

From Sin to Science: The Cancer Revolution of the Nineteenth Century

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ABSTRACT

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This dissertation analyzes the critical importance of the late nineteenth century to the development of a novel, radical approach to cancer that continues into the twenty-first century. From the 1870s to the 1890s, physicians and the public came to understand cancer in an entirely new light, founded upon the application of scientific principles, methods, and instruments to cancer medicine as well as upon a major change in the social perception of the disease.

Cancer as it was conceptualized, diagnosed, and treated prior to this revolutionary transformation will be explored. The birth of cellular pathology will set the stage for the transition of cancer from a macroscopic, eponymous malady to a microscopic, cellular disease.

The founding of an institution devoted solely to the care of cancer patients and the investigation of the disease will illustrate how societal beliefs, combined with personal tragedy, philanthropy, and medical expertise, legitimized the disease and fostered cancer research.

The histories of the cancers of two Presidents of the United States, Ulysses S. Grant and Grover Cleveland, who were diagnosed with the disease only nine years apart during these critical years, will be compared and contrasted for the insights they provide on this great transformation.

The scientific underpinnings of these changes will be examined from their roots in physics, chemistry, and biology to their applications in microscopy, anesthesia, and antisepsis. Modern cancer will be shown to be based firmly on the medical microscope and the advent of scientific surgery that occurred in the late nineteenth century.

Contents

Abstract

Introduction *1*

Section I: Traditional Cancer

1. Traditional Cancer *24*
2. Institutional Beginnings in America *60*

Section II: From Traditional to Modern Cancer

3. General Grant's Cancer: Twilight of the Traditional *91*
4. The Reflection of Modern Cancer: The Secret "Anxious Summer" of the President *199*
5. From Grant to Cleveland: Small Steps and Giant Leaps *306*

Section III: Science and the Making of Modern Cancer *325*

6. New Visions, Newer Insights: The Birth of Medical Microscopy and The Rise of Modern Cancer *327*
7. The Treatment of Cancer: From Ancient Antidotes to the Golden Age of Surgery *671*

Conclusion *1036*

Epilogue *1044*

Selected Bibliography *1060*

ILLUSTRATIONS

Figures

1. A Modern Light Microscope	<i>page</i> 461
2. Zeiss Apochromats Microscope Objective (1886)	465
3. Abbe Condenser Optical Pathway	469
4. Leeuwenhoek Microscope (circa late 1600s)	484
5. Surgical Utensils – Roman Period (1 st Century CE)	686
6. Puerperal Fever (Monthly Mortality Rates 1841-1949)	932
7. Pasteur Drawing (A)	961
8. Pasteur Drawing (B)	962
9. Civil War Surgery	988
10. Book cover of Lister’s <i>Antiseptic Principle</i>	988
11. Lister and his Carbolic Acid Spray	992
12. The Chamberland Autoclave	1003
13. An Operating Suite in 1900	1004
14. The Left Hand of Frau Rontgen (1895)	1047
15. Mrs. Mary Lasker (USPS Stamp 2009)	1054

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library and always made me welcome. Arlene Shaner, who had recently begun her work at the Malloch Rare Book Room at the Academy (now the Drs. Barry and Bobbi Collier Rare Book Reading Room), found me the best sources and the best light to see them in. Conversations with Arlene always led my research in the right direction. My travels to archives at the College of Physicians of Philadelphia, which holds the best original sources on President Grover Cleveland's secret cancer, were enhanced and made pleasurable by Ed Morman (who had by then moved to the CPP), Charles Greifenstein, and the late Gretchen Worden of the incomparable Mütter Museum.

As a physician, I learned long ago that the practice of medicine (and the beauty of life) is so much more than words on a page. A patient's history is so much less meaningful without feeling his handshake, looking him in the eyes, and hearing the tone of his voice. So it has been with my work in history. Those mentioned above have provided humanity as well as materials to make this the work that it is, but there are others whose classification by institution or archive is not so obvious who also deserve thanks. Albert S. Lyons MD (1912-2006), co-author of the magisterial *Medicine: An Illustrated History*, opened his Central Park West apartment to me and shepherded me through the early stages of my investigations into the history of medicine. Mrs. Ann Wandell, daughter of prolific cancer history author Francelia Butler, shared her insights with me into her mother's interest in cancer and her relationship with Memorial Hospital in general and Dr. Hayes Martin specifically. I will always cherish her gift of her mother's work to me. In the Fall of 1999, I had the unequalled pleasure of speaking with Mrs. Helen Coley Nauts in her Park Avenue apartment, surrounded by photographs of her family, including

her father, Dr. William Bradley Coley (1862-1936). My research into Dr. Coley's writings from the late nineteenth century first piqued my interest in cancer history, so the ability to speak one on one with his daughter (63 years after his death) was incredible. To her enormous credit, Mrs. Nauts carried on her father's work as founder of the Cancer Research Institute. She also kindly bestowed upon me a rough draft of the biography of her father that she had been working on for many years. There were many others, but one other personal interview of note was with Dr. Paul Marks, then President and CEO of the Memorial Sloan-Kettering Cancer Center. He generously gave of his time to me as I researched the evolution of the culture of cancer over the course of the nineteenth and twentieth centuries. MSKCC is arguably the premier institution for the treatment of cancer in the world. Thus, when I asked him what he considered to be the greatest advance in cancer in the past century, I expected a response related to cancer therapies, which made enormous strides in the twentieth century. His answer struck me: "earlier diagnosis." Of course, he was correct, for cancer is a physical presence — generally easier to expunge earlier in its course. And time has more than proven his answer right, from the halls of medicine to the politicization of cancer diagnosis in the Affordable Care Act.

Without my family, there would have been little reason to undertake this work. A brother in mind if not blood, Irwin ("Win") Robins, Esq. made this work possible. It is safe to say that without his steadfast encouragement, gentle (and sometimes not-so-gentle) prodding, and infinite hospitality (with wife Sue), this work would never have come close to completion. He is an editor's editor, with a command of the English language and love

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DEDICATION

To

Barbara Ann Kapelman MD MS (Microbiology) MS (Medical Informatics)

**My love and lover, without whom this work and the world it lives in would have no
meaning**

INTRODUCTION

CANCER.

The very word strikes fear into the heart of every adult. As it should. In 2012, cancer killed more than 8 million people worldwide, of whom about 577,000 were Americans.¹ It is the second leading cause of death in the United States, behind cardiovascular diseases.² And if current trends continue, cancer will become the most common cause of death sometime during this second decade of the twenty-first century. On an individual level, the pain and suffering caused by cancer and its treatments—surgery, immunotherapy, radiation, and chemotherapy—are comprehensible only to those who have experienced them. The importance of cancer transcends the medical world. A culture of cancer influences what we eat, where we live, and even our choice of romantic partners.

THESIS

The study of "cancer" can be approached from a panoply of perspectives, including the historical, the scientific, the medical, and the cultural. This dissertation weaves these strands together to reveal the major period of change in the nineteenth century – change that transformed cancer from a death sentence with end-stage heroic medical intercession to a scientifically understood disease with social, economic, and political overtones caught up within a web of research and industry. The cancer revolution was part and parcel of the scientific revolution that swept over medicine in the mid-to-late nineteenth century. This thesis argues that specific elements of this transformation revolutionized the understanding of cancer. Indeed, the investigation, diagnosis, and treatment of the phenomenon of nature that became the modern

¹<http://www.cancerresearchuk.org/cancer-info/cancerstats/world/cancer-worldwide-the-global-picture> and <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-031941.pdf> accessed November 14, 2012.

² In 2009, the last year of finalized mortality data, heart disease accounted for 599, 413 deaths in the United States; cancer for 567, 628 deaths. <http://www.cdc.gov/nchs/fastats/lcod.htm> accessed November 14, 2012.

disease were in many ways uniquely positioned to benefit from the scientificization of medicine and the medicalization of cancer that occurred at that time.

In essence, the transformation of cancer as viewed from the socio-religio-medical standpoint by physicians in the eighteenth to mid-nineteenth century – which I call "traditional cancer" – gave rise to a new comprehension of the disease by the end of the nineteenth century – which I name "modern cancer." Modern cancer was born not in the twentieth century – as most historians suggest – but in the late nineteenth century. How that nineteenth-century transformation came about and, in particular, the ideas, protagonists, and instruments involved – reified in the diagnostic and therapeutic modalities of our time – is the subject of this dissertation.

The late nineteenth-century revolution in the history of cancer is remarkable not only for its creation of entirely new ways of diagnosing and treating the disease, but also for its redirection of emphasis from the prevention of cancer to its treatment. Theories and practices for the prevention of cancer abounded before the twentieth century. Those who believed in the heritability of cancer could offer little to offspring born into these families. On the other hand, climate, the physical environment, diets, and living styles were remediable causes and all were addressed as preventable causes of cancer at one time or another. The use of the microscope in cancer diagnosis and prognosis, in conjunction with the rise of surgery as the most desired response to cancer, were critical in highlighting the role of treatment over prevention. The germ theory of cancer offered a return to thoughts of prevention, for germs were external agents that potentially could be avoided. Nevertheless, the theory of cancer causation by germs, so prominent in the 1890s, soon disappeared under the critical eye of James Ewing and others in the first decade of the twentieth century, not to be revived until the environmental movement of the

1960s and 1970s spotlighted preventable external causes of cancer. For many other reasons – economic, political, and social – the 21st century remains a time when the emphasis on treatment far outweighs that on prevention. The late nineteenth century was the key turning point in this debate. Currently at stake are billions of dollars, tens of thousands of jobs, and hundreds of thousands of lives.

HISTORIOGRAPHY

Although physicians and laymen have written about cancer from time immemorial, few have addressed its history. Those who have tackled this past tend to do so from either a scientific/medical or a social/political/economic perspective, as though these two world views were mutually exclusive. Most important, their focus on the mid-to-late twentieth century as the revolutionary period in cancer is misdirected.

The *Bulletin of the History of Medicine* and the *Journal of the History of Medicine and Allied Sciences* contain numerous articles dealing with people and events related to the history of cancer in the nineteenth century, but their subjects and foci are narrow. Indeed, the majority of secondary works on cancer history, be they articles or books, pay mere lip service to the paradigm shift in cancer history that occurred in the late nineteenth century. Most rapidly jump to the post-Second World War era of chemotherapy, radiotherapy, and their ilk.

This dissertation contends that the turning point in cancer was the late nineteenth century. During that time the incidence of cancer began to explode, the microscope became the instrument of cancer diagnosis and prognosis, the advent of anesthesia made procedures more tolerable, and innovations in antisepsis made them safer. As a result, surgery became the treatment of choice for cancer. The culture of cancer then began a transformation in the popular psyche from an inescapable guilt-laden death sentence to a disease that could and should be

treated and, ultimately, cured. The goal here, therefore, is to return the debate on the history of cancer to the late nineteenth century. The subsequent developments of the twentieth century and beyond that dominate writings on the history of cancer – cancer chemotherapy, radiotherapy, immunotherapy, even genetics – were derivative to those of the late nineteenth century. The earlier emphasis on the mid-to-late twentieth in cancer histories is short-sightedness.

A few historians have included a meaningful discussion of cancer in the late nineteenth century. For example, L. J. Rather's *Genesis of Cancer* focuses on cell theory and its implications for theories of cancer causation in the first half of the nineteenth century, but ends abruptly before addressing those of the late nineteenth century.³

Similarly, Henry Sigerist, head of the Institute of the History of Medicine at Johns Hopkins from 1932 to 1947, emphasized social conditions. His best-known work, *The Great Doctors*, includes essays on Johannes Müller, Rudolf Virchow, Ignaz Semmelweis, Louis Pasteur, Robert Koch, Joseph Lister, and Paul Ehrlich, but cancer is rarely discussed.⁴ And Sigerist died before completing his projected eight-volume series on the history of medicine that may have contributed more to cancer history. Richard Shryock, who directed the same Johns Hopkins Institute from 1949-1958, also wrote medical history from more of a social than an establishment perspective, as did Dr. George Rosen at Columbia, but their studies do not examine the rise of modern medicine in the late nineteenth century and cancer was at most tangential to their main concerns.

³L. J. Rather, *The Genesis of Cancer: A Study in the History of Ideas* (Baltimore: The Johns Hopkins University Press, 1978). Dr. Rather, a pathologist, subsequently wrote a text on *Johannes Müller and the Nineteenth Century Origins of Tumor Cell Theory* (1986), solidifying his interest in cancer pathology theories of the first half of the century.

⁴Henry E. Sigerist, *The Great Doctors: A Biographical History of Medicine*, trans. Eden and Cedar Paul (Garden City, NY: Doubleday & Company, Inc., 1933; repr., 1958).

The advent of the social history of medicine as a more mainstream approach in the 1960s reduced the emphasis on the physician and looked at questions of medical history from the "bottom up." Nevertheless, physicians continued to write about the history of cancer from a doctor-oriented point of view. *The Theory and Practice of Oncology, Historical Evolution and present principles*, written by the surgical oncologist Ronald Raven mentions little about the cancer revolution of the late nineteenth century.⁵ Numerous other oncology texts, often written by physicians for physicians, include a historical essay that glosses over the watershed era of the late nineteenth century. Dr. Michael Shimkin's profusely illustrated *Contrary to Nature* (1977), published in the "War on Cancer" era after the National Cancer Act (1971), is a series of short hagiographic essays touching on the histories of physicians from antiquity to the mid-twentieth century to illuminate the contributions of individuals to progress in cancer medicine.⁶ More recent work by physician researchers, including Steven A. Rosenberg's *Transformed Cell* (1992)⁷ and Robert A. Weinberg's *Racing to the Beginning of the Road* (1998)⁸ are personal essays that discuss theories of cancer causation from a presentist perspective; i.e., how contemporary theories of cancer led to their own work in immunology and molecular biology, respectively. These books are compelling, but their historical contributions are not through the contextualization of history. And little is mentioned of cancer before their own times.

⁵Ronald Raven, *The Theory and Practice of Oncology, Historical Evolution and Present Principles* (Carnforth, UK: The Parthenon Publishing Group, 1990).

⁶Michael B. Shimkin, *Contrary to Nature: Being an Illustrated Commentary on Some Persons and Events of Historical Importance in the Development of Knowledge Concerning Cancer* (Washington, D. C.: United States Government Printing Office, 1977).

⁷Steven A. Rosenberg and with John M. Barry, *The Transformed Cell: Unlocking the Mysteries of Cancer* (New York: Avon Books, 1992).

⁸Robert A. Weinberg, *Racing to the Beginning of the Road: The Search for the Origin of Cancer* (New York: W. H. Freeman and Company, 1998).

Thus, even in the last few decades, historians of cancer tend to treat developments in cancer as building blocks in the gradually constructed but inevitable wall of cancer knowledge – akin to Lord Acton's expectations for the ineluctable completion of historical knowledge almost a century earlier. Few note the importance of historical context to developments in cancer medicine and fewer still realize that "progress" is a punctuated historical phenomenon, running at full speed at times and crawling at others. The full-out sprint of the late nineteenth century, when rapid change was the norm in cancer medicine, remains unrecognized in these works.

A "social" approach to history of cancer took hold in the 1970s. James Patterson's *The Dread Disease* (1987) is typical of non-physician writings. Indeed, his work is the culmination of years of the application of social history and politics to cancer history.⁹ But Patterson's book was not a history of cancer so much as an attack on the government-sponsored cancer "establishment." He touches on the nineteenth century, but his interest clearly lies in the mid-to-late twentieth. His chief concerns were the inadequacies and wrongs perpetrated by "the cancer industry" and, in particular, the parade of false cures trumpeted by that industry over the course of the 20th century.

The Cancer Wars (1995),¹⁰ by Robert Proctor, emphasized the often conflicted interplay between cancer researchers and industry in the twentieth century, a relationship Proctor called the "politics of cancer"¹¹ and the "social construction of ignorance."¹² He exposes the failings of government and scientists to regulate and publicize pollutions that can lead to cancer. Other

⁹James T. Patterson, *The Dread Disease: Cancer and Modern American Culture* (Cambridge, MA: Harvard University Press, 1987).

¹⁰Robert Proctor, *The Cancer Wars* (New York: Basic Books, 1995).

¹¹After Samuel S. Epstein, *The Politics of Cancer* (Garden City, NY: Anchor Press/Doubleday, 1978). and others.

¹²Proctor, *Cancer Wars*, 12.

writings on fears of poisoning (carcinogenic or otherwise) derive from the larger struggles between manufacturers and individuals in the industrial age. They can be seen in descriptions of soot-filled air in the nineteenth century, including those of Charles Dickens¹³ and Harriet Beecher Stowe,¹⁴ and find more recent and specific application to cancer in the works of the modern environmental movement from Rachel Carson's *Silent Spring* (1962)¹⁵ to Jonathan Harr's *A Civil Action* (1995)¹⁶ to Devra Davis' *The Secret History of the War on Cancer*.¹⁷ These compelling works neglect what made cancer a household word in the first place – its separation in the nineteenth century from infectious "tumors" and its ability to be discerned under the microscope and treated with the surgical knife. They describe a glass half empty by neglecting the late nineteenth-century contributions to the current diagnosis of cancer, for cancer was a different disease before the medical microscope.

Other authors select a component of the scientificization of medicine at the end of the nineteenth century and carry it through to the present from a cultural point of view. Nancy Tomes' *The Gospel of Germs* (1998)¹⁸ is an example of this genre, with its relation of the rise of germ theory following the sanitation movement and how theory translated into practice. This focus might have been a welcome addition to the history of cancer, for the germ theory of cancer

¹³Charles Dickens and George Cruikshank, *Oliver Twist; or, the Parish Boy's Progress*, [1st ed., 3 vols. (London,: R. Bentley, 1838).

¹⁴Harriet Beecher Stowe, "The Chimney-Corner for 1866. Vii. Bodily Religion: A Sermon on Good Health," *Atlantic Monthly*, July 1866.

¹⁵Rachel Carson, *Silent Spring* (Boston: Houghton Mifflin, 1962).

¹⁶Jonathan Harr, *A Civil Action* (New York: Random House, 1995).

¹⁷Devra Lee Davis, *The Secret History of the War on Cancer* (New York: BasicBooks, 2007).

¹⁸Nancy Tomes, *The Gospel of Germs: Men, Women, and the Microbe in American Life* (Cambridge, MA: Harvard University Press, 1998).

originated during her "gospel emergent" era, but Professor Tomes' major interest is the relation of germ theory to the AIDS epidemic, not the role of germ theory in cancer history.

Barron Lerner, in *The Breast Cancer Wars* (2001),¹⁹ mentions the ancient history of breast cancer and rapidly skips to the nineteenth century as the beginning of a science-informed surgery for breast cancer. This is certainly true. Dr. Lerner's purpose is to establish William Halsted's radical mastectomy of the late nineteenth century as a target for twentieth-century attacks on (male-dominated) breast cancer surgery.²⁰ The focus is not on the chemistry and science of medical advances that led to expand the technique of earlier breast-excision surgeries, but rather on the "wars" fought in post-Second World War period that adjudicated the most appropriate breast cancer treatment (and making the effort to discover it) for the women who suffered from the disease. Dr. Lerner's superficial treatment of the late nineteenth century is understandable given his primary interest in the dynamic interactions among patients, physicians, and the public advocates in the latter half of the twentieth century, but his brief relation of the great insights and developments that led to their conclusion in Halsted's radical mastectomy falls short of the invaluable history that led to the procedure. Indeed, from the perspective of the cancer revolution of the late nineteenth century, William Halsted's radical mastectomy was more a culmination than a beginning.

Another genre in the writing of cancer history illuminates the history of the cancer institution, which first became a reality in the United States during the late nineteenth century. Although there have been many hagiographic essays on hospitals and cancer institutions,²¹ one

¹⁹Barron H. Lerner, *The Breast Cancer Wars: Hope, Fear, and the Pursuit of a Cure in Twentieth-Century America* (Oxford: Oxford University Press, 2001).

²⁰"The ways in which male physicians conceptualized the cancerous female breast further promoted its radical removal." *ibid.*, 89.

relatively recent example of this is James Olson's *Making Cancer History* (2009),²² a work of fileopietism created as an act of appreciation for the institution, The University of Texas M. D. Anderson Cancer Center, that saved his life again and again. "I had cancer. I have cancer. I will always have cancer."²³ But Olson devotes only four pages to cancer before the twentieth century, quickly noting that "Rudolf Virchow had first exposed cancer at the cellular level"²⁴ but with little on the people, innovations, discoveries, and events in the nineteenth century that made the M. D. Anderson possible. His elitist history and its lack of historical context miss the *sine qua non* of modern cancer history. This dissertation relates the conception of another great cancer institution, the New York Cancer Hospital (today Memorial Sloan-Kettering Cancer Center in New York), founded in 1884, but roots it firmly in the radical social, institutional, and scientific changes of that era that led to its creation.

Siddhartha Mukherjee's *The Emperor of all Maladies* (2010) is a synthetic narrative subtitled "a biography of cancer."²⁵ It is a magisterial work, deserving of the praise that it has received, that purports "to highlight the large themes that run through this 4,000-year history."²⁶ But it is not a biography or history of cancer as much as it is a biography of those affected by

²¹For the Memorial Sloan-Kettering Cancer Center alone, there are several examples, including Memorial Hospital Archives, "New York Cancer Hospital (Old Memorial)," in *Hayes Martin Collection* (New Yorkn.d.), probably from the 1930s, Bob Considine, *That Many May Live: Memorial Center's 75 Year Fight against Cancer*, 1 vols. (New York: Memorial Center for Cancer and Allied Disease, 1959; repr., August 1982)., and Archives Committee of Memorial Sloan-Kettering Cancer Center, "A Century of Commitment: A History of Memorial Sloan-Kettering Cancer Center," (New York: Memorial Sloan-Kettering Cancer Center, 1984).

²²James S. Olson, *Making Cancer History: Disease & Discovery at the University of Texas M.D. Anderson Cancer Center* (Baltimore: The Johns Hopkins University Press, 2009).

²³Ibid., ix.

²⁴Ibid., 12.

²⁵Siddhartha Mukherjee, *The Emperor of All Maladies: A Biography of Cancer* (New York: Scribner, 2010).

²⁶Ibid., xiii.

cancer – patients, physicians, researchers, and politicians. He provides little discussion of events before the twentieth century and much of that discussion is given to highlight how those past events foreshadowed developments in the twentieth century – a presentist approach.

Mukherjee's focus is once again on the post-Second World War period. His heroes are Dr. Sidney Farber, who founded modern chemotherapy in the 1940s, and Mary Lasker, who began a public campaign against cancer at about the same time and played a critical role in the politicization of cancer culminating in the National Cancer Act of 1971. To him, events in cancer history before the twentieth century are more prequel than focus. The social history of cancer prior to the twentieth century is summarized as "once a clandestine, 'whispered-about' illness"²⁷ without attention to the great upheavals that the diagnosis of cancer caused in the lives of its victims when cancer was conceived as punishment for sin – up to and including the nineteenth century. This is a biography in the etymological sense of the word as a picture of lives, but Mukherjee speeds to his interests in the twentieth century – the deification of Dr. Farber and Mrs. Lasker, the post-Second World War history of chemotherapy, the "War on Cancer," environmental carcinogens, the genetics of cancer, targeted therapies, and other developments firmly rooted in the latter half of the twentieth century. It cursorily mentions the foundational early years to rush to the perceived exciting events later in life that made the biographee famous. In this case, however, Mukherjee misses the point that the foundational years are critical to all subsequent history, including his own.

Thus, Mukherjee gives short shrift to the crucial period that allowed his heroes to comprehend and treat cancer in a different way from that in which it had been understood and managed for centuries. When describing John Hunter's surgical skill he correctly notes that "if

²⁷Ibid.

the pain *during* surgery were not bad enough, the threat of infections *after* surgery loomed."²⁸ However, only two paragraphs describe the entire history of anesthesia, and he devotes only a scant page to the history of antiseptics. Mukherjee summarizes two of the three greatest discoveries crucial to the making of modern cancer, anesthesia and antiseptics (the third being the development of the medical microscope), in one sentence: "Antiseptics and anesthesia were twin technological breakthroughs that released surgery from its constraining medieval chrysalis."²⁹

In spotlighting the achievements of the recent twentieth-century past and glossing over the innovations of the nineteenth, Mukherjee misses the seminal innovations of that earlier period. There were Dr. Farbers (like Oliver Wendell Holmes, Sr., Ignaz Semmelweis, and the dentist Horace Wells) and Mrs. Laskers (like Elizabeth Hamilton Cullum and Charlotte Augusta Astor, wife of John Jacob Astor) in the nineteenth century without whom it is unlikely that Sidney Farber and Mark Lasker could have achieved what they did, but these giants of cancer history do not appear in Mukherjee's *Emperor*. Surprisingly, neither do General Ulysses S. Grant or President Grover Cleveland, whose cancer histories (especially Grant's) played a key role in increasing public awareness of the disease that led to Dr. Farber's "seismic transformation...from a clinician into an advocate for cancer research"³⁰ half a century later – and to Mary Lasker's success in the politicization of cancer. But recognition of the importance of this earlier period is absent. It is like writing a history of the tree, glorifying its leaves and branches, without appreciating the role of its roots.

SOURCES

²⁸Ibid., 56.

²⁹Ibid., 58.

³⁰Ibid., 100.

This dissertation on the history of cancer during the nineteenth century focuses is on the United States, but since much of American cancer history during this period derived from Germany, Great Britain, and France, many sources originate in these countries. Fortunately, primary sources are abundant include newspaper articles, medical textbooks of the period, and, especially, collections of private letters, papers, and manuscripts.

This investigation began on the second lower level of the Health Sciences Library at Columbia University. Over the years, I found myself coming back to those journal articles, medical textbooks, and popular books. The *Boston Medical and Surgical Journal* (forerunner of *The New England Journal of Medicine*), the *Journal of the American Medical Association*, *The New York Medical Journal*, and the *British Lancet*, among others, span the nineteenth century and spotlight how dramatically the "cancer" of the early century differed from that late in the century. The proximity of the Archives and Special Collections in that same Library led to personal papers, student notes, surgical charts, and other manuscripts that created a *mise en scene* of the times.

Each chapter of this manuscript represents an exploration into new and different sources. The New York Academy of Medicine's Rare Book Room in particular, contains incomparable sources of primary works on pathology, microscopy, General Grant's cancer, President Cleveland's doctors, and many other topics.

No history of what was is currently named the Memorial Sloan-Kettering Cancer Center can be written without the invaluable works in the Memorial Hospital Archives and the Rockefeller Archives. The Hayes Martin Collection and the papers of John Parsons, first President of the New York Cancer Hospital, in the Memorial Hospital Archives illuminate without equal the promises and pitfalls of the first major cancer hospital in the United States as

they reveal intimate correspondence between Mrs. Astor, Mrs. Cullum, and Mr. Parsons. The papers of John D. Rockefeller Jr., place the reader right next to the youthful future philanthropist in the 1890s as he suffers over the death of his good friend to cancer. They then explicate how that loss was a primary motivation for his devotion to cancer projects and his donation of millions of dollars to Memorial Hospital.

General Grant's throat cancer, which did so much to remove the stigma from cancer and change the course of the social history of the disease in the late nineteenth century, may be culled from primary writings found in the New York Academy of Medicine and elsewhere as much as from the newspaper articles of the day. Every aspect of General Grant's cancer, including quotations and analyses gleaned from Grant's physicians on a daily basis, was reported in detail and widely disseminated, making newspaper and magazine articles excellent primary source materials. Weekly medical journals at the time described aspects of Grant's cancer and its complications for a more specialized audience. In addition, these medical journals illuminate the understanding of cancer by physicians in the late nineteenth century. Reviewing articles in those same journals over the decade following the General's death reveals the remarkable change in the conceptualization of cancer that occurred during that short interval.

The papers of Dr. William Williams Keen in the archives of the College of Physicians of Philadelphia (CPP) allow a first-hand look into President Cleveland's "secret surgery" for cancer. Newspaper articles of the day are valuable for the subterfuge perpetrated against the public and the press by the President's associates, but they also show how the public perception of cancer had dramatically transformed since General Grant's death. One need only go downstairs at the CPP, to the Mütter Museum, to see the remnants of the President's cancerous jaw removed that summer's day in 1893!

Sources for the history of the microscope range from primary archives mentioned above to medical journals to magazines and newspaper articles. There are many excellent articles on specific subjects in the *Bulletin of the History of Medicine*, the official publication of the American Association for the History of Medicine, and the *Journal of the History of Medicine and Allied Sciences*, without which no well-researched history of medicine or history of cancer can be written.

Primary sources are, however, just that – sources. They are starting points that provide a fertile soil upon which the seminal and revolutionary period in the history of cancer that is the late nineteenth century may be explored and cultivated.

PLAN & SCOPE

This dissertation is an attempt to answer the What? When? Who? Where? How? and, with greater difficulty, the Why? of this transformation in the history of cancer that occurred in the last decades of the nineteenth century. The goal is to examine how cancer physicians and others came to think of modern cancer, beginning with "traditional" cancer as it was before the great transformation, analyzing the transformative elements from the mid-to-late nineteenth century, and culminating in the early twentieth century with a foundation that serves as the underpinning for thinking about cancer in general and cancer research in particular.

This history unfolds as a series of topical essays. Each contributes to a picture of the transformation wrought by these powerful elements in the last decades of the nineteenth century. At times it reads like a series of medical and scientific biographies linked by a common modality such as pathology, the microscope, or surgery. There are stories of influential physicians and scientists like J. Marion Sims, Oliver Wendell Holmes Sr., Joseph Lister, and Louis Pasteur and their contributions to cancer. Other sections delineate the roles of influential people and

powerful families, such as the Astors, Rockefellers, and Emperor Friedrich of Germany, whose personal tragedies and support for novel solutions to the problem of cancer propelled the culture and study of cancer in entirely new directions. The medical lives and social contexts of two Presidents, one who died from his cancer and the other who was cured of it, serve to highlight in personal and societal terms the demise of traditional cancer and the rise of modern cancer. Where appropriate, I have examined in detail the technology of the diagnosis and treatment of cancer; ancient technology that served as tools of treatment for over two millennia and modern technology for diagnosis and treatment that yielded deeper insights and broader understandings of the disease that is modern cancer. All of these focused biographies, technologies, and, ultimately, analyses have a unified goal: a new historical understanding of cancer as it was and how it came to be what it is.

THE LANGUAGE OF CANCER

Some terms require definition. "Cancer" is a word at once recognizable to all and yet most difficult to define. Everyone has heard the word, but to pin down its exact meaning in all venues—connotative, denotative, scientific, medical, sociological—is a challenge. "Cancer" has meant different things to different people at different places and times. As a scientific and medical term, I wish to use the word as "an uncontrolled proliferation of cells, typically with invasion and destruction of adjacent normal tissue, and often with metastatic spread to distant parts of the body."³¹ But this is a modern definition that excludes most of the meanings of cancer before the late nineteenth century as well as the deeper psychological and sociological meanings in both the past and the present. Nevertheless, one must start somewhere. Common contemporary divisions of uncontrolled growths into benign, malignant, and metastatic, for

³¹Oxford English Dictionary, "*Cancer, N. And Adj.*" (Oxford University Press). Accessed November 22, 2012.

example, were rare before the late nineteenth century, but common thereafter. There are still other ideas of paramount importance to a historical analysis of cancer – Was cancer one disease or many? Was cancer a heritable illness? A contagion? A consequence of environmental poisoning? Answers to these questions are proposed in their proper places within the text. Other ways of understanding the meaning of "cancer" before the late nineteenth century – epidemiologic, demographic, etiologic – are necessary, and these also are explained in the text where appropriate.

For all these reasons and more, "cancer" as a general term is too non-specific and ahistorical to use for contexts both before and after the revolutionary period of the late 1800s. Thus, I have constructed the term "traditional cancer" to summarize and describe the socio-medical meaning of cancer from the eighteenth century well into the nineteenth century. Many elements of traditional cancer existed before the eighteenth century, but their variability and connotation make strict ascription of the term to earlier centuries problematic. Nevertheless, the term traditional cancer must sometimes be used prior to the eighteenth century in order to simplify explanations. My experience with writings before the era of modern cancer is that one assumes he understands the definition of cancer in use at the time only at one's own peril. But even when applied to the Enlightenment, Romantic, and early Industrial Ages, the meaning of traditional cancer is much more than its definition, for it assumes within itself not only pathological swellings of all sorts (tumors and localized infections) that no one today would consider cancer, but also a host of connotations peculiar to this disease or set of diseases involving their prevention, diagnosis, treatment, and prognosis – even when considered in a solely medical context. In short, the history of cancer before the end of the nineteenth century is laden with definitional difficulties.

"Modern cancer" is the term that I use to summarize and describe the meaning of cancer after the great transformation of the late nineteenth century. This definition is more than a term set in time (post-1880s), for it is meant to contain within itself a new set of relationships – between medical disciplines, institutions, people, and technologies – as well as to differentiate modern from traditional cancer. For example, whereas traditional cancer was anatomic and macroscopic, based upon didacticism and empiricism, modern cancer is histologic and microscopic, based upon science and experimentation. Whereas traditional cancer was predicated upon constitutional beliefs of total-body propensities and an avoidance of surgery until all else had failed (and often refrained from even then, with the exception of very superficial lesions), modern cancer is predicated upon a belief that the disease begins in one location and only gradually achieves a nexus from a nidus, thereby making surgery early in the disease process desirable and potentially curative. From a societal perspective, whereas traditional cancer was stigmatized (often linked to venereal, contagious, and infectious diseases conceived as punishments for sinful behavior) and individualized (leaving most patients on their own until the late nineteenth century), modern cancer is patient-centered and institutionalized, from research facilities to hospitals devoted exclusively to the care of cancer patients. And on the individual level, cancer transfigured from a highly stigmatized punishment to a legitimized medical disease – from sin to science.

Above all, therefore, whereas traditional cancer was a state of mind centered on repression, avoidance, and pessimism, modern cancer is a science focused on increased awareness, action, and – although difficult to discern in the immediacy of the moment versus the long trail of time – optimism.

The revolution that led from traditional to modern cancer is one of the greatest stories of progress in human history. Although it is as yet a story without an ending, it is likely to be one of the most outstanding triumphs of man. How "we" (and the "we" will become clearer over the course of this work) came to know what we know of cancer today is therefore of critical importance, for the path taken not only excludes many other possible paths but is also highly determined by the starting point or points. The importance of the history of cancer to the goal of the cure of cancer cannot be overstated, for the germ of the future is in the present as the roots of the present are discernible in the past.

BEFORE TRADITIONAL CANCER

The focus of this dissertation is the transformation of cancer that occurred in the last half of the nineteenth century. Nonetheless, a few words are required to set the stage for what I came to call traditional cancer. More will be evident in the ensuing chapters.

The disease called cancer in 2013 is discoverable (through the use of contemporary diagnostic techniques) in writings and remains from Dynastic Egypt³² and Ancient Greece.³³ In those times and places cancer was an unusual cause of morbidity and mortality. Indeed, before the industrial revolution in Western Europe and America, cancer was not as significant an influence on everyday life as it is today.³⁴ The past century and a quarter, however, have witnessed remarkable changes in the problem of cancer.

³²James Henry Breasted, ed. *The Edwin Smith Surgical Papyrus*, Two vols., vol. One & Two, The University of Chicago Oriental Institute Publications (Chicago: The University of Chicago Press, 1930; reprint, 1984), 403. Note especially "Bulging Tumors on the Breast," Case Forty-Five, XV 9-19.

³³Hippocrates, *The Aphorisms of Hippocrates*, trans. Thomas Coar, Special ed., The Classics of Medicine Library (London: A.J. Valpy, 1822; repr., 1982), 177. See specifically, Section VI, Aphorism XXXVIII.

³⁴The death rate from cancer in the United States in 1850 was estimated to be 9/100,000. W(illiam) Roger Williams, *The Natural History of Cancer with Special Reference to Its Causation and Prevention* (London: William Heinemann, 1908), 76. In 2009, the last year of reported statistics, the death rate from cancer in America was 173.2/100,000. <http://www.statehealthfacts.org/comparemaptable.jsp?cat=2&ind=67> accessed November 29, 2012.

In addition, from the earliest historical records to the middle of the nineteenth century, cancer was not perceived as the pathological entity that it is today. Nor did the average American dread cancer as much as the epidemics, childhood diseases, and pneumonias that swiftly snuffed out life. Fear of cancer was present, but its incidence was so low as to preclude common concern.³⁵ In addition, living long enough to develop cancer was to some a victory over the deadly acute infectious diseases of the age, because cancer was deemed a disease of “old age.”³⁶

Hippocrates is believed to have coined the Greek word “karkinos” in the fifth century BCE to describe his impression of cancer as crab-leg-like veins running over the surface of highly vascular growths.³⁷ Galen used the word in the second century CE to describe *tumoribus praeter naturam* (“tumors contrary to nature”) and his views on tumors and cancers held sway until the nineteenth century.³⁸ The terminology of cancer has always been problematic,³⁹ and even as late as the 18th and early 19th centuries, the terms “cancer,” “tumor,” and “growth” were often used interchangeably. Not until the late 19th century did the rise of the use of the microscope for diagnostic pathology and correlated clinical medicine allow a clearer visual and cognitive distinction between benign and malignant tumors, the latter of which are today

³⁵Ibid.

³⁶In the 1880s, old age meant “over 40 years of age.” Francis R. Baker, compiler. Reported and Arranged by E.A. Tucker, “Dr. Francis Delafield's 'Lectures on the Practice of Medicine,'” in *Archives & Special Collections of the Health Sciences Library of Columbia University* (New York 1888), 51. See especially Lecture 10, “Cancer of the Liver.”

³⁷Mark Barrow, “Portraits of Hippocrates,” *Medical History* 16(1972): 85-88.

³⁸Galen, mimicking Hippocrates (as he often did), said of breast cancer, “Just as a crab's feet extend from every part of its body, so in this disease the veins are distended, forming a similar figure.” Henry Alan Skinner, *The Origin of Medical Terms*, 2nd ed. ed. (New York: Hafner Publishing Company, 1970), 88.

³⁹Despite the general acceptance of cancers today as site specific (e.g., lung cancer, breast cancer), neoplastic growths continue to be reclassified as new discoveries and technical innovations find some cancer characteristics more important than others.

commonly called cancers.⁴⁰ Thus, the modern meaning of the word “cancer” arose in the critical period of the late 19th century.

Concurrent with the acceptance of “cancer” as a distinct clinicopathological entity was the separation of cancer from its traditional cultural connotations. Because cancer was often deemed inherited, contagious, or even venereal, it was cast in the public mind—and often in the professional mentalité—as a stigma. Those afflicted felt self-blame and shame, assuming that cancer was punishment for sin. In the more religious culture of pre-Darwinian, pre-Civil War America, this aura of disgrace took on heightened meaning. Consequently, cancer victims and their families often did not seek attention from medical professionals or clergymen until the growth was beyond any hope of cure. Some never sought help. Those who did typically received a diagnosis of uncertain validity and were commonly treated with topical or ingestible *materia medica* which, if they were fortunate, did no harm.

Even those few whose masses were deemed cancerous and amenable to surgery (and were able to afford it) could, if they agreed to undergo resection, endure the greatest horrors imaginable. Fanny Burney’s chilling first-person narrative of her breast cancer surgery in 1811 recounts in gory detail her personal experience with the excruciating pain and suffering of cancer surgery in the pre-modern era.⁴¹ As a result, cancer surgery in the traditional era was associated with high morbidity and mortality rates – facts not lost on the doctors and patients of the day. The most experienced and conscientious surgeons wisely followed Hippocrates’s two-thousand-year-old directive to operate as early as possible in the course of the disease – but only if the

⁴⁰Even today, however, some will still use the term “cancer” to describe a benign tumor rather than a malignancy.

⁴¹Fanny Burney, “A Mastectomy of 30 September 1811,” in *Excerpts from the Journals and Letters of Fanny Burney (Madame D'arblay. Volume Vi, France 1803-1812, Letters 550-631)*, ed. ed. Joyce Hemlow (Oxford: Oxford University Press, 1975).

lesion was superficial. Otherwise, do not operate or, in my paraphrase, “if it’s deep, let it keep.”⁴² In the years before the discovery of analgesia, anesthesia, and antisepsis in the middle decades of the nineteenth century, cancer surgery was uncommon and therefore the antisocial, reproachable conceptualization of cancer meant that most of its victims suffered among their family with limited outside involvement or support.

The advent of microscopic pathology, in conjunction with modalities that made cancer treatments safer, more effective, and more acceptable, led to a marked change in the professional and societal image of cancer. As these transformative forces drove the decline of the traditional conception of cancer in the closing decades of the nineteenth century — the Gilded Age and Progressive Era in the United States — it was gradually replaced by new thoughts and actions.

OUTLINE

The agents of this transformation were scientific, institutional, social, technological, and professional. Each will be explored as a contributor to the making of modern cancer.

This dissertation is divided into three sections. The first section, focused on traditional cancer, consists of two chapters. The first sets the stage by comparing some elements of the diagnosis, treatment, and conceptualization of cancer as it is generally viewed today with similar considerations during the era of traditional cancer. The focus then shifts to anatomic pathology, the medical mainstay of traditional cancer. The second chapter further explores social and economic aspects of traditional cancer, highlighting the founding of the first major hospital in the United States devoted exclusively to the care of patients with cancer and the reasons behind such a radical undertaking.

⁴²Hippocrates, *Aphorisms*, 177. “It is better not to cure occult cancers, for they who are cured quickly perish; whilst they who are not cured live longer.”

The second section, consisting of three chapters, illustrates the transition from traditional to modern cancer through the stories of two Presidents of the United States diagnosed with cancer, General Grant who succumbed to his disease, and Grover Cleveland, only a few years later, who, with the application of some of the new diagnostic and therapeutic techniques of modern cancer, triumphed over it and lived many years thereafter free of cancer. The history of General Grant's fatal cancer is directly counterpoised against that of President Cleveland's cured cancer in the third chapter of the section, where similarities and differences between the two cases are used to highlight social and cultural, as well as medical, changes that occurred over the course of the great transformation.

The third section, based on the role that the rise of medical science played in the history of modern cancer, explores the revolutionary changes in the diagnosis and management of cancer that were critical to this critical period in the history of cancer. These are some of the most remarkable changes that occurred in cancer medicine over the course of the nineteenth century, but are hardly appreciated today. The first of two large chapters in this section explains the role of the application of technology to cancer diagnosis – highlighted by the advent of the medical microscope – that was and continues to be integral to the conceptualization of cancer. The second chapter explores the roots and applications of the new science of chemistry (as opposed to alchemy), and the novel chemicals that emerged as a consequence of that new knowledge over the nineteenth century, to medicine and surgery in general and the treatment of cancer in particular. This is not a discussion of cancer chemotherapy which, although very much a twentieth-century phenomenon, has deep roots in the nineteenth, as we shall discover. Rather, this chapter examines the chemicals – anesthetics, analgesics, antiseptics – that led to a major expansion in the role of surgery for the treatment of cancer. In fact, these new chemicals were

the basis of modern cancer surgery, which could not have occurred without them. They initiated an era of approximately fifty years during which surgery was the treatment of choice for cancer – the golden age of cancer surgery.

Completing this analysis of the great transformation in the history of cancer is an epilogue that, informed by these foundational elements of the rise of modern cancer, carries the story forward into the twentieth and twenty-first centuries. Above all, the epilogue emphasizes how the great transformation from traditional to modern cancer wrought in the last decades of the nineteenth century revolutionized the conception and connotation of cancer to provide the framework for all that has and will come after. In 2013, we live very much in the shadow of this previously unheralded great cancer transformation.

SECTION I
TRADITIONAL CANCER

Chapter 1

“Cancer as it was: The Hallmarks of Traditional Cancer”

O dread disease
What vile form accompanies thy name
What suffering trails thy wake
What sorrows after thy passage

Begone!
And leave in our remembrance
Nothing but
A History

Dr. William A. Rockefeller the Celebrated Cancer Specialist

On a clear day in 1853, William Avery Rockefeller, vagabond father of the young John D. Rockefeller, stood up in his horse-drawn buggy in Richfield, Ohio to hawk his cancer medicine. Earlier that day, Big Bill, as he was called due to his nearly six-foot, thick-chested frame, had checked into the best room at the local hotel and posted a sign in the lobby: “Dr. William A. Rockefeller, the Celebrated Cancer Specialist, Here for One Day Only. All cases of cancer cured unless too far gone and then can be greatly benefited.”¹ He had no formal medical training—let alone a specialty in cancer—and any celebration was purely of his own creation. Cancer, uncommon though it was in the mid-nineteenth century, attracted a curious audience.² As the crowd gathered to hear the beguiling oratory of this impressive man in his silk hat and

¹Ron Chernow, *Titan: The Life of John D. Rockefeller, Sr.*, First Vintage Books Edition (New York: Vintage Books, 1998): 38.

²William Roger Williams, *The Natural History of Cancer with Special Reference to Its Causation and Prevention* (London: William Heinemann, 1908): 76.

black frock coat with the diamond pin, one wonders what must have been going through the minds of his listeners. “Twenty-five dollars a bottle” (an enormous sum in those days), they heard. Most, including the town physician, probably had little knowledge of cancer. Many had never heard of a patient with cancer. They knew only of its notorious reputation for prolonged suffering and incurability. “Less money for lesser medicine,” he continued. “Doc” Rockefeller, as he was known to his home-town neighbors from that time on, sold his wares, collected his earnings, and moved on through the Midwest and Canada, often for months at a time, in pursuit of his flimflam livelihood.³ His medicine, probably a mixture of herbs derived from his mother’s backyard “physic bush,” was not unusual treatment for cancer in his day.⁴

A BRIEF LOOK AT MODERN CANCER

In 2012, it is hard to imagine a similar scene occurring in the United States. “Modern cancer,” the legitimized medical disease of the present, is ubiquitous and in the forefront of the public consciousness. A culture of cancer emerged in the twentieth century that affects, among other things, what we eat, where we live, who we choose for our sexual partners, when we wear a hat in the sun, and why, in general, we take precautions undreamed of in the nineteenth century. Screening tests like mammograms, Pap smears, fecal occult blood smears, and prostate specific antigens are household terms.⁵ Prodigious government and private institutions have sprung up that gather data, perform research, and investigate potential causes,

³Chernow, 6.; Allan Nevins, *Study in Power: John D. Rockefeller, Industrialist and Philanthropist*, 1st ed., 2 vols., vol. I (New York: Charles Scribner’s Sons, 1953): 30.

⁴Chernow, 6.

⁵Mammograms are low-dose radiographs of the breast. They are used to discover early, treatable breast cancer. Pap smears, named after George Papanicolau of Cornell University Medical College, are cytological examinations of vaginal, cervical, and uterine cells. Again, the aim of the Pap smear is early cancer detection of those organs. The fecal occult blood smear is a test of the stool for small quantities of blood, as might be caused by colon or stomach cancer. The prostate specific antigen, or PSA, is a blood test that quantifies the level of a prostate protein that increases with prostate cancer. Its use has also been earlier detection of cancer.

diagnostic techniques, treatments, and cures. The daily newspapers and the nightly television broadcasts are peppered with sound bite versions of their findings. This massive cancer industry is fueled by tax dollars from all levels of government and private donations to the American Cancer Society and sister organizations that result from requests for money that daily fill our mailboxes. Regardless of these efforts, however, more than one of four deaths in the United States in 2009 related to cancer.⁶ Rare in this day and age is the individual whose personal life has not been adversely influenced by a relative or friend who has, has had, or died from the disease.

The present-day cancer process for the individual patient is complicated, expensive, time-consuming, and frightening—and quite different from that of antebellum America. To understand the past it is necessary first to offer a brief description of what the contemporary patient experiences from the time of initial detection of a cancer to the dénouement of the natural disease. The potential patient of today is usually the first to discern a problem, although routine or screening tests of blood, urine, and/or other bodily fluids may reveal something abnormal. A woman, for example, may feel a lump in her breast. A man may note a change in his cough after years of smoking, or perhaps a change in his pattern of urination. There is fear—sometimes great fear—especially if a family history of cancer is known. There may be reluctance to visit the doctor because of that fear, but there is no concern about being shunned for having the disease. Cancer is just too common today.

The woman or man visits the physician for explanation and treatment of her or his localized symptoms. S/he has become a patient. The physician, more likely than not highly cognizant of the symptoms (the patient's "subjective" sensations) and signs (the health practitioner's "objective findings") of cancer, takes a medical history, performs a physical

⁶<http://www.cdc.gov/nchs/fastats/lcod.htm> accessed November 14, 2012.

examination, and initiates a series of tests—some in the office, some in a hospital or stand-alone facility—meant to expose and highlight an abnormality if one is present *and* discoverable. Some tests meant to catch cancer in its earlier stages depend upon chemical reactions, such as a blood test to measure the level of prostate specific antigen in a man, or a stool test for blood that might suggest colon cancer. Other tests include imaging procedures. The breast lump could be visualized with a low-dose radiation study called a mammogram. Or it might be “seen” as a result of a transducer emitting and receiving sound waves through tissue, known as an ultrasound or sonogram. An ultrasound, CAT (Computerized Axial Tomography), or MRI (Magnetic Resonance Imaging) procedure would visualize the prostate gland and surrounding tissues to detect an abnormality and, if cancer is suspected, to “see” whether or not there is evidence of spread of the disease beyond the borders of the gland. Visualization of a “suspicious” lesion (i.e., an abnormality suggestive of cancer) usually leads the surgeon or radiologist to take a biopsy—a tissue sample excised from the area in question. A highly-trained technician receives the sample, puts it through an automated series of chemical reactions to stain the tissue to highlight certain features at the expense of others, and delivers the slides to a pathologist for microscopic examination. The pathologist examines the processed biopsy slides, describes his or her findings, and offers a conclusion as to the nature of the abnormality. Pathologist and clinician serve as judge and jury in answering the fatal question: Is it cancer or isn’t it? If yes, what type of cancer is it, and has it spread beyond the confines of the original tissue? If so, where and to what extent has it disseminated? Further diagnosis may entail more examinations or even—more rarely today than before the advent of the imaging procedures—exploratory surgery to ascertain the extent of disease. For most patients, however, their involvement with the diagnostic phase ends with the biopsy.

If the biopsy confirms the suspicion of cancer, treatment is begun unless the disease has spread to such an extent that therapy is likely only to worsen the predicted remaining life of the patient.⁷ The definitive and curative treatment for most “solid” tumors, like those in the lung, prostate, and colon, is surgical extirpation of the cancerous tissue. Radiation therapy, directly derived from Wilhelm Röntgen’s late 1895 discovery of the X-ray, is used alone or in conjunction with other treatments to disrupt the machinery of the uncontrolled cancer cell. Chemotherapy—born in the late nineteenth-century chemistry laboratory of Paul Ehrlich and raised (as the silver lining in a very dark cloud) in the nitrogen mustard-filled trenches of the First World War—circulates throughout the liquid and solid portions of the body. The hope is to effect the destruction of every cancer cell without damaging normal cells. Immunotherapy, nurtured in the United States by Dr. William B. Coley at The New York Hospital and the New York Cancer Hospital, stimulates the body to mount its own internal defense system (the immune system) against the cancer cells. Other adjunctive therapies, like BCG—also from the late nineteenth century, serve to augment the surgical, chemotherapeutic, and radiation “attacks” on sensitized tumor cells. If the patient responds to therapy, he or she is often “followed up” and continued on maintenance therapy for lengthy periods. Some cancers are curable. Others, depending upon their location and the extent of disease at the time of discovery (their “stage” in the language of medicine), are virtually incurable. Survival for five or more years after surgical removal or other treatment of the cancer is usually considered a cure. The whole process is like a war, and the words used to describe it—“battle,” “invasion,” “spread,” “containment,” “stage,” and “control”—are lexical shortcuts for the way our society interprets natural cancer.

⁷“Prediction” is derived from decades of accumulated statistics about the course of the disease.

Behind the treating physicians and cancer-care teams stands an enormous industry of cancer institutions. Some, like the National Cancer Institute, created by federal legislation in 1937 during the blizzard of progressive legislation known as the New Deal, fund research “relating to the cause, prevention, and methods of diagnosis and treatment of cancer.”⁸ Others, like the private American Cancer Society, founded in 1913, have as their mission the education and consciousness raising of a cancer-prone public. Hospices for the terminally ill palliate the incurable. The emphasis on technology, chemotherapeutics, radiation physics, and many other specialties requires a highly-trained corps. The present-day cancer network is a complicated and far-reaching behemoth.

TRADITIONAL CANCER

The cancer industry did not exist in “Doc” Rockefeller’s day. Indeed, Americans of the mid-nineteenth century would not recognize the technology, institutional nature, and social attributes of modern cancer because its roots lie firmly in the late nineteenth and early twentieth centuries. But to understand the transformation to modern cancer it is first necessary to dissect the disease cancer as it was conceived before its metamorphosis. What were the hallmarks of this “traditional” cancer, and what forces began to act upon it to effect the development into modern cancer? This chapter will give a glimpse of traditional cancer from social and medical perspectives.

First, a disclaimer. This work is a history of the “disease” cancer. Disease is a social construction of a natural-world phenomenon named, defined, and characterized by human beings. Traditional cancer of the nineteenth century—the subject of this chapter—and modern cancer of the late nineteenth and twentieth centuries are diseases. This is *not* a history of

⁸The National Cancer Act of 1937 may be accessed at <http://legislative.cancer.gov/history/1937>.

nature's cancer ("natural cancer")—a process of biological change unfiltered through the mind of man. I know of no such work and have no idea how it could be accomplished. I have searched, however, for evidence to discern whether the pathoanatomy of cancer has changed over time. Did natural cancer have the same causation, histological attributes, and natural history in the nineteenth century that it does today? In short, has nature's cancer evolved? Humans, bacteria, and viruses—common causes of disease—evolve over time.⁹ Why not cancer? In rare cases, such as President Grover Cleveland's secretly excised mouth tumor from 1893, twentieth-century pathologists using contemporary standards of interpretation re-examined nineteenth-century tissue specimens.¹⁰ New diagnoses were applied to old terminology, but the evolution of natural cancer cannot be discerned this way any more than the historian of today can divine the otherwise-unexpressed intent of the personage of the past solely through extant manuscripts. Do not let the ancient genealogy of the word 'cancer' from Hippocratic Greece deceive. It is not the same disease. Rather, the disease cancer has transformed with time as generations age and their political, economic, and cultural climates change. Many historians of medicine ahistoricize natural cancer. Would evolution of nature's cancer alter the form and substance of this work? Yes, it would add layers of complexity in many dimensions, because the cause, diagnosis, treatment, and cure of cancer—and society's interpretation of these variations—would most likely change with the natural entity. Nevertheless, such speculation is a topic for another time. For the purposes of this work, I will assume, rightly or wrongly, that natural cancer has remained the same. The human element, which informs the history of the disease cancer, changed.

THE TRAVAIL OF TRADITIONAL CANCER

⁹ See, for example, Paul W. Ewald, *Evolution of Infectious Disease* (Oxford: OUP, 1994).

¹⁰ John J. Brooks, Horatio T. Enterline, and Gonzalo E. Aponte, "The Final Diagnosis of President Cleveland's Lesion," *Transactions & Studies of the College of Physicians of Philadelphia* 2, no. 1 (1980): 1-25.

Social and medical connotations remarkably unlike those of today invested traditional cancer of the nineteenth century. Cancer was a social problem and a medical disaster. Patients were excluded, stigmatized, deprecated, and often left on their own to deal with the pain and suffering of their deadly disease. There were no cancer hospitals, hospices, or medical networks to aid the cancer patient in America. Oncologists, the medical and surgical cancer specialists of today, did not exist.¹¹ Indeed, for most of the century there was no consensus on exactly which pathologic lesions were cancer and which were not. Victims often suffered long periods with increasingly severe symptoms. They sought relief from many sources when the pain, disfigurement, or ulceration became intolerable, in part because treatment was a lesser of evils. Was it better to die from the terrifying knife that gave scant hope of cure, or to wither away relying upon a nostrum that at best did no harm? No wonder cancer in the nineteenth century was deemed incurable.¹² The horror of cancer magnified its importance in the public psyche.

The traditional cancer patient of the first three quarters of the nineteenth century lived under a cloud of fear and death from beginning to end. Take today's woman with a lump in her breast and transport her back in time to the early nineteenth century. Most likely she discovered the lump herself, not through self-examination—a post-Victorian twentieth-century invention—but as a result of an injury to the breast or perhaps as a consequence of the growth of the lesion to the extent that it caused pain or disfigured her breast.¹³ If a poor woman, her chance for respite might be limited to a dispensary or perhaps consolation from a close relative. More

¹¹ 'Oncology,' meaning 'tumor,' is derived from the Greek *onkos*, meaning bulk or mass. The word 'oncology,' according to *Webster's Ninth New Collegiate Dictionary* (1991), was first used in 1857. Nevertheless, the American Society of Oncologists was not founded until 1964.

¹²S. D. Gross, M. D., "On the Results of Surgical Operations in Malignant Diseases," *Transactions of the American Medical Association* 6(1853).

¹³ Evidence that periodic mammograms clearly reduced breast cancer mortality rates was not publicized until the 1960s. (*JAMA* 176 (1961): 1114-16)

likely, she would treat the lump herself with a mixture of salves or poultices gleaned from a popular medical book or a local friend.¹⁴ She might be reluctant to tell anyone else, including her husband. If the lesion was indeed a malignancy, which she might intuit from the continued growth, increased pain, and progressive derangement of the contour of the breast, she might seek the aid of a physician, fearful of the cost and the treatment. During the middle years of the nineteenth century there were doctors of different persuasions in the era of democratic medicine that has been called the Age of Jackson. “Regular” physicians practiced a “heroic” medicine that included much bloodletting, purging, and the use of mercurials, regardless of the disease under treatment. “Irregular” physicians, who may or may not have been licensed,¹⁵ used herbs and other alternative “natural” medicines for a panoply of disorders, including cancers. Families of means were treated at home, not in a hospital. A poor woman in an urban setting with a tumor might seek admittance to a mid-nineteenth century hospital if ambulatory medical therapies failed—as they inevitably did if the diagnosis of cancer was accurate. These charitable institutions, more moral way stations than the temples of science they would become in the twentieth century, required a letter of introduction from a priest or other notable to present to the philanthropist who funded the bed that the patient might occupy for a stay of several weeks to months. The philanthropist, based upon the reference and often in conjunction with a consulting

¹⁴ See, for example, William Buchan, M.D., Chapter XLVI, “Of a Schirrus and Cancer,” in *Domestic Medicine; or, the Family Physician: Being an Attempt to render the Medical Art more generally useful, by shewing people what is in their own power both with respect to the Prevention and Cure of Diseases*, 2d American ed., (Philadelphia: Joseph Crukshank, 1774), pp 361-65. This popular and practical how-to medical text underwent many editions well into the nineteenth century.

¹⁵ Medical licensure was not required to practice medicine for many years in the second quarter of the nineteenth century. New York State, for example, which had required licenses to practice medicine by 1807, repealed licensing laws in 1844 only to reinstitute state controls in 1853. Joseph F. Kett, *The Formation of the American Medical Profession: The Role of Institutions, 1780-1860* (New Haven: Yale UP, 1968), 181-82.

physician, would decide whether the patient was worthy to be admitted.¹⁶ This “class-structured institution,” as Charles Rosenberg called it, one of many in the nineteenth century, included ardent Victorian reformers—usually women—and physicians from the upper classes who sought to hone their surgical skills and build a reputation by operating on the poorer elements of society to enhance their private practices.¹⁷ Most cancer patients, however, were shunned and refused admission to voluntary hospitals for a variety of reasons, including the fact that they were deemed incurable.¹⁸ She might have been admitted to a religious hospital or a municipal care facility for terminal care, but, though the poor leave few written records, the result was most likely a painful, lonely death.

Surgeons must be very careful
When they take the Knife!
Underneath their fine incisions
Stirs the culprit,—Life!

—Emily Dickinson

The wealthy woman with a breast lump had another opportunity—surgery in a private setting by the physician of her choice. Fanny Burney (1752-1840), the noted early nineteenth-century English novelist and wife of General Alexandre d’Arblay, is famous in the annals of medical history for the letter she wrote to her sister about her mastectomy in the fall of 1811.¹⁹ Madame d’Arblay, as she was known in official circles, “began to be annoyed by a small pain in

¹⁶ Charles E. Rosenberg, *The Care of Strangers: The Rise of America's Hospital System* (Baltimore: The Johns Hopkins University Press, 1987), p22-27.

¹⁷Ibid., 105. See also Morris J. "The Transformation of the American Hospital Vogel, 1850-1920." In Susan Reverby and David Rosner, Phil: Temple UP, 1979. LK has article., “The Transformation of the American Hospital, 1850-1920,” in *Health Care in America: Essays in Social History*, ed. Susan M. Reverby and David Rosner (Philadelphia: Temple University Press, 1979), pp114.

¹⁸Ibid., 113.

¹⁹ This section is derived from Fanny Burney’s Letter to Ester Burney. Fanny Burney, “A Mastectomy of 30 September 1811,” in *Excerpts from the Journals and Letters of Fanny Burney (Madame D’arblay. Volume Vi, France 1803-1812, Letters 550-631)*, ed. ed. Joyce Hemlow (Oxford: Oxford University Press, 1975).pp596-616.

my breast” in August 1810.²⁰ Despite the medicines of numerous physicians, “the pains became quicker & more violent.”²¹ Surgery was considered a last resort, because the prevalent constitutional theory of the nature of disease (s.v.) suggested that surgical excision was useless to cure the disease. In addition, the absence of anesthesia, satisfactory analgesia, and antisepsis made the treatment potentially worse than the disease. By the summer of 1811, however, the pendulum had swung toward the necessity of surgery. “I felt the evil to be deep, so deep, that I often thought if it could not be dissolved, it could only with life be extirpated.”²² Three surgeons, including the eminent Baron Dominique-Jean Larrey, “Napoleon’s surgeon,” were consulted and informed Madame d’Arblay that they would operate in her home, as was the practice for the wealthy in the nineteenth century.²³ Only the poor went to the charitable hospitals. No urgency was manifest, for the surgery was to be palliative, not curative. Fanny did the only rational thing a person could do under such circumstances—she made out her will.²⁴ Another physician advised Fanny that she was making a great mistake. The cancer had already progressed too far for surgery, he declared on the basis of her symptoms without any more compelling evidence, and surgery would only “accelerate [sic] my dissolution” “to that most frightful of deaths.”²⁵ On September 30, 1811, unannounced, “7 Men in black”—the three surgeons, two physicians, and two students—entered her home, gave her some wine to serve as

²⁰Ibid., 598.

²¹Ibid., 600.

²²Ibid., 603.

²³Larrey (1766-1842) was the French army surgeon who invented the “flying ambulance,” known today as the army field hospital. J. Henry Dible published his biography of Larrey, *Napoleon’s Surgeon*, in 1970.

²⁴Burney, 605.

²⁵Ibid., 607.

her only anesthetic, and held her fast to her own “Bed stead.”²⁶ A soft, transparent handkerchief through which she saw “the glitter of polished Steel” covered her face as the knife began to cut into her breast.²⁷ “When the dreadful steel was plunged into the breast—cutting through veins—arteries—flesh—nerves—I needed no injunctions not to restrain my cries. I began a scream that lasted unintermittingly during the whole time of the incision— & I almost marvel that it rings not in my Ears still! so excruciating was the agony.”²⁸ A brief respite, and then “the terrible cutting was renewed— & worse than ever, to separate the bottom, the foundation of this dreadful gland from the parts to which it adhered—Again all description would be baffled—yet again all was not over,—Dr. Larr[e]y rested but his own hand, & —Oh Heaven!—I then felt the Knife rackling against the breast bone—scraping it!—This performed, while I yet remained in utterly speechless torture.”²⁹ The entire operation lasted but twenty minutes. For Fanny, nevertheless, it was an eternity she could never forget.³⁰ The operation was a rare success. She had undergone the ultimate, life-threatening treatment of traditional cancer and won. Fanny Burney lived another twenty-nine years to the age of eighty-eight. Few in her time were so fortunate.³¹

What of the man with lung or prostate cancer? No technology existed to diagnose such “internal” tumors ante mortem in the age of traditional cancer. Clinical examination with

²⁶Ibid., 610.

²⁷Ibid., 611.

²⁸Ibid., 612.

²⁹Ibid.

³⁰Ibid., 613.

³¹The stories of women who underwent breast surgery in the pre-anesthetic, pre-analgesic, pre-antiseptic, pre-antibiotic days of the mid-nineteenth century are related by other writers. Few wrote as dramatically as Fanny Burney. See, for example, Samuel Warren, “Cancer,” in *Passages from the Diary of a Late Physician* (Edinburgh: William Blackwood and Sons, 1844).

anatomic-pathologic correlation was in its infancy in the nineteenth century,³² so clinical diagnoses of internal abnormalities were fraught with inaccuracies. Only “external” tumors like those of the skin, mouth, breast, and cervicouterus could be diagnosed with any reliability. Symptoms dictated therapy.³³ Pain warranted opium and its derivatives. The outcome was uniformly fatal.

THE SOCIAL PROBLEM OF TRADITIONAL CANCER

The case histories of the anonymous poor woman with breast cancer and Fanny Burney highlight many of the problems of traditional cancer. What role did class, ethnicity, and race—factors that loomed large in public and professional attitudes toward other nineteenth-century diseases—play in traditional cancer? Why did it take so long for symptoms to lead to help? Why was there such reluctance to discuss the problem with friends, family, and physicians? Why were the sick and destitute with cancer excluded from charitable hospitals at the same time that patients with a wide variety of other essentially untreatable conditions were admitted? Why were cancer patients shunned and stigmatized? In essence, what were the causes of the social problem of traditional cancer?

VISIBILITY

The social problem of cancer in the nineteenth century was not due to a high frequency of cancer in the population. On the contrary, the incidence was much less than it is today in both absolute and relative terms. Dr. Fordyce Barker (1817-1891), an eminent New York surgeon who devoted much effort to the treatment of cancer, estimated in the late nineteenth century that

³² Henry E. Sigerist-1, *The Great Doctors: A Biographical History of Medicine* (1933).. See especially chapters 28 (Auenbrugger), 32 (Corvisart and Pinel), and 33 (Laennec and Broussais).

³³ Leo Tolstoy, *The Death of Ivan Ilych and Other Stories*, trans. Aylmer Maude and J. D. Duff (New York: A Signet Classic from New American Library, 1886). is the most chilling account of the psychological terror of traditional cancer, and of the futility of treatment.

about thirty people died from cancer out of one hundred thousand living in the period 1850-1854.³⁴ Although mortality statistics from the nineteenth century are rare and of poor quality compared to those of the present, there is reason to believe that cancer death rates had not changed appreciably for tens and perhaps hundreds of years before the middle of the nineteenth century.³⁵ In 1998, by contrast, the mortality rate from cancer was almost two hundred per hundred thousand living—an almost seven-fold increase.³⁶ Moreover, these statistics include the fact that more people are cured of cancer today (and therefore do not die from it) than ever before. Instead, more Americans in the antebellum era died from infectious diseases than cancer—the reverse of the present antibiotic era. Cancer was less visible than it is today, but it was no less feared.

CLASS AND THE SOCIAL PROBLEM OF TRADITIONAL CANCER

Nor was the social problem of traditional cancer based solely upon class, ethnicity, or race, three common categories of discrimination in nineteenth-century America. It is easy to assume that the poor, immigrants, and African Americans who suffered with cancer during the socially-stratified Victorian era were stigmatized on the basis of their personal characteristics rather than their disease, but the evidence does not support this contention. The rich and native European Americans were as likely to suffer the slings and arrows of cancer stigmatization as “the Others”—and to hide their diagnosis accordingly. Newspaper obituaries in the nineteenth century rarely named cancer as the cause of death—even when cancer was the cause known to the family. Neither the death certificate nor the obituary of Mrs. John Jacob Astor III (1825-

³⁴ New York Cancer Hospital, *Second and Third Annual Report 1886-1887* (New York: New York Cancer Hospital, 1887), Annual Report, 2.

³⁵ Scotto, Joseph and John C. III Bailarr. "Rigoni-Stern and Medical Statistics. A Nineteenth Century Approach to Cancer Research." *Journal of the History of Medicine and Allied Sciences* 24 (1969): 65-75.

³⁶ World Almanac 2000.

1887) mentioned the fact that she died of cancer.³⁷ Mrs. Elizabeth Hamilton Cullum (1831-1884), one of the first cancer activists who worked to overturn the social problem of traditional cancer, sought to make a strong point by insisting that the true cause of her death—cancer—be cited in her public obituary.³⁸

Neither was the stigmatization of cancer based upon an increased frequency of the disease among the poor. The lower classes, so often the target of infectious diseases and youthful demise due the ramifications of poverty, were no more likely to develop cancer than the rich. “Cancer attacks all classes of people,” wrote Dr. Thomas Weeden Cooke, pathologist at the London Cancer Hospital, the first hospital in the world devoted exclusively to the care of cancer patients.³⁹ “The poor are not more its victims than the well-to-do.”⁴⁰ Indeed, Cooke noted that the poor were less likely to acquire cancer than the rich. “The crowded courts and alleys of our large towns yield even fewer cases of cancer than are to be found distributed over the green pastures and the fertile fields” of the gentry.⁴¹ The implied urban-rural/poor-rich differentiation in cancer incidence recurred again at the end of the nineteenth century, but, for Cooke and others of the Victorian era, cancer was not despised as a class-based disease of the lower orders.

ETHNICITY AND THE SOCIAL PROBLEM OF TRADITIONAL CANCER

Ethnicity played a relatively minor role in furthering the stigmatization attendant to cancer and whatever influence it had came late in the era of traditional cancer and could work for

³⁷Memorial Hospital Archives, Record Group 500 Hayes Martin Collection, Box 5, folder 84, "Obituaries 1887-1961."

³⁸See Chapter 2 of this dissertation for a more extensive discussion of both women.

³⁹Thomas Weeden Cooke, *On Cancer: Its Allies and Counterfeits*, 2 vols., vol. 1+2 (London: Longmans, Green, and Co., 1865), 10-11.

⁴⁰*Ibid.*

⁴¹*Ibid.*, 11.

or against cancer prejudice. The population of the United States was most homogeneous from an ethnic and religious point of view in the early 1840s.⁴² Thereafter a series of catastrophes across the Atlantic served to push Europeans—Irish, Germans, Italians, Russians—toward America’s shores. The “Great Immigration” did not begin, however, until the 1880s, a time when traditional cancer was already fading under the influence of multiple forces. Those who cared for cancer patients in the earlier decades of the nineteenth century sometimes blamed the disease on ethnic habits of immigrants, but more likely the physician was attempting to fit the alien habits of the victim into the physician’s concept of cancer causation. Dr. Richard Carmichael, who believed that irritation caused cancer—a common belief at the time—explained the frequency of lip cancer among the Irish thus: “frequent irritation of a part, such as the peasantry of Ireland are in the habit of inflicting on their under lips in the act of smoking, from the habit of constantly using short and heated tobacco pipes, may occasion carcinoma in the most healthy, young, and robust persons.”⁴³ On the other hand, less anecdotal evidence could cut the connection between cancer and stigma in an otherwise disparaged ethnic group. Eastern European Jews, for example, often considered to be carriers of tuberculosis and other diseases,⁴⁴ were reportedly less likely to suffer the ravages of cancer. “The available indications,” wrote the cancer researcher W. Roger Williams in the early twentieth century, “point clearly to the

⁴²Jeremy Atack and Peter Passell, *A New Economic View of American History from Colonial Times to 1940*, 2nd ed., (New York: W. W. Norton & Company, 1994): 229-34, 238.

⁴³Richard Carmichael, *An Essay on the Origin and Nature of Tuberculous and Cancerous Diseases* (Dublin: Hodges and Smith, College-Green, 1836): 35.

⁴⁴Irving Howe with the assistance of Kenneth Libo, *World of Our Fathers* (New York: Schocken Books, 1989): 149; and Alan M. Kraut, *Silent Travelers: Germs, Genes, and the "Immigrant Menace"* (New York: BasicBooks, 1994): Chapter 6, “*Gezunthayt iz besser vi Krankhayt: Fighting the Stigma of the “Jewish Disease,”* especially 155.

conclusion, that the liability of Jews to cancer varies with their mode of life, approximating to that of the people among whom they dwell, but generally being somewhat inferior to it."⁴⁵

RACE AND THE SOCIAL PROBLEM OF TRADITIONAL CANCER

The social stigma of traditional cancer did not devolve from the widespread prejudice against African Americans. The predominantly ill-housed, ill-clothed, and ill-fed agricultural workers of the antebellum and postbellum South suffered from high rates of infant mortality and a host of indigenous diseases, but cancer was not one of them.⁴⁶ Cancer epidemiologists in the early twentieth century collected data from the South retrospective to the mid-nineteenth-century census. They concluded that cancer was rare among African Americans.⁴⁷ Indeed, as cancer came to be considered by many in the late nineteenth century a "disease of civilization," the poor black farmer was emphatically excluded from those likely to develop cancer.⁴⁸

CAUSES AND CONSEQUENCES

The exclusion of cancer victims from the mainstream of American life and its nineteenth-century hospitals was based upon the chronicity of the disease, fear, abhorrence, and economic factors. Natural cancer differs from many other ailments in the subtleness of its initial symptoms and the longevity of its course. A pain or change in bodily habits may be a symptom of temporary distress or the first indication of a mortal illness. Frequently only time will tell. As a result, diagnosis in the nineteenth century was usually delayed or suspended. Only when

⁴⁵William Roger Williams, *The Natural History of Cancer with Special Reference to Its Causation and Prevention*, 1st ed., 1 vol. (London: William Heinemann, 1908): 16.

⁴⁶Todd L. Savitt and James Harvey Young, eds. *Diseases and Distinctiveness in the American South*. Knoxville: The University of Tennessee Press, 1988.

⁴⁷Williams, 66.

⁴⁸Willard Parker, M.D., "Willard Parker, M.D. Papers, 1884," manuscript letters and papers, Willard Parker Papers: #37-59, New York. Folder #57, Autograph letter signed by Edmund B. Fowler (1811-1879) to Willard Parker, M.D., NY, 12/7/1878; Folder #59, Letter to Mrs. J.H. Armsby, Palatine Bridge, NY, 6/14/1881, Malloch Rare Book Room, The New York Academy of Medicine.

symptoms were clearly intolerable and chronic did the afflicted seek help. By that time little of substance could be done. Practitioners sought to alleviate symptoms as the cancer grew and caused pain, distortion of bodily features, and fungating ulcers for all around to experience and relate to their community. Probably for this reason leprosy, to which cancer was invariably compared, was considered more curable than cancer.⁴⁹ In consequence, the chronicity of cancer and its multiple manifestations engendered social interpretation and the development of cultural attitudes toward the disease and the stricken patient.⁵⁰ These biases were strongly condemnatory in the age of traditional cancer.

Ignorance is the mother of prejudice.

—J. Bright, *London Times*, July 18, 1861⁵¹

Fear of cancer dominated the prejudice of society against traditional cancer. Causation beliefs were key to the trepidation and stigmatization of cancer. The cause of cancer was unknown, but beliefs and hypotheses were rampant.⁵² The religious character of antebellum America colored causation beliefs, and most blamed the victim. The period of religious fervor in the second quarter of the nineteenth century, known in America as the Second Great Awakening, tempered the steel hand of Jonathan Edwards's unforgiving Calvinist God of the century before, but piety still stayed the tenor of antebellum angst.⁵³ God was the ultimate judge and the cause

⁴⁹“Cancer Hospital Project in New York City,” *The New York Times*, March 8, 1884, 8:2. The quotation was from Dr. James Marion Sims.

⁵⁰Certainly there are cancers like leukemia that killed swiftly before the advent of effective chemotherapy in the mid-twentieth century. It is interesting to note that leukemia was one of the last cancers to be characterized (by Donné, Virchow, and others about 1845)—perhaps because the fulminant course of most acute leukemias differed so much from solid tumors and therefore, to some, did not behave like a “cancer” at all.

⁵¹From the *Oxford English Dictionary* for ‘prejudice,’ 1933 edition, 1275.

⁵²I have compiled a list of reputed cancer causes predominantly from the nineteenth and twentieth centuries that runs in excess of ten pages.

⁵³Charles E. Rosenberg, *The Cholera Years: The United States in 1832, 1849, and 1866*, 1st ed., 1 vols. (Chicago: The University of Chicago Press, 1962).p4-5.

of all illness. Cancer was punishment for sin. No specific sin was tied to the development of cancer, but surely the sin had been egregious, because the illness was grievous. Victorian women with cancer were deemed especially iniquitous because they were viewed by men through two lenses of sinfulness—one of gender, the other of cancer.⁵⁴ A horrendous consequence of this belief that cancer was punishment for evil was that mortal attempts to cure God-given disease were considered unrighteous at best and blasphemous at worst. Better to let the disease follow the course that God intended. Let the sinful one fester as punishment for her sins.⁵⁵

By the third quarter of the nineteenth century, a more materialistic and secular American society began to blame cancer on new causes, but with similar social consequences. Contagion and inheritance came to dominate concepts of disease causation, just as much of natural cancer today is explained in the dominant paradigm of molecular biology and genetics. Cancer fit well into both nineteenth-century scenarios. The idea of contagion has Greek roots, but it was not until the mid-seventeenth century that Athanasius Kircher (1601-1680), a German Jesuit, observed living microorganisms in the blood of plague victims and believed that they were the cause and vehicle of the disease.⁵⁶ Germs, as they were eventually called, gave contagion one explanation. But there were many other competing notions of the cause of contagion during the nineteenth century, including miasma (polluted air) and filth. As Robert Mitchell opined in

⁵⁴G.J. Barker-Benfield, *The Horrors of the Half-Known Life: Male Attitudes toward Women and Sexuality in Nineteenth-Century America*, 1st ed., 1 vols. (New York: Harper & Row, 1976), p282. I plan a much longer exposition of female gender and cancer for Chapter 6.

⁵⁵Rosenberg, *Rosenberg, Care of Strangers*.p376FN12. Also note that pain-killing anesthesia was initially shunned for similar reasons during this same period. See Deborah Kuhn McGregor, *From Midwives to Medicine: The Birth of American Gynecology* (New Brunswick, NJ: Rutgers University Press, 1998), p203.

⁵⁶“The Germ Theory of Disease,” Henry Alan Skinner, *The Origin of Medical Terms*, 2nd ed. ed. (New York: Hafner Publishing Company, 1970), p190.

1879, “The imputed cause of many diseases is impurity of atmosphere from dense population, want of ventilation, and the decay and decomposition of animal and vegetable matters, aggravated by poverty and its consequences, imperfect nutrition, and want of cleanliness.”⁵⁷

The germ theory of contagion was revived by Jakob Henle (1809-1885), the student of Johannes Müller (1801-1858) and teacher of Robert Koch (1843-1910), and established on firm footing in Europe in the mid-nineteenth century.⁵⁸ The theory may or may not have been slow to catch on in the United States, but long before there were “cancer germs” there were advocates for the contagiousness of cancer.⁵⁹ It was not unusual for more than one member of a family to contract the disease—implying contagion. Servants were known to “catch it” from their master or mistress. By the 1870s, hospitals routinely excluded cancer patients from their wards, citing fears of contagion.⁶⁰ The belief that cancer was contagious fueled the social stigma against the disease.

A derivative of the contagion theory of cancer causation was the belief that the disease was venereal in origin.⁶¹ How many Victorian women were shunned because two of the most

⁵⁷Robert Mitchell, *A General and Historical Treatise on Cancer Life: Its Causes, Progress, and Treatment*, 1st ed. (London: J. & A. Churchill, New Burlington Street, 1879): 9-10.

⁵⁸Henry E. Sigerist, *The Great Doctors: A Biographical History of Medicine*, trans. Eden and Cedar Paul (Garden City, NY: Doubleday & Company, Inc., 1933; repr., 1958), 350.

⁵⁹See Phyllis Allen, "Etiological Theory in America Prior to the Civil War," *Journal of the History of Medicine and Allied Sciences* 2 (1947)., Phyllis Allen Richmond, "American Attitudes toward the Germ Theory of Disease (1860-1880)," *Journal of the History of Medicine and Allied Sciences* 9 (1954)., and for a more contemporary contrary opinion as to the acceptance of germ theory in America, see Nancy J. Tomes and John Harley Warner, "Introduction to Special Issue on Rethinking the Reception of the Germ Theory of Disease: Comparative Perspectives," *Journal of the History of Medicine* 52 (Ja 1997): 7-16. LK copy, 990322. 52, no. January (1997).

⁶⁰Hayes Martin, Harry Ehrlich, and Francelia Butler, "J. Marion Sims--Pioneer Cancer Protagonist," *Cancer* 3, no. 1950 (1950)., p199.

⁶¹Edwin A. Mirand, "Dr. Roswell Park's Lasting Legacy to the World in Developing the Concept of a Cancer Center," in *Medical History in Buffalo 1846-1996*, ed. Lilli Sentz (Buffalo: State University of New York at Buffalo, 1996)., p193.

common cancers diagnosable in the nineteenth century (before internal cancers could be visualized), breast and uterus, were firmly felt to be the consequence of illicit or excessive sexual intercourse or even merely desire! How unfortunate that more than half of women's cancers in double-standard Victorian America were those of their sexual organs!⁶² At least two sources of purported confirmatory evidence were invoked that cancer was venereal. One was that cundurango, a plant derivative touted in the early 1870s as a cure for cancer, was also a treatment for venereal disease.⁶³ How could the bark of the vine ameliorate both illnesses, asked the cognoscenti of the time, if they were not of the same origin? Secondly, Dr. Novinsky, a Russian veterinarian, showed in 1876 that venereal sarcoma of dogs could be transplanted from one animal to another.⁶⁴ A venereal cancer had been proven contagious in dogs. Surely men—and women—were no different from dogs. Thus, Victorian attitudes toward gender and sex, coupled with seemingly incontrovertible evidence during the 1870s that cancer was a venereal contagious disease, combined to make women with cancer into social pariahs.

The social stigma of traditional cancer was compounded by the presumed inalterable nature of inheritance and the fixed hierarchical structure of society that dominated American culture before the acceptance of Charles Darwin's reconceptualization of man's understanding of the universe. Although Darwin noted to a friend as early as 1844 that "I am almost convinced (quite contrary to the opinion I started with) that species are not (it is like confessing a murder)

⁶²Of the 278 patients admitted to the New York Cancer Hospital from Dec 1887 to Jan 1, 1889, for example, 53 had breast ca, and 94 uterine ca. Bob Considine, *That Many May Live: Memorial Center's 75 Year Fight against Cancer*, 1st ed., 1 vols. (New York: Memorial Center for Cancer and Allied Disease, 1959).p22

⁶³Dr. Casares, Quito, January 4, 1870 [Accompaniment A.] Flores & Wing, "Cundurango," ed. Mr. Fish (Washington: 1871). p6.

⁶⁴Michael B. Shimkin, *Bicentennial of Medicine in the United States, 1776-1976* (Atlanta, GA: Department of HEW, PHS, NIH, NLM), Videotape.

immutable,”⁶⁵ he did not publish *On the Origin of Species* until 1859. And to write that his ideas were immediately accepted would fly in the face of history. Throughout most of the nineteenth century, therefore, the child was thought to mirror the parent. Cancer, or rather the constitutional tendency to cancer, was believed to be inherited. Hence the disease was not viewed like the plague, which felled everyone who was exposed to it. Rather there had to be a susceptibility to the contagiousness of cancer, and that proclivity was inherited. Further, Lamarckianism—the belief in the heritability of acquired characteristics—was strong. Even Darwin subscribed to it. Once a member of a family developed cancer, his or her descendants were at increased risk for the same fate. These notions were well accepted and carried the prejudice against cancer from one generation to the next—like a Biblical curse. As Carmichael sermonized in his 1836 essay "On The Origin and Nature of Tuberculous and Cancerous Diseases," "the punishment inflicted thus upon the children, and reflected back again upon the parents in anxiety and sorrow, explains and justifies that apparently harsh, but natural and necessary law, that 'the sins of the parents are visited upon the children, even to the third and fourth generation.'"⁶⁶ The stigma against cancer was powerful in Carmichael and his colleagues. He concluded his essay with the wish that those with cancer should cease to exist on the face of the earth: "Then, fortunately, perhaps, a degenerated race may cease to possess the power of propagating its kind."⁶⁷

⁶⁵Martin Gardner, ed. *Great Essays in Science*, 1st ed., 1 vols., The Pocket Library (New York: Pocket Books, Inc., 1957).p1.

⁶⁶Carmichael, 51.

⁶⁷Ibid. It is important to remember that the concept of 'race' in the nineteenth century was very different from that today. 'Race' then referred to a group of people—usually different from one's own. There was the Jewish race, the Italian race, and the Irish race—as well as that "degenerated race" of Carmichael that included all people with cancer.

Nineteenth-century concepts of contagion and inheritance intertwined with Victorian mores and an inflexible layered society to condemn cancer victims—unlike most other sufferers of disease—to the margins of the community.

EXCLUSION OF THE REVOLTING

The transmogrifying physical effects of cancer further offended Victorian sensibilities. The social stigmatization of traditional cancer kept the diseased away from help longer.⁶⁸ Fear of surgery removed hope of effective treatment. Therefore, most nineteenth-century cancers were essentially untreated.⁶⁹ Superficial cancers, like those of the skin or breast, that went unattended ultimately ate away at the flesh to create a rotting lump of unbearable stench that left the staunchest soldier quivering.⁷⁰ Bloom, Richardson, and Harries, who examined the records of untreated breast cancer patients from 1805 into the twentieth century, found that “in the absence of primary treatment [i.e., surgery] patients often linger for many months or years with large, foul ulcerating breast tumours which penetrate deep into the chest wall and produce much pain, discharge, and intermittent haemorrhage.”⁷¹ Cancer patients were rejected because of the “offensive odors” produced by these fungating and ulcerating lesions. In 1873, for example, a woman with cancer admitted under false pretenses to the Woman’s Hospital of the State of New York caused a tumult and the undying anger of the administrators because “the Ward was made so very offensive from the nature of the disease that two or three patients actually left and others

⁶⁸H. J. G. Bloom, W. W. Richardson, and E. J. Harries, "Natural History of Untreated Breast Cancer (1805-1933)," *British Medical Journal* 2, no. 5299 (1962): 215.

⁶⁹Ibid., 214; *ibid.*

⁷⁰Ibid., 215.

⁷¹Ibid., 219.

complained bitterly of the discomfort to which they have been subjected.”⁷² Hospitals and medical caregivers rejected cancer patients not only because of the assault of the advanced disease on their senses, but because it drove away others whose diseases were deemed more responsive to Victorian moral and medical care. Those with cancer were considered unworthy and were ostracized.

THE ECONOMIC FACTOR

The high cost of caring for cancer patients compounded their exclusion from hospitals and added a measurable justification to their social stigmatization. Cancer costs exceeded those of other diseases for numerous reasons. The family of the stricken, at a time when disability and health insurance were essentially nonexistent, lost the benefit of all future earnings, had to hire more help at home, and, depending upon the circumstances, might be forced to pay something out of pocket for hospital care—if they could find admission to a non-voluntary hospital that would take them. The cost to those facilities that would admit cancer patients was excessive because of the special daily needs of the cancer patient as well as the chronicity of the disease. Attorney John E. Parsons, president of both the Woman’s Hospital—which excluded cancer patients—and the New York Cancer Hospital, knew well the cost of cancer. “The nature of the disease requires a richer and more liberal diet, and for medical supplies it involves a cost per patient quite beyond what is required in an ordinary hospital.”⁷³ Nursing requirements were also high because the near-terminal cancer victim—the most likely to seek hospital care—required much attention to bandages, feedings, and the activities of daily living. In addition, the New York Cancer Hospital did not discharge chronic cases. “This is

⁷²Deborah Kuhn McGregor, *From Midwives to Medicine: The Birth of American Gynecology* (New Brunswick, NJ: Rutgers University Press, 1998), 192. on Minutes of Ladies Board, 3 Jun 1873)

⁷³John E. Parsons, “Report of the President, *Seventh Annual Report*,” (New York: New York Cancer Hospital, 1891), 8-9.

peculiarly so in view of the fact that until all the room of the Hospital is required for treatment cases, we have not felt at liberty to reject or dismiss cases chronic in their character.”⁷⁴ Despite the fact that most voluntary hospitals in the nineteenth century were run by wealthy individuals, their balance sheets were always precarious. Most voluntary hospitals subsisted on a shoestring from “an eclectic mixture of contributions from local government, endowment income, the proceeds of community fundraising, and the fees of occasional private patients.”⁷⁵ Economic panics and downturns, such as those of 1873 and 1893, dried up funding. Perhaps hospitals of the nineteenth century were correct to exclude cancer patients on *economic* grounds. They could jeopardize the financial health of the hospital, as Mr. Parsons found out. By the end of the nineteenth century, the New York Cancer Hospital, near bankruptcy, was forced to change its name and its mission away from a near-exclusive focus on cancer patients toward a hospital population with general diagnoses.⁷⁶

TRANSITION: THE SPECTRE OF INCURABILITY

The incurability of cancer haunted Traditional Cancer in Victorian times. This cultural notion, which persists today in a more circumscribed form, serves to bridge the ideological divide between the social and medical interpretations of cancer in the mid-nineteenth century. The evidence that cancer was incurable was incontrovertible.⁷⁷ Laymen needed no prodding to accept the incurability of cancer, because it was common knowledge that cancer inexorably killed. Physicians, who have labored for centuries to prognosticate disease by means of

⁷⁴Ibid., 9.

⁷⁵Charles E. Rosenberg, *The Care of Strangers: The Rise of America's Hospital System* (Baltimore: The Johns Hopkins University Press, 1987; repr., 1995), 238-39.

⁷⁶John E. Parsons, "Report of the President, *Fourteenth Annual Report*," (New York: New York Cancer Hospital, 1898).

⁷⁷Gross, "On the Results of Surgical Operations in Malignant Diseases," 157, 61.

symptoms and signs into curable and incurable, consistently considered cancer as belonging to the latter category. Hippocrates, the father of medicine, pleaded that the disease was best left alone under most circumstances to come to its natural conclusion.⁷⁸ Survivors like Fanny Burney were so rare as to be notable—and to question the accuracy of the original diagnosis.

In 1853, Dr. Samuel D. Gross (1805-1884), one of the most prominent American physicians of the nineteenth century, presented a study *On The Results of Surgical Operations in Malignant Diseases* to the fledgling American Medical Association. He surveyed the results of surgical operations and other methods of treating cancer worldwide and throughout history. Cancer, he concluded in one of the most extensive investigations of the disease in the nineteenth century, was “incurable.”⁷⁹ Notions of medical futility and psychological hopelessness set the framework for the alienation and exclusion of traditional cancer victims from society.

THE MEDICAL PROBLEM OF TRADITIONAL CANCER

It is one of the worst aspects of our present developmental stage in medicine that the historical knowledge of things diminishes with each generation of students. Even independent young research workers can normally be assumed to have a historical knowledge of no more than three to five years at a maximum. Anything published more than five years ago does not exist.
—Rudolph Virchow (1870)

The medical problem of traditional cancer was the constitutional theory of disease. The incurability of cancer, for example, was more than a realistic conclusion based upon experience. It was also the inescapable result of this prevalent medical concept. Cancer, like most other diseases in the early nineteenth century, was formulated within the framework of a constitutional ideology. This idea, alien to most twentieth-century practitioners and investigators—but now undergoing a revival in the genomic era, held that susceptibility to disease was inherent to one’s

⁷⁸Hippocrates, *The Aphorisms of Hippocrates*, trans. Thomas Coar, Special ed., The Classics of Medicine Library (London: A.J. Valpy, 1822; repr., 1982), 177.

⁷⁹Samuel David Gross, M. D. (1805-1884), *On the Results of Surgical Operations in Malignant Diseases*, *National Library of Medicine* (Philadelphia: T. K. and P. G. Collins, Printers, 1853), Microfilm, 161 pages, NLM 01613193 2.

being. Language has continued this notion to the present under the guise of his or her “constitution.”

CONSTITUTIONALISM

The concept is of constitutionalism ancient. Hippocrates (c.460-c.377 BCE) attributed the cause of cancer to a humor called black bile (melan chole) that circulated throughout the body.⁸⁰ The Greek physician Galen (129-c.199) furthered the notion of cancer as a non-localistic, historical process. His explanation of disease based on the four humors held sway in many parts of the Atlantic community well into the nineteenth century.⁸¹

Why was the constitutional theory of disease the medical problem of traditional cancer? It made cancer incurable and therefore, by definition, hopeless. Remove a cancer from one part of the body and the belief was that it would simply arise elsewhere because the entire organism was prone to the disease. All empirical evidence bore this out. If, for example, a patient suffering from breast cancer submitted to surgery in the nineteenth century, and if she survived the dangerous procedure without succumbing to postoperative infections and other complications, the probability was that she would experience a local or distant recurrence. Why? Because cancer was intrinsic to that human body. The constitutional concept of cancer predicted the futility of operation. Consequently, surgery became a last-ditch effort to palliate a manifestly incurable disease. Cure was theoretically impossible. Fanny Burney was most fortunate. If her growth was a malignancy,⁸² then she was lucky that it was removed, based upon twentieth-

⁸⁰See, for example, Mark Barrow, "Portraits of Hippocrates," *Medical History* 16 (1972): 8.

⁸¹De Moulin, 70; Maulitz, 3, 17, 337; John S. Haller, Jr., *American Medicine in Transition 1840-1910*, (Urbana: University of Illinois Press, 1981), 9.

⁸²Pathological examination of tissue removed by surgery was not routinely performed until the late nineteenth and early twentieth centuries. (See James R. Wright, Jr. "The Development of the Frozen Section Technique, the Evolution of the Surgical Biopsy, and the Origins of Surgical Pathology," *BHM* 59 (Fall 1985): 295-

century notions of cancer, before it invaded local tissues and the lymphatic system. What we call metastases were believed to be new tumors recurring in a fertile cancerous soil.⁸³ Not until the nineteenth century was it discovered that metastases, which were not named as such until that time and literally denote a ‘change in place,’ were parts of the original cancer that took root in another site within the body.⁸⁴ The incurability of traditional cancer was more a consequence of the dominant paradigm of constitutionalism than extant than of the natural disease itself.

How many more could have been saved if early removal of cancerous growths had then been advocated! In a cruel twist of fate, a theory that had been the basis of medical practice for centuries retarded the very actions that could have saved lives. The influence of theory on practice and the effect of those practices on cultural sentiments unnecessarily led many to an early grave.

THE FRAGMENTATION OF THE WHOLE

And as for Intellectual concerns, I do with some confidence expect a Revolution, whereby Divinity will be so much a Loser, and Reall Philosophy flourish, perhaps Beyond men’s Hopes.

—Robert Boyle (1627-1691)

The disintegration of the constitutional theory of disease was part and parcel of the fragmentation of society brought on by capitalism, nationalism, and secularism. The communitarian unity fostered by the Church during the Middle Ages fell apart as artisanal workshops manufactured goods through a division of labor, armies rolled over Europe promoting

326.) Therefore the cancer diagnosis of Fanny Burney’s skin lesion was made on purely clinical grounds, increasing the probability that the tumor was not a malignancy at all.

⁸³Howard W. Haggard and G. M. Smith, "Johannes Muller and the Modern Conception of Cancer," *Yale Journal of Biology and Medicine* 10, no. 5 (1938): 422.

⁸⁴Joseph Claude Recamier, *Recherches Sur Le Traitement Du Cancer, Par La Compression Methodique Simple Ou Combinee, Et Sur L’histoire Generale De La Meme Maladie* (1829). J.C.A. Recamier (1774-1852), named *metastasis* (vol 2, p 110, lines 3-7) and recognized how cancer spread.

the dissociation of the Continental Empire into nation-states, and Christianity split into ever-more-numerous sects.

Medical practitioners, being of society as well as in it, were sensitive to these changes. American medicine, until the last decades of the nineteenth century, grew up in the shadow of European medicine, so it is natural to explore first the Continental roots of modern medicine before returning to the States.

Vesalius (1514-1564), the great Belgian anatomist, flouted convention by personally dissecting human cadavers. His major text, *De humani corporis fabrica* (1543), repudiated Galenic tradition and began a long series of investigations that to this day continue to fragment the human body into smaller and smaller units.⁸⁵ Giovanni Morgagni (1682-1771), an Italian physician, applied the new (and contested) human anatomy to pathology—the study of human disease. His major work, *De sedibus et causis morborum per anatomen indagatis (The Seats and Causes of Diseases investigated by Anatomy)* (1761), emphasized the internal organs rather than the body as an indivisible whole, earning Morgagni the status of father of pathological anatomy.⁸⁶ Xavier Bichat (1771-1802) who, during his short but productive life, pioneered the study of human tissues (which he called ‘membranes’), further narrowed the focus of medicine away from the corpus. In doing so, he honed the process that was to serve as the model for nineteenth century medicine; viz., that anatomical change is the foundation of human pathology.⁸⁷

⁸⁵Andreas Vesalius, Joannes Oporinus, and Jan Stephan van Calcar, *Andreae Vesalii Bruxellensis, Scholae Medicorum Patauinae Professoris, De Humani Corporis Fabrica Libri Septem* (Basileae: Ex Officina Joannis Oporini, 1543).

⁸⁶Giambattista Morgagni, *The Seats and Causes of Diseases*, trans. Benjamin Alexander, Special ed., 3 vols., The Classics of Medicine Library (Birmingham, Ala.: The Classics of Medicine Library, 1983).

⁸⁷Xav. Bichat, *A Treatise on the Membranes in General, and on Different Membranes in Particular*, trans. John G. Coffin. (Boston: Cummings and Hilliard, 1802; repr., 1987). Also see Michel Foucault, *The Birth of the*

By the nineteenth century, as social and economic forces continued the division of society by breaking up/cleaving the family through the departure of men and children to workplaces away from the home and leaving women with the domestic chores,⁸⁸ medical practitioners began to question the viability of the holistic constitutional concept. An enlightened group of eight practitioners in Edinburgh, calling themselves the Medical Committee of the Society for Investigating the Nature and Cure of Cancer, asked thirteen profound questions that dissected the nature, causation, course, and treatment of cancer.⁸⁹ One of the queries directly confronted the prevailing constitutional concept of cancer:

Query 7th.--*May cancer be regarded at any period, or under any circumstances, merely as a local disease? Or does the existence of cancer in one part afford a presumption that there is a tendency to a similar morbid alteration in other parts of the animal system?*

No answer was offered. These far-seeing men set the agenda for the demise of the constitutional theory of cancer during the nineteenth century by asking the right questions.

CELL THEORY

All diseases are in the last analysis reducible to disturbances,...of large and small groups of living units (cells), whose functional capacity is altered in accordance with the state of their molecular composition and is thus dependent on physical and chemical changes of their contents.

—Rudolph Virchow (1855)⁹⁰

The microscope, the greatest technological development of medicine in the nineteenth century, replaced theory with observation. Technological improvements to the microscope, as

Clinic: An Archaeology of Medical Perception, trans. A. M. Sheridan Smith (New York: Vintage Books, 1963; repr., 1994).

⁸⁸The literature on the sundering of the family and the cult of domesticity is vast. See, for example, Nancy F. Cott, *The Bonds of Womanhood: "Woman's Sphere" in New England, 1780-1835* (New Haven: Yale University Press, 1977).

⁸⁹Matthew Baille et al., "Questionnaire from the Institution for Investigating the Nature and Cure of Cancer," *Edinburgh Medical and Surgical Journal* 2(1806): 382-90.

⁹⁰Cited in Harold M. Malkin, *Out of the Mist: The Foundation of Modern Pathology and Medicine During the Nineteenth Century* (Berkeley: Vesalius Books, 1993; repr., 1995), 143.

we shall see, fostered the cell theory of disease and signaled the death knell of constitutionalism and its sway over the ideology of traditional cancer medicine. Although the microscope in a recognizable form was probably invented in the late sixteenth century, chromatic and spherical aberrations of the projected image made it effectively unusable for the study of human biology. During the 1820s, Europeans improved the instrument to allow the reliable observation of biological structure.⁹¹ In 1838, two German biologists, Matthias Schleiden (1804-1881) and Theodor Schwann (1810-1882), advanced cell theory—i.e., that the fundamental functional unit of the organism is the cell.⁹² The body had been fragmented from a whole into organs, tissues, and then cells.⁹³ The cell became the basic unit of the body. Disease was conceived as an abnormality of the cell. In 1840, Johannes Müller (1801-1858), the colleague/mentor of Schleiden and Schwann, published a remarkable tract that, for the first time, applied the reborn microscope and cell theory to the study of tumors.⁹⁴ Decades passed before the use of the microscope in the study of cancerous diseases was accepted by practitioners and surgeons as well as pathologists. Nevertheless, Müller and his students, especially Rudolph Virchow (1821-

⁹¹Brian Bracegirdle, "J. J. Lister and the Establishment of Histology," *Medical History* 21(1977): 187-91.

⁹²Contemporaries of Schleiden and Schwann gave credit for the cellular unit to "The fact that the material elements of all organic beings—plants and animals—originate from minute cell-organisms, was first announced by Oken [Die Zeitung. Frankfurt, 1805]; it has been ably illustrated and enforced by Schleiden, Schwann, Barry, and other physiologists; and is now universally concurred in, as a truth of the highest interest and importance to physiology, and practical medicine." William Addison, M.D., F. R. S., *On Healthy and Diseased Structure and the True Principles of Treatment for the Cure of Disease, Especially Consumption and Scrofula; Founded on Microscopical Analysis*, 1st ed. (London: John Churchill, 1849).p 1. L. J. Rather, Patricia Rather, and John B. Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, trans. L. J. Rather, 1st ed. (Canton, MA: Science History Publications, 1986).p v. Rather gives a compelling historical argument for the existence of cell theory long *before* Schleiden and Schwann, but they are usually given credit for the discovery of cell theory.

⁹³The process of reducing the investigatory unit of the body to smaller and smaller pieces continued with cellular 'organelles,' DNA, base pairs, and the chemicophysical bonds of life, although deciphering the "language" of DNA continues to be the main focus for examining the etiology of cancer at the microscopic level.

⁹⁴Johannes Müller, "On the Finer Structure and the Forms of Morbid Tumors (Ueber Den Feinern Bau Und Die Formen Der Krankhaften Geschwulste; Berlin, 1838)," in *Johannes Müller and the Nineteenth-Century Origins of Tumor Cell Theory* (Canton, MA: Watson Publishing International (Science History Publications, U.S.A.), 1838).

1902)—the father of cellular pathology—laid the groundwork for a revolutionary new conceptualization of cancer based upon local rather than systemic notions of disease.

For cancerous diseases, the greatest clinical advance of the nineteenth century was the application of the microscope to the study of cancer. The result, the cell theory of cancer, overthrew constitutional theory and constructed a new ideology of disease founded upon the new pathology. Cell theory succeeded because it was based on the firm foundation of pathology, lent itself to a more accurate differentiation between benign and malignant tumors, created a framework of understanding that improved treatment results, and gave new hope where there had been none. As a result, cell theory helped to dissipate the social stigma against cancer.

AVANT-GARDE PATHOLOGY

Pathology was the most advanced discipline of medicine for most of the nineteenth century. Based on the new reductionist organ-tissue-cell model of localized disease, it provided a radical way of looking at the body and disease. Müller and Virchow, who, with their students, dominated the German school, published tracts on the microscopic nature of cancer that assumed the local nature of cancer.⁹⁵ Their work created a new nosology of cancer—a classification based upon the appearance of cancerous tissue under the microscope.

LIFTING THE VEIL

The definition of cancer had been one of the major problems of cancer medicine for centuries. An exasperated Virchow exclaimed in the 1860s that "no human being can define,

⁹⁵Johannes Müller, "Ueber Den Feinern Bau Und Die Formen Der Krankhaften Geschwulste (on the Finer Structure and the Forms of Morbid Tumors)," in *Johannes Müller and the Nineteenth-Century Origins of Tumor Cell Theory* (Canton, MA: Watson Publishing International (Science History Publications, U.S.A.), 1838; reprint, 1986). Rudolf Virchow, *Die Krankhaften Geschwulste. Dreissig Vorlesungen Gehalten Waehrend Des Wintersemesters 1862-1863 an Der Universitaet Zu Berlin* (Berlin 1863-1867).

even under torture, exactly what a tumour is."⁹⁶ The word ‘tumor,’ literally ‘swelling’ from the Greek, had been used to describe growths as diverse as boils and malignant cancers. Agreement on terminology was confusing and without convention well into the nineteenth century. Thus physicians could not agree on the name of what they were examining, let alone what to do about it. Tumors were classified in vague descriptive terms unrecognizable today. ‘Scirrhus,’ meaning hard, was frequently used to describe breast cancers, but could apply to other cancers as well. Additional commonly-used terms included ‘encephaloid’ or ‘cerebriform,’ like the texture of brain tissue; ‘colloid,’ like gelatin; ‘fungus hæmatodes,’ full of blood; and ‘sarcoma,’ flesh-like. Of these, only the last is still used today, but even ‘sarcoma’ has taken on a new definition more consonant with modern medicine.

The microscope engendered the creation of new terminology that was more precise and reproducible—hallmarks of the scientific endeavor. Precision resulted from microscopic analysis of tissues into their component layers: epithelial (outer), mesothelial (middle), endothelial (inner). Reproducibility was a consequence of the remarkable new discovery that cancers from the same organ—regional or metastatic—looked the same under the microscope. This new method of classifying tumors and cancers, although adopted slowly over decades, opened a new world into the investigation of benign and malignant diseases. Part and parcel of this momentous change was the result that meaningful communication between investigators, practitioners, and others increased tremendously once the Babelic confusion of tongues had been dissipated.⁹⁷ A veil had been lifted from the hidden visage of natural cancer.

⁹⁶Cited by Williams, *Williams, Natural History of Cancer*, 3. From Virchow, *Die Krankhaften Geschwuelste*, 3.

⁹⁷The terminology of cancer continues to change as the pathophysiology of the disease is better defined. I suspect that the language of cancer will not be concretized until the cause(s) is/are ascertained – and then in the language of the time, be it molecular, atomic, or subatomic.

The medical world is alive to these inquiries, and research will develop facts but little thought of heretofore. Science is progressing, and facts are stubborn things. The developments of physiology, materia medica, and chemistry will finally make these subjects plain, when preconceived opinions, and old threadbare theories, will yield to the development of true knowledge, and many a disease that has hitherto been an opprobrium medicorum will yield to the true light of science, and our profession will rise higher and higher in the scale of science, and the whole world will be blessed thereby.

—J. W. Bright (1871)⁹⁸

The local theory of cancer development promoted by microscopic analysis also revolutionized treatment. A new culture of cure developed. Constitutional theory predicted that early tumor excision was futile. Local theory encouraged the opposite belief. The greatest—if not the only—opportunity for cure lay in the early removal of the lesion. Surgeons, whose approach to medicine had foreshadowed a localistic view of disease,⁹⁹ had surmised this for centuries, but never before had there been an ideological framework to support early treatment. The “golden age of surgery” in the 1880s and 1890s was the result of both theoretical and practical advances. The three-fold miracles of analgesia, anesthesia (1840s), and antisepsis (1860s-70s)—themselves offspring of the revolution in nineteenth-century chemistry—reduced the pain and complications of surgery. No longer was surgery for cancer solely an attempt at terminal palliation. An increasingly literate public on both sides of the Atlantic read of these changes and sought the aid of practitioners earlier and more frequently than ever before. The possibility of cure by early extirpation began to undermine the pervasive assumption of incurability and hopelessness that had been attached even to superficial cancers. Technological and ideological advances began to transform the belief systems surrounding traditional cancer.

⁹⁸J. W. Bright, M.D., *Cancer: Its Classification and Remedies* (Philadelphia: S. W. Butler, M.D., 1871), 105; *ibid.*

⁹⁹Owsei Temkin, "The Role of Surgery in the Rise of Modern Medical Thought," *Bulletin of the History of Medicine* 25(1951): 259.

Several storm clouds, however, were forming beyond the horizon. The incidence of cancer rose dramatically in the last decades of the nineteenth century and with it new charlatans touted quack medicines as never before. Internal cancers in particular, formerly invisible to all but the autopsy prosector, seemed to become more frequent. And a new explanation for disease in the last quarter of the nineteenth century—bacteria—held out hope for the prevention of cancer at the same time that a post-Darwinian world envisioned new threats of contagion from previously unimagined invaders struggling for their own existence. As time and tide moved westward, America began to face the challenge of cancer more and more on its own with new institutions, technology, and research.

THE COMING OF THE END FOR TRADITIONAL CANCER

The social stigma and constitutional basis of traditional cancer were deeply rooted in the American psyche. The local theory of cancer formation, based upon the microscope and cell theory, slowly reversed the cycle of incurability and hopelessness that enveloped cancer. That transformation is still continuing. But the trend toward earlier surgery that gained dominance in the late nineteenth century, favored by the notion of site-specific cancer, went a long way toward removing the abhorrence attendant upon the smell and sight of advanced disease. Timely surgery, defined by the late nineteenth century as early surgery, markedly reduced the incidence of fungating and ulcerating cancers. It is rare to see such lesions today. The role of class, ethnicity, and race underwent an ironic alteration. The poor, descendants of immigrants, and African Americans developed increased incidences of cancer toward the end of the Victorian era as epidemiologic data improved and the number of new cases increased throughout all levels of society. Medical care for previously excluded cancer patients became more expensive as the cost of technology added to the cost of care, but new sources of revenue from paying patients

and other institutions ameliorated these increases to the point where economic cost no longer engendered stigmatization.

Nevertheless, the fear of cancer persisted. Old “Doc” Rockefeller, the cancer curer, found an audience for his fraudulent nostrums well after the advent of cell theory, early surgery, and the demise of the hallmarks of traditional cancer. New cancer theories and treatment earlier in the course of the disease did not remove the threat of suffering and death. The cause and cure of cancer remained unknown. New institutional, medical, technological, and social forces evolved that served to legitimize the disease cancer, but dread remained.

By the last quarter of the nineteenth century some social stigmatization, particularly in the American hospital system, endured. Nevertheless, as we shall see in the next chapter, nascent institutions rose to accept the challenge of cancer and dispelled even that vestige of traditional cancer.

Chapter 2

Institutional Beginnings in America

The belief systems upon which traditional cancer rested – social stigmatization and medical constitutionalism – died a slow death. They persisted vigorously into the last decades of the nineteenth century, when the rising incidence of cancerous diseases and the concurrent increase in knowledge thanks to pioneering pathologists armed with microscopes, began to affect a new generation of Americans. These Progressives, as they were called in later years, combined a faded memory of the Civil War with a new-found optimism bolstered by an industrializing economy and a nascent middle class. Many were dedicated to the belief that social amelioration was the *summum bonus* of mankind. Institutions became the vehicle of social progress, and, as in other endeavors, the institution, for many, assuaged the ravages of cancer. Still, the first cancer institution was not built in repudiation of the medical and social stigmas that bastardized cancer earlier in the nineteenth century, but rather as a result of growing unmet needs.

Medical history is iatrogenic.

—Henry Sigerist

The historiography of cancer institutions in America parallels that of other fields in the history of medicine. Dr. Michael B. Shimkin, an oncologist and prominent historian of cancer who wrote and lectured mainly during the third quarter of the twentieth century, opined that to understand the history of cancer in the United States one need look no further than the physician.¹ Great medical doctors—almost always men—charted a course, he said, of ineluctable progress from one discovery to another with the seemingly natural result that cancer patients received the best possible diagnosis and treatment, usually in hospitals. On a parallel

¹See especially Michael B. Shimkin, *Contrary to Nature: Being an Illustrated Commentary on Some Persons and Events of Historical Importance in the Development of Knowledge Concerning Cancer* (Washington, D. C.: United States Government Printing Office, 1977).

course, outstanding physicians also led growing cancer research facilities in an attempt to solve the enigma of cancer.² Cancer institutions, in Shimkins' hagiographic iatrohistory, arose and persisted in a physician-dominated universe. From time to time wealthy laymen and eventually the government contributed money to assist the physician in the quest. Nevertheless, medical professionals were the principals of creation and transformation, insulated from the mundane concerns of society and culture. Physicians, according to Shimkin, were the agents of the rise of cancer institutions and the legitimization and popular medicalization of cancer.

Research into the engines of change in cancer ideology in the late nineteenth century does not confirm Shimkin's conclusions. Physicians were actors, but the play was written and choreographed by philanthropists, nonprofessional activists, and, increasingly, politicians. Further, the entire drama occurred within a cultural context that increasingly valorized science and lifted the medical profession along with it.³ Physician-researchers and surgeons made great advances in cancer detection and patient care at the end of the nineteenth century, but these changes were more effect than cause. Physicians were not passive bystanders during the institutional beginnings of modern cancer, but neither were they protagonists.

Traditions: Contagion and Reclusion

Before the 1880s, there were no cancer institutions in the United States and few in Europe. Abbot Jean Godinot, the canon of the church of Rheims, France, donated the then

²Ibid., and Harold Rusch, "The Beginnings of Cancer Research in the United States," *Journal of the National Cancer Institute* 74, no. 2 (1985): 391-403.

³ Here I am somewhat at odds with Paul Starr, who believed that physicians, with cultural support, were the agents of their own "sovereign profession." Paul Starr, *The Social Transformation of American Medicine: The Rise of a Sovereign Profession and the Making of a Vast Industry* (New York: Basic Books, Inc., 1982), Chapter 3, "The Consolidation of Professional Authority, 1850-930"

enormous sum of 25,000 Livres in 1740 to establish a cancer ward in the town.⁴ Consumed by dread of contagion from the inmates, neighbors quickly sought the relocation of the eight-bed “Hôpital Saint-Louis.” Consequently, the patients were confined to the hospital.⁵ In 1792, the British philanthropist Samuel Whitbread established a specialty ward in Middlesex Hospital, London, to give Dr. John Howard the opportunity to care for the cancerous poor and “study 'the natural history' of the disease.”⁶ These wards were anomalies, begun by philanthropists with laudable intentions, but stifled by a critical and fearful community. If cancer was contagious or retribution for iniquity, as was then believed, then surely the disease and the person suffering from it must be shunned. Dr. William Marsden founded the first permanent institution completely devoted to cancer patients in England in 1851. This “old Cancer Hospital” later served as a model for institutions around the world, including the United States, through its combination of philanthropy, clinical care, and, eventually, research.⁷ In America, *sans* institutions, those few cancer patients who were treated by physicians were treated at home.⁸

Conventions and convictions excluded cancer patients from traditional general hospitals in America until the end of the nineteenth century. A hospital in the middle of the century was,

⁴ About USD \$100,000 in the 1940s. “Abstracts from ‘History of the Hospices and Hospitals of Rheims,’” Typewritten letter from Professeur Agregé Romieu to Hayes Martin, M.D. dated “Tuesday April 17/56”, Memorial Hospital Archives, Record Group 500 Box 2 Folder 37 “H. Martin Collection.”

⁵Ibid.

⁶Daniel De Moulin, *A Short History of Breast Cancer* (Boston: Martinus Nijhoff Publishers, 1983), 50.

⁷D.A. Brunning and C.E. Dukes, “The Origin and Early History of the Institute of Cancer Research of the Royal Cancer Hospital,” *Proceedings of the Royal Society of Medicine* 58(1965). In 1954, the name of the cancer hospital was changed to the Royal Marsden Hospital. Ibid.

⁸Seale Harris and with the collaboration of Frances Williams Brown, *Woman's Surgeon: The Life Story of J. Marion Sims*, First ed. (New York: The Macmillan Company, 1950), 270.

in Charles Rosenberg's words, in many ways similar to "a well-run boarding house."⁹ They were charitable institutions administered with a heavy dose of paternalism and authoritarianism by well-heeled Victorians.¹⁰ In a world that perceived disease as punishment for sin, inmates were treated for moral turpitude as well as physical illness. Philanthropists endowed beds and controlled admissions to them. Admission criteria often required a good reference from a respectable clergyman as much as an ailment worthy of care. Notions of cure rested on moral as well as physical improvement. How, then, could cancer—an illness perceived as just punishment for sin—become a legitimate indication for hospitalization?

One agent of the change from stigma to legitimacy was the cancer institution, a direct descendant of the nineteenth-century general hospital. Founded in the United States amidst turmoil and tragedy, cancer hospitals, research facilities, and homes for cancer "incurables" served to legitimize cancer for society at large by the end of the nineteenth century. The first of these cancer institutions was the hospital. The first American all-cancer institution, the New York Cancer Hospital (today the Memorial Sloan-Kettering Cancer Center), established in 1884, represents the complex mix of changes in ideology and practice that led to a new view of the disease—from traditional to modern cancer.¹¹

The origin of the New York Cancer Hospital was rooted in the conflict spawned by the ban on the admission of cancer patients to the Woman's Hospital of the State of New York,

⁹Charles E. Rosenberg, *The Care of Strangers: The Rise of America's Hospital System* (Baltimore: The Johns Hopkins University Press, 1987), 119.

¹⁰Morris J. Vogel, "The Transformation of the American Hospital, 1850-1920," In Susan Reverby and David Rosner, *Health Care in America: Essays in Social History* (Philadelphia: Temple University Press, 1979), 108.

¹¹ Most of the following material is derived from the Memorial Hospital Archives. Specific references will be given as warranted. I am indebted to Kathy Frumento, former Director of Library Services, and her staff at the Medical Library, Nathan Cummings Center at Memorial Sloan-Kettering Cancer Center for their wonderful support, cheerful searching, and comfortable working atmosphere.

passed in January 1874.¹² "If one hospital can be the mother of another," wrote John E. Parsons in 1885, President of the fledgling New York Cancer Hospital and also a Board Governor at the Woman's Hospital, "I look upon the Woman's Hospital as the mother of [the New York Cancer Hospital]."¹³

The ideological innovation realized in the construction of the New York Cancer Hospital can be understood through exploration of the reasons for the exclusion of indigent cancer patients from general hospitals and, in particular, the Woman's Hospital. Such patients required special diets, expensive long-term nursing care that increased costs to the poorly capitalized charitable hospital, and their presence disturbed other patients.¹⁴ Before the advent of X-rays, other internal imaging techniques, and biological cancer markers, few internal cancers could be diagnosed other than at postmortem examination. Consequently, most detectable cancers until the last years of the nineteenth century were located in body areas amenable only to external inspection: the skin, throat, breast, and cervix/uterus. When ulcerating tumors turned bodies into foul-smelling, repugnant masses, it was not only proper Victorian matrons who recoiled in horror.

The perceived immorality of cancer and the revolting physical features of the disease conspired to make exclusion of cancer patients from the charitable hospital unquestioned. Physicians and laymen alike confused cancer with syphilis before the histopathologies of the two diseases were delineated in the nineteenth and early twentieth centuries. Syphilis, with its pejorative overtones, was a disdained disease known in Victorian times to be associated with

¹²Harris and Browin, *Woman's Surgeon*, 298.

¹³John E. Parsons, "The Secretary's Report, *First Annual Report*," (New York: New York Cancer Hospital, 1885), 21.

¹⁴"Report of the President, *Seventh Annual Report*," (New York: New York Cancer Hospital, 1891), 8-9.

“misconduct” through its venereal origins.¹⁵ The clinical features shared by the two maladies—foul discharges, ulceration, neurologic changes—invited comparison if not equivalence when clinical description based upon observation was the mainstay of popular and regular medicine. To Victorians, sexuality, sex, women, the uterus, and venereal diseases had shameful ties.¹⁶ Syphilis was clearly contagious. Why not cancer? “In brief,” wrote the physician-historian Hayes Martin, cancer “was a disease unacceptable in the wards of any hospital.”¹⁷

Cancer Clash: The Woman’s Hospital vs. Dr. Sims

The Board of Lady Supervisors of the Woman’s Hospital, the cream of New York’s Gilded Age society, was the force behind the official ban against the admission of cancer patients. The Ladies’ Board, as they were known, was responsible for the day-to-day operations of the Hospital. Their sway over the Board of Governors, the final arbiters of policy, transcended their daily roles. They supervised the caretakers and supplies, visited patients, and played a major role in fundraising for the Hospital.¹⁸ When they called for a change in hospital policy, the Board of Governors listened.

In 1872, one particular patient with an ulcerated carcinoma was directly responsible for the exclusion of cancer patients from the Woman’s Hospital.¹⁹ On December 7, a physician admitted “an advanced cancer case” for surgery over the objections of the Ladies’ Board.

¹⁵Hayes Martin, Harry Ehrlich, and Francelia Butler, “J. Marion Sims--Pioneer Cancer Protagonist,” *Cancer* 3, no. 1950 (1950). and Hayes Martin, “Historical Note No. 6,” “J. Marion Sims--Pioneer Cancer Protagonist,” July 1945, TMs, p10. Memorial Hospital Archives, Box 5, Folder 81a.

¹⁶See, for example, John S. Haller, Jr. and Robin M. Haller, *The Physician and Sexuality in Victorian America* (Urbana: University of Illinois Press, 1974).

¹⁷Martin, “Historical Note No. 6,” 10.

¹⁸Ibid.

¹⁹“Editorial Interview with Dr. J. Marion Sims,” *St. Louis Clinical Record* IV/#6 (Sep 1877): 153-172. *Memorial Hospital Archives*, “Sims, J. Marion: Biographical c1860-83,” Record Group 500, Hayes Martin Collection, Box 7 folder 108a.

Unfortunately, the surgery had to be postponed and the cancer became, as the physician described it, “far advanced into a sloughing which produced a fearful stench, poisoning the air of the ward. Some patients were about to leave, or had left the hospital in consequence of this, and the Lady Managers very naturally made a great row about it.”²⁰ The Board of Governors responded to the Ladies’ outcry and explicitly prohibited cancer patients from admission to the Hospital.²¹

Dr. James Marion Sims, the “Father of American Gynecology” and physician-founder of the Woman’s Hospital (as well as its on-again, off-again chief surgeon), objected to the decision. He had battled entrenched forces from his poor but proud upbringing in the South, and he was not about to abandon his beliefs at the age of sixty. As a youth, he had gone against his father’s wish for him to be a lawyer or minister in order to become physician.²² During the 1840s, he had performed multiple controversial gynecological operations on unanaesthetized slave women in Alabama in an attempt to cure them of debilitating and offensive openings that developed between the vagina and the bladder (vesicovaginal fistulae) during traumatic childbirths.²³ In 1855, this “autocrat of the sick-chamber”²⁴ flouted the medical establishment to found his own

²⁰ Ibid., 167.

²¹ Harris and Browin, *Woman's Surgeon*.

²²In 1833, Sims's father was very disappointed in his son’s career choice. He said, "It is a profession for which I have the utmost contempt. There is no science in it. There is no honor to be achieved in it; no reputation to be made, and to think that *my* son should be going around from house to house through this country, with a box of pills in one hand and a squirt in the other, to ameliorate human suffering, is a thought I never supposed I should have to contemplate." J. Marion Sims, *The Story of My Life*, ed. H. Marion-Sims (New York: Da Capo Press, 1884; repr., 1968), 114-16.

²³ The consequence of a vesicovaginal fistula is a persistently malodorous vaginal discharge and chronic vaginitis. Patients suffered persistent vaginal symptoms and social ostracism. Sims operated on Anarcha, who suffered through thirty times without anesthesia in the late 1840s before he happened upon the silver sutures that would hold the fistula closed. Ibid., 245.

²⁴The term was used by Sims. Ibid., 436.

hospital for women—the Woman’s Hospital of the State of New York.²⁵ Sims’s Southern sympathies caused him to lose power at the hospital when he immigrated to Europe during the Civil War, but, in 1868, he was restored by the Board of Governors to the position of chief surgeon. In 1870, he returned to Europe and engaged in dashing exploits during the Franco-Prussian War with Napoleon III and Florence Nightingale. After the war, Sims returned to the Woman’s Hospital and began admitting cancer patients over the objections of the Ladies’ Board. Indeed, the 1872 patient who touched off the prohibition of cancer admissions had been his case.²⁶

It is not clear why Sims refused to accept the conventional dogma of cancer contagiousness and patient ostracism. Dr. Thomas Addis Emmet, Sim’s fellow Southerner and long-time co-surgeon on the Medical Board of the Woman’s Hospital, believed that the high prevalence of cancer in women was the reason. He remarked that Sims refused to deny admission to women with cancer, insisting instead “that a disease from which so large a proportion of women died should be treated in a hospital devoted to the diseases of the sex.”²⁷ Perhaps it was, as Seale Harris implied, an optimistic altruism that drove Sims to find a cure for women’s cancers.²⁸ Perhaps it was a matter of fees;²⁹ cancer patients, as today, required numerous costly medical and surgical interventions for their relatively chronic condition.

²⁵Rosenberg, *Rosenberg, Care of Strangers*. Rosenberg elaborates on the desire of elite physicians to build their remunerative private practices by caring for indigent patients in charitable hospitals in mid-century. See also Sims, *Story of My Life*, 269-70.

²⁶The role of local hospital politics should not be denigrated when analyzing such decisions. Harris and Browin, *Woman’s Surgeon*, 296-98, elaborated on the political infighting of the Medical Board, Ladies’ Board, and Board of Governors that played a role in the ruling.

²⁷Thomas Addis Emmet, *Incidents of My Life: Professional—Literary—Social, with Services in the Cause of Ireland* (G. P. Putnam’s Sons, 1911), 195.

²⁸Harris and Browin, *Woman’s Surgeon*, 296-97.

²⁹Sims, *Story of My Life*, 192, 432.

Nevertheless, John Parsons, a member of the Board of Governors of the Woman's Hospital, had another suggestion. He wrote in 1885 that Sims had had a professional interest in treating cancer patients for many years:

As far back as nearly thirty years ago, when Dr. Sims began the movement which ended in the organization of the Woman's Hospital, I believe that it was in his mind that cancer cases should be treated there. I believe that it was his intention that cancer cases should be introduced into the wards of that hospital, and for the reason that in his opinion there was no more danger in bringing into association with other patients those who were suffering from cancer than those who were suffering from headache or any other ordinary ailment to which human nature is subject.³⁰

Sims, contrary to the dominant cancer causation theory in his day, believed the disease was not contagious. Unlike future cancer physicians, however, Sims sought no proof to sustain his radical opinion. His "experiments," as irate members of the Ladies' Board referred to his cancer surgeries, were really nothing more than clinical observations. There was little scientific method in his traditional cancer ideology. He had operated upon cancer patients in his own facility since his days in Alabama in the 1840s,³¹ but at the Woman's Hospital he could not overcome the anticancer prejudices of the Hospital's managers. The Boards held the power and they stayed his hand.

The impetuous Dr. Sims disdainfully accepted the Boards' prohibition on the admission of cancer patients but was enraged by the "spy" they sent to make sure he complied with the rules.³² On November 19, 1874, the occasion of the festive nineteenth Annual Meeting of the Woman's Hospital, Sims lost control of his anger and denounced the Board for intruding into

³⁰Parsons, "President's Report," *First Annual Report*, 19.

³¹Harris and Browin, *Woman's Surgeon*, 270.

³²*Ibid.*, 302. The "spy" was a hospital employee. It should also be pointed out that Sims was less affected by the hospital cancer ban than other surgeons because he rented private space not far from his home where he performed cancer surgery without interference. *Ibid.*, 358.

what he believed should be physicians' decisions.³³ "In the matter of cancer," he asserted, "I have no hesitation in saying that you have transcended the bounds of your authority."³⁴ The fashionable Victorian crowd, expecting pleasantries and sweet music, was shocked by the outburst from the world-renowned surgeon. But Sims, not realizing his powerlessness in the face of the local controlling moneyed interests, continued. "For myself, I have never heeded your edict and never will; and if you are aggrieved at this you can have my resignation at your next meeting if you wish it."³⁵ The audience was stunned. An uneasy silence filled the banquet hall. Sims's friends sought to adjourn the meeting, but to no avail. Colonel George T. M. Davis, a leader of the Board of Governors, had had enough of Sims. "In biting phrases he denied the justice of the accusations Sims had made and censured him sharply for selecting so inopportune an occasion to air his personal grievances."³⁶ The personal had become political and Sims, whose professional identity was wrapped up in the Woman's Hospital, lost. On December 5, 1874, he tendered his resignation to the Board of Governors with a penitent but ineffective apology. Sims believed that physicians should control the hospital. Reality was otherwise. The 1874 hospital was an institution run by and for philanthropists. Cancer was excluded.

An ultimately unsuccessful return to the Woman's Hospital in 1881 only confirmed that Sims's desire to admit cancer patients was incompatible with the traditional care structure of the nineteenth-century hospital. He still could not convince the Board to permit the admission of cancer patients. The Hospital had experienced falling revenues after Sims's termination and the Boards, perhaps sensing a change in Sims's mien since his near-fatal bout with pneumonia the

³³"Woman's Hospital of New York Anniversary," *The New York Times*, 20 Nov 1884, 2:6.

³⁴Ibid.

³⁵Ibid.

³⁶Harris and Browin, *Woman's Surgeon*, 302.

previous winter, were eager to have him back on staff. He was appointed Senior Consulting Surgeon. Other hospitals still refused to admit cancer cases, but Sims misunderstood his reappointment to be an affirmation of the right to admit cancer patients and soon began doing so.³⁷ The Medical Board was initially behind him, but the Ladies' Board again complained bitterly. On March 13, 1882 the Medical Board, *sans* Sims, gave up: "The members of the Medical Board of the Woman's Hospital desire to withdraw their recommendation to the Board of Governors regarding the admission of cancer cases—they have in no wise changed their opinion on this subject, but they deem it expedient to withdraw their request, in order to avoid fruitless discussion and harmonize the action of the respective Boards."³⁸ The Boards were still firmly in control. They would not tolerate cancer patients in the Woman's Hospital. Sims left the Hospital he had founded once and for all time.

Personal Tragedy, Civic Progress:

The Founding of the New York Cancer Hospital

The medicalization and reduced stigmatization of cancer in the public eye was promoted by the cancer institution, the first of which was established after Sims's final departure from the Woman's Hospital. In 1881, Sims rose like a surgical phoenix from the ashes of his own 1874 hot-headedness to return to the Hospital not only because of his international fame and surgical prowess, but, perhaps more importantly, because he had powerful dissident sympathizers on the Ladies' Board and Board of Governors who agreed with his stance on cancer. He was handsome and persuasive, and, from the establishment of the Woman's Hospital in 1855, Mrs. William B.

³⁷Ibid. 357-58.

³⁸Hayes Martin, "Sims and the Woman's Hospital," (no date) typescript, TMs, *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 7 folder 108a, "Sims, J. Marion: Biographical," 21.

Astor—daughter-in-law of famed John Jacob Astor—was his ally.³⁹ In 1872, by which time a new generation of elite Victorian women constituted the Ladies' Board, her daughter-in-law, Charlotte Augusta Gibbes Astor (Augusta or Charlotte Augusta to her friends), wife of John Jacob Astor III, became a member.⁴⁰ The younger Mrs. Astor's cousin, Mrs. Elizabeth Hamilton Halleck Cullum—granddaughter of Alexander Hamilton, widow of the Chief of Staff of the Union Army General Henry Halleck, and riding partner of Mrs. Abraham Lincoln—joined the Board three years later.⁴¹ Contrary to the anticancer tide of Victorian conformity, they became strong supporters of the idea that cancer patients, rich and poor, should be granted admission to hospitals.

Mrs. Astor and Mrs. Cullum had compelling reasons for urging the institutionalization of cancer. In the last quarter of the nineteenth century cancer, was conceived predominately as a woman's disease because women were more than twice as likely as men to be diagnosed with the disease.⁴² Most diagnosable cancers were, as noted previously, externally visible or palpable. (Later male-dominated cancers of the lung and prostate were still invisible.⁴³) Both women believed it their sacred duty to help the poor and sick. Mrs. Cullum served as vice-president of the Woman's Hospital, established the Helping-Hand Society, the diet kitchen of St. Thomas's

³⁹Sims, *Story of My Life*, 292.

⁴⁰New York Cancer Hospital. *Second and Third Annual Report 1886-1887*, 41.

⁴¹Bob Considine, *That Many May Live: Memorial Center's 75 Year Fight against Cancer*, 1 vols. (New York: Memorial Center for Cancer and Allied Disease, 1959; repr., August 1982), 19.

⁴²William Roger Williams, *The Natural History of Cancer with Special Reference to Its Causation and Prevention* (London: William Heinemann, 1908), 57. The exact ratio given by Williams was 2.2:1.

⁴³Cigarette smoking was highly gendered until the third decade of the twentieth century. Cigarettes first made their appearance in the United States in 1867, but not until the invention of the rolling machines in 1883 and the monopolization of the industry under the American Tobacco Company, led by James Buchanan Duke, in 1890, did smoking become popular for men. Cigarette smoking was so highly gendered that a woman was arrested in New York on September 28, 1904 for smoking while riding in an automobile. "You can't do that on Fifth Avenue," said the arresting policeman." Gorton Caruth, *The Encyclopedia of American Facts and Dates* (New York: HarperCollins, 1993), 401 (quotation) and passim.

Home, and multiple other charities in New York and San Francisco.⁴⁴ Mrs. Astor, a South Carolinian by birth like Dr. Sims, was the driving force behind the legendary Astor philanthropy. Although John Jacob Astor III got the credit, it was actually Charlotte who gave away millions of dollars raked from the vast Astor real estate holdings in burgeoning New York.⁴⁵ “He furnished the money; she distributed it.”⁴⁶

Personal reasons and sentimental experiences helped to galvanize contributors. Mrs. Cullum and Mrs. Astor were present at a meeting of the Ladies’ Board when Dr. T. Gaillard Thomas, one of the four surgical members of the Medical Board at the Woman’s Hospital, and later a surgeon at the New York Cancer Hospital, related the story of a young woman with cancer who came to him for surgery. “I asked her if I could not perform the operation at her house. She said I could not and asked if I could not send her somewhere where I could treat her. ‘I could not.’ One of the ladies asked Dr. Thomas if he operated upon her and he replied that he did not. When asked the result, he said that she was dead. When asked what the result might have been if he could have performed the operation, he said that ‘she might have lived.’ ‘She might have been cured; I think it is safe to say that 15 years might have been added to her life.’”⁴⁷ Such stories could melt the heart of all but the most adamant board members.

Cancer struck the Cullum and Astor families closer to home. In 1882, when Sims finally abandoned all hope of treating cancer patients at the Woman’s Hospital, Cullum’s only son died

⁴⁴George W. Cullum, "The National Cyclopædia of American Biography," (1897).

⁴⁵John Jacob Astor (3d), "The National Cyclopædia of American Biography," (1924), 104-5.

⁴⁶Ibid.

⁴⁷Untitled typewritten manuscript by Hayes Martin on cancer history, TMs, *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, folder 82a, "Memorial Hospital, history."

of cancer at the age of twenty-six.⁴⁸ Mrs. Cullum was herself diagnosed with uterine cancer at about the same time. She underwent three operations, perhaps by Dr. Sims, and died of the disease at the age of fifty-three in September, 1884.⁴⁹ At a time when few would even verbally admit to having cancer, Mrs. Cullum defiantly insisted that it be listed on her death certificate as the cause of death.⁵⁰ Her cousin Charlotte Augusta Astor suffered a similar fate. Mrs. Astor, according to Drs. Hayes Martin and Seale Harris, probably also suffered from uterine cancer.⁵¹ Mrs. Astor died in December, 1887 at the age of sixty-two, six days after the official opening of the New York Cancer Hospital.⁵² These personal tragedies laid the foundation for the first cancer institution in America. Mrs. Astor, writing about her cousin, Elizabeth Cullum, four days after the dedication of the New York Cancer Hospital in May, 1884, said: “her pain has been made fruitful of refreshment to many.”⁵³

⁴⁸Hayes Martin, “The Organization of the NYCH,” “Historical Note No. 3,” Apr 1945, *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, Folder 81a, page 9.

⁴⁹“Memorial to Mrs. Cullum,” *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, folder 83, “New York Cancer Hospital (old Memorial).”

⁵⁰Death certificate from Thomas J. Duffield, Director, Bureau of Records and Statistics, City of NY, Department of Health, Bureau of Records, 125 Worth Street NY, NY 13; March 16, 1945; *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, folder 83, “New York Cancer Hospital (old Memorial).”

⁵¹The *New York Tribune* article of April 29, 1884 is the major source for this statement. “Historical Note No. 4, “The Cornerstone Laying Ceremony of the NYCH, Hayes Martin, May 1945, *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, Folder 81a, p11; and Harris, 358 and 379.

⁵²City of New York Death Certificate No. 9627. Dr. Fordyce Barker, Charlotte Augusta Astor’s physician, listed the cause of death as “chronic catarrhal and enteritis” secondary to “general and cerebral asthenia and acute ischemia.”

⁵³Augusta Astor, “From Augusta Astor to John E. Parsons,” in *The Parsons Collection; Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, *Box 5, folder 82a; “Memorial Hospital, history”* (New York 1884). Handwritten letter from Augusta Astor to John E. Parsons dated May 21, 1884. *The Parsons Collection: Letters Addressed to Mr. John Parsons Concerning the Cancer Hospital. Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, folder 82a, “Memorial Hospital, history.” Underlining in the handwritten original.

An institution is the lengthened shadow of one man.

—Ralph Waldo Emerson

(or woman—the editor)

The story of the founding of the New York Cancer Hospital reveals the intrigue and devotion that even the most wealthy and influential philanthropists needed to bring to bear in a traditional world where power was personal and cancer was taboo. On March 5, 1883, Mrs. Astor summoned her husband's personal attorney and Woman's Hospital Board member, Mr. John E. Parsons, to the Astor residence to discuss an urgent matter. "I am prepared, by Mr. Astor," she wrote, "to make a precise proposal to you. And yet, particularly on my side, there are reasons that make delay inconvenient."⁵⁴ Mrs. Astor wished the well-connected Mr. Parsons to make an anonymous offer to the Woman's Hospital to build a "Pavilion to be used solely for the treatment of Cancer Cases."⁵⁵ Mr. Astor, wrote Augusta, was willing to pay \$170,000 for the erection of the desired pavilion.⁵⁶ On April 9, when Parsons presented the anonymous offer to the Woman's Hospital, the majority of the Ladies' Board objected. They claimed that cancer was contagious and would drive away other patients. Mrs. Astor countered with a proposal to the Board to seek "expert advice"—a suggestion consonant with the spirit of the times. Submit a series of "precise questions," she wrote, "to a large number of prominent surgeons & physicians—asking from each a written answer to the entire series of questions" about cancer.⁵⁷

⁵⁴Mrs. Astor's "reasons" for urgency likely relate to her recent cancer diagnosis. Handwritten letter from Mrs. Charlotte Augusta Astor to Mr. John E. Parsons, entitled "Sunday," *ibid.* *The Parsons Collection: Letters Addressed to Mr. John Parsons Concerning the Cancer Hospital. Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, folder 82a, "Memorial Hospital, history." This letter and those that follow are not dated by year. It is possible that they were written in 1882 rather than 1883. Based upon contextual events, I believe, the 1883 date is most likely.

⁵⁵Fragment of a draft from Augusta Astor to John E. Parsons, (before 1884). *The Parsons Collection*.

⁵⁶*Ibid.*

⁵⁷Handwritten letter "From Augusta Astor to JEP[John E. Parsons], November 8, (1883), Saturday Novr. 8th." *The Parsons Collection*.

Not surprisingly, the anonymous offer sent the Boards into a snit. A committee was formed with Parsons as chairman. On April 14, 1883, the committee reported that at least \$185,000 was necessary. Meetings on May 7 and 22 ended with indecision. On May 29, the discussion of the gift was tabled by the Board of Governors with a vote of 12-6.⁵⁸ By June 10, the anonymous offer was all but rejected, “poisoned,” wrote Mrs. Astor, by the Ladies’ Board.⁵⁹ Parsons tried compromise again and again and even offered to eliminate the word ‘cancer’ from the cancer pavilion. He shortened the dimensions of the pavilion to house fewer patients. He banned all “incurables” to reduce the “offensive” nature of the disease to a minimum.⁶⁰

In the summer of 1883 Parsons sought the aid of the most famous living American woman’s physician, Dr. J. Marion Sims. It may not have been a wise choice, for the Woman’s Hospital Boards professed no love for Sims over the cancer problem. But Parsons was a wily advocate. He must have known that even if the Woman’s Hospital rejected the Astor offer—as he must have felt it would—the strength of Sims’s international reputation might be used toward other means to accomplish the goal. In a word, Parsons and the Astors used Sims. Nevertheless, Sims responded with what can justifiably be labeled as a preamble to the history of modern cancer. “A cancer hospital is one of the great needs of the day,” wrote Sims,

and it must be built. We want a cancer hospital on its own foundation—wholly independent of all other hospitals. If we had one properly organized, it would call out and develop the talent necessary for its success. But a cancer hospital we must have.

Let this organization draw to itself men and women who will earnestly give their time and energies to its successful working. Let its promoters procure a site, build a hospital and organize a board of medical counsellors at once. There should be a department for men and another for women. Its medical board ought to be men who go

⁵⁸“From the minutes of the Board of Governors--Woman's Hospital.” Hayes Martin manuscript of The Woman's Hospital. TMs. *Memorial Hospital Archives* Record Group 500 Box 2 Folder 37. “H. Martin Collection.”

⁵⁹From C.A. Astor to JEP, June 10, (probably 1883): “Sunday June 10th. *The Parsons Collection*. “Poisoned,” she wrote, “in connection with matters that now seem to have taken their place among the things that have, no longer, life! —”

⁶⁰Extracts from minutes of the Parsons committee, June 11, 1883. *The Parsons Collection*.

into it with zeal, determined not only to give temporary relief to human suffering, but also to do something towards discovering better methods of treatment.

We are now making great progress in every department of medicine. Why should not cancer derive some benefit from this general onward movement? Doubtful points of practice can only be settled in the wards of a great hospital. And success in treatment can only here be demonstrated.

We want a medical board composed of men of large and liberal views. I would take knowledge wherever it can be found. I would invite any man who claimed to have a specific to come and try his remedies, under the supervision of a committee specially appointed for that purpose. I would offer a large premium for any improvements, whether in constitutional or local treatment. I would do everything to obtain practical knowledge on this subject, regardless of the source from which it emanated. If you can get money enough to furnish it and launch it on the sea of discovery and experimental research, rest assured that money will come as soon as the community is made aware of the existence and the objectives of the hospital.

We have hospitals for lepers, and leprosy is more incurable than cancer; and we have but one cancer hospital in all Great Britain and none in our own country. It is time we turn a listening ear to the cries of humanity. Build a cancer hospital, provide it with the necessary comforts and the highest skill in treatment, and rest assured that patients will come from all quarters, too glad to avail themselves of such kindness and care as in your wisdom and generosity will be provided for them.

And if there are any who favor a special hospital for cancer (and I hope there are some) let me beg you to take steps at once to inaugurate a movement which must culminate in a great work so much needed here and now. The subject of cancer is too large and its interests too great to be lodged in a pavilion subsidiary to any other hospital, whether special or general.

(Signed) J. Marion Sims
Pittsfield, Mass., September 23, 1883.⁶¹

Less than two months later Sims died from an acute heart disorder at the age of seventy.⁶²

The Sims letter did not forestall the rejection of the anonymous Astor offer by the Woman's Hospital. The divided Ladies' Board and Board of Governors could not find common ground. On December 8, in a last-ditch effort to appease the wealthy dissidents—perhaps because the anticancer majority believed that Astor, Cullum, and company would no longer support the Woman's Hospital—the Ladies' Board elected Elizabeth Cullum president. She, however, would not suffer their transparent ruse and spurned the presidency. Parsons withdrew the Astor offer on January 14, 1884. "The withdrawal of the proposal, it should be understood,"

⁶¹Sims's letter is in *The New York Academy of Medicine*. It is quoted in Martin, Ehrlich, and Butler, "Martin, Sims," 202-3.

⁶²Sims, *Story of My Life*, 22.

he wrote, “is coerced, not voluntary. I wish to put myself on record as protesting against the unwillingness to accept a gift of near \$200,000 in the direction of legitimate work.”⁶³ On January 18, 1884, the Board of Governors, not to be outdone, resolved that “it is inexpedient and detrimental to the interest of the Hospital to accept a generous proposal made them to donate \$185,000 towards the erection of a Cancer Pavilion on the grounds of the Institution.”⁶⁴ The majority of the Boards of the Woman’s Hospital, steeped in the stigma of traditional cancer and having no compelling personal reason to embrace the institutionalization of cancer, put an end to Astor’s magnanimous offer to append cancer to the legitimate work of the general hospital.

Augusta Astor’s reasoning was correct. The Boards had been poisoned by “a deeply seated prejudice [that] has all the force of an established fact.”⁶⁵ Poisoned by the perception of cancer as a contagious disease. As a venereal disease. As a disease that invited prejudice and disgust wherever it was found. But the Astors were complicitous: Why, for example, was the offer anonymous? Perhaps it was a selfless desire to spotlight the donation and not the donors. Perhaps it was an act of noblesse oblige, a small donation of \$185,000 from a man who was worth about \$100,000,000.⁶⁶ More likely, the Astors, doyens of society, did not feel that they could reveal their true beliefs about cancer—that cancer was not a disease to be shunned—nor bring attention to the probability that Mrs. Astor herself had cancer. Nevertheless, the philanthropist Augusta Astor knew that something had to be done about the cancer problem. She

⁶³Harris and Browin, *Woman's Surgeon*, 377-78.

⁶⁴Handwritten letter "From Charles N. Talbot [Woman's Hospital Secretary] to JEP [John E. Parsons], January 18, 1884": "The Woman's Hospital in the State of New York, Corner 49th Street and 4th Avenue, New York, January 18, 1884." *The Parsons Collection*.

⁶⁵Handwritten letter "From Augusta Astor to JEP [John E. Parsons], (probably between January 14 and 23, 1884). "Wednesday eve.g." *The Parsons Collection*.

⁶⁶Astor’s “estimated worth at the time of his death was between \$75,000,000 and \$100,000,000.” *The National Cyclopædia of American Biography*, Volume VIII, 1924, 105.

knew from personal experience that cancer *was* a legitimate problem that required good men and women working together. Augusta Astor had seen the institution and believed in it. She took Henry James's words of 1879 to heart: "The best things come from the talents that are members of a group; every man works better when he has companions working in the same line, and yielding the stimulus of suggestion, comparison, emulation. Great things of course have been done by solitary workers: but they have usually been done with double the pains they would have cost if they had been produced in more genial circumstances."⁶⁷ Less than a week after the final rejection of the Astor offer, Augusta Astor made plans for "the establishment of a distinct Cancer Hospital."⁶⁸ The jaundiced, traditional view of cancer, filtered through the personal tragedies of the heretical philanthropists, instigated the birth of what would become the first modern cancer institution.

Charity sees the need not the cause.

–German proverb

Mrs. Astor was not alone in her quest for a specialized facility. Elizabeth Cullum had independently devised a similar plan. "I must begin by telling you," wrote Augusta to Parsons, "that Mrs. Cullum (with whom my relations hold both an affection and a confidence that are beyond the usual demands of kinship) addressed me a few days since -- in entire ignorance of Mr. Astor's association with the offer to the Woman's Hospital --, some proposals in connection with her own present plan of shaping, so far as might be possible to her, the establishment of a distinct Cancer Hospital --"⁶⁹

⁶⁷Jr. Schlesinger, Arthur M., ed. *The Almanac of American History*, Revised and Updated ed. (New York: Barnes & Noble Books, 1993), 335-6.

⁶⁸Handwritten letter "From Augusta Astor to Mr. Parsons, January 23, (1884)." *The Parsons Collection*. Underlining in the original.

⁶⁹Letter "From Augusta Astor to Mr. Parsons, January 23, (1884)." *The Parsons Collection*. Underlining in the original.

MRS. ASTOR'S FOUR CONDITIONS

The solution to the problem of cancer was institutionalization. The efforts of many working together for a common cause would create synergy such that the whole was greater than the sum of its parts. Bring the best, most talented, and most committed together under the aegis of a specialty hospital and the problem would be solved. Still, the hospital must be administered with an eye toward sustaining revenue. With one eye on the past and one on the future, Mrs. Astor, in a letter to Mr. Parsons dated January 23, 1884, set forth conditions that “had to be fulfilled” in order to pursue “a plan so beneficent.”⁷⁰ First, there had to be enough land to allow “air and sunshine sufficient.” Second, the original pavilion built with \$180,000 “should be exclusively devoted to the care of Women.” Third, “incurables”—those without “reasonable expectation that they were susceptible to benefit from operations, or special modes of treatment”—would be excluded. Fourth, “while liberal provision should be made for poor patients, the Hospital should be so arranged as to invite within its walls, those of the better class, who should make payment in accord with the accommodation furnished.”⁷¹

On February 7, 1884, a meeting was held at the home of General George Washington Cullum and Mrs. Elizabeth Cullum at 261 Fifth Avenue in New York for the purpose of founding a cancer hospital. Many of the rich and famous alighted from their carriages that evening, relieved to find a means to unburden themselves of the injustice they believed had been perpetrated by the majority of Board members at the Woman’s Hospital over the cancer question. Mrs. Astor, of course, was there. John E. Parsons, confidante extraordinaire, accepted the presidency of the new hospital at the urging of Mrs. Astor and her cousin Elizabeth Cullum.

⁷⁰Ibid. Underlining in the original.

⁷¹Ibid.

Morris K. Jesup—merchant, banker, philanthropist—was elected vice president. Joseph Drexel, who had associated with the young J. Pierpont Morgan only a few years before to found Drexel, Morgan & Company, became Treasurer. Cornelius Vanderbilt II, grandson of the Commodore and heir apparent to the family fortune, lent his expertise. Miss Schuyler, Mrs. Townsend, and Mrs. Reid joined the group. Since the founders of the cancer hospital were women, it is perhaps not surprising that four of the six members who would oversee the daily functioning were women. A few physicians were present. Dr. William T. Bull, the famous surgical innovator, and four other physicians (including a pathologist) were founders. In all, seven of the fifteen “incorporators” of the New York Cancer Hospital were from the Woman’s Hospital—the minority cancer dissidents.⁷²

The criteria mandated by Mrs. Astor in her January 23rd letter to Mr. Parsons established the framework for the hospital. Before 1884, cancer was effectively banned from the hospital. With the opening of the New York Cancer Hospital in 1887, this was no longer true. Little did Mrs. Astor know that her four provisions for the founding of the hospital were nothing less than a blueprint for the institutionalization and popular medicalization of cancer.

Form Follows Fear: The Architectural Reification of Germ Theory

Mrs. Astor’s first mandate was “air and sunshine sufficient.”⁷³ The relationship between disease and the environment was suggested by the Ancient Greeks, but the miasma theory predominant during the nineteenth century specifically linked bad air and poor light with disease. The industrialization of America in the last half of the century led critics like Harriet Beecher

⁷²Handwritten letter “From Elizabeth H. Cullum to Mr. Parsons, (early in 1884).” ALS. *The Parsons Collection*.

⁷³Handwritten letter “From Augusta Astor to Mr. Parsons, January 23, (1884).” ALS. *The Parsons Collection*.

Stowe to link “airless” factories with the “unnatural” and, by implication, the unhealthful.⁷⁴ By the 1870s and 1880s, the slowly growing popularity of the germ theory in America⁷⁵—espoused by Pasteur, Koch, and others in Europe—transformed the locus of disease from the miasmatic environment to the infected individual. Blame shifted from the local government functionaries responsible for the environment to the individual who had acquired the disease, a change implicit in the prejudice against cancer patients and the fear of cancer contagion. Dr. Sims had not believed in the contagiousness of cancer, but the Astors, Elizabeth Cullum, Parsons, and Charles C. Haight, the architect of the New York Cancer Hospital, were not so sure. Ironically, although they built the hospital in part to overcome the bias against cancer, they constructed it with the most up-to-date sanitation and bacteriological safeguards—as though cancer was an infectious disease.⁷⁶

The location of the New York Cancer Hospital in a sparsely populated area at Central Park West and 106th Street was a concession to the complaints of neighbors about contagion (and fears of falling property values) that the executors of Abbot Godinot had experienced at Rheims almost a century and a half earlier.⁷⁷ But the relatively isolated site just west of the newly

⁷⁴Harriet Beecher Stowe, “The Chimney-Corner for 1866. Vii. Bodily Religion: A Sermon on Good Health,” *Atlantic Monthly*, July 1866, 85-93.

⁷⁵Phyllis Allen Richmond, “American Attitudes toward the Germ Theory of Disease (1860-1880),” *Journal of the History of Medicine and Allied Sciences* 9(1954): 428-54. Also see the excellent introduction and Chapter I by Nancy Tomes, *The Gospel of Germs: Men, Women, and the Microbe in American Life* (Cambridge, MA: Harvard University Press, 1998).

⁷⁶‘Contagiousness’ requires direct physical contact. ‘Infectious’ does not. ‘Communicable’ subsumes both method of the spread of disease. Of course, many diseases are both contagious and infectious. For a clear description of the distinction between these terms, see *The Gospel of Germs*. Tomes, *Gospel*, 20.

⁷⁷Hayes Martin, “The Organization of the New York Cancer Hospital,” “Historical Note No. 3,” (April, 1945), 10.

completed Central Park also afforded the bounty of clean air, unobstructed natural light, and a new city sewer system.⁷⁸

The design of the hospital was the reification of the newly popular germ theory. Bacteria were believed to lurk in dark, dirty corners. Stench, a throwback to the miasmatic era, warned that germs were near. The hospital structure thus had to be flooded with natural light,⁷⁹ devoid of dirty corners, and furnished with the best ventilation and plumbing systems available.⁸⁰ The New York Cancer Hospital was constructed to be all that and more. The wards were circular, like the round towers of a castle. Some called it “the Bastille.”⁸¹ The circular design afforded light streaming in the high windows almost the entire day. There are no corners in a circle, so bacteria could not hide and mops easily whisked away what few bacteria survived. Cleanliness was assured. The heads of the patient’s beds were arranged outward in a radiate design, so contagion between patients was reduced. Nurses cared for a large number of patients from the focus of the circular ward, a very different perspective from the predominant style of the traditional parallelogram-shaped hospital pavilion common at that time.⁸² The large, circular wards were connected by open-air verandas where patients could breathe fresh air and feel the

⁷⁸The sewer system was deemed so important to the new Hospital that the official opening of the New York Cancer Hospital was postponed until December 6, 1887—less than one month after the completion of the Eighth Avenue city sewer line that serviced the Hospital. New York Cancer Hospital. *Second and Third Annual Report 1886-1887. Memorial Hospital Archives*, p9.

⁷⁹The Edison Electric Light Company was established in New York City on October 15, 1878, but it was not until September, 1882 that the Pearl Street central station began to supply electricity to lower Manhattan. Schlesinger, *The Almanac of American History*, 338, 50. The cancer Hospital was not electrified until 1901. General Memorial Hospital, "Seventeenth Annual Report for the Year 1901," (New York: General Memorial Hospital for the Treatment of Cancer and Allied Diseases, 1902), 15.

⁸⁰Tomes, *The Gospel of Germs*. discusses these features from the residential point of view. Also see the excellent paper presented by architect Jeanne Kisacky at the Seventy-Fourth Annual Meeting of the American Association for the History of Medicine, “Redefining Isolation: Hospital Diseases, Hospital Architecture, and the New York Hospital,” in Charleston, South Carolina, April 20, 2001.

⁸¹Rusch, "The Beginnings of Cancer Research in the United States," 392.

⁸²New York Cancer Hospital, *Second and Third Annual Report 1886-1887*, 10.

warmth of sunlight. Connecting the wards on each floor of the circular towers were ventilation, plumbing, and temperature control systems that were the models of their day.⁸³ The ventilation system allowed “the air of each ward [to be] changed completely every five minutes,” so that there was “almost absolute freedom from unpleasant odors”⁸⁴—the original bugaboo of the Ladies’ Board at the Woman’s Hospital. Plumbing was state of the art, so there was no risk of contamination between the water supply and sewage that Victorians feared.⁸⁵ Heating coils at the base of each “hot-air pipe” allowed the temperature of each room to be adjusted separately so the air did not become “vitiated.”⁸⁶

The architecture of the New York Cancer Hospital applied germ theory to the care and treatment of patients. In consequence, the rapidly rising medical sciences of bacteriology and pathology met the cancer patient in the hospital to begin the institutionalization of the disease cancer. Mrs. Astor’s “air and sunshine” mandate brought together germs and cancer—an ideological combination that would have great influence on the development of modern cancer.

“Exclusively devoted to the Care of Women”

The woman’s pavilion of the New York Cancer Hospital, the only section of the Hospital planned until almost six years later, was dedicated on May 17, 1884. “Remember,” the New York Tribune quoted Mr. Parsons at the cornerstone ceremony, “that the hospital is to be appropriated by the conditions of the gift to the exclusive treatment of women afflicted with cancer. It is sad to reflect that it is more prevalent and is more severe among women than among

⁸³Charles Coolidge Haight, “The Report of the Architect,” New York Cancer Hospital, *Second and Third Annual Report 1886-1887*, 12.

⁸⁴New York Cancer Hospital, *Second and Third Annual Report 1886-1887*, 9-10.

⁸⁵Annmarie Adams, *Architecture in the Family Way: Doctors, Houses, and Women, 1870-1900* (Montreal: McGill-Queen's University Press, 1996), 36.

⁸⁶“Enlarging the Hospital to Relieve Cancer Victims,” *New-York Daily Tribune*, July 20, 1890.

those of the other sex."⁸⁷ The New York Cancer Hospital would not have been founded had the Woman's Hospital accepted the Astor gift, so Mrs. Astor's focus on a pavilion exclusively for women was not surprising. In addition, cancer was, as early epidemiological statistics appeared to make clear, a disease that disproportionately affected women.⁸⁸

This emphasis also revealed the cultural context of a woman's place in Victorian America. Women were different from men, not equal. The family wage, the exclusion of women from most non-domestic jobs,⁸⁹ and the accent on the household as the repository of morality, all revealed the fragile nature of the second sex in the virile job market of late nineteenth-century industrial America. Who would care for the women who were poor? abandoned? widowed? Who would tend the unfortunate with cancer who shouldered the woman's double burden of caring for herself and her family? Who would lend the moral uplift that religion appeared unable to deliver after the ruin of the Civil War? Indeed, who would provide a moral anchor for the women immigrants and rural migrants who flocked to New York in great numbers as urbanization and industrialization pulled families and individuals from their roots? Labor associations were not the answer. Mrs. Astor had witnessed the devastation and fear that ran through her circle during the nation-wide strikes of 1877. The politicians of Tammany Hall were corrupt and dangerous. The solution was private charity. Social control and cohesion through moral suasion. Teach the poor by giving to them and they would be less likely to take. The Woman's Hospital was a moral as well as a medical institution, but the majority of its Boards had refused the cancer patient. So Mrs. Astor and her cousin, Mrs. Cullum, created a new woman's hospital for those with cancer—the New York Cancer Hospital,

⁸⁷"The New Cancer Hospital," *New York Tribune*, May 18, 1884, 1.

⁸⁸Williams, *Natural History of Cancer*.

⁸⁹Except teaching and, later, nursing.

and one year—to the day—after Augusta’s death, Mr. Astor announced that he was donating \$145,000 to the New York Cancer Hospital to build a pavilion for men.⁹⁰ It was named for Charlotte Augusta Astor.⁹¹

The exclusive emphasis on women in the early days of the New York Cancer Hospital helped to drive the medical profession toward specialization, particularly the specialties of gynecology and oncology. Dr. Thomas Addis Emmet, Marion Sims’s hand-chosen successor at the Woman’s Hospital and a consulting surgeon at the New York Cancer Hospital, called himself “the first specialist” in gynecology because he was in the unique position, he explained, of “being a pioneer” in the midst of patients (“extensive resources” he called them) with the same or similar diseases.⁹² Under such circumstances he found that he “could not successfully do general practice and practice gynecology together.”⁹³ “I thus,” wrote Emmet, “as a generally-educated physician became the first specialist, while there had been before me many Especialists, who from taste, or from the force of circumstances, had gradually given more attention to the treatment of some one special class of diseases than to another...No one seemed to recognize that the unusual hospital advantages which I had experienced, and this advantage alone, had fitted me for being a specialist.”⁹⁴ The specialist did not create the institution. The institution created the specialist. The cancer hospital produced the cancer specialist, further institutionalizing and legitimizing cancer.

⁹⁰“New-York Cancer Hospital; Men's Pavilion Erected by J.J. Astor," *The New York Times*, Dec. 13, 1888.

⁹¹Handwritten letter "From J. J. Astor to John E. Parsons, January 10, 1889." ALS. *The Parsons Collection*.

⁹²Emmet, *Incidents of My Life: Professional—Literary—Social, with Services in the Cause of Ireland*, 203.

⁹³Ibid.

⁹⁴Ibid.

“The Exclusion of Incurables”

Many of the reasons for Mrs. Astor’s insistence on the exclusion of cancer patients deemed hopeless were set forth by the traditional Ladies’ Board at the Woman’s Hospital. Incurable cancer patients were costly to maintain, exuded fetid odors, required excessive nursing care, offended other patients, were most likely contagious, and probably contracted the ailment by some means of incontinence. Mrs. Astor’s concerns were different. Years before, she had heard the plaintive cry of Dr. Thomas’ silenced cancer victim whose life might have been saved—or at least significantly extended—if he had been able to operate on her in the hospital. Mrs. Astor knew that early surgery was the only known cure for cancer.⁹⁵ The goal of the New York Cancer Hospital was the cure and treatment of cancer, not the care of those beyond hope. The proper place for incurables was the traditional religious institution and its descendants—not the hospital.⁹⁶

The spotlight the New York Cancer Hospital focused on treatable cancer served as an early effort to educate the public to bring their persistent swellings to the doctor as soon as possible. Before 1913, when the American Society for the Control of Cancer (the original name

⁹⁵Hayes Martin wrote that “cancer was until the founding of this hospital an eldorado for rapacious quacks because the stigma was so great attached to the disease that such patients were shunned.” “Untitled piece by Hayes Martin on cancer history,” TMs, Memorial Hospital Archives, Record Group 500 Hayes Martin Collection, Box 5, folder 82a, “Memorial Hospital, history.”

⁹⁶Rose Hawthorne Lathrop, the daughter of Nathaniel Hawthorne, founded the first home for incurables, St. Rose’s Free Home for Cancer Incurables, in New York in 1899. The former Mrs. Lathrop, who had become Sister Alphonsa after her conversion to Catholicism following the death of her only son and her divorce, had probably been a nurse at the New York Cancer Hospital in 1893. Charles W. Bell, “Care of Dying Is Nuns’ Calling,” *New York Daily News*, Dec. 6, 1997. See also Patricia Dunlavy Valenti, *To Myself a Stranger: A Biography of Rose Hawthorne Lathrop*, 1st ed. (Baton Rouge: Louisiana State University Press, 1991), 279. Secondary sources, such as Francelia Butler’s “Early Cancer Nursing,” *RN* (Oct 1954): 40, state unequivocally that Rose Hawthorne Lathrop was a graduate nurse at the New York Cancer Hospital in 1893 for three months, but the Annual Reports of the time, which listed the names of the trainee nurses, do not list her among the matriculants. I am indebted to Kathy Brennan, Memorial Hospital Archivist, for bringing this discrepancy to my attention.

of the American Cancer Society) was founded,⁹⁷ there were few organizations to alert the public to the growing problem of cancer. The attention lavished on the Cancer Hospital by newspapers, however, functioned to publicize cancer and the importance of early diagnosis and treatment. Mrs. Astor excluded the hopeless incurables, but in doing so she included those whom she believed could be helped by earlier recognition of their cancers.

“To invite within its walls, Those of the Better Class”

Before the 1880s, traditional private charitable hospitals, like the Woman’s Hospital, routinely served some paying patients.⁹⁸ Often these were worthy citizens with respectable occupations who were separated from their far-off families and adrift in the anonymity of the expanding city. Absent home care from family or friends, they often went to the hospital when they needed medical attention for a significant illness. Mrs. Astor knew this “better class” because she had seen them at the Woman’s Hospital. First and foremost, she knew that they were a source of revenue to supplement contributions from private donors. The additional income also cushioned the effects of the inevitable financial downturns that seemed to occur about every twenty years during the nineteenth century and that affected hospitals as well as other philanthropic facilities dependent upon contributions.⁹⁹ The Astor money to the New York Cancer Hospital was intended only to pay for construction costs. The Hospital had to seek endowment and operating funds elsewhere.¹⁰⁰

⁹⁷The American Society for the Control of Cancer became the American Cancer Society in 1945.

⁹⁸Rosenberg, *Rosenberg, Care of Strangers*, 32.

⁹⁹Major economic recessions/depressions began in 1819, 1837, 1857, 1873, and 1893. President Parsons complained bitterly about the “serious pecuniary depression” and its effect on New York Cancer Hospital revenue. *Eleventh Annual Report, 1895*, 9.

¹⁰⁰Mr. Parsons spent most of his time as president of the Woman’s Hospital (1889-1915) and the New York Cancer Hospital (1884-1915) fundraising to meet operating expenses. The New York Cancer_Hospital, *Annual Reports*, passim.

Mrs. Astor was prescient inviting the “better class” to the Cancer Hospital. “Pay patients,” as Mr. Parsons called them, supplied an increasing percentage of hospital operating revenue between the opening of the woman’s pavilion in 1887 and 1897.¹⁰¹ In an early example of cross-subsidization, “receipts coming from this source [“pay patients”] aid in taking care of patients who are without means.”¹⁰² Private patients may have saved the institution from financial ruin during the 1893-1897 “Great Depression.”¹⁰³ The Hospital allowed non-cancer admissions when beds were available, especially to the pricier “Private Rooms and Special Wards.”¹⁰⁴ By the end of the nineteenth century, private patient revenue increasingly substituted for philanthropic donations.¹⁰⁵

The admission of private patients also served to increase the acceptance of cancer as a legitimate focus for physicians and hospitals. By 1897, a decade after the opening of the first cancer wards at the hospital, physicians, wrote President Parsons, increasingly “interest themselves in sending us patients.”¹⁰⁶ In addition, “there is a disposition on the part of private patients to recognize the advantages of [the New York Cancer] hospital treatment.”¹⁰⁷

Larger demographic changes also helped fuel the rise of the cancer hospital. The ballooning middle class became mindful of the advantages of operating suites and special

¹⁰¹New York Cancer Hospital. *Twelfth Annual Report 1896*. Memorial Hospital Archives, 10.

¹⁰²*Ibid.*

¹⁰³“President’s Report,” New York Cancer Hospital. *Thirteenth Annual Report 1897*. Memorial Hospital Archives, 17.

¹⁰⁴Anna Meredith Lawson, “A Synopsis of the History of the NYCH, Now known as The Memorial Hospital For the Treatment of Cancer and Allied Diseases.” *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 5, folder 82a, “Memorial Hospital, history.”

¹⁰⁵“Statement by the President,” *Twelfth Annual Report 1896*, 10.

¹⁰⁶*Ibid.*

¹⁰⁷*Ibid.*

nursing care provided within the hospital setting. Transformations in the urban family, which left fewer members at home to care for the sick, propelled the move to the hospital.

Improvements in municipal transportation and communication reduced the time between hospital patient and loved ones, as well as between physicians and their hospitalized patients. The New York Cancer Hospital, in particular, offered state-of-the-art antibacterial architecture and facilities to reduce germs in an increasingly “antisepticonscious America.”¹⁰⁸ More and more, cancer became a disease to be treated by surgeons in hospitals. An increasingly cancer-conscious society realized it was their best—and sometimes only—hope.¹⁰⁹

John Jacob Astor III and Charlotte Augusta Astor eventually donated at least \$465,000 to establish the New York Cancer Hospital.¹¹⁰ Over the course of less than two decades the Hospital achieved the four mandates of Mrs. Astor and more. A cancer hospital had been founded “on its own foundation,” as Sims wrote, “determined not only to give temporary relief to human suffering, but also to do something towards discovering better methods of treatment.”¹¹¹ But if the words were Sims’s, the materialization of the first Cancer Hospital in the United States was born out of the tragedies of the Astor and Cullum families. By the turn of the twentieth century, the hospital incorporated both the prestige of medical science and the demographically important middle class to lend legitimacy to a traditional social ailment that was rapidly becoming a modern medical problem. The hospital, founded for the cure and

¹⁰⁸The term is from Tomes, *The Gospel of Germs*, Chapter 7.

¹⁰⁹The increasing incidence of cancer was publicized by the statistician Frederick Ludwig Hoffman of Prudential Insurance Company long before he urged the formation of the American Society for the Control of Cancer in 1913. Frederick L. Hoffman, *Journal of the American Medical Association* 19(1901): 101.

¹¹⁰“Enlarging the Hospital to Relieve Cancer Victims,” *New-York Daily Tribune*, July 20, 1890. John Jacob Astor III donated \$445,000 in his name and \$20,000 in Mrs. Astor’s name.

¹¹¹Letter from J. Marion Sims to John E. Parsons, September 23, 1883. Martin, Ehrlich, and Butler, “Martin, Sims,” 202-3.

treatment of a stigmatized sickness, served to transform cancer into a disease state as established as influenza or cholera. “When the project of a cancer pavilion in connection with the Woman’s Hospital was started,” reflected John Parsons in 1897, “the prejudice was so strong that it compelled the abandonment of the scheme. At that time there was a general objection to the treatment of cancer cases in general hospitals. This naturally led to the establishment of our Hospital. Since then the situation has changed. The Hospital has itself assisted in lessening the prejudice against the disease. Now cancer cases are received in most of the hospitals.”¹¹²

By the final years of the nineteenth century, the institution served to ameliorate the stigma attached to cancer and, in its place, legitimize cancer. In return, cancer moved into the institution.

¹¹²John E. Parsons, *Twelfth Annual Report 1896*, The New York Cancer Hospital, 11.

Section II

TRANSITION: FROM TRADITIONAL TO MODERN CANCER

Chapter 3

General Grant's Cancer: Twilight of the Traditional

It all started with a peach.

On June 2, 1884, slightly more than two weeks after the dedication of the New York Cancer Hospital, General Ulysses S. Grant, revered commander of the Union armies during the Civil War and former President of the United States, was enjoying lunch at his summer home in fashionable Long Branch, New Jersey when he came to his favorite fruit, the peach.¹ Instead of the sensual pleasure he had come to expect from the juicy, plump fruit, Grant suffered severe pain in his throat and face that forced him from the dining table. A little more than a year later, on July 23, 1885, the General died of the cancer that had caused that first episode of pain. In between, he suffered mightily.² Indeed, so much publicity surrounded the ordeal of Ulysses S.

¹Many attest to the General's fondness for peaches. See John Y. Simon, ed. *The Personal Memoirs of Julia Dent Grant [Mrs. Ulysses S. Grant]*, The Ulysses S. Grant Association (New York: G. P. Putnam's Sons, 1975), 328.; George W. Childs, *Recollections of General Grant: With an Account of the Presentation of the Portraits of Generals Grant, Sherman, and Sheridan* (Philadelphia: Collins Printing House, 1890), 41.; and Robert M. Steckler and Donald P. Shedd, "General Grant: His Physicians and His Cancer," *The American Journal of Surgery* 132(1976): 509.

²The best general reviews of Grant's battle with cancer are the historical (Thomas M. Pitkin, *The Captain Departs: Ulysses S. Grant's Last Campaign* (Carbondale: Southern Illinois University Press, 1973)., the medical (Rodney B. III Nelson, "The Final Victory of General U. S. Grant," *Cancer* 47, no. 3 (1981): 433-36.and—from a nuanced perspective with an eye on the twentieth century—the cultural (James T. Patterson, *The Dread Disease: Cancer and Modern American Culture* (Cambridge, MA: Harvard University Press, 1987). The diary of Doctor James H. Douglas, now in the Library of Congress; George F. Shradly's weekly writings in *The Medical Record*; and the newspapers of the day are the best contemporary sources of information on the General's fatal illness. To my knowledge, no one has presented the story of Grant's malignancy in the medical-historical contextual framework that I have chosen to best exemplify traditional cancer.

Grant that he thrust the disease cancer forcefully into the forefront of the national consciousness.³

Traditional Sin, Modern Science

During the last two decades of the nineteenth century, a major transition took place in the medical and public perception of cancer. Grant's fatal illness, and the notoriety that surrounded his personal agony, brought a new understanding to the meaning of the disease. Not only did cancer become a subject of legitimate medical inquiry, but the disorder also took on a new public persona. If prominent and beloved figures like General Grant could suffer the throes of cancer, how could cancer be "contrary to nature"?⁴ Heretofore, only the most heinous sins deserved its punishment. Yet the venerated hero of the Republic⁵ endured the tragic disease, so how could scorn and denigration attach to others with cancer? Grant's travail altered the culture of cancer from a stigmatized, fatal disease to a legitimate concern of the national community. Importantly, these changes occurred as the incidence of the disease rose dramatically.

General Grant was not alone in sparking the transition of the culture of cancer from sin to science. Earlier in the nineteenth century, innovative discoveries in pathology ushered in new perspectives on the medical aspects of traditional cancer. The founding of the first cancer hospital in America served to recruit the forces of the institution to contend with the burgeoning

³William S. McFeely, one of Grant's many recent biographers, wrote that "in a century that relished the spectacle of dying there was, in America at least, no deathwatch the equal of Grant's....With Grant, the nation for eight months read almost daily in the newspapers of the progress of the disease, of the devouring of the victim by the unmentioned cancer, and of the valiant battle of the old warrior, before getting the news of his final surrender." William S. McFeely, *Grant: A Biography*, The Library of the Presidents Collector's Edition ed. (Norwalk, CT: The Easton Press, 1981; repr., 1987), 509.

⁴The expression is attributed to Galen (129-c.199). See Jeremiah Reedy, "Galen on Cancer and Related Diseases," *Clio Medica* 10, no. 3 (1975): 234-35.

⁵General Grant, although he made overtures to heal the rift between North and South during his presidency, was revered, of course, predominantly above the Mason-Dixon Line. My references to Grant as hero should be borne with that geographical and political qualification in mind.

social problems of traditional cancer. The microscope, a plaything for amateur naturalists well into the 1870s,⁶ came of age in medicine with theories of germs in the 1880s and 1890s to provide a new—but at first tentative—solution to the problem of diagnosis. In addition, new theories of the pathogenesis of cancer in the waning years of the nineteenth century propelled the medical investigation of the disease to previously unimaginable prominence within the unifying medical profession and, subsequently, with the public. In 1893, therefore, only eight years after the Grant's death, when President Grover Cleveland noted oral symptoms—not dissimilar from those experienced at first by General Grant—the diagnosis and treatment of Cleveland's tumor were strikingly different from those experienced by Grant. Although the transition to the disease cancer in its modern form was far from complete when Cleveland's cancer was first diagnosed, it had taken giant strides in an untested direction in a remarkably short span of time.

This chapter portrays the great import of General Grant's illness to the history of cancer. It also begins an analysis of the profound differences between traditional and modern cancer through a comparison of the medical and social case studies of the two American Presidents with cancer in the last years of the nineteenth century—Grant and Cleveland.

“The Nation's Greatest Hero”

Who was Grant and how did he draw such attention to the disease cancer? The General, as he was customarily called even after his two terms in the White House (1869-1877), was an enigma. He was a man of great contradictions—stoicism and pathetic suffering, monumental achievements and naïveté. Above all, however, he was a savior to those who believed in the Union. From this he derived his enormous popularity.

⁶John Harley Warner, "Exploring the Inner Labyrinths of Creation: Popular Microscopy in Nineteenth-Century America," *Journal of the History of Medicine and Allied Sciences* 37(1982): 19.

By the 1880s, however, he had little interest in publicity.⁷ Indeed, he had retreated to the reticence that developed from a natural credulity that caused him trouble on several occasions.⁸ An episode in his youth revealed this aspect of his nature long before he attained the highest elected office in the United States. Jesse Grant sent his eight-year-old son Ulysses to purchase a horse.⁹ The boy, when asked how much he was willing to pay for the animal, eagerly explained to the horse's owner that his father had told him to offer twenty dollars and, if that was not accepted, to eventually raise the offer to twenty-five dollars.¹⁰ His fame, of course, rested not on the achievements of his presidency—of which there were many—but squarely on his battlefield victories. Following the assassination of Lincoln,¹¹ Grant “symbolized the war, the victory, the reunion.”¹² “The Nation’s Greatest Hero,” as *The New-York Times* called him, accepted Robert E. Lee’s surrender in April, 1865 at Appomattox Court House and was intimately involved in

⁷“I made what reputation I have as a soldier,” not as a politician or president, he wrote on May 23, 1885. From Major General Ulysses S. Grant 3rd, “Grant’s Last Victory,” in *Ulysses S. Grant: Warrior and Statesman* (New York: William Morrow & Company, Inc., 1969), 449.

⁸Upon leaving office in 1877, Grant assured Congress that “failures have been errors of judgment, not of intent.” John Y. Simon, ed. *The Papers of Ulysses S. Grant*, 24 vols., The Ulysses S. Grant Association (Carbondale: Southern Illinois University Press, 1967-).

⁹Actually, his father probably called him “Lyss.” Ulysses S. Grant had been born Hiram Ulysses Grant. After boyhood, his family called him Ulysses (pronounced *U-lis-sis*), but the congressman who appointed him to West Point erroneously listed his name as Ulysses S. Grant, possibly thinking of his mother’s maiden name, Hannah Simpson. Ulysses S. Grant, *Personal Memoirs of U. S. Grant*, 2 vols. (New York: C. L. Webster & Co., 1885-86), 6 Footnote 3. Grant adopted the S., but never translated the letter as Simpson. McFeely, *Grant*, 524 Footnote 2.

¹⁰Ulysses Simpson Grant, *Personal Memoirs of U. S. Grant*, ed. Editor with Notes and an Introduction E. B. Long, The Library of the Presidents Collector’s Edition ed. (Norwalk, CT: The Easton Press, 1885; repr., 1989), 9-10.; The (New York) World, “Gen. Grant’s Departure: Preparations for His Trip to Mount Macgregor Completed,” *The World*, 16 June 1885, 3:1.

¹¹General Grant, a great hero in his time, was himself no hero-worshipper. Thus, his adoration of President Lincoln was even more notable. He related to one of his closest physicians, Dr. George F. Shrady, that he “was profoundly impressed by [Lincoln’s] modesty, sincerity, and earnestness. He was justice, humanity, and charity all in one.” Lincoln, related Grant, was “the greatest man he had ever known.” George F. Shrady, M.D., *General Grant’s Last Days, with a Short Biographical Sketch of Dr. Shrady* (New York: Privately Printed, 1908; repr., One of 50 privately printed copies), 34.

¹²John Lauber, *The Inventions of Mark Twain*, The Library of Great Lives Collector’s Edition ed. (Norwalk, CT: The Easton Press, 1990; repr., The Easton Press (MBI, Inc.), 1995), 219-20.

Andrew Johnson's impeachment as the President's Secretary of War *ad interim* in 1868.¹³ His allegiance to Congressional Republicans—and Civil War renown—made him a prime candidate for the Presidency that year.

In 1868, Grant was elected the eighteenth and youngest President of the United States.¹⁴ The Reconstruction of the South continued during his tenure, but contemporaries remembered the Grant administration most for its corruption. These were the times that Mark Twain and Charles Dudley Warner labeled the “Gilded Age”—for its superficial patina with deceptive underpinnings.¹⁵ Grant came away from the experience chastened but unindicted.¹⁶ Nor did he seem to learn shrewdness from the malfeasance of those around him. His trip around the world in 1879 somewhat restored his public image, but the scandalous failure on May 6, 1884, of his namesake investment company,¹⁷ Grant & Ward, brought him back into the scathing public limelight as the dupe of Ferdinand Ward, previously known as the “Young Napoleon of

¹³The source of the appellation is The New York Times, "A Most Fitting Burial Place: The Nation's Greatest Hero Should Rest in the Nation's Greatest City," *The New York Times*, 25 July 1885, 1:4-5. President Johnson appointed Grant Secretary of War in order to incite a court test of the Tenure of Office Act that required Congressional approval for the President to remove confirmed appointees from office. Grant accepted the secretaryship in August, 1867, but, despite a putative promise to Johnson that he would stay in the War office, resigned in January, 1868 when Congress insisted upon Edwin M. Stanton's reinstatement.

¹⁴Grant was elected President when he was forty-six years old—the youngest of all presidents before him. John F. Kennedy, of course, became the youngest elected president in 1960 (age 43), but Theodore Roosevelt, who assumed the presidency upon the assassination of William McKinley in 1901, was the youngest president ever to hold the office (age 42). Grant's relative youth contributed to his candidacy for the presidency in 1872 (which he won), 1876, 1880, and even 1884. In 1884, the year Dr. Douglas diagnosed his throat cancer, he was only sixty-two years old—seven years less than the age at which Ronald Reagan was inaugurated as the fortieth President of the United States.

¹⁵Mark Twain and Charles Dudley Warner, *The Gilded Age: A Tale of Today* (Hartford, CT: American Publishing Company, 1873; repr., New American Library, 1985).

¹⁶The Reverend Henry Ward Beecher said of Grant that “his mistakes lay in fidelity to friends,” and that “the mistakes of his Administration lay at the door of the good qualities of the man. The New-York Times, "Gen. Grant's Condition: Earnest Remarks by Mr. Beecher at the Plymouth Church Prayer Meeting," *The New York Times*, March 14 1885, 2:2. Also see McFeely, *Grant*, 385.

¹⁷Grant's son, Ulysses, Jr., was a partner and the actual “Grant” in Grant & Ward. Few investors seem to have known this. Nevertheless, the General put his own money into the firm and encouraged friends and family to do the same.

finance.”¹⁸ The collapse of the firm ruined Grant financially.¹⁹ Such was the perpetually trusting nature of Grant’s personality, and such was the behavior that he exhibited during interactions with his physicians only a short time later.

Besides his credulity and the devotion to his wife, Julia, perhaps only two things remained constant in his life—cigars and whiskey.²⁰ His bad habits were widely known—then and now.²¹ Both may have contributed to the development of his cancer.²² Following Ward’s embezzlement of the firm’s assets, Grant maintained his introspective, brooding nature to his final days. This was the demoralized personal state in which, less than a month after the fall of the investment house of Grant & Ward and the loss of his financial security, the infamous peach episode signaled the onset of the General’s last great battle.

Eras do not die like living creatures; they merge and blend into one another.

—Ronald Walters, *American Reformers*

General Grant was a principal—although involuntary—agent in the transition from traditional to modern cancer. Before the last decades of the nineteenth century, shame and blame mixed with fear and dread to create an unconscionable social and medical burden upon those

¹⁸Pitkin, *The Captain Departs*, 1.

¹⁹The New-York Times, "Mr. Beecher's Remarks on Gen. Grant." Adam Badeau, Grant’s military secretary during the Civil War and, later, one of his first biographers, wrote dramatically—and metaphorically—“this sorrow [the failure of Grant & Ward] was a cancer indeed.” Adam Badeau, *Grant in Peace: From Appomattox to Mount Mcgregor, a Personal Memoir* (Freeport, NY: Books for Libraries Press, 1887; repr., 1971), 422.

²⁰Edmund Wilson, *Patriotic Gore: Studies in the Literature of the American Civil War* (Boston: Northeastern University Press, 1962; repr., 1984), 135-38. Grant may have decreased the frequency of his drunken debauches during and after the Civil War. Nelson, "The Victory of U. S. Grant," 433. The amount of whiskey he consumed by the early 1880s is unclear. Steckler and Shedd, "Grant's Physicians and Cancer," 511-12.

²¹An unlikely source suggests the notoriety of General Grant’s smoking and drinking. Joanne Gordon, "Stone the Authors," *Forbes*, July 9, 2001, 54.

²²Today it is well accepted that the combination of alcohol and smoking is a great risk factor for throat cancer. National Institute of Dental Research, "Causes and Prevention of Mouth and Throat Cancers," (Bethesda, MD: National Institute of Dental Research, 2001). at http://cancernet.nci.nih.gov/wyntk_pubs/oral.htm. Accessed May 23, 2001.

stricken with the disease. In the early decades of the century, hope of God's salvation sustained the sufferer's will. Following the Civil War and the gradual acceptance of Darwinism, however, even God's proffered succor mitigated. Desolation and isolation wracked cancer victims more than ever. Society's old-line doyens, burnt over with the desire to uplift the sick through philanthropic almshouse-hospitals, aided stigmatization by barring the cancerous poor in the name of dignity and order. At the same time, nineteenth-century (primarily European) medical scientists who explored the newfound world of cancer microscopy added novel insights to the nomenclature and taxonomy of the disease. By the end of the century, the disease cancer took on a new gloss of medical legitimacy through scientific worthiness. In addition, increased public awareness followed the personal travail that persuaded the rebellious few—visionary proponents of institutional cancer care like Dr. J. Marion Sims, Mrs. Charlotte Augusta Astor, Mrs. Elizabeth Hamilton Cullum, and Mr. John E. Parsons—to establish a fledgling hospital for the care of the poor with cancer on the upper West Side of Manhattan—only about two miles from General Grant's 3 East 66th Street brownstone residence.

What a coincidence that John Jacob Astor III (husband and patron of Augusta's causes), Ulysses S. Grant, and Louis Pasteur were all born in 1822!²³ All three were born in the age of traditional cancer and contributed to a revolution that culminated in the birth of modern cancer.²⁴ Astor, his wife Augusta, and her "dear Cousin" Elizabeth,²⁵ attempted to right what they believed was the wrongful refusal of the Woman's Hospital to serve the cancerous poor. Their

²³Astor (1822-1890) was a subject of Chapter 2. This chapter discusses Grant (1822-1885). Louis Pasteur (1822-1895), chemist slayer of spontaneous generation and a father of germ theory, will be discussed in Chapter 7. Interestingly, Gregor Mendel, the father of experimental genetics—a field that currently plays a major role in the investigation of cancer—was also born in 1822.

²⁴Note that I am not implying that they were born under the astrological sign of cancer.

²⁵Augusta and Elizabeth were very close. For the exact epithet used here, see Augusta Astor, "From Augusta Astor to John E. Parsons," in *The Parsons Collection; Memorial Hospital Archives, Record Group 500 Hayes Martin Collection, Box 5, folder 82a; "Memorial Hospital, history"* (New York 1884).

solution, a stand-alone in-patient cancer facility, the first of its kind in the Western Hemisphere, was dedicated to the treatment and care of those with the dread illness. Thereby they lent brick and mortar to an ideology of salvation urged on by the demographic displacements of industrial capitalism and the increasing incidence of the disease. Nevertheless, perceptions of traditional cancer permeated their actions. As Mr. and Mrs. Astor had attempted to circumvent the social problem of traditional cancer with anonymity, so General Grant also sought to avoid the spotlight. They all failed—such was already the nature of the press even in their day²⁶—but in the face of tragedy and in the spotlight of publicity they transformed the culture of cancer toward increased openness, acceptability, and the scrutiny of a new approach to medicine founded upon the principles of science and the practice of laboratory investigation.

There is properly no history; only biography.

—Ralph Waldo Emerson²⁷

The General did not intend to become a *cause célèbre*. Dr. George F. Shrady, one of his personal physicians, stated clearly that Grant was happiest as “an ordinary private citizen.”²⁸ Nevertheless, his cancer became one of the most publicized events of the 1880s and was the most prevalent newspaper story of 1885. Indeed, the amount of news coverage devoted to the war hero’s final months was called “staggering.”²⁹

²⁶Grant believed the press to be rapacious, sensational, and inaccurate. Mary Drake McFeely and William S. McFeely, *Ulysses S. Grant: Memoirs and Selected Letters. Personal Memoirs of U. S. Grant. Selected Letters 1839-1865* (New York: Penguin Books USA Inc., 1990), 1113.

²⁷Ralph Waldo Emerson, "History," in *Essays, First & Second Series, The 100 Greatest Masterpieces of American Literature* (Franklin Center, PA: The Franklin Library, 1841; reprint, 1984), 11.

²⁸Shrady, *Grant's Last Days*, 25.

²⁹Pitkin, *The Captain Departs*, 155.

Grant's fight with cancer is a model of denial, prevarication, suffering and fear, and, ultimately, a coming to terms with himself and his illness. The story represents the timeless cycle of hope and despair associated with the disease. Further, its occurrence in a figure of such renown in the 1880s during the critical period in the making of modern cancer lent special agency and importance to his inadvertent contribution to the history of cancer.

**GENERAL ULYSSES S. GRANT:
A CASE STUDY IN TRADITIONAL CANCER**

Grant's clinical course is illustrative of the model of traditional cancer. Grant's case creates a privileged window into the workings and limitations of the disease at that time and—through the changes wrought by his agony—the beginnings of modern cancer. Grant arguably received the best clinical care available. Certainly, the press, the public, and Grant himself believed this to be so.³⁰³¹ Nevertheless, only a few years later the notion of the “best” cancer treatment underwent a major transformation.

We cannot thoroughly understand the modern perception of cancer without knowing its roots. Moreover, we cannot understand its roots without investigating the people, institutions, and culture that made it so. Grant, like William Avery Rockefeller and the Board of Lady Supervisors of the Woman's Hospital of the State of New York, represents that past.

No one could have predicted that the General, a stout man of barely sixty-two years, would change the course of cancer history—least of all Grant himself. In one of his most famous notes to his throat specialist, Dr. John Hancock Douglas, the dying Grant summed up his own life as a series of unintended consequences:

³⁰The New York Times, "Faith in His Doctor's Skill. Gen. Grant's Written Expression of His Satisfaction with Their Treatment.," *The New York Times*, 24 July 1885, 6:2-3. George W. Childs, the General's publisher friend from Long Branch, also quoted Grant's admiration for his physicians and the medical care they provided. Childs, *Recollections*, 41-42. Also see George F. Shradly, M.D., "The Surgical and Pathological Aspects of General Grant's Case," *The Medical Record* 28(1885): 123., and Grant 3rd, "Ulysses S. Grant," 449.

If I live long enough I will become a sort of specialist in the use of certain medicines, if not in the treatment of disease. It seems that man's destiny in this world is quite as much a mystery as it is likely to be in the next. I never thought of acquiring rank in the profession I was educated for; yet it came with two grades higher prefixed to the rank of General officer for me. I certainly never had either ambition or taste for political life; yet I was twice President of the United States. If anyone had suggested the idea of my becoming an author, as they frequently did, I was not sure whether they were making sport of me or not. I have now written a book which is in the hands of the manufacturers. I ask you to keep these notes very private lest I become an authority on the treatment of diseases. I have already too many trades to be proficient at any.³²

—July 8, 1885, 4:00 A. M.

He never did become a specialist in the use of cocaine, the main medication used to treat the pain of his throat malignancy, but he did provide an unexpected spotlight on the problem of cancer and, in doing so, altered the history of the disease forever.

October 22, 1884—The Medical Office of Dr. John Hancock Douglas:

Grant: Is it cancer?

Douglas: General, the disease is serious, epithelial in character, and sometimes capable of being cured.³³

Grant's health began to decline before the fateful peach of June, 1884. He personally traced the beginning of the deterioration of his physical health to Christmas Eve, 1883.³⁴ On that cold and misty night he alighted from a coach on New York's Upper East Side and turned quickly to give the coachman a gift of twenty dollars for the holidays. But the pavement was icy and as he turned he slipped and fell.³⁵ Grant was diagnosed with a ruptured muscle in the upper part of his thigh. Only a few days after the accident, immobilized and bedridden, he developed an excruciating pain in his chest that blossomed into pleuro-pneumonia and pleurisy. In the tradition of the day (decades before the advent of antibiotics) he was confined to bed for a

³²McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1118.

³³Quoted by Horace Green, *General Grant's Last Stand; a Biography* (New York, London,: C. Scribner's Sons, Ltd., 1936). from the diaries of Dr. John H. Douglas, Library of Congress. Also quoted in Steckler and Shedd, "Grant's Physicians and Cancer," 509.

³⁴The New-York Times, "His Fatal Illness: The Progress of the Malady to Which He Succumbed," *The New-York Times*, 24 July 1885, 5:2.

³⁵Badeau, *Grant in Peace*, 416.

lengthy period.³⁶ He could have died, as had Dr. J. Marion Sims only a month before, but he recovered despite the immobility-induced bedsores that increased his risk of infection and sepsis. For the rest of his life, however, he never again walked without the use of crutches or a cane.³⁷ Nevertheless, he survived the Christmas Eve trauma and feeling “healthy, rich, and happy”³⁸ entered the spring of 1884 with high hopes for himself and his growing family. In short order, however, his money disappeared with the speculator Ward and—in a twist on the downfall of Adam and Eve—he ate the peach. Then, as in the case of our Biblical progenitors, the denial began.

DENIAL

(June-October, 1884)

The peach symptoms greatly troubled General Grant initially. He immediately mentioned them to his friend and Long Branch neighbor, George W. Childs—a well-known Philadelphia publisher.³⁹ Childs had invited his friend Dr. Jacob Mendez Da Costa, a Philadelphia surgeon, for a weeklong stay in Long Branch. The physician was famous for Da Costa’s Syndrome—a form of battle fatigue with which Grant had firsthand knowledge.⁴⁰

³⁶Ibid., 417.. Although the medical record is unclear, it is possible that a blood clot that traveled from his immobilized leg to his lungs—a pulmonary embolism—caused Grant’s acute chest pain. If so, bed rest might have killed him, because the continued bed confinement (long before modern anticoagulants) may have engendered even more potentially fatal clots rushing to his lungs.

³⁷McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1157.

³⁸Badeau, *Grant in Peace*, 416.

³⁹Childs’ role in Grant’s illness in the summer of 1884 is elaborated upon in his *Recollections* and further expanded in a duplicative narrative intended more for popular consumption (and personal aggrandizement) in Childs, *Recollections*.

⁴⁰Richard Goldhurst, *Many Are the Hearts: The Agony and Triumph of Ulysses S. Grant* (New York: Thomas Y. Crowell Company, 1975), 141. Da Costa’s Syndrome is also known as neurocirculatory asthenia. Da Costa himself called the soldier’s condition “irritable heart.” Abnormal function of the neurologic and circulatory systems with increased susceptibility to fatigue, palpitations, dyspnea, rapid pulse, anterior chest pain, and anxiety characterizes the Syndrome. Da Costa first recognized the syndrome during the Civil War. Today Da Costa’s Syndrome would most likely be classified amongst the post-traumatic stress syndromes. Thomas Lathrop Stedman,

Childs offered the doctor's services and Grant accepted forthwith. Indeed, Childs was so concerned about Grant that he brought Dr. Da Costa to see him shortly after the doctor's arrival.⁴¹ The surgeon examined Grant's throat on the porch of his summer house using the sun's light for illumination. Medical devices for internal visualization of human body cavities were then in their infancy and—as was the case with reflected candlelight—sometimes dangerous. Exactly what Da Costa thought he saw is unclear. Childs, who made every effort to portray his Philadelphia friend positively, reported years later that “Dr. Da Costa knew at once the disease was cancer.”⁴² Others, however, did not concur in the accuracy of Da Costa's initial impression.⁴³ Regardless, he did not tell Grant his suspicions. Instead, he gave him a prescription and told him to contact his family physician, Dr. Fordyce Barker, “at once.”⁴⁴

There is more here than meets the eye. Da Costa and Grant were observing longheld customs that, true to the tenets of traditional cancer, threatened Grant's well being. Whatever the surgeon thought he saw was apparently quite small and, given the surgical knowledge of the day, most likely amenable to extirpation at that stage.⁴⁵ But Da Costa followed a code of secrecy—by not telling Grant his diagnosis—that essentially removed the patient from participation in his

Illustrated Stedman's Medical Dictionary, 24th ed. (Baltimore: Williams & Wilkins, 1982), 133., and <http://meltingpot.fortunecity.com/tenison/308/ptsd/history.htm>. Accessed 30 May 2001.

⁴¹The vast majority of sources place Dr. Da Costa's examination of Grant in June, 1884. Mrs. Grant, however, recollected years later that the doctor saw her husband “early in August, I think.” Simon, *Julia Dent Grant*, 329.

⁴²Childs, *Recollections*, 141-42.

⁴³For example, Goldhurst related that the surgeon “saw something. What it was Da Costa didn't know, it was too minute to tell.” Goldhurst, *Many Are the Hearts*, 141.

⁴⁴Many sources corroborate the prescription: Nelson, “The Victory of U. S. Grant,” 433.; Childs, *Recollections*, 41.; Goldhurst, *Many Are the Hearts*, 141. Unfortunately, the medication prescribed is not known, so an attempt to divine Da Costa's diagnosis from the medicine he prescribed for Grant is not possible. The Finding Aids for the Da Costa archives at Jefferson Medical College make no mention of Grant: (http://jeffline.tju.edu/SML/archives/collections/finding_aids/pdfs/jmdacosta.pdf (accessed 30 May 2001).

⁴⁵McFeely, *Grant*, 496. McFeely's medical advisor was Solomon Cohen, M. D. (Ibid., 558-9 Footnote 3).

own care and, not coincidentally, made the patient more dependent on the physician. In addition, the Philadelphia surgeon implicitly acknowledged a code of exclusivity by referring Grant back to his personal doctor. Indeed, he may have been embarrassed for seeing the General in the first place without the explicit consent of the eminent Dr. Barker.⁴⁶

Grant was also complicit in his own demise. He knew that Dr. Barker, true to his annual wont, was in Europe for the summer months, but he did not relay this information to Da Costa. In addition, Grant's symptoms recurred repeatedly throughout the summer months.⁴⁷ Indeed, the intermittent throat symptoms so affected the General that he eventually sought Dr. Da Costa's Philadelphia address from Childs. He told Childs that he planned to pay the surgeon a visit from Long Branch for the purpose of further diagnosis and treatment.⁴⁸ However, Grant's symptoms temporarily improved shortly thereafter and he never went.⁴⁹

The old soldier repressed his symptoms with his well-known stoicism and did not visit a physician for more than four months. During that time the pea-sized tumor continued to grow. Grant's code of repression, commonly followed in the nineteenth century when the treatment for cancer was often worse than the disease,⁵⁰ served him ill. His wife urged him to seek medical attention but Grant, still in denial, told her repeatedly that "it will be all right directly, and I will

⁴⁶Nelson, "The Victory of U. S. Grant," 433.

⁴⁷Childs, *Recollections*, 41.

⁴⁸Note that it was the physician, Dr. Da Costa, who followed the code of exclusivity—not Grant.

⁴⁹Goldhurst, *Many Are the Hearts*, 142.

⁵⁰See Chapter 1. In particular, note the famous quotation attributed to Hippocrates concerning the treatment of non-skin cancers: "It is better not to cure hidden cancers, for they who are cured quickly perish; whilst they who are not cured live longer." Hippocrates, *The Aphorisms of Hippocrates*, trans. Thomas Coar, Special ed., The Classics of Medicine Library (London: A.J. Valpy, 1822; repr., 1982), 177. Also, envision the tribulations of Fanny Burney, who underwent surgery for her breast tumor in 1811.

not have a doctor.”⁵¹ Of course, he, like many other cancer victims before and since, may have surmised that he had cancer and assumed hopelessness based upon a code of futility. The October 22, 1884 exchange between Grant and Douglas in the above epigraph suggests as much. Indeed, during the traditional era the word ‘cancer’ was so anathema to Grant and others that “he never after the first instance called it cancer.”⁵²

The Grants returned to New York from Long Branch in early October, but the General did not request Dr. Barker’s assistance for several weeks.⁵³ Mrs. Grant noted that her husband continued to deny the severity of his problem and instead focused on writing his memoirs⁵⁴—his true source of nourishment and the sustainer of his life.⁵⁵ “All that summer was spent by my dear husband in hard work: writing, writing, writing for bread.”⁵⁶ Finally, on or about October 20, Grant visited Dr. Fordyce Barker.⁵⁷ By the 1880s, Barker had become a well-respected

⁵¹Simon, *Julia Dent Grant*, 329.

⁵²McFeely, *Grant*, 502.

⁵³There may be another reason why Grant delayed his visit to Dr. Barker for throat symptoms. Fordyce Barker had developed a “partial paralysis of the vocal cords” around 1850 that affected his speech for the rest of his life. Since the General had been Barker’s patient for some years, he must have known of the physician’s disability and, perhaps, feared its development in himself. Henry R. Viets, “Barker, Benjamin Fordyce, (May 2, 1818 - May 30, 1891),” in *Dictionary of American Biography* (New York: American Council of Learned Societies, 1928).

⁵⁴Simon, *Julia Dent Grant*, 329.

⁵⁵Lauber, *Mark Twain*. and William S. McFeely, “To Write a Book: To Be a Man,” in *Grant: A Biography* (Norwalk, CT: The Easton Press, 1981; reprint, 1987). concentrate heavily upon the contribution of Grant’s *Memoirs* to his mental well being in the last months of his life. Grant, despite unbearable pain, completed the second and final volume of the *Personal Memoirs of U. S. Grant* on July 18, 1885—only days before his death.

⁵⁶Simon, *Julia Dent Grant*, 329. After the failure of Grant & Ward, the loss of the Grant family’s savings, and default on a \$150,000 loan from William H. Vanderbilt that Grant had taken at Ward’s request, Grant supported his family by writing a series of articles on the Civil War for *The Century Magazine* at \$500 per article.

⁵⁷The exact date of the General’s first visit to Dr. Barker for his throat symptoms is unclear. Most authors claim that Grant saw Barker on October 22, 1884. Mrs. Grant, however, believed that her husband visited Barker on October 20. *Ibid.* Mrs. Grant’s knowledge was first-hand, so I accept her date.

physician renowned for his considerable knowledge of cancer.⁵⁸ Indeed, the New York Cancer Hospital selected him as the keynote speaker at their dedication only five months before.⁵⁹

Barker was shocked by Grant's throat and immediately referred the General to the best oropharyngeal specialist in New York—Dr. John Hancock Douglas.⁶⁰

General Grant first consulted Dr. Douglas on October 22, 1884—more than four and a half months after the episode of the painful peach. Grant and Douglas were hardly strangers. Their paths first crossed when Grant marched against Fort Donelson in the spring of 1862. Douglas was then Associate Secretary of the United States Sanitary Commission and Grant was a ne'er-do-well who had not long before been “drummed out of the army in California for drunkenness.”⁶¹ Nevertheless, Douglas admired Grant and the soldier reciprocated.⁶² They served together at Shiloh and the Wilderness—the doctor responsible for establishing and managing the field hospitals—but it was Donelson they remembered best.⁶³ Indeed, the Union capture of Fort Donelson was the first major victory for the North and started Grant on his

⁵⁸Dr. Fordyce Barker, physician to Presidents Garfield and Grant, was an eminent personality—although not without controversy—in his own right. Earlier in 1884, members of the New York Academy of Medicine had accused Barker of practicing without the diploma that he claimed to have received from the Ecole de Paris in 1844. He was later exonerated (although he actually *did not* receive his diploma at that time), but not until the end of 1884. Memorial Hospital Archives, "New York Cancer Hospital (Old Memorial)," in *Hayes Martin Collection* (New Yorkn.d.), Box 1, Folder 15: Bequests, Astor, J. J., 1884; 926-927. Nevertheless, he was a *bon vivant* who befriended Charles Dickens, Washington Irving, and Oliver Wendell Holmes. In addition, Barker helped Dr. J. Marion Sims found the Woman's Hospital of the State of New York, served as Augusta Astor's physician during her fatal illness, and played a prominent role in the launch of the New York Cancer Hospital. The biography of this famous and influential physician remains to be written.

⁵⁹Dr. Barker's dedicatory address was given at the laying of the cornerstone of the New York Cancer Hospital, May 17, 1884, on 106th Street just off Eighth Avenue (now Central Park West). New York Cancer Hospital, "Second and Third Annual Report 1886-1887," (New York: New York Cancer Hospital, 1887), "Address of Dr. Fordyce Barker, Consulting Physician," Memorial Hospital Archives, 28-35.

⁶⁰Rodney Nelson III referred to Douglas as “the best known otolaryngologist in New York.” Nelson, "The Victory of U. S. Grant," 434.

⁶¹*Ibid.*, 433.

⁶²Goldhurst, *Many Are the Hearts*, 142.

⁶³*Ibid.*

ascendancy. It was at Donelson that Grant acquired the moniker “Unconditional Surrender” for the terms of surrender he demanded from the Fort’s Confederate commander Simon Bolivar Buckner and the initials of his first two names, U(lysses). S.⁶⁴ Grant and Douglas remained fast friends. Grant could have bypassed the vacationing Dr. Barker and visited his old friend Douglas for throat pains long before October if he had not been in denial.

Douglas was appalled by what he saw in Grant’s throat. Not only was a mass present in the right tonsillar area to the side of the tongue, but Douglas noted an enlarged lymph gland under the crook of the jaw—a sign suggesting that the cancer might have spread beyond its original confines.⁶⁵ The doctor treated Grant expectantly, meaning that he applied solutions of iodoform, salt water, dilute carbolic acid, and permanganate of potash and yeast to the lesion to decrease inflammation and irritation.⁶⁶ A topical cocaine solution controlled the pain.⁶⁷ No biopsy was performed and no further consultations were sought. There is no evidence that the specialist even considered surgery at this stage. Instead, he continued to apply the topical solutions for months.

Why no surgery?

Surgery is the mainstay of modern cancer therapy. However, it was hardly the treatment of choice for Grant because the disease was well known to be incurable and operative complications could be devastating. Nevertheless, Douglas considered surgery later in the General’s course. Why did he not consider it sooner?

⁶⁴Nelson, "The Victory of U. S. Grant," 434.

⁶⁵Steckler and Shedd, "Grant's Physicians and Cancer," 508-09.

⁶⁶Steckler and Shedd believed, based primarily on the evidence provided by Dr. Douglas in his diary, that on October 22, 1884 Grant had—in modern parlance—a T1N1 squamous carcinoma of the right tonsillar pillar. *Ibid.*, 509, Figure 6 on 11.

⁶⁷*Ibid.*, 509.

Did Dr. Douglas misdiagnose Grant's throat lesion? Did the doctor believe the condition to be more benign than it actually was and therefore that surgery was unwarranted? No—to both questions. Douglas knew immediately upon first examination that the disease was, as he wrote, “serious, epithelial in character, and sometimes capable of being cured.”⁶⁸ (Epithelioma, today known as squamous cell carcinoma, was indeed Grant's final diagnosis.) If he thought the lesion benign, he would not have used such equivocal language to a personage of Grant's stature. Further, Douglas informed Mrs. Grant shortly thereafter that her husband's illness was “fatal.”⁶⁹

Did Dr. Douglas believe that the lesion, although cancerous, was not amenable to surgery? Again no. Douglas first examined Grant in October, 1884. Five months later, after considerable growth of the mass, he still deemed surgery possible.⁷⁰ If he had been uncertain about the feasibility of surgery, he would have called in a surgical consultant for another opinion—as he and Dr. Barker did months later.

Did Douglas believe that surgery was contraindicated because other underlying medical conditions made Grant a poor surgical risk? Surely he was enfeebled by his fall on the ice the previous Christmas Eve—especially since that fall compounded the aggravation of a leg lesion he first suffered in New Orleans during the Civil War.⁷¹ After the Christmas of 1883, he always walked with crutches or a cane. Otherwise, however, he seemed in good health. He was active and traveled to Dr. Douglas' office and elsewhere by public transportation, which was no more genteel in Grant's day than in ours. Julia Dent Grant, who carefully observed her husband daily,

⁶⁸Ibid.

⁶⁹Simon, *Julia Dent Grant*, 329.

⁷⁰The New York Times, "His Fatal Illness. The Progress of the Malady to Which He Succumbed.," *The New York Times*, 24 July 1885, 5:3.

⁷¹McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1157.

also commented that he was well. “My husband was healthy, temperate, strong,” she wrote shortly after Grant’s first visit to Douglas.⁷²

Did Dr. Douglas—like Grant—deny the seriousness of the General’s malady? This is unlikely, given the nature of his response to the General when Grant asked him during their first consultation if the growth was cancer.

Was Douglas’ failure to recommend surgery bad judgment—even malpractice? Not by the standards of his time. The medical and surgical consultants did not criticize his treatment plan.⁷³ Indeed, Grant’s other physicians went so far as to concur publicly with Douglas’ treatment plan.⁷⁴ In addition, the press—which continually challenged the consultant’s diagnosis when the General showed the slightest sign of improvement⁷⁵—did not condemn Douglas for avoiding surgery.

Was surgery appropriate treatment for the General in October, 1884? No and Yes. The date is the key. No, because surgery for such tumors at the time was discouraged by the best of authorities. Indeed, although surgery was the only well-accepted cure for cancer in the 1880s, it was usually deferred—often forever. Textbooks of the era decried surgical intervention as a cure for oral cancers.⁷⁶ Nevertheless, William S. McFeely, one of Grant’s biographers, wrote that a medical authority he consulted suggested “surgery in 1884 was sufficiently advanced so that a

⁷²Simon, *Julia Dent Grant*, 329.

⁷³Shrady, "Grant's Case," 121.

⁷⁴Ibid.

⁷⁵See, for example, *The New-York Times*, "Astonishing His Family: Gen. Grant Joining Them at the Lunch Table. Taking His Old Place and Eating with Relish--Continued Improvement Locally and Generally," *The New York Times*, 17 April 1885, 1:3. and "Gen. Grant Holds His Own: No Apparent Change in His Conditions. The General Appears at His Window--His Family Hopeful--What the Doctors Say of His Improvement," *The New York Times*, 19 April 1885, 9:1.

⁷⁶Morell Mackenzie, *A Manual of Diseases of the Throat and Nose Including the Pharynx, Larynx, Trachea, Oesophagus, Nasal Cavities, and Neck*, vol. 1 (London: J. & A. Churchill, 1880), 84.

carcinoma...of the throat could have been completely excised.”⁷⁷ As early as 1880, for example, Dr. Emil Kocher, a Swiss surgeon, had performed a radical excision of the tongue for cancer.⁷⁸ “Cures” from charlatans like William Avery Rockefeller abounded, but regular physicians acknowledged at the time that only surgery could assuage the disease.⁷⁹ Grant’s physicians apparently agreed, although the surgery they contemplated was for palliation, not cure. When the General took a turn for the worse in early 1885, Barker and Douglas consulted Drs. Shrady and Henry B. Sands, both surgeons. As late as March, 1885—by which time the cancer had grown larger than a plum and showed signs of invasion of the right neck—the surgeons believed that surgery was still “mechanically possible.”⁸⁰ But they did not operate because the tumor had grown to such a size that there was no assurance that even “radical” surgery could remove every last vestige of the cancer “without immediate risk to life by severe shock to a constitution already much enfeebled.”⁸¹ In short, it was too late for surgery. Why did Douglas not suggest surgery sooner? The answer may lie within the primary causes of traditional cancer—irritation and constitutionalism.

Felix qui potuit rerum cognoscere causas.⁸²

—Virgil

⁷⁷McFeely, *Grant*, 496. McFeely did not cite the historical source used for the medical opinion given by his consultant, Dr. Solomon Cohen.

⁷⁸H. S. J. Lee, ed. *Dates in Oncology*, Landmarks in Medicine Series (Pearl River, NY: The Parthenon Publishing Group Inc., 2000), 57.

⁷⁹Dr. Samuel D. Gross, chairman of the American Medical Association’s 1853 investigation into the surgical treatment of cancer, wrote that although “I have never had any confidence whatever in the curative agency of excision in genuine cancer of this [penis] or any other part of the body,” “a great majority of [surgeons] have always been, and still are, in favour of operation.” S. D. Gross, M. D., “On the Results of Surgical Operations in Malignant Diseases,” *Transactions of the American Medical Association* 6(1853): 143.

⁸⁰The New York Times, “His Fatal Illness,” 5:3.

⁸¹Ibid.

⁸²Happy is he who has been able to know the causes of things.

Causality is the most slippery of slopes, an endless conundrum of proof and speculation. It is not, however, a philosopher's idle fancy without consequences. Mankind incessantly seeks the causes of things and often finds them—true or not. Causal relations are important because they lead to theories that govern practices, and theories and practices—in the field of medicine—guide treatment. Such is the case today with cancer research under the sway of genomics and molecular biology, and such was the situation with theory and practice in General Grant's day.

Irritation

Dr. Douglas believed that “irritation” caused Grant's lesions⁸³—the most common “exciting” cause ascribed to cancer in the age of traditional cancer.⁸⁴ The nineteenth-century medical term ‘irritation’ meant much more than it does today. The present-day definition of ‘irritation’ includes notions of “soreness, roughness, or inflammation of a bodily part.”⁸⁵ Duration and context are not major components of today's ‘irritation.’ In contradistinction, nineteenth-century ‘irritation,’ as applied to cancer causation, included a significant element of chronicity—irritation of long standing—and a fertile soil in which irritation could induce cancer; i.e., a suitable constitution. Dr. Rudolph Virchow, the famous German pathologist and social activist of the nineteenth century who published three volumes on cancer a decade before General Grant's fatal illness,⁸⁶ vigorously promoted the idea that chronic irritation caused

⁸³The New York Times, "His Fatal Illness," 5:2.

⁸⁴Sciences The Encyclopedia Britannica: A Dictionary of Arts, and General Literature, *Cancer*, Ninth ed., The Encyclopedia Britannica: A Dictionary of Arts, Sciences, and General Literature (Edinburgh: Adam and Charles Black, 1876), 801.

⁸⁵Frederick C. Mish, ed. *Webster's Ninth New Collegiate Dictionary* (Springfield, MA: Merriam-Webster Inc., 1991), 640. *Stedman's Medical Dictionary* gives a similar definition. Stedman, *Stedman's*, 727.

⁸⁶Rudolf Virchow, *Die Krankhaften Geschwuelste. Dreissig Vorlesungen Gehalten Waehrend Des Wintersemesters 1862-1863 an Der Universitaet Zu Berlin* (Berlin 1863-1867).

cancer.⁸⁷ Irritation alone, however, was necessary but not sufficient to cause cancer. The cancer victim required a constitutional tendency to cancer—an internal proclivity to develop the disease if provoked by an external stimulus.

Smoking

Dr. Shrady acknowledged that the cause of the General's throat cancer was "conjectural," but then proceeded to embrace the dominant causal explanation of the day. It "starts from local irritation.... There must, however, aside from [irritation], be a latent tendency toward cancerous troubles which is more pronounced in some individuals than in others, otherwise we should be unable to explain why simple and continued irritation would induce the disease in one case and not in another."⁸⁸ What irritant caused Grant's cancer? Smoking, offered Shrady—eighty years before the Surgeon-General's report on the link between cancer and tobacco.⁸⁹ General Grant had been an inveterate cigar smoker since his conquest of Fort Donelson more than twenty-two years earlier.⁹⁰ Thereafter cigars habitually protruded from his mouth.⁹¹ "It is...quite probable,"

⁸⁷Daniel De Moulin, *A Short History of Breast Cancer* (Boston: Martinus Nijhoff Publishers, 1983), 68.

⁸⁸Shrady, "Grant's Case," 123.

⁸⁹It is important to realize that doctors and others made a causal connection between tobacco and cancer long before the 1950s and 1960s. Observational connections of cause and effect between tobacco and cancer date from at least the mid-seventeenth century when John Hill, a London apothecary, reported the association in his 1761 tract. See John Hill, *Cautions against the Immoderate Use of Snuff Founded on the Known Qualities of the Tobacco Plant; ... And Enforced by Instances of Persons Who Have Perished Miserably of Diseases, Occasioned, ... By Its Use*. By Dr. J. Hill, (London: printed for R. Baldwin, and J. Jackson., 1761), <http://www.columbia.edu/cgi-bin/cul/resolve?clio5123161>. The best "scientific" studies that demonstrated the link, however, were not performed before the twentieth century. For a brief but interesting review of the history of smoking see Fredric N. Jackson and Rolf H. O. Holle, "Smoking: Perspectives 1985," *Primary Care* 12, no. 2 (1985).

⁹⁰Grant smoked "a dozen very large, strong cigars a day." Childs, *Recollections*, 42-43. The frequently drunken soldier smoked little until he was forty years old. The newspapers, he insisted, were to blame for his cigar habit. Horace Green, a Grant biographer, quoted the General later in Grant's life: "In the accounts given in the papers, I was represented as smoking a cigar in the midst of conflict [at Fort Donelson]; and many persons, thinking no doubt that tobacco was my chief solace, sent me boxes of the choicest brands from everywhere in the North. As many as 10,000 were received. I gave away all I could get rid of but having such a quantity on hand, I naturally smoked more than I would have under ordinary circumstances, and I have continued the habit ever since." Steckler and Shedd, "Grant's Physicians and Cancer," 511.

wrote Shrady, “that the irritation of smoking was the active cause of the cancer in General Grant’s case, or, at least, it is fair to presume that he would not have had the disease if his habit had not been carried to excess.”⁹²

Other physicians vehemently disagreed that the irritating cause of Grant’s throat cancer was cigar smoke. On November 8, 1884, Fordyce Barker called in Frank Abbott, M.D. to treat a neuralgia that the General had developed on the right side of his head. Dr. Abbott extracted all three of Grant’s right superior molars over the course of six days. He was certain that the poor dentition, not the smoking, was the instigator. The irritation caused by the abrasion of the tongue chafing against the rotten teeth, he determined, was as a major contributor to the tumor that by then had invaded the base of the right side of the tongue:

If we take into consideration the highly irritable condition of that region of his mouth, the extension of the inflammation into the vault and down that side of his throat, the rough and ragged surfaces of a broken tooth, and the tartar incrustations, against which the side of his tongue was almost constantly rubbing, I believe that I am quite justified in concluding that here may have been a factor, at least, in the localization of the painful disease from which the General is now suffering, instead of attributing it altogether to the habit of smoking, which seems to be the prevailing opinion, at least among the laity.⁹³

The editor of the *Independent Practitioner* was even more adamant that smoking was an unlikely cause of cancer. In an editorial published shortly after the General’s death, he pointedly referred to the popular link between Grant’s cigars and his cancer:

General Grant was a smoker, and every anti-tobacco crank in the country immediately jumps to the conclusion that the disease that is slowly but surely eating out the life of the most distinguished man of his age is the direct fruit of the cigar; whereas,

⁹¹See Artist unknown, "A Cartoonist's View of Grant as a Traveler," (Washington: Library of Congress, 1981). The illustration can also be found in McFeely, *Grant*, 452.

⁹²Shrady, "Grant's Case," 123.

⁹³Frank Abbott, "General Grant's Condition," *Independent Practitioner: A Monthly Journal devoted to Dental and Oral Science* 6(1885): 219.

aside from the fact that the smoker's mouth is seldom in a cleanly condition, tobacco probably had little or nothing do to [*sic*] with the origin of the tumor.⁹⁴

Alcohol

Grant's whiskey habit, interestingly, was not held to be a causative irritating factor. Today the association between alcohol, smoking, and throat cancer is well established.⁹⁵ Forces in the nineteenth century, however, conspired to conceal the danger. Was the General at risk, and why was the peril unseen? The General was well known for his imbibitions of spirits at a time when the per capita consumption of alcohol in Victorian America was lower even than that of today—and substantially lower than when Grant was in his youth.⁹⁶ In addition, Grant had been a substantial drinker for some time—long before the victory at Fort Donelson. However, his intake must have diminished thereafter because John Rawlins, the General's Chief of Staff during the Civil War, became the self-appointed “keeper of Grant's conscience” and succeeded in significantly curtailing his commander's drinking.⁹⁷ Rawlins had a personal incentive to keep his chief sober because his father had been a drunk who left the family in poverty. Thereafter Grant continued to drink alcohol to some extent, but just how much is not clear.⁹⁸ Regardless, the alcohol-induced injury to the lining of his mouth may have occurred in youth.

⁹⁴Editorial, “The Case of General Grant,” *ibid.*, 210.

⁹⁵National Institute of Dental Research, “Causes and Prevention.” Accessed at http://cancernet.nci.nih.gov/wyntk_pubs/oral.htm on May 23, 2001.

⁹⁶W. J. Rorabaugh, *The Alcoholic Republic: An American Tradition* (Oxford: Oxford University Press, 1979), See Chart 1.1, “Annual Consumption of Distilled Spirits per Capita, in U. S. Gallons,” 8; and Table A1.2, “Alcoholic Beverage Consumption, absolute alcohol for each beverage, per capita of drinking-age (15+) population, in U. S. gallons,” 233.

⁹⁷Steckler and Shedd, “Grant's Physicians and Cancer,” 511-12.

⁹⁸*Ibid.*, 511. Grant had alcohol as late as the month of his death—July, 1885—for he wrote to Dr. Douglas that alcohol was not having its usual effect on him. McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1114, 17.

Observational and epidemiological studies in the twentieth century established a strong link between alcohol and throat cancer—a connection almost as prevalent as the nineteenth-century association between tobacco and throat cancer.⁹⁹ It is surprising that the link between alcohol and throat cancer was not established earlier. But perhaps not that surprising. In the nineteenth century, alcohol, unlike cigars, had medicinal value. Alcohol gave elixirs their sweet taste and evoked a sense of well being. And, although “in the nineteenth century it was widely accepted that people drank because they were undisciplined, ungodly, or degenerate,” alcohol was also believed to have the virtue of relieving anxiety—a common focus of medical and lay attention during the deracinating years of the American industrial revolution at the close of the nineteenth century.¹⁰⁰ The people and the press may also have been reluctant to criticize their exalted hero for exhibiting the weakness of a common man.

It is a feature of many systems of thought, and not only primitive ones, that they possess a self-confirming character. Once their initial premises are accepted, no subsequent discovery will shake the believer's faith, for he can explain it away in terms of the existing system. Neither will his convictions be weakened by the failure of some accepted ritual to accomplish its desired end, for this too can be accounted for. Such systems of belief possess a resilience which makes them virtually immune to external argument.

—Keith Thomas, *Religion and the Decline of Magic*

The causal belief in the constitutional nature of Grant's throat cancer influenced Dr. Douglas' non-surgical treatment of the General. Indeed, constitutionalism argued against most “curative” treatments, for if the cancer was inherent to one's constitution, then how could one

⁹⁹See <http://www.nci.nih.gov>. The combination of the two major risk factors for squamous cell carcinoma of the throat—alcohol and tobacco—yields the highest probability known today for the development of oropharyngeal cancer. General Grant, of course, smoked cigars and drank whiskey for more than a score of years before the onset of his cancer symptoms.

¹⁰⁰Rorabaugh, *Alcoholic Republic*, 241. On the prevalence of anxiety in the last two decades of the nineteenth century, see S. Weir Mitchell, "Nervousness and Its Influence on Character," in *Doctor and Patient* (Philadelphia: J. B. Lippincott Company, 1888). The modern meaning of 'nervous' as a form of anxiety (previously the word was used in a 'sinewy' sense), Mitchell explained, was probably begun by Robert Whytte in 1765—at the beginning of the English industrial revolution. As we shall see, many physicians, philosophers, and others felt that cancer was a disease of 'civilization'—i.e., a consequence of the industrial revolution. *Ibid.*, 115.

eradicate the disease without eliminating the diseased? The cigar smoke—the exciting cause—had already done its dirty work. The cancer was there. Stop smoking cigars and the cancer would remain. Excise the cancer and it would reappear elsewhere. Surgical experience for centuries had borne out the validity of this theory.¹⁰¹ Constitutionalism implied that cancer was one disease, not many. It involved the entire body, not just one organ or region. How else could the rate of recurrence after surgery be so high? Why else would cancer spread to parts of the body far from the original cancer?¹⁰² Surgeons averred that operations to remove cancers might actually increase the probability of reappearance.¹⁰³ The constitutional theory of cancer causation predicted that surgical treatment of Grant’s cancer was futile, and that the disease was incurable. Dr. Samuel Gross summarized the prevalent position of the medical profession toward cancer surgery a few years earlier in his ground-breaking monograph when he stated that “nature never cures a disease of this kind; nor can this be effected by any medicine or internal remedies known to the profession.”¹⁰⁴ Surgery played no role in this *mentalité*. “I have...no confidence in any operation for malignant diseases,” he wrote.¹⁰⁵ Dr. Douglas followed the precepts and practices of his time. Adam Badeau, the General’s military secretary, summed up the mood of physician and patient alike after Grant’s first visit to Dr. Douglas in October, 1884:

¹⁰¹Dr. Samuel D. Gross’ 1853 review of the surgical cancer literature is an excellent source to support these observations. Gross, "On the Results of Surgical Operations in Malignant Diseases," 153-313.

¹⁰²The concept that cancer disseminated to different parts of the body from a single locus of disease (metastasis) was suggested by Recamier in 1829, but was relatively slow to catch on—especially in the United States. Joseph Claude Recamier, *Recherches Sur Le Traitement Du Cancer, Par La Compression Methodique Simple Ou Combinee, Et Sur L'histoire Generale De La Meme Maladie* (1829), volume II, 110 (lines 3-7).

¹⁰³Gross, "On the Results of Surgical Operations in Malignant Diseases," passim.

¹⁰⁴*Ibid.*, 157.

¹⁰⁵*Ibid.*, 161.

“There was disquietude and even alarm, —the terrible word cancer was itself almost a knell.”¹⁰⁶

It was to be a long and trying course for the General, his family, and the nation—fostered to no small extent by the prevailing theories of the day.

PREVARICATION

(October, 1884-February, 1885)

General Grant’s realization in the fall of 1884 that denial was not an effective method to deal with his worsening pains led to prevarication and equivocation by himself, his family, and his physicians. Keeping such things private was the order of the day for men like Grant and women like Mrs. Astor, for the stigma of cancer ran deep.¹⁰⁷ Many victims of cancer in the nineteenth century concealed their illness, but the General—seemingly always, albeit reluctantly, in the public spotlight—could not. His inability to keep the nature of his ailment secret had significant repercussions for Grant and those around him in the short term and, over the next several years, for the making of modern cancer.

The General did not accept the seriousness of his condition until after lengthy discussions with Drs. Barker and Douglas in late October 1884. Mrs. Grant recalled in her *Personal Memoirs* that “it was then he realized for the first time that his malady was of a serious nature.”¹⁰⁸ No longer could he deny his symptoms and their significance to himself. However, even after he was convinced as to the life-threatening nature of his throat trouble he continued to deceive his wife and family from the truth. “The General did not inform me of the physicians’

¹⁰⁶Badeau, *Grant in Peace*, 427.

¹⁰⁷Dr. Fordyce Barker, who was also Mrs. Astor’s physician, did not include the diagnosis of cancer on her death certificate (City of New York Death Certificate #9627; signed 12 December 1887), although there is good evidence that her death was caused by end-stage uterine cancer. (See Chapter 2 and, in particular, *The New York Tribune*, 29 April 1884.) Not listing a diagnosis of cancer on a death certificate was commonplace in the nineteenth century.

¹⁰⁸Simon, *Julia Dent Grant*, 329.

opinion of his trouble for some time after he had learned it,” confessed Mrs. Grant.¹⁰⁹ Julia was distraught. She knew from her husband’s behavior that something was terribly wrong. Nevertheless, confronting him would be useless. He had already denied the obvious. Therefore, Mrs. Grant and her eldest son, Col. Fred Grant, rode to Dr. Douglas’ office to question the physician directly. “I then went myself to the specialist and learned the dreadful truth but still could not believe the malady was a fatal one. I asked again and again if it were not curable and was answered that there had been instances when it had been cured. Then hope returned to me.”¹¹⁰

Dr. Douglas misled Mrs. Grant. He knew that an accurate diagnosis of epithelioma had no chance for spontaneous regression. Instead, he compassionately told her what she most wished to hear. It worked. “Down in my heart,” wrote Julia, “I could not believe that God in his wisdom and mercy would take this great, wise, good man from us, to whom he was so necessary and so beloved. It could not be, and I surely thought he would recover.”¹¹¹

The astute and politic Douglas also slyly laid the seeds of troubles to come. He told them that the General had “a cancerous tendency” that required “daily prophylaxis...to keep the affliction from smelling offensively as it grew.”¹¹² Douglas had already decided against surgery—if he ever seriously considered it—for surgery could have been performed for palliation to keep the size, smell, and ulceration of the cancer to a minimum as well as for cure. In addition, Douglas informed them that Grant’s constitution required fortification “to enable

¹⁰⁹Ibid.

¹¹⁰Ibid.

¹¹¹Ibid.

¹¹²Goldhurst, *Many Are the Hearts*, 144.

him to resist the ravages of the disease.”¹¹³ Finally, the specialist predicted that “the disease would have a long course, and that during it the General would alternate between despair and hope.”¹¹⁴ Mrs. Grant deceived herself—perhaps purposely, perhaps wisely—when she chose to embrace hope rather than despair. She continued to fool herself and remained in denial to the end. “Even at the moment which everyone else thought would prove his last,” wrote Adam Badeau, “she could not realize the imminence of the end.”¹¹⁵ No one—least of all Mrs. Grant or the General—would have benefited from her acceptance of the ultimate truth. She had every faith that her husband, who had waged and won many battles, would again be victorious. She prayed vigorously for his recuperation.

Misleading Symptomatic Improvement

Recover he did—for the first few weeks. Day after day, from late October to late November when the weather turned colder, General Grant, venerated hero of the Civil War and eighteenth President of the United States, traveled on the public street-car two miles from his home to Douglas’ office for local throat applications.¹¹⁶ The treatments appeared to ameliorate Grant’s symptoms, for the General felt better and improved steadily.¹¹⁷ Some days after Thanksgiving, Grant decided he was well enough to discontinue visits to Dr. Douglas.¹¹⁸ The specialist, unfortunately, did not know whether his solutions were affecting the symptoms or the disease, for cancer symptoms in the early stages can be fickle. They often wax and wane in the

¹¹³Ibid.

¹¹⁴Ibid.

¹¹⁵Adam Badeau called Mrs. Grant’s behavior “a mystery.” Ibid.

¹¹⁶Badeau, *Grant in Peace*, 427.

¹¹⁷McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1159.

¹¹⁸Ibid.

beginning, even as the disease follows its natural course of destruction. Cancer can be its own prevaricator.

As the weeks passed, Grant realized that cigars were his enemy. Smoking irritated his throat and exacerbated his symptoms. He tried to help himself by eliminating them. Breaking this habit of at least twenty-two years was arduous. He had long ago become addicted to cigars. After Fort Donelson, he smoked “stronger and stronger brands” of twelve to fifteen cigars daily to get the same “relaxing and thought-provoking effects.”¹¹⁹ In the summer of 1884, he noted with some surprise that smoking cigars irritated his throat. He later informed Childs that “he was smoking fewer and milder cigars”—sometimes only three each day.¹²⁰ Grant’s doctors, divided on whether the cigars caused his cancer, agreed that throat irritation suggested that the General should decrease his smoking. Their advice to Grant is curious. Barker and his consultants suggested that he restrict his cigar consumption to “the first half of three cigars a day” because they “thought it probable that it was the nicotine which accumulated in the last half of the cigar that produced the irritation.”¹²¹ Nevertheless, the General’s body told him otherwise. Grant took matters into his own hands. First half or last, the cigars had to go. On November 20, 1884, while visiting friends at a horse farm in Goshen, New York, he astonished his company by stating, “Gentlemen, this is the last cigar I will ever smoke.”¹²² True to his words, he never smoked again. His throat felt better after abstaining from cigars. He was no longer in denial and the suggested compromises of his doctors, well-intentioned as they may have been, were of no more concern to him than if they had made the ridiculous suggestion that his soldiers

¹¹⁹Shrady, *Grant's Last Days*, 15-16.

¹²⁰Childs, *Recollections*, 42-43.

¹²¹The New-York Times, "Gen. Grant in Better Health," *The New York Times*, 12 January 1885, 2:2.

¹²²Goldhurst, *Many Are the Hearts*, 149.

compromise their fighting to achieve only partial subjugation of the enemy. To the General, victory on the battlefield or against cancer was the same. It was all or none.

Truth Revealed, Truth Dismissed

For most of 1884 only Grant, Drs. Barker, Douglas, and Abbott knew the General had cancer. This small group took Grant's closest friends and family into confidence at the end of the year. Then, as the gods would have it, a seemingly trivial event occurred that brought the General's condition to the attention of the world. In early December, Grant developed an upper respiratory infection and his throat pain recurred with a vengeance.¹²³ Indeed, he could no longer swallow solid foods and relied for sustenance on "liquid food."¹²⁴ His symptoms compelled him to renege on a speaking engagement that he had scheduled with E. F. Beale, a man he hardly knew. The General—in his inimitably honest fashion—naively penned a note to Beale that persistent pain in his throat prevented him from fulfilling his promised appearance. Beale thanked Grant by transmitting the note to a newspaper reporter who publicized Grant's travail.¹²⁵ The secret was out that something was terribly wrong with the General's health—or so they thought—but for the ingenuity and equivocation of Grant's doctors. Grant learned his lesson from the Beale disclosure. Thereafter he avoided reporters and communicated with the outside world only through his physicians. They spun his story for the press.

Long before the Beale disclosure General Grant was news: local, national, and international. The focus on celebrity was no less then than now. Only the professions of the luminaries were different. The media, which at that time consisted primarily of legions of

¹²³Badeau, *Grant in Peace*, 427.

¹²⁴*Ibid.*

¹²⁵McFeely, *Grant*, 502.

newspapers and other periodicals,¹²⁶ suspected before December that the General had “cancer of the mouth.”¹²⁷ However, they had no proof. Drs. Barker and Douglas refused to confirm the rumors. Beale’s leak appeared to be *prima facie* evidence that they were true. Nevertheless, Grant’s physicians again denied what they knew so well. The General’s note to Beale broke in a Philadelphia newspaper in early January, 1885.¹²⁸ The press confronted Barker and Douglas and again they prevaricated.

Cover-up—1885 Style

Grant’s physicians neither lied nor completely told the truth. Instead, they sought to deceive and mislead. Initially they succeeded. In early January, for example, *The New-York Times*, a newspaper that the General came to loathe,¹²⁹ interviewed both Fordyce Barker and John H. Douglas about Grant’s health.¹³⁰ Dr. Barker admitted that the General had had mouth pain, but asserted that its cause was a “swelling.”¹³¹ A bad tooth, he continued, probably led to the swelling. Finally, he concluded, Grant’s “excessive” cigar habit exacerbated the problem. Barker offered nothing about cancer, so the insistent reporter asked whether smoking caused cancer of the tongue. Barker, again protecting his patient with half-truths, proceeded to educate the newspaperman in the contemporary knowledge of cancer. Yes, Barker claimed, “cancer of

¹²⁶In the 1880s, New York City alone had dozens of newspapers. Some, like Joseph Pulitzer’s *World* had two editions daily and on Sunday. Kenneth T. Jackson, ed. *The Encyclopedia of New York City* (New Haven: Yale University Press, 1995), 813.

¹²⁷The New-York Times, "Gen. Grant in Better Health," 2:2.

¹²⁸Goldhurst, *Many Are the Hearts*, 150.

¹²⁹McFeely and McFeely, "Ulysses S. Grant: Memoirs and Selected Letters," 1113. Grant was not sanguine about newspapers in general. Nelson, "The Victory of U. S. Grant": 435.

¹³⁰"General Grant in Better Health," *The New-York Times*, 2:2.

¹³¹*Ibid.*

the tongue has originated from smoking strong tobacco in clay pipes.”¹³² Grant, however, was not a clay pipe smoker. Nevertheless, Barker continued that clay pipes “may have been a local cause of inducing (cancer of the tongue) where a constitutional predisposition to the disease existed.”¹³³ End of interview.

Strictly speaking, Barker had not lied. Grant did indeed have a swelling in his mouth. The rotten teeth did scrape the tongue when they rubbed against it. Cigar smoke does irritate an inflamed throat. For years, physicians knew that clay pipe smokers suffered an increased incidence of mouth cancer. Moreover, doctors and laymen alike knew that irritation alone without a susceptible constitution was not enough to induce cancer. Nevertheless, Barker did not tell the truth when asked if the General had cancer. Barker was fortunate that common sense supported his equivocation. The newspapermen had only to spy the General from their street-side vantage point to know that he was up, walking about, and received numerous visitors. They kept Grant and his East Side townhouse under constant surveillance. From all that they knew and believed, the General did not fit the picture of traditional cancer.

The newspapermen also queried Dr. Douglas about Grant’s medical condition. The rumor was that the General had cancer of the tongue. The “*Times* man,” as the General called the reporter for the New York newspaper, asked the physician bluntly if Grant had cancer of the tongue. Douglas answered straightforwardly that “Gen. Grant has not cancer of the tongue.”¹³⁴ Again, denial and half-truths. Grant’s cancer was originally cancer of the throat, not the tongue. Douglas had noted that the growth began near the right tonsil. Nevertheless, by December, 1884

¹³²McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1113.

¹³³*Ibid.*

¹³⁴The New-York Times, "Gen. Grant in Better Health," 2:2.

it was clear that the disease also involved the tongue.¹³⁵ Douglas had been treating his patient for secondary ulcerations of the tongue—perhaps caused by regional spread of the cancer—for weeks. Precisely speaking, however, Grant’s condition was not cancer of the tongue. It was an epithelioma of the right tonsillar pillar. Too bad the reporter did not ask about that.

Thus, the physicians protected their patient’s privacy. General Grant similarly struggled to protect his wife and family from the consequences of his illness, but he could not hide his symptoms from their everyday proximal gaze. Dr. Douglas initially sought to protect Grant when he equivocated about the presence of cancer. Why all the efforts at “protection” through equivocation and prevarication? Such behavior is present in a much less guarded form today,¹³⁶ but it began with traditional cancer. Little could be gained through openness and honesty. Cancer, everyone knew, was an incurable disease. It fostered pain, ulcerations, and masses. It bred stench, destruction, and corruption of the body. In short, it was an affront to Victorian sensibilities. No wonder people deemed cancer punishment for sin earlier in the nineteenth century—especially during the Second Great Awakening and the religious revivals that followed. No wonder physicians and laymen alike believed that there had to be some intrinsic physical contribution by the victim—his or her constitution—to the genesis of the disease. A diagnosis of cancer carried a burden much heavier than just any disease. Grant, his family, and his doctors knew this. The moral turpitude of equivocation and prevarication was a small price to pay to conceal the General’s true disease from the public.

Recrudescence

¹³⁵The New York Times, "His Fatal Illness. The Progress of the Malady to Which He Succumbed.," *ibid.*, 24 July, 5:2.

¹³⁶Kudos in this effort go to the courageous publicization of breast cancer by Betty Ford in the 1970s, colon cancer by President Reagan in 1984, the recent spate of prostate cancer announcements by politicians, and numerous others. It is also much harder to keep such knowledge secret today. Ironically, the new federal “medical privacy” laws may actually open more personal medical records to public scrutiny.

General Grant returned to Dr. Douglas in December when the respiratory infection brought back his throat pain. From that time on he was continually under the throat doctor's care. Cocaine, which had only recently been introduced into the United States,¹³⁷ was the balm used to assuage the vicious pains the General suffered in his throat, neck, and the side of his head.¹³⁸ The severity of Grant's clinical symptoms fluctuated greatly over the next two months. His sometimes-healthy appearance allowed his doctors to claim with visible evidence that he did not have cancer. The press was kept at bay.

On January 13, 1885, for example, the General felt better. He was able to eat, drink, and speak without pain for the first time in weeks. Nevertheless, Dr. Douglas' examination that day revealed progression of the cancer.¹³⁹ The symptomatic improvement temporarily dissuaded the press from pursuing the morbid truth. Grant took advantage of the welcomed respite to work steadily on his memoirs. He kept very much to himself on the second floor of the New York townhouse.¹⁴⁰ Rarely did he receive the many visitors who called at the townhouse, especially when in the throes of pain. At times, he would not even join his family at dinner. His inability to chew and swallow without pain embarrassed him. Worse, he dreaded the ever-present possibility of regurgitation of food through his nose.¹⁴¹ Consequently, the General subsisted

¹³⁷David Musto, "The First Cocaine Epidemic," in *New York Academy of Medicine Lecture Series* (New York NY1999). Dr. Musto noted that cocaine was first used as a local anesthetic in the United States in 1884.

¹³⁸General Grant usually received muriate of cocaine, the chloride form of the painkiller.

¹³⁹The New-York Times, "Sinking into the Grave: Gen. Grant's Friends Give up Hope," *The New York Times*, March 1 1885, 2:3. The clinical correlation between symptoms and signs in the first stages of cancer may be poor. This apparent contradiction did not fluster Grant's doctors, but the press could not understand that cancer symptoms may seem to improve early in the clinical course of the disease even though the pathology worsened.

¹⁴⁰McFeely, *Grant*, 499.

¹⁴¹Shrady, "Grant's Case," 123.

primarily on dairy-based liquids for the last six months of his life.¹⁴² Without surgery, there was little active intervention the family, friends, or doctors could do other than protect him from the rapacious inquisitiveness of the hounding press. Prevarication and equivocation were the order of the day.

The General's inconstant symptoms also fooled the medical press. Dr. George F. Shrady, founder and editor of *The Medical Record*, announced boldly to a confounded nationwide medical and lay audience in the February 21, 1885 edition of his weekly medical magazine that Grant assuredly did not have cancer—if he ever did have the disease. “We are gratified to learn from his attending physician that all these signs of epithelioma have passed away, that the ulcerated surfaces have healed, and the adjoining tissues have regained their natural suppleness.”¹⁴³ The medical diagnosis passed along to Shrady by Fordyce Barker and J. H. Douglas was “chronic superficial inflammation of the tongue.”¹⁴⁴ No microscope evidence was offered or sought to confirm or refute the diagnosis—another major aspect of traditional cancer. But times and the General's condition were changing. Indeed, microscopical findings on Grant's tumor were available when Shrady published his ill-informed, notorious editorial, but the surgeon, not yet a member of the General's team of consultants, did not know it. Nevertheless, the microscopic findings ended the prevarication and equivocation into which the Grant household and medical staff felt coerced by the social problem of traditional cancer.

THE AGONY OF SUFFERING AND FEAR

(February-June 1885)

¹⁴²Ibid.

¹⁴³Editorial and George F. Shrady, M.D., Editor, "General Grant's Condition," *The Medical Record* 27(1885): 213. *The Medical Record* had weekly updates on the General's medical status from February-July, 1885.

¹⁴⁴Ibid.

General Grant took a turn for the worse on February 17 from which he never fully recovered.¹⁴⁵ He caught “a severe cold” during that time of deepest winter and found that his symptoms of pain on swallowing, regurgitation, and loss of appetite all worsened.¹⁴⁶ Drs. Barker and Douglas were alarmed and became “anxious to make a more satisfactory investigation of the nature of the disease than was possible by examining Gen. Grant’s mouth.”¹⁴⁷ Not only had the gross appearance of the throat mass and its invasiveness become more difficult to interpret, but the General also developed increasing pain when struggling to open his mouth for the physicians’ ever-more-frequent probes. In short, the doctors were confused and concerned, so they searched for some form of independent verification of their diagnosis. Barker and his consultants decided to use an old instrument, the microscope, for a new purpose—medical diagnostics. They were hardly the first, but gross clinical judgment marginalized the microscope when deciding the nature of the patient’s ailment. Before this critical period in the history of cancer, microscopic sections of pathologic tissue were primarily utilized in America to diagnose abstruse lesions or differentiate between benign and malignant tumors.

The next day, Dr. F. C. Riley sprayed the General’s throat with a four percent solution of hydrochlorate of cocaine to anesthetize the biopsy area. Then he excised a section of the tumor about the size of a “small pea.”¹⁴⁸ The doctor obtained the tissue section from the edge of an ulcer that had eroded into the site of the original mass at the back of the throat on the right side.

¹⁴⁵The New York Times, "His Fatal Illness," 5:2-3.

¹⁴⁶Ibid., 5:2.

¹⁴⁷Ibid., 5:3.

¹⁴⁸George R. Elliott, "The Microscopical Examination of Specimens Removed from General Grant's Throat," *The Medical Record* 27(1885): 290.

The objective was to perform a “microscopical examination.”¹⁴⁹ This was the first time the consultants sought a microscopic confirmation of the General’s clinical diagnosis. Dr. Douglas had diagnosed ‘epithelioma’ based on gross visual inspection four months earlier. Grant suffered his initial cancer symptoms eight months before. Such a period was an eternity in the life of the growth of a mature cancer. The average life expectancy with epithelioma was known at the time to be ten and a half to thirteen months, so by the standards of the day the biopsy was performed when the General was far along in the course of his cancer.¹⁵⁰

“Microscopical Examination”

On February 19, 1885, two days after Grant’s symptomatic relapse, Dr. George R. Elliott, an expert at microscopic pathology called in by Dr. Douglas, hardened the General’s biopsy specimen submitted by Dr. Riley for twenty-four hours in alcohol and then stained the thin sections cut from the excised tissue. Staining is a biochemical process. Tissues soaked in colored chemicals absorb the dyes and highlight the morphological contrast between different cells and stromal elements.¹⁵¹ Elliott’s conclusion gave Barker and Douglas a sense of relief but served only to create even more distress—if possible—for the General, his family, and his friends.

Dr. Elliott pondered long and hard over his microscopic diagnosis. Indeed, his introspective deliberations were fraught with angst. He was a firm believer in the value of the

¹⁴⁹The New-York Times, "Sinking into the Grave."

¹⁵⁰Quoted from the *Medical News* (Philadelphia), March 21, 1885 by "Chatting with a Friend: A Pleasure Which Gen. Grant Greatly Enjoys. A Long Talk with Mr. Edwards Pierre-Pont Yesterday--the Physicians Discussing a Surgical Operation," *The New York Times*, 20 March 1885.

¹⁵¹Elliott, "Microscopical Examination," 289-90. The thin sections were stained with “hæmatoxylon [*sic*], Bismarck brown, and hæmatoxylin and eosin.” Paul Ehrlich, the “father of modern chemotherapy,” in his youth (he was only thirty in 1884), combined his interest in chemistry and histology to discover many histologic staining techniques long before he invented his first major “magic bullet,” Salvarsan, on his six hundred and sixth experiment. Henry E. Sigerist, *The Great Doctors: A Biographical History of Medicine*, trans. Eden and Cedar Paul (Garden City, NY: Doubleday & Company, Inc., 1933; repr., 1958), 384-85.

microscope for medicine in general and medical diagnostics in particular. His viewpoint, however, was in the minority at the time.¹⁵² His concern was not so much his final diagnosis (he felt certain of that) but rather how to convince the medical establishment—and then, ideally, the public—of the merit of his findings. His first goal, he decided, must be accuracy. He was well aware of the importance of the case. After all, the stature of the patient, the eminence of Grant's physicians, and the tenuous, fledgling standing of the microscope in the realm of medical diagnosis assured him widespread publicity. Further, his belief in the usefulness of the microscope in medical diagnostics came at a time when most doctors considered the microscope more of a "toy" than a precision instrument of medical diagnosis.¹⁵³ He certainly did not wish to appear hesitant or confused because renowned clinicians had criticized the subjectivity of microscopical interpretations for decades.¹⁵⁴ After much thought, Elliott concluded in the most precise medical language of the day that "the more or less lobulated appearance of the epithelial mass; the actual existence of some 'cell-nests'; the great diversity in the shape of the cell elements; the marked evidences of epithelial proliferation, and the peculiar appearance of the stroma, warrant the diagnosis of epithelioma of the squamous variety."¹⁵⁵ Although Elliott found "marked uniformity" amongst the cellular elements—usually a sign of benignity—there was also "a tendency of the new cell-formation to burrow into the deeper parts of the underlying tissue."¹⁵⁶ Such invasiveness is characteristic of a malignant cancer, and that was his diagnosis.

¹⁵²Warner, "Popular Microscopy," 19.

¹⁵³Steckler and Shedd, "Grant's Physicians and Cancer," 510.

¹⁵⁴Deborah Jean Warner, "The Campaign for Medical Microscopy in Antebellum America," *Bulletin of the History of Medicine* 69(1995): 382.

¹⁵⁵Elliott, "Microscopical Examination," 290.

¹⁵⁶*Ibid.*

Nevertheless, given the stakes, Dr. Elliott felt the need for a higher order of certainty. Again, he reviewed the clinical history with an eye toward any details that could change or sustain his initial impression.¹⁵⁷ He felt the necessity, as he later wrote in his analysis of the microscopic investigation published in *The Medical Record*, to affirm to the medical community that he desired to exclude “all possibilities of error.”¹⁵⁸ To further bolster the accuracy of his diagnosis he did what any self-respecting specialist would do—he consulted another expert. Dr. T. E. Satherthwaite, a well-known pathologist, concurred with Elliott’s diagnosis.¹⁵⁹ In addition he asked Dr. Shrady, the very same physician who had been misled by Barker and Douglas only days before into publishing the errant information that Grant did not have cancer, to review the tissue sample under the microscope. Elliott refused to tell Shrady the name of the patient from whom the specimen had been obtained. Although not Elliott’s intention, this cruel game of medical mystery was often perpetrated upon medical microscopists during the 1880s in order to ridicule them, thereby demeaning the value of the microscope to medicine.¹⁶⁰ Elliott’s purpose, on the other hand, was to seek corroboration for his critical diagnosis, not to challenge and deride. Shrady, recent president of the New York Pathological Society¹⁶¹ and a plastic surgeon of local repute, examined the tissue under the microscope and spontaneously concluded that “this specimen comes from the throat and base of the tongue and is affected with cancer.”¹⁶² Elliott, seeking as much assurance as possible, asked Shrady if he was certain. “Perfectly sure,”

¹⁵⁷Ibid.

¹⁵⁸Ibid.

¹⁵⁹Ibid.

¹⁶⁰Francelia Butler, "General Grant's Fight against Cancer," *National Republic*, November 1953, 6.

¹⁶¹Shrady was President from 1883-1884. Shrady, *Grant's Last Days*, 4.

¹⁶²Goldhurst, *Many Are the Hearts*, 145.

responded Shrady, “this patient has a[n]...epithelioma.” Elliott then informed Shrady that “this patient is General Grant.” “Then General Grant is doomed,” replied Shrady.¹⁶³ The judgment was mournful for the General and those who loved and revered him, but Elliott received the validation he deeply desired. Finally, he declared to Drs. Barker and Douglas that the microscopic picture was “characteristic of that form of cancer known as the epithelioma.”¹⁶⁴

The future of microscopy in medicine hung on the accuracy and acceptance of Elliott’s diagnosis. How he wanted to prove the worth of the instrument! Elliott noted some of the problems with medical microscopy, but wanted all to know that “this case illustrates the peculiar value of the microscope as an aid in diagnosis, since without it a positive conclusion could not have been reached upon the exact nature of the disease.”¹⁶⁵ Not all would have agreed that the microscope provided the final word on the General’s diagnosis, but the instrument had triumphantly passed a crucial test. The burgeoning newspaper network immediately promulgated the histologic diagnosis of Grant’s cancer to every city and hamlet in the United States and around the world covering “Gen. Grant’s condition.”¹⁶⁶ The microscope had come of age.¹⁶⁷

“Formal Consultation”

¹⁶³Ibid.

¹⁶⁴Elliott, "Microscopical Examination," 290. In the 1970s, Drs. Robert M. Steckler and Donald P. Shedd reviewed Elliott’s line drawings of Grant’s microscopy from the March 14, 1885 issue of *The Medical Record*. They concluded that the illustrations “clearly illustrate what we recognize today as squamous carcinoma with keratin pearl formation.” Steckler and Shedd, "Grant's Physicians and Cancer," 510. Elliott’s microscopic diagnosis, according to these reviewers ninety years later, was correct.

¹⁶⁵Elliott, "Microscopical Examination," 290.

¹⁶⁶“Gen. Grant’s Condition” and variations thereon were the banner headlines frequently used by *The New-York Times* and other publications during the Spring and Summer of 1885.

¹⁶⁷In 1950, Dr. Elliott’s widow presented General Grant’s microscope slides to the Armed Forces Institute of Pathology. Butler, "Grant's Cancer," 6. I have found no published evidence that the slides have been re-examined recently.

The microscopic diagnosis vindicated Drs. Fordyce Barker and John H. Douglas. Nevertheless, they, like Dr. Elliott, felt the need for further confirmation of their diagnosis and, in particular, of their treatment. On February 19, 1885, the day that Elliott first examined the microscopical sections, they met in consultation with Dr. Thomas M. Markoe, soon (like Barker and Shrady) to be a consultant on the staff of the new Cancer Hospital that was being constructed on 106th Street, and Dr. Henry B. Sands, a renowned surgeon, to review the General's case and plan a course of action. All agreed that no change was necessary. "The diagnosis of epithelioma was...unanimously confirmed and the judiciously conservative treatment of Drs. Barker and Douglas was fully endorsed."¹⁶⁸ Grant was doomed, felled by the reluctance of his primary physicians to use or believe in the value of the microscope to achieve a precise diagnosis at an early stage of disease and the reticence of his surgeons to excise a local mass in an age of constitutionalism. Both are pervasive hallmarks of traditional cancer. "From the time of that consultation," wrote *The New-York Times*, "the certainty of Gen. Grant's death from the cancer was accepted by the doctors."¹⁶⁹

Solace in a Sea of Suffering

At the end of February, plans were made for the General's death. The pain in his mouth became more frequent and less amenable to relief by topical cocaine. He became more forlorn and isolated.¹⁷⁰ Eating was more of a problem than ever. Speech was labored—sometimes even impossible. Simply opening his mouth wide enough for the doctors' examinations and local treatments was torture.

¹⁶⁸Shrady, "Grant's Case," 121.

¹⁶⁹The New York Times, "His Fatal Illness," 5:3.

¹⁷⁰The New-York Times, "Chatting with a Friend: A Pleasure Which Gen. Grant Greatly Enjoys. A Long Talk with Mr. Edwards Pierre-Pont Yesterday--the Physicians Discussing a Surgical Operation," *ibid.*, 20 March, 5:1-2.

How does a man dying of cancer live? He chose that which gave him the most pleasure. Alone in the midst of his family, Grant worked on his memoirs days and nights with near frenzy, mustering all the remaining strength in his emaciating body to finish the corpus he believed would be his final and enduring legacy.¹⁷¹ “The General’s memoirs,” recalled Mrs. Grant, “occupied every leisure moment. He even wrote at night sometimes when sleep would not come to him.”¹⁷² The herculean task of writing became his most successful therapy in an otherwise nightmarish existence. In penning his personal memoirs, he found solace, money, and distraction—the sustainers of life he previously lacked and most desired.¹⁷³ “It was a happy thought that suggested that book”—“his labor of love” Julia called it—despite “his health gradually failing.”¹⁷⁴ The therapeutic nature of the memoirs derived from both ethereal catharsis and the worldly promise of royalties. For once he—and not those inaccurate and sometimes untrustworthy authors who sought to write for him¹⁷⁵—had the chance to recollect history as he saw it.

Samuel L. Clemens, who admired Grant at least from the time they became friends at a reunion of the Army of the Tennessee five years before, learned on February 21st that Grant was dying and reiterated his offer to publish the memoirs on the best terms for the General’s family.¹⁷⁶ No one expected Grant to live long enough to reap any monetary reward from his

¹⁷¹Grant 3rd, “Ulysses S. Grant,” 449-50.

¹⁷²Simon, *Julia Dent Grant*, 330.

¹⁷³*Ibid.*, 329.

¹⁷⁴*Ibid.*, 330.

¹⁷⁵I am here alluding to General Adam Badeau, Grant’s military secretary, with whom Grant had a major falling out over the writing of the *Memoirs*. Badeau later sued (and collected a settlement from) the Grant family for what the General had promised him. Pitkin, *The Captain Departs*, 37-43., admirably told the story of the two very different personalities.

¹⁷⁶McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1159.

efforts. George W. Childs, the Philadelphia publisher who had referred Grant to Dr. Da Costa in Long Branch when the General ate the peach of foreboding an eternity before, strongly urged Grant to accept Clemens' offer.¹⁷⁷ By March 2, the General and the savvy humorist struck a deal that eventually made the Grant family financially whole again.¹⁷⁸ The General felt relieved of a great burden and dove deeply into the writing of his memoirs, casting the symptoms of his cancer aside as best he could.

Newspaper Frenzy: Grant's Doom

The two major sources of evil for the General, the cancer and the press, would not be denied. Grant's pain and swallowing difficulties recurred throughout the last days of February and the first days of March.¹⁷⁹ The number of dignitaries and other visitors to the East Side townhouse increased dramatically, a sure sign that family and friends believed the end was near.¹⁸⁰ The General was increasingly confined to his library and bedroom on the second floor.¹⁸¹ Vague diagnoses and promises of impending improvement could no longer restrain the press, which kept vigil on the sidewalk, across the street, and sometimes from less respectable

¹⁷⁷McFeely, *Grant*, 504.

¹⁷⁸Ibid., 500-501. The popularity of General Grant's two-volume *Personal Memoirs* was enormous. Julia Dent Grant received \$450,000 from Charles L. Webster & Company, Clemens' publishing house. This was more than enough to repay William H. Vanderbilt and all their other creditors with plenty to spare. Clemens made more than \$100,000 on the publishing deal.

In a twist of fate, \$450,000 is also close to the amount of money that the Astors donated toward the construction of the New York Cancer Hospital. It is difficult to determine who did more for the making of modern cancer—the institution or the national hero.

¹⁷⁹The New York Times, "Gen. Grant's Condition—Cancer Threatens Death: Illness Reviewed," *The New York Times*, 1 March 1885, 2:3.

¹⁸⁰"The Patient in the Sick Room. His Bravery While Suffering and His Thoughtfulness for Others," *The New York Times*, 24 July 1885, 5:5.

¹⁸¹Times, "His Fatal Illness: The Progress of the Malady to Which He Succumbed," 5:3.

points of observation.¹⁸² Onlookers and the press needed only spy Grant in his second-floor window to know that the rosy reports of his return to health issued from the home were untrue. Crowds of newspapermen grew so large that frequently neighbors and friends summoned the New York City police to disperse them in order to allow vehicles to pass through the street and carriages to discharge visitors at the townhouse entrance.¹⁸³ “Reporters ‘covering the case,’” wrote Shrady in his spirited telling of “General Grant’s Last Days” twenty-three years after the General’s death, “were so constantly on guard in the street that it seemed impossible for anything of importance to occur in the house without their knowledge.”¹⁸⁴

The reporters established a “clearing-house” in the basement of a house on the east side of Madison Avenue just south of Sixty-sixth Street—around the corner from the Grant home. Newspapermen from the *Herald*, Pulitzer’s *World*, *The New-York Times*, the Associated Press, and other periodicals and agencies gathered there to share stories and relay their articles across the nation and around the globe.¹⁸⁵ A barricade of professional bowdlerization could no longer hide the secret of the General’s cancer. Once the diagnosis seemed as certain as it would ever be—based upon the old clinical assumptions and new microscopic findings—and once Grant’s condition required his confinement to the observable second-story rooms fronting East Sixty-sixth Street, the secret of the General’s cancer could no longer be protected, prevaricated, or equivocated. The “formal consultation” among Drs. Barker, Douglas, Markoe, and Sands in late February, when all concurred in the diagnosis of epithelioma and the hopeless prognosis,

¹⁸²Shrady, *Grant's Last Days*, 54.

¹⁸³Ibid., 61. Street congestion from masses of spectators continued until the General left the City in June. The New-York Times, "Gen. Grant Much Worse: Another Severe Attack Yesterday Morning. The End Thought to Be at Hand, but He Rallies Again--His Condition Hopeless.," *The New York Times*, 2 April 1885, 1:5.

¹⁸⁴Shrady, *Grant's Last Days*, 53.

¹⁸⁵Ibid.

signaled the end of any serious efforts on the part of Grant and his doctors to keep the cancer secret. Ulysses S. Grant himself decided to bring the truth to light. “The public,” admitted Shrady, “was officially informed of the grave and fatal character of his malady. From that time every symptom...was freely discussed” with the press.¹⁸⁶ He never wished to make his plight public, but he believed he had no choice. It was an act that required as much courage as any battle he fought during the Civil War, for even the Confederate army was more controllable and predictable than the press corps.

The General’s cancer became public knowledge on March 1, 1885. On that day, *The New-York Times* confirmed that Grant, after “weeks of conflicting press reports,” was dying of cancer.¹⁸⁷ From that time on General Grant and his cancer became even bigger news than before. No efforts were spared to obtain—by hook or crook—all the news fit to print, and then some. The “newspaper watch,” as one biographer called it, was relentless.¹⁸⁸ Reporters besieged Grant, his family, his visitors, household members, and the medical consultants with requests for information about his cancer. The recent memory of the death of President James Garfield exacerbated the problem. Only four years earlier, Charles Guiteau had assassinated Garfield. Misleading and contradictory bulletins dominated the news on the President’s condition for the two months Garfield lived thereafter. The press would not be so easily deceived so soon. The initial obfuscation of Grant’s true medical condition revived a fetid bitterness in the reporters and columnists who had lived and worked during the Garfield crisis.¹⁸⁹

¹⁸⁶ Ibid., 50.

¹⁸⁷The New-York Times, "Sinking into the Grave." The quotation based upon *The New-York Times* article is from McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1159. Also included in the *Times* article is a summary of Grant’s medical history from June, 1884 to that day.

¹⁸⁸Goldhurst, *Many Are the Hearts*.

¹⁸⁹Shrady, *Grant's Last Days*, 53.

Ironically, George F. Shrady and Fordyce Barker had also been Garfield physicians.¹⁹⁰ The press would not brook a repeat of the Garfield debacle—and neither would Shrady, Barker, and the other physicians. Shrady, of course, had a special incentive to provide accurate reports. He had himself recently suffered public humiliation at the hands of Grant’s consultants for printing misinformation engendered by the opprobrium of traditional cancer.¹⁹¹

General Grant and his physicians established a medical bulletin service to ensure accurate reports for the news media. Three “bulletin-boys” relayed information constantly from the Grant townhouse to, amongst others, “the Western Union telegraph and cable service, the Associated Press, and the United Press.”¹⁹² Bulletins were usually issued three, four, and five times a day. When the General took a turn for the worse, as he did during his spring of suffering in 1885, the consultants released public notices every hour or less.¹⁹³ Nevertheless, the bulletins were insufficient to satisfy the insatiable rapaciousness of the press for any and all news about the General and his cancer. Grant and his family rarely spoke directly to the press, but everyone around them did.

The General approved the official bulletins released by the physicians to the bulletin-boys, but he could not deny the endless stream of visitors their fleeting moment in the spotlight. Some enjoyed the attention they received when calling upon the Grant family. Congressmen, Civil War generals (from both North and South), and the rich and famous exited from their

¹⁹⁰Francelia Butler, "The Search for a Cure," in *Memorial Hospital Archives, Hayes Martin Collection: Record Group 500, Box 2, folder 42: Cancer therapy Publications 1782; 1822; 1942; 1944* (New York 1950), 2.

¹⁹¹George F. Shrady, ed., "Why the Medical Record Took Such a Favorable View of General Grant's Case.," *The Medical Record* 27(1885): 270.

¹⁹²Shrady, *Grant's Last Days*, 53.

¹⁹³The New-York Times, "Grant Much Worse; "Gen. Grant Much Worse: Sleeping Only Two Hours Saturday Night. Another Severe Coughing Spell Last Evening--Failing During the Last Week--a Talk with Dr. Newman.," *The New York Times*, 13 April 1885.

condolence calls at 3 East 66th Street to invariable buttonholing at curbside. The next day their utterances—no matter how trivial—appeared in the newspapers.¹⁹⁴ Some of the less celebrated sought to become more notable at the General’s expense. They noted the mania surrounding the Grant townhouse and used their wives to take advantage of it. Wallace Brown, self-proclaimed “specialist in the treatment of cancer,” came from northern Massachusetts to gratuitously treat the General with his “specific.” Dr. Barker inquired as to the chemical composition of the proprietary solution, but Brown refused to divulge its “secret.” The physicians sent him home without seeing Grant. Nevertheless, the ruckus he caused at the front door of the townhouse gave him instant fame. All the newspapers reported his story and he received free nationwide publicity.¹⁹⁵ Brazil, not to be outdone by the “cancer cure” Cundurango discovered near the Andes in Ecuador a decade earlier,¹⁹⁶ sent their own sure cure for the disease through the State Department. The General’s doctors would not permit such therapy to rival their treatments.¹⁹⁷ After a few months of this medicinal and media mayhem, Grant sent an exasperated note to Dr. Douglas claiming that the newspaper “is an advertising medium for quack medicines prepared by ignorant people.”¹⁹⁸

¹⁹⁴“A Sudden Morning Alarm: Drs. Shradly and Sands Summoned to Gen. Grant's Aid. The Rev. Dr. Newman, Ex-Senator Chaffee, and Gen. Badeau Also Sent for--a Sudden Change for the Worse," *The New York Times*, 7 April 1885, 1:1-2.

¹⁹⁵“Gen. Grant's Condition: The Continued Progress of the Disease," *The New York Times*, March 13 1885, 5:3.

¹⁹⁶J. W. Bright, M.D., *Cancer: Its Classification and Remedies* (Philadelphia: S. W. Butler, M.D., 1871), 183. “Cundurango” is an alternate spelling for this plant derivative that touched off a scandal that reached the highest echelons of government, including the Hon. Schuyler Colfax—President Grant’s Vice President.

¹⁹⁷The New-York Times, "Gen. Grant's Improvement. Taking a Short Walk and Showing Signs of Better Health," *The New York Times*, 22 April 1885, 4:6.

¹⁹⁸Nelson, "The Victory of U. S. Grant," 435.

Others did not seek celebration, but found it anyway—or, in rare cases, used it for the benefit of others. John Jacob Astor III and his wife Charlotte Augusta, whose generosity funded the initial construction of the New York Cancer Hospital, were visitors. Joseph W. Drexel, wealthy scion of the Philadelphia Drexels and first Treasurer of the Cancer Hospital, also paid his respects. Indeed, ties between the fledgling Cancer Hospital and the travail of General Grant were close.¹⁹⁹ The reporters did not miss this connection, and John E. Parsons, Astor's attorney and the first President of the New York Cancer Hospital, took advantage of the publicization of cancer to raise an endowment for the cancer institution.²⁰⁰

The tenacity of the press never ceased to amaze Grant's physicians. An extensive interview inevitably followed even the most routine visit by any of the General's several physicians. The "anxious interviewers," as Shrady called the newspapermen, filled their notebooks verbatim but then peppered their stories with as much fantasy as fact.²⁰¹ At times, the reporters sent "dummy patients" feigning Grant's symptoms to the private medical offices of the consultants. Their objective was to obtain inside information on the nature, progress, and prognosis of the disease. To the astonishment of the physician, the offhand remarks gleaned by

¹⁹⁹Pitkin, *The Captain Departs*, 58. Pitkin also noted that Drexel was one of two co-signatories to work with Grant a year earlier to raise money to pay for the pedestal of the Statue of Liberty. U. S. Grant, William M. Evarts, and Joseph W. Drexel, "Letter to George E. Jones, Esq.," in *The George E. Jones Papers, The New York Public Library* (New York 1884).

²⁰⁰John E. Parsons, "Report of the President, *Tenth Annual Report*," (New York: New York Cancer Hospital, 1894), 9. The Astors paid for the construction of the New York Cancer Hospital, but left the problem of an endowment to others. During the dark days of the 1890s, President Parsons entreated William Astor, the son of John Jacob III and Augusta, to continue his parents' generosity to the Hospital, but he refused. President John Parsons headed fundraising during his more than thirty years (1884-1915) as President of the New York Cancer Hospital.

²⁰¹Shrady, *Grant's Last Days*, 53.

the imposter during the office visit appeared in the newspaper the next day as a formal interview!²⁰²

Constant observation of Grant's second-floor windows from the public streetways was also insufficient to satisfy the voracious appetite of the press. Bribes to gain an advantage over the competition were commonplace. Subterfuge was accepted as a necessary cost of doing business. One newspaperman, for example, offered a Grant servant money in order to spy on the General from the yard behind the house rather than from the street in front.²⁰³ Another seduced a chambermaid in one of the townhouses across from the Grant residence in order to gain unfettered access to her room. Love? Passion? No, he desired a better view of the General's living quarters from the higher vantage point of the maid's upper-floor room.²⁰⁴ The General's case put cancer under the microscope—both literally and figuratively. In 1885, General Grant was news and the news was General Grant.

Oftentimes he regretted his decision to go public with his malady. Nevertheless, he knew that disclosure was inevitable. Once the physicians knew the microscopic findings, and once Barker invited Dr. Shrady, editor of *The Medical Record*, to become a Grant consultant, secrecy was impossible. Toward the end of his life, worn out, angry, and despondent from the objectionable media attention, he begged the press to leave him and his family alone. Near death, he singled out one newspaper in particular—perhaps the greatest offender—for condemnation. “I see the (*New-York Times*) man,” he wrote in a note to Dr. Douglas, “keeps up the character of his dispatches to the paper. They are quite as untrue as they would be if he

²⁰²Ibid., 53.

²⁰³Ibid., 54.

²⁰⁴Ibid., 54.

described me as getting better from day to day. I think he might spare my family at least from reading such stuff.”²⁰⁵

Congressional Saviors

In early March, during the depth of the General’s physical and emotional trials and tribulations with cancer and the press, one brief but shining moment lifted his spirits and temporarily eased his suffering. It was an act of Congress. Living in the faultfinding, antihero world of today, it is difficult to imagine the depth of awe and adoration the public held for General Grant. Honors, gifts—even houses—were bestowed upon him. His trip around the world just a few years earlier revealed that people around the world had an interest in the man.²⁰⁶ The shocking news in late February and early March that Grant was dying from cancer intensified the Union’s inestimable reverence for him. Leaders in the House and Senate, attuned, as always, to the buzz of the populace, revived a previously-failed bill that honored Grant as a retired general—with full pay. Opponents of the bill had decried the favoritism that it implied, but the news of Grant’s cancer, along with a Congressional ruse, silenced the naysayers.

Time was short, for the Republicans had lost the presidency and the new Democratic president was to take office at 12 noon on the fourth of March.²⁰⁷ Joseph E. Johnston, Confederate General and now Congressman, introduced the bill to create the highest rank in the military—General of the Army. However, in a political sleight of hand for which Congress is well known, the bill did not name Ulysses S. Grant to the post. Instead, the president was to

²⁰⁵Handwritten note from Ulysses S. Grant to Dr. John H. Douglas, June 30, 1885, P. M. McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1113.

²⁰⁶See, for example, McFeely, "Grant," 450. McFeely called the world-wide tour of Julia and Ulysses Grant “perhaps the grandest tour an American couple had ever made.”

²⁰⁷Grant, of course, had served as a Republican President. The Twentieth Amendment to the Constitution, which established January 20 as the day of presidential transition, was not adopted until 1933.

appoint the titleholder. The Senate passed the bill and rushed it to the House on the morning of March 4, where the Representatives approved it by acclamation.²⁰⁸ Outgoing Republican President Chester Arthur, in the last minutes of his administration, signed the bill into law and immediately named Grant as the new General of the Army. It was the last action of his presidency. At 11:54 A.M. on the morning of March 4, 1885, the Senate of the United States set aside all business and gave its Constitutional “Advice and Consent” to the Grant nomination “unanimously amid tumultuous applause.”²⁰⁹ Signing Grant’s commission as General of the Army fell to the new President. Indeed, it was the Democrat’s first official duty. He did so.

In a wry twist of fate, the man who presented the good news to the General in New York was George W. Childs, the same Long Branch friend who may have been the first to hear the reputed bad news from Philadelphia’s Dr. Da Costa after the painful peach episode. Grant was quiet, even stoical, upon hearing the news, but Julia Grant was exultant. “Hurrah,” she cried, “our old commander is back!”²¹⁰ Despite his outward calm, the honor quickened Grant’s pulse and gave him a short-lived respite from his cancer woes. Perhaps it even extended his life, for Samuel Clemens, who happened to be visiting that day, noted that the General was quite moved. “The effect upon him was like raising the dead.”²¹¹

Red-Clover, Cocaine, and Therapeutic Control

Grant’s health continued to deteriorate despite the psychological lift from the Congressional kudos and the well wishes that poured in from across the land as his travail became widely known. Nevertheless, the media frenzy was a two-edged sword that mostly cut

²⁰⁸Jean Edward Smith, *Grant* (New York: Simon & Schuster, 2001), 625.

²⁰⁹*Ibid.*

²¹⁰Pitkin, *The Captain Departs*, 30.

²¹¹*Ibid.*

deep into his sense of self and also aggravated his physical decline. Cancer and the press, however, were not the only enemies with which his body did battle. His medicines, though administered with good intentions and the best knowledge available at the time, contributed to his decline, as they did to many in the days of traditional cancer.

Many of the General's medicines were a consequence of worsening throat pain. Four percent cocaine, salt water, and other palliatives no longer assuaged his pain.²¹² Friends from around the world sought to aid him. Wallace Brown and the country of Brazil were hardly the only contributors. Grant received putative cancer therapies from seemingly everywhere.²¹³ The General and his family deferred therapeutic decisions to the more learned and experienced judgment of the consultants. Routinely the physicians rejected the outside suggestions.

In one particular instance, however, the family broke their custom and urged the physicians to administer red-clover.²¹⁴ Like many other natural nostrums of the time—akin to today's untested “complementary” and “alternative” therapies—it was thought to ameliorate cancer.²¹⁵ The doctors consented and gave the red-clover. Why did the consultants agree to prescribe red-clover when they rejected numerous therapies from Brazil, North America, and the far reaches of the Earth? The age of therapeutic nihilism—the twilight zone in the history of pharmacy between empty medicinal claims and efficacious ethical drugs that encompassed the belief that no medicine was better than a medicine of uncertain value—came of age in the last

²¹²Shrady, "Grant's Case," 123.

²¹³The advice Grant received transcended medications. “Letters reach him from all over the country with suggestions for help in his disease,” the Rev. Dr. Newman related to *The New-York Times*, “but he pays no attention to them. They all go to the doctor.” *The New-York Times*, "Gen. Grant's Suffering. Dr. Douglas Summoned to Him Early This Morning.," *The New York Times*, 29 March 1885, 2:3.

²¹⁴Butler, "Grant's Cancer," 7. Red clover is a phytoestrogen—plant compounds that the digestive tract converts into estrogens. The hyphen in red-clover commonly applied in the nineteenth century is no longer used.

²¹⁵*Ibid.*

two decades of the nineteenth century.²¹⁶ Proponents believed that any therapy, red-clover included, should at the very least not injure the patient. Red-clover suffered no history of therapeutic iniquity. The consultants gave the General a trial of several weeks. The only discernible result was a mild laxative effect.²¹⁷ No adverse reactions were noted.²¹⁸ Grant made few specific therapeutic requests of his doctors. The patient and the family left the physicians almost completely on their own to select medications as they saw fit. Red-clover seemed a small price to pay for therapeutic hegemony. The doctors approved it because, as Dr. Shrady testified, they deemed it “the least harmful of medicines of its sort for continuous administration.”²¹⁹ Red-clover appeared to fulfill the physician’s mantra of therapeutic nihilism—above all, do no harm.

Cocaine initially relieved Grant’s pain but later bedeviled him. The narcotic was the mainstay of the therapeutic armamentarium used by Dr. Douglas and the other consultants, but its addictive properties were largely unknown to them. It required no special proponent to champion its use, for the General’s major symptom, at least in the earlier stages, was localized pain. In 1885, cocaine was a wonder drug touted for such affliction.

The treatment of pain was one of the great triumphs of nineteenth-century science and medicine. As the case study of Fanny Burney intimated,²²⁰ alcohol was the most common

²¹⁶Lewis Thomas, *The Youngest Science: Notes of a Medicine-Watcher* (New York: The Viking Press, 1983), 19-20.

²¹⁷Shrady, "Grant's Case," 123.

²¹⁸Red clover (*Trifolium pratense*) may have actually stimulated General Grant’s cancer growth. Phytoestrogens may have both estrogenic (feminizing) and antiestrogenic effects. One recent oncology study revealed that a similar phytoestrogen increased breast cell proliferation. It is unclear whether red clover may have further stimulated the growth of Grant’s squamous cell carcinoma of the throat. Although Dr. Shrady noted that red clover was administered “continuous”ly, the dosage used on Grant is unknown—a frequent problem with nineteenth-century drugs in the pre-standardization era that was part of the age of traditional cancer. The Medical Letter, "Phytoestrogens," *The Medical Letter On Drugs and Therapeutics* 42, no. 1072 (2000): 17-18.

²¹⁹Shrady, "Grant's Case," 123.

²²⁰Dissertation Chapter 1, 11-13.

analgesic at the beginning of the century. Morphine was isolated from opium during the first decade of the 1800s and at first analysis appeared to be a gift from the gods.²²¹ By the 1880s, however, in yet another example of high hopes dashed by experience, those who had originally reveled in its awe-inspiring properties learned the horrors of its addictive tendencies. Many attempted without success to discover treatments for morphine addiction. But it was not until 1884 that Karl Koller, working at the General Hospital in Vienna with another young Austrian physician by the name of Sigmund Freud, discovered that the application of the crystalline extract of the leaf of the Peruvian coca plant—cocaine—made the eye of a frog oblivious to pain.²²² The expanding medical news networks of the day quickly promulgated Koller and Freud’s findings. Within a year this new miracle drug had been used as a local anesthetic on thousands of patients in Europe and America,²²³ thus allowing surgeons and others to bypass the twin dangers of respiratory and circulatory collapse not infrequently associated with general anesthetics like ether and chloroform.

New as it was, cocaine appeared the ideal treatment for the General’s throat pains. At first, they responded well to the topical solution. Grant’s own analysis of “the question of the use of cocain [*sic*]” is memorable for its textbook-like description:

Taken properly it gives a wonderfull [*sic*] amount of relief from pain. Gradually the parts near those where the medicine is applied become numb and partially paralyzed [*sic*]. The feeling is unpleasant but not painful. Without the use of it the parts not effected with disease are pliable but of no use because their exercise moves the diseased parts and produces pain.²²⁴

²²¹Indeed, the name ‘morphine’ derives from Morpheus, the Greek god of dreams.

²²²John Walton, Paul B. Beeson, and Ronald Bodley Scott, eds., *The Oxford Companion to Medicine*, 2 vols., vol. 1 (Oxford: Oxford University Press, 1986; reprint, Gryphon Editions, Inc., 1988), 48.

²²³*Ibid.*, 677.

²²⁴McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1120.

As the months passed, however, the usual applications no longer mitigated the lancinating pains. “Cocaine,” penned the dolorous Grant to his physician in late June 1885, “ceases to give the relief it did.”²²⁵ Grant had become tolerant to “the Peruvian exhilarator.”²²⁶ Indeed, he probably knew that he was on the road to addiction. By early July, he confessed that “I feel the want of [cocaine] very much.”²²⁷ The old warrior must have witnessed addiction to the older drug morphine more often than he wished to recount. The painful war wounds of tens of thousands of soldiers felled during the War Between the States—the amputated limbs, the shattered bones, the swollen infections heralded by “laudable pus”—were treated with morphine.²²⁸ The General knew that the only remedy for such tolerance and addiction was withdrawal. “If its use can be curtailed,” he confided to Dr. Douglas, “I hope it will soon have its effect again.”²²⁹ The consultants only temporarily diminished the drug dose. Morphine was used on a regular basis to calm the suffering patient and allow short-lived respites from the days—and especially nights—of suffering.²³⁰ Alcohol was added as a stimulant and adjunct painkiller. Its effects, however, after decades of tolerance developed from Grant’s hard liquor consumption, were insufficient to quell the escalating cancer pains.

The physicians controlled the medications. The consultants considered the General’s comments, but made drug decisions based upon their perceptions and experience. The goal of therapy, under the rubric of palliation, was to keep Grant as comfortable as possible. The clarity

²²⁵Grant 3rd, “Ulysses S. Grant,” 446.

²²⁶McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1112.

²²⁷Grant 3rd, “Ulysses S. Grant,” 447.

²²⁸Jane Stuart Woolsey, *Hospital Days: Reminiscence of a Civil War Nurse* (Edinburgh Press, 1868; repr., 1996), 55.

²²⁹Grant 3rd, “Ulysses S. Grant,” 446.

²³⁰Shrady, *Grant's Last Days*, 67.

of the General's mind, as judged by his ability to concentrate on his memoirs, was used as the measure of the upper limit of the narcotic dose. The balance between overdose and underdose of cocaine was minded well and, as a result of the magnification and global dissemination of news of the General and his cancer, unknowingly served to spread the initially unrecognized evil of the drug throughout the western world.²³¹ Cocaine, new and hopeful yet inadequate and already intimating danger, was another example of good intentions gone awry. By the end of his illness, the analgesics long administered and controlled by the consultants were virtually ineffective.²³² The popularity of the General and the publicization of his cancer and its treatments inadvertently brought both cancer and cocaine into the modern era.

Necessary Deliberations

On March 8, symptoms worsened despite red-clover, cocaine, and morphine. The physicians undertook yet another re-examination of the problematic microscopical slides.²³³ Grant's unexpectedly rapid downward clinical course in late February and early March provoked Drs. Barker, Douglas, and Sands to again question their clinical judgment and the histologic interpretation. The General officially consulted George F. Shrady, M. D. for the first time that day due to his expertise in microscopic pathology. From then on he devoted himself to Grant's case and claimed that he and the General became quite close.²³⁴ The consultants, swollen in number, once again agreed that epithelioma was the most likely diagnosis.²³⁵ They treated the

²³¹A pharmacist in Atlanta, Georgia concocted Coca-Cola shortly after the General's death. The initial ingredients included an extract of the African kola bean and cocaine. Grant's cancer agony, as it served to change the face of cancer, also promoted the use of cocaine. "The Cola Wars," (The History Channel, 2001).

²³²Grant 3rd, "Ulysses S. Grant," 450.

²³³The New York Times, "His Fatal Illness," 5:3.

²³⁴Dr. Douglas also claimed to have developed a friendship with General Grant. Goldhurst, *Many Are the Hearts*, 147. The General's thoughts on the matter are unknown.

²³⁵Shrady, "Grant's Case," 122. and The New York Times, "His Fatal Illness," 5:3.

General with a 5:1000 solution of hot salt water—enough to lessen some secondary throat inflammation, but not nearly enough to ameliorate the worsening cancer pain. The results of the clinical examination performed that day were shocking. The physicians discovered to their dismay that the speedy decline in Grant's condition was due to the natural but uncharacteristically rapid progression of the tumor. The cancer had invaded deep into the throat and neck.²³⁶

One week later General Grant was in more pain and losing weight rapidly on his liquid diet. Overall, his clinical condition worsened markedly.²³⁷ Drs. Barker, Douglas, Sands, and Shrady met on March 15 to decide upon their next course of action.²³⁸ Nine months after the onset of symptoms and five months after Dr. Douglas's initial cancer diagnosis, the consultants contemplated surgery for the first time. Sands and Shrady, the surgeons, noted that an operation on Grant's cancer "would involve the division of the lower jaw in the median line, the extirpation of the entire tongue and the greater part of the soft palate, together with the removal of the ulcerated and infiltrated fauces and the indurated glandular structures under the right angle of the lower jaw."²³⁹ In short, surgery at this advanced cancer stage would involve the removal of most of the bottom right portion of the General's face, throat, and neck. The result would be unimaginable disfigurement.

The probability that surgery could completely extirpate the cancer at this late stage approached zero. In addition, surgery (especially of the head and neck) in the traditional era,

²³⁶"His Fatal Illness," 5:3.

²³⁷Ibid., 5:2.

²³⁸Ibid., 5:3.

²³⁹Ibid.

before the general acceptance of antiseptic techniques, carried with it the risk of hastening Grant's demise. Operative and postoperative complications like infection and hemorrhage were common. Against all odds, the consultants believed that curative surgery was still possible, but that the General's "constitution" would not survive. The prospect of surgery—perhaps the only hope Grant ever had to defeat the epithelioma when still in its early stages—was finally and conclusively abandoned. Drs. Barker and Douglas dismissed Dr. Sands, whose services had been specifically retained to perform surgery, from the consulting group on April 1.²⁴⁰ The termination of Dr. Sands was the ultimate sign that the last vestige of hope for the General was abandoned.

Near Death

The General's failing health brought him to the edge of life during the third week of March, 1885. The analgesics became less effective and pain worsened. Grant's "eating," a euphemism for his attempts to swallow his liquid diet, became more laborious. Vomiting was frequent. Weight loss was rapid. His weight declined from about 180 pounds in 1884 to less than 125 pounds.²⁴¹ Except for his face, which is often preserved in appearance beyond other parts of the body during cachexia (physical wasting associated with chronic disease), he was a skeleton. Worst of all, he could no longer work on his beloved memoirs.²⁴² The loneliness of

²⁴⁰The New-York Times, "Gen. Grant's Sufferings: Strength Gained after Passing Very Low. Sad Scenes of the Night and Early Morning, When the Family Were Twice Called to His Side.," *The New York Times*, 3 April 1885, 1:1.

²⁴¹The New York Times, "The Patient in the Sick Room. His Bravery While Suffering and His Thoughtfulness for Others," *ibid.*, 24 July, 5:5. The Rev. Dr. Newman noted in his diary that Grant's weight had declined from 200 to 145 pounds by the end of March. Stefan Lorant, "Baptism of U. S. Grant: Newly Discovered Diary of a Minister Tells the Intimate Story of the Spiritual Battle the General Waged in His Dying Days," *LIFE*, 26 March 1951, 92.

²⁴²The New York Times, "Patient in the Sick Room," 5:5.

cancer pervaded his downtrodden mien. Life lost meaning.²⁴³ In late March, one of an endless parade of eminent callers proclaimed to the press that Grant “has had so much loneliness lately that it has become oppressive to him.”²⁴⁴ Were it not for the March 20 visit of his only daughter, Mrs. Nellie Sartoris, he might have died then.²⁴⁵ The press, hovering like hungry vultures around the Grant townhouse, sensed the end. They questioned visitors emerging from 3 East 66th Street in excruciating detail. Bulletins from the household increased in frequency.²⁴⁶ The General and his family tied loose ends with haste. On March 26, for example, Grant testified extensively from his home in connection with the lawsuits that encumbered Grant & Ward.²⁴⁷ The General became front-page news almost continuously until the day of his death—and for weeks thereafter.

In late March, frightful choking episodes began. On Sunday, March 29, at about 1 A. M., the General came closer to death than ever before. That night, the family noticed he was tossing more than usual in his sleep. Suddenly Grant awoke and began gasping for breath. He complained of a painful, intractable choking sensation in his throat. Dr. Douglas was immediately summoned and, arriving about thirty minutes later, “found Gen. Grant suffering from a secretion in the throat which he was unable to reject.”²⁴⁸ His airway was clogged and

²⁴³The New-York Times, "Chatting with a Friend: A Pleasure Which Gen. Grant Greatly Enjoys. A Long Talk with Mr. Edwards Pierre-Pont Yesterday--the Physicians Discussing a Surgical Operation," *ibid.*, 20 March, 5:1.

²⁴⁴*Ibid.*

²⁴⁵The New York Times, "His Fatal Illness," 5:3.

²⁴⁶The New-York Times, "A Day of Less Suffering: Gen. Grant Showing Marked Improvement. More Comfort and Strength Enjoyed after a Night of Anxiety to the Physicians and Family.," *ibid.*, 1 April, 2:1.

²⁴⁷The New York Times, "His Fatal Illness. The Progress of the Malady to Which He Succumbed.," *ibid.*, 24 July, 5:4.

²⁴⁸The New-York Times, "Gen. Grant's Condition: The Crisis through Which He Passed Yesterday. In Great Danger for Several Hours--the Family at His Bedside and the Physicians Summoned.," *ibid.*, 30 March, 1:1.

each breath became more labored. As he gasped for air, Douglas' attempts to clear the breathing passage failed. At 3 A. M. Grant summoned his last strength to jump from his bed and exclaim in a choking but barely audible voice: "I can't stand it! I'm going to die."²⁴⁹ Dr. Douglas responded to this outburst with brandy and chloroform hypodermically. To the great relief of Mrs. Grant, the inspissated (thickened) secretions cleared spontaneously. The doctor was unable to do anything directly to prevent the General from suffocating in open air. The choking episode horrified Grant. For the rest of his life, he insisted that one of his consultants remain within hailing distance at all times. The physicians drew up a schedule and abided by it.²⁵⁰ Dr. Douglas was most affected. He gave up his practice to devote himself unconditionally to the General's care. "He regarded it," explained *The New-York Times* in the doctor's obituary, "as a patriotic duty imposed on him—something far above the usual case in importance—and presenting claims other than those of medical practice."²⁵¹

One consequence of the near-fatal choking incident was that the General "slept" upright in a chair from that day forward until the night before his death.²⁵² The General noted after that first occurrence that whenever he assumed a recumbent position secretions would pool in his throat and he would be unable to breathe.²⁵³ The cancer at least partially obstructed his upper esophagus, for he could no longer clear his natural secretions, which are normally swallowed.

²⁴⁹Ibid. The Rev. Dr. Newman recorded more telling words in his diary: "Oh I can't stand it! I must die! I must go!" Lorant, "Baptism of U. S. Grant," 92.

²⁵⁰The New-York Times, "Gen. Grant's Weakness: A Wearisome Day and Night for the Sufferer. Sleeping in His Chair to Prevent a Recurrence of the Painful Coughing Spells--a Great Loss of Strength," *The New York Times*, 31 March 1885, 1:1.

²⁵¹The New York Times, "Dr. J. H. Douglas," *ibid.*, 3 October 1892, 4:7.

²⁵²Editorial and George F. Shradly, M.D., Editor, "At Last," *The Medical Record* 28(1885): 99.

²⁵³The New-York Times, "Grant's Weakness," 1:1.

Instead, they spilled over into his airways and lungs. Lying in a supine position in bed only hastened the onset of the pooling and choking sensations. Sitting up or standing (were he not so weak) allowed some clearance of the saliva and reduced the risk of choking. The General, proud standard-bearer of the Union forces, was effectively relegated to two chairs for the rest of his life—one for his emaciated frame and one on which to rest his legs.

The General grew more frail despite his new upright position. Two nights later he suffered another violent choking spell.²⁵⁴ All prepared for the General's death. The consultants believed that even their efforts to palliate the cancer had become fruitless. They decided "to let matters take their natural course."²⁵⁵ The physicians seemed not to understand that the "natural course" had been their plan—wittingly or unwittingly—from the beginning. In reality, their intervention had been minimal. Palliation, they never acknowledged, was a miserable failure. The General, they now believed, was in God's hands.

The media smelled blood. The authorities attempted without success to quell the uproar. The police arrested Thomas Kehoe, for example, on the corner of Broadway and Twenty-Ninth Street for selling "extras" about the death of the General. The judge sentenced him to time in prison.²⁵⁶ Some out-of-town newspapers, seeking to get a jump on the competition, also reported Grant's death. Others delayed their morning editions for a few hours in anticipation of his demise.²⁵⁷ General William Tecumseh Sherman, Grant's "most trusted corps commander,"

²⁵⁴"Less Suffering," 1:7.

²⁵⁵*Ibid.*, 2:1.

²⁵⁶The New-York Times, "Obtaining More Sleep: A Quiet Night and Day in the Grant Household. Safely Passing the Critical Period of the Morning--a Day of Comparative Comfort for the Sufferer.," *The New York Times*, 4 April 1885, 1:3.

²⁵⁷"Less Suffering," 2:1.

begged the insistent newsmen to preserve the dignity of their dying leader.²⁵⁸ “I do not believe in the clamor and hubbub that is being made in Gen. Grant’s last hours. He has suffered greatly and should be allowed to die in peace.”²⁵⁹ Nevertheless, the “silence and sorrow” called for by Grant’s friend of fifty years became commercialized frenzy in the clutches of the predatory press.²⁶⁰ The General was not dead, but the newspapers proceeded to bury him in St. Louis or Washington, D. C.²⁶¹

Instead, the General clung to life. Wednesday, April 1, passed in relative quiet—at least inside the Grant residence. Early the next morning, however, the General suffered another life-threatening episode of near-asphyxiation. The doctors believed that his constitution was too weak to withstand further assault. *The New-York Times* captured the terror of suffocation and the futility of his medical treatments:

At 3:30 [A. M.] o’clock Gen. Grant suddenly awoke. He gasped for breath and then coughed violently and spasmodically. Dr. Douglas was instantly at his side. The fit of coughing momentarily grew more violent. Harrison [Grant’s servant] rushed into the room to render assistance. An attempt was made to administer the usual remedies. This was unsuccessful, as the patient was struggling and gasping in his efforts to breathe. His efforts were too great for his overtaxed strength and he fainted. Quickly revived by restoratives, he fainted again.²⁶²

The next day, outside throngs of newspapermen and passers-by hung like vultures at a carrion feast. The frequency of the bulletins increased to more than one per hour to satisfy the burgeoning crowds. Nightfall brought even larger crowds. Family and neighbors called the police more than once to clear the doorway and the street. “The police dispersed the staring

²⁵⁸William L. Barney, "William Tecumseh Sherman," in Eric Foner and John A. Garraty, eds., *The Reader's Companion to American History* (Boston: Houghton Mifflin Company, 1991), 988.

²⁵⁹The New-York Times, "Obtaining More Sleep," 1:3.

²⁶⁰Ibid.

²⁶¹Ibid.

²⁶²The New-York Times, "Grant Much Worse."

main crowd about 8 o'clock [P. M.], but could not lessen the number of promenaders."²⁶³ Even at midnight "loungers still idled their time along the block."²⁶⁴

Baptism

Grant also sensed the end. The Rev. Dr. John P. Newman, a Methodist Episcopal minister, baptized the General, never a man of deep religious devotion,²⁶⁵ after a particularly fierce episode of choking and coughing.²⁶⁶ Mrs. Grant and the women of the family, true to the religious division of the sexes at the time, were heartened that the General agreed to baptism.²⁶⁷ Without it, they believed, he could never enter the kingdom of Heaven. The men of the family did not share the same belief. Colonel Fred Grant, who most often made the family decisions

²⁶³Ibid.

²⁶⁴Ibid.

²⁶⁵Henry Ward Beecher called him a "Christian" despite the fact that he was essentially irreligious. Beecher's reasons for doing so are intriguing and lay in assumed morality rather than known behavior. The New-York Times, "Mr. Beecher's Remarks on Gen. Grant," 2:2.

²⁶⁶The exact date of the baptism is open to question. One would like to believe that the diary of the Rev. Dr. John Philip Newman, who baptized the Ulysses S. Grant, would be most accurate. Newman gave the date of baptism as April 2. However, two other observers who frequented the Grant residence at that time—Senator Jerome Chafee, whose daughter married one of Grant's sons, and Mark Twain—questioned Newman's diary entries. Lorant, "Baptism of U. S. Grant," 92. William S. McFeely placed the date of baptism as March 28, 1885. McFeely, *Grant*, 503. Francelia Butler dated the baptism to April 1. Butler, "Grant's Cancer," 7. Dr. George F. Shrady declared that the baptism occurred on April 5. McFeely's source appears to be Pitkin, but the latter did not specify an exact date of baptism—only that it was performed "in one of these crises" between the end of March and the beginning of April. Pitkin, *The Captain Departs*, 34. Ms. Butler's source is unclear. Shrady was present but did not pen his memoir of *Grant's Last Days* until 1908. Shrady, *Grant's Last Days*, 60. *The New-York Times* did not mention the event during the days in question.

The date is important because it pinpoints when the General abandoned all hope of regaining a normal life and, psychologically, succumbed to the cancer. It was also a sign that Grant and his loved ones accepted his imminent demise.

²⁶⁷Lorant, "Baptism of U. S. Grant," 92. and Pitkin, *The Captain Departs*, 34.

during his father's final months, commented that "it would do no harm."²⁶⁸ The General, unable or unwilling, no longer resisted the Christian sacrament.²⁶⁹

The conflict between religion and science was never more evident than on this microcosmic scale. For, as the Reverend baptized the General, Dr. Shrady administered "hypodermics of brandy."²⁷⁰ Grant immediately responded and became more alert. He even appeared a bit energized. What caused his response—the rite or the shot? The Reverend, who apparently spent little time not praying, was certain they had all witnessed a miracle as a result of the baptism. Dr. Shrady was more circumspect. "I was inclined to attribute the result to the brandy," he wrote.²⁷¹ The sensational press championed the Reverend Doctor's stance.²⁷² Grant was more persuaded by the good doctor's point of view. Newman's evidence was faith; Shrady's experience.

Grant's rejuvenation was transient. The cancer, temporarily silent but inexorable, reminded all of its persistence about midnight on April 7 when the General hemorrhaged.²⁷³ Dr. Shrady reported in *The Medical Record* that the amount of the bleed from his mouth was four ounces.²⁷⁴ Blood loss over a short time of that quantity, though minimal by most standards, may seem a veritable flood. Worse, his general condition—as measured by the standards of the

²⁶⁸*The Captain Departs*, 34.

²⁶⁹McFeely, *Grant*, 503. The Rev. Dr. Newman, whose observations were suspect to Chafee, Twain, and others, claimed in his personal diary that Grant said, "I had intended to take that step [of baptism] myself." Lorant, "Baptism of U. S. Grant," 92. Nevertheless, he was not baptized until near death.

²⁷⁰Shrady, *Grant's Last Days*, 60.

²⁷¹*Ibid.*

²⁷²McFeely, *Grant*, 503.

²⁷³The New-York Times, "Gen. Grant Much Weaker: Dragged Down by an Attack of Hemorrhage. A Sign of the Last Stages of the Disease--Little Hope That He Will Survive Long.," *The New York Times*, 8 April 1885, 1:2.

²⁷⁴Editorial and Shrady, "General Grant's Condition," 410.

day—failed rapidly. Shrady noted that the pulse became “feeble” and his temperature rose to 102° Fahrenheit.²⁷⁵ The consultants continued their attempts at analgesia and palliation by increasing the dose of morphine, but there was really nothing they could do but watch and wait with countless others around the globe. Grant, to the surprise of all, survived the night. The bells that stood ready to peal their mournful dole at the death of the General remained silent.

Resurrection

General Grant fooled them all. He felt better the next morning. His speech was thick, probably related to increased mucus production, but his swallowing was easier and he was able to clear his secretions with less effort.²⁷⁶ Most likely, the hemorrhage resulted from the relentless invasion of the cancer into the surrounding tissues of the head and neck. The mucous membrane sloughed and exposed the underlying blood vessels, causing them to bleed. The hemorrhage also helped his respiration, for when the cancerous tissue broke off part of the obstruction to his intake of air caused by the tumor was relieved. Grant swallowed and breathed easier. The first hemorrhage was not his last, but over the next two weeks the improvement in his clinical condition appeared nothing short of miraculous.

The doctors underestimated Grant’s constitution. Despite the burdens he bore of traditional cancer—late diagnosis, inadequate or absent effective treatment, insufficient or excessive doses of medicines, adverse reactions to attempts at palliation and analgesia, and the competition between religion and science for the cancer consciousness of the public—the

²⁷⁵Ibid.

²⁷⁶Shrady, "Grant's Case," 122.

General lived on. His desire to finish the memoirs acted like a shield against death. The family believed that Grant's recovery was nothing short of a "resurrection."²⁷⁷

The press concluded that the physicians' diagnosis of cancer was in error. It is even possible that the General "remarked that he did not think that his was cancer."²⁷⁸ All knew that no one survived traditional cancer. Logic led to the ineluctable conclusion that if he was better he could not have cancer. The press derided the consultants, considered the microscope and the microscopic findings a humbug, and blamed the physicians for misleading the public.

Newspapers, encouraged by the Grant's stalwart personality, concluded "the patient's chances of recovery were good."²⁷⁹ Every additional day the General lived augmented and transformed the public's knowledge of cancer as the apotheosis of Ulysses S. Grant reached new heights.

There were psychological as well as physical explanations for the General's improvement. Grant's memoirs, more than ever, became his *raison d'être*. He felt an inner drive to complete them. They would be a gift of financial security to his family and his legacy to the world.²⁸⁰ First he had to muster his remaining physical and mental strength in spite of the cancer that the doctors insisted had never resolved. Then he had to convince a wary public that the memoirs were his and not the product of some mercenary or ghostwriter.²⁸¹ By the week of April 20, he was still in pain but nonetheless strong enough to resume work on his book,

²⁷⁷The New-York Times, "Obtaining More Sleep," 1:1.

²⁷⁸Lorant, "Baptism of U. S. Grant," 93.

²⁷⁹Shrady, "Grant's Case," 122.

²⁸⁰Grant 3rd, "Ulysses S. Grant," 449-50.

²⁸¹The twenty-year relationship between General Grant and Adam Badeau, his military secretary and biographer, is complicated and intriguing. Suffice it to say that on April 29, 1885, the *New York World* reported that Badeau was the real author of Grant's *Memoirs*. Grant shot back with a public letter claiming that the writing was all his own. Further disagreements followed. Grant dismissed Badeau on May 5. Nevertheless, Badeau's own not-so-subtly-entitled *Personal Memoirs of U. S. Grant* remain a valuable first-hand source on the General. Badeau, *Grant in Peace*.

primarily by dictation.²⁸² “It is my life. Every day, every hour is a week of agony. I am easier when employed,” he wrote.”²⁸³ Time and again, the cancer made speech more difficult and dictation temporarily ceased.²⁸⁴ Nevertheless, the General rallied his spirits in April and early May and dove deeply into the tasks of organizing his recollections; checking references, maps, and battle plans; and writing what would become one of the most famous works of military history.²⁸⁵ Many narratives had been written about Civil War battles (including many about Grant), but few offered the intimate involvement and depth of feeling with which Grant suffused his *Personal Memoirs*. They are, indeed, truly personal. In his dying months the General felt the urgency of time brought on by the propagating cancer, but he also felt the tug of posterity and knew that only he could do justice to the memory of the War. In his honesty to himself, he was honest with others. In the context of his times he instilled life into his *Memoirs* with his dying breath.

A Respite Too Short

By the end of April, 1885, the General’s stable physical condition encouraged even the doctors—though they never doubted the reality and relentlessness of Grant’s cancer. Dr. Fordyce Barker wrote a letter to another physician in early May explaining that the improvement

²⁸²The New York Times, "His Fatal Illness," 5:4.

²⁸³Lorant, "Baptism of U. S. Grant," 93.

²⁸⁴The New York Times, "His Fatal Illness," 5:4.

²⁸⁵The admirers of Ulysses S. Grant’s *Personal Memoirs of U. S. Grant* are legion. Matthew Arnold found the book rich and compelling (but criticized Grant’s grammar). Nelson, "The Victory of U. S. Grant," 435. Gertrude Stein believed the *Personal Memoirs* was one of the best works ever written by an American. See Gertrude Stein and Thornton Introduction Wilder, *Four in America* (New Haven: Yale University Press, 1947). Edmund Wilson offered the highest praise for Grant’s *Memoirs* when he reflected that they revealed the depth and passion of Grant’s soul because “perhaps never has a book so objective in form seemed so personal in every line.” Wilson, *Patriotic Gore*, 143.

in Grant's health could be attributed to the breakdown and sloughing of cancer tissue.²⁸⁶ "There has been ulceration and slough of the tonsil, and front of the uvula," he wrote. "The slough has now cleaned off—the offensive discharge has, in a great measure, ceased, pain in articulation and deglutition [swallowing] is now greatly diminished." Caution was the watchword, however, for "the local induration remains, and the carcinoma is slowly but manifestly progressing."²⁸⁷

Although the press and street gawkers continued to habituate East Sixty-Sixth Street between Fifth and Madison Avenues, some of the furor abated. The urgency to see the General before he left this life diminished, and the street became unblocked. On occasion, reporting on Gen. Grant's condition was even relegated to the second or later page of the newspaper.

Nevertheless, if the General ever doubted that he had cancer, all disbelief was dissipated by the beginning of May, 1885. Much to the dismay of the General and his family, he again became front-page news on May 1. He never relinquished that dubious position for the rest of his life. The head and neck pains became worse. Regurgitation, choking, and bleeding recurred. Grant hurriedly but diligently continued to construct his memoirs of the Civil War. He decided to stop the history at Appomattox Court House in 1865—almost exactly twenty years before he wrote them. The cancer transmogrified the General's naturally introspective and reticent disposition into a brooding shell of pain and hopelessness. However, the anger, petulance, and/or vengefulness that might be expected of weaker personalities in such unfortunate circumstances were missing. He would not use his memoirs as a springboard for criticism and vindictiveness. There would be no mention of the brouhaha with President Johnson over

²⁸⁶Benjamin Fordyce Barker, "Letter to Dr. John Rogers, Concerning a Description of General U. S. Grant's Epithelioma. Barker Wrote "Gen'l Grant Has Epithelioma, Involving Left Tonsil, Uvula, Pharynx, Base of the Tongue, and Enlargement of Right Cervical Glands...I May Add That the Microscopic Evidence Seems Conclusive That the Disease Is Epithelioma...," in *The New York Academy of Medicine. Rare Books Collection. Presented by Dr. Arthur S. McQuillan* (New York 1885).

²⁸⁷Ibid.

Secretary Stanton and the Tenure of Office Act, no reflections on his gullibility and the corruption during the two terms of the Grant presidency, no reference to being mulcted by Ferdinand Ward,²⁸⁸ and, above all, no mention of the cancer that was inexorably destroying his body. As he refused to mention the word ‘cancer’ after Dr. Douglas’ initial diagnosis in October, 1884, so he would not include it in the story of his life. The Civil War defined and encased his identity. All else—including his final illness—was postscript.

On May 16, the consultants noted that the General was unusually depressed.²⁸⁹ There was no evidence that a sudden worsening of his cancerous condition or the immediate focus of his memoirs contributed to his altered mental state. Indeed, the physicians and the family agreed that were it not for the memoirs, Grant was ready to give up. The consultants convened to consider the cause and concluded that it was “due to the state of the weather.”²⁹⁰ They prescribed a change of climate for the fast-approaching summer months.²⁹¹

Weather, Climate, and Cancer

The perceived influence of weather and climate during the nineteenth century on medicine in general, and on traditional cancer in particular, cannot be overestimated. As one’s constitution made disease person-specific, so climate made disease region-specific. In the eternal historical seesaw between the belief in external and internal causes of disease, the constitution was internal and climate external. To conceive of cancer separate from the

²⁸⁸The word ‘mulct,’ meaning to swindle, was commonly used at the time to describe the Grant & Ward debacle.

²⁸⁹The New-York Times, "Grant's Sufferings," 5:4.

²⁹⁰Ibid. Paradoxically, the weather on May 16 was, by most standards, most salubrious. *The New-York Times* noted "for the Middle Atlantic States, fair weather, variable winds, slightly warmer in southern portion, stationary temperature in northern portion." The temperature ranged from the mid-50s to the low 70s. The New York Times, "The Weather Indications," *ibid.*, 16 May, 2:7.

²⁹¹Lorant, "Baptism of U. S. Grant," 97.

individual who harbored it was incongruous to the nineteenth-century physician. Each individual had a unique family background, social standing, life course, and climatological history.

Weather was to climate as a short-term influence on cancer was to a longer-term effect. The poor weather that was thought to have depressed Grant in mid-May was only a transient atmospheric affect compared to the more permanent impact of the mid-Atlantic climate on the General's health during the last years of his life. Both weather and climate were deemed to be unhealthy and contributory to Grant's tragic cancer.

Knowledge of the importance of weather and climate to health and disease, including cancer, derived from at least the time of Hippocrates.²⁹² To the Ancients and their ideological descendants, disease resulted from an imbalance between man and environment. Humoral theory, which persisted into the eighteenth and even nineteenth century, was a derivative of this holistic idea.²⁹³ An inharmonious excess of black bile, melan chole, in light of this prevalent theory, elicited cancer.²⁹⁴ John Hunter, the famous eighteenth-century British surgeon and anatomist, considered climate in his discussion of the "predisposing causes" of cancer. In his *Lectures on the Principles of Surgery*, he noted in his discussion of malignancies that "perhaps climate also has considerable effect."²⁹⁵ Less than a decade after Dr. John Howard inaugurated the first British cancer ward at the Middlesex Hospital in London in 1792, the Society for

²⁹²Francis Adams, ed. *The Genuine Works of Hippocrates*, Special ed., 2 vols., vol. 2, The Classics of Medicine Library (London: The Sydenham Society, 1849; reprint, 1985), Section III, 715-22.

²⁹³See Dissertation Chapter 1, page 28.

²⁹⁴In his aphorism, Hippocrates attributed melan chole, the cause of cancer, to the Spring and, especially, Autumn in his Mediterranean climate. Adams, *The Genuine Works of Hippocrates*, Section III: 20, 719 and Section III, 22, 20.

²⁹⁵Jessie Dobson, "John Hunter's Views on Cancer," *Annals of the Royal College of Surgeons of England* 25(1959): 177. His other predisposing factors were "age, parts [i.e., some body parts are more susceptible to cancer than others] and hereditary predisposition."

Investigating the Nature and Cure of Cancer was formed by a group of eight prominent Scottish and English physicians.²⁹⁶ In 1802, the Medical Committee of the Society published a pamphlet that posited thirteen queries they believed were essential for the study of cancer.²⁹⁷ “Query 8th” asked “Has climate or local situation any influence in rendering the human constitution more or less liable to cancer, under any form, or in any part?” Their conclusion was that it was “necessary to observe the effects of climate” in order to comprehend cancer.²⁹⁸

Medical practitioners and the public in the nineteenth century believed that weather and climate played a role in both the causation and treatment of diseases, including cancer. As scientists and the public paid more attention to the general notion of “measurement,” tabulations of temperature and humidity were correlated with health and disease. In 1849, the practical application of climate to disease led the then-ailing Dr. J. Marion Sims, the provocateur of increased cancer awareness at the Woman’s Hospital of the State of New York and a seminal influence on the founders of the New York Cancer Hospital, to forsake his beloved South “to go to the North...for a necessary change of climate.”²⁹⁹ He was certain that his dysenteric bowel

²⁹⁶Bruce S. Schoenberg, "A Program for the Conquest of Cancer: 1802," *Journal of the History of Medicine and Allied Sciences* 30(1975): 3.

²⁹⁷*Ibid.*, 10. The queries and comments were republished as a “Report” in the The Medical Committee of the Society for Investigating the Nature and Cure of Cancer, “Thirteen Queries,” *Edinburgh Medical and Surgical Journal* 2(1806): 382-89. Also see “The Questionnaire from the First Cancer Society: 1806,” in *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, “*Cancer therapy Publications 1782; 1822; 1942; 1944*” (New York 1944).

²⁹⁸Schoenberg, “The Conquest of Cancer: 1802,” 12.

²⁹⁹J. Marion Sims, *The Story of My Life*, ed. H. Marion-Sims (New York: Da Capo Press, 1884; repr., 1968), 248.

condition was “a chronic disease of the climate”³⁰⁰ and that “if I could change my climate entirely I believe that even yet I might be cured and restored to health.”³⁰¹

In May, 1884, Dr. Fordyce Barker, physician to Mrs. Astor, President Garfield, and General Grant, gave the Medical Address at the dedication of the New York Cancer Hospital.³⁰² Examination of the 1880 United States Census, he noted, revealed that the incidence of cancer was increasing. Dr. Barker then analyzed the number of cancer cases by climate correlated with site of origin and found that the disease was more common in the North than in the South—and especially “prevalent in New York.”³⁰³ The location of his domicile thus doubly hexed General Grant. First, for years he had been exposed to the climate of a State with one of the highest measured incidences of cancer.³⁰⁴ Second, the physicians believed, oppressive weather made him melancholy and “enervated.”³⁰⁵ The solution, all agreed, was to vacate to a more salubrious climate.

FINAL DAYS

(June-July 1885)

Mount McGregor

³⁰⁰Ibid., 252.

³⁰¹Ibid., 264.

³⁰²New York Cancer Hospital, "Nych, Annual Report, 1886-1887," 28-35.

³⁰³Ibid., 29. Barker's interpretation of the incidence of cancer throughout the United States based upon the 1880 census figures is open to question. The lowest incidence of the disease, for example, was noted in Mississippi, where the accuracy of census reporting is in doubt. See also W(illiam) Roger Williams, *The Natural History of Cancer with Special Reference to Its Causation and Prevention* (London: William Heinemann, 1908), 76.

³⁰⁴Dr. Roswell Park, Buffalo, New York cancer researcher and surgeon, added, "the death rate from cancer (in western NY) is greater than in any other part of the continent." Quoted by Andrew A. Gage, "Roswell Park, M.D. -- the Parasitic Theory of the Cause of Cancer," in *Medical History in Buffalo 1846-1996*, ed. Lilli Sentz (Buffalo, NY: State University of New York at Buffalo, 1996), 165. from the New York Medical Journal, *New York Medical Journal* 57(1893): 233-37.

³⁰⁵The (New York) World, "Gen. Grant's Departure: Preparations for His Trip to Mount Macgregor Completed," 8:1.

The newspapers learned of the consultant's recommendation that the General leave New York City for a healthier clime immediately after they made the decision. The news, as with all information about "The Old Hero," spread almost instantly across the nation. The Grant summer house at Long Branch, held for estate purposes in the name of Mrs. Grant after the General's losses in the Grant & Ward fiasco, was rejected because of its hot, seabreeze-humid atmosphere billowing in off the Atlantic Ocean. The General's family received summer residence offers from all over the country, including California, the Catskills, and the Adirondacks.³⁰⁶ Most of the solicitations (and they were solicitations because it was no secret that the presence of the General in one's community brought instant fame and probable wealth to the vicinity), consonant with the beliefs of the time, were from cool, dry habitats.

The Grants, after consulting with Dr. Douglas, accepted Joseph W. Drexel's offer to summer at his cottage on Mount McGregor, eleven miles north north-east of renowned Saratoga Springs, New York.³⁰⁷ There were many reasons why the General and Mrs. Grant favored Drexel's proposal above all others. Personal ties were paramount. Joseph W. Drexel, a principle in the banking house of Drexel, Morgan and Co., was the son of the founder of the original Drexel & Co., and the brother of *the* Drexel [Anthony J.] of Drexel, Morgan and Co. Importantly, A. J. Drexel also co-owned the Philadelphia *Public Ledger* with George W. Childs, Grant's good friend who summered in Long Branch. In addition, Joseph W. had been close to the General in other ways. He was one of only two other co-signatories to work with Grant a year earlier in their effort to raise money for the construction of the pedestal of the Statue of Liberty—a monument conceived by Bartholdi to memorialize abolition rather than immigrant

³⁰⁶The Commercial Advertiser, "Strength for Gen. Grant: Finding a Summer Home for Him at Mount Macgregor. Accepting Joseph W. Drexel's Offer and to Start for His Resting Place the Latter Part of This Month," *The New York Times*, 12 June 1885, 5:1.

³⁰⁷Ibid.

freedom and thus closer to the General's past.³⁰⁸ Joseph Drexel also had significant links to the nascent cancer community and its fledgling institutions. He was the first Treasurer of the New York Cancer Hospital, and his philanthropic efforts, though short-lived, sustained the institution at its beginning.³⁰⁹ Not surprisingly, many of the General's handpicked physicians (Barker, Shrady, and Markoe) were soon to be on the staff of the new cancer hospital under construction across Central Park from Grant's townhouse.

The personal relationship between the two men was not the only reason for the selection of the Drexel summer home. The cottage and environs embodied the epitome of a salutary climate for the stricken General. The reputation of the area for the rejuvenation of health was incomparable. Mohawk Indians, long before British-American settlement in the region, were aware of the healing properties of the springs.³¹⁰ In 1767, they took their Colonial friend and ally, Sir William Johnson, to the springs to recover from his ailments.³¹¹ He regained his health. Word of this remarkable cure by the waters led to the founding of a cottage health industry in the first years of the nineteenth century. Spas, well-appointed hotels, boarding houses, and even a water-bottling company—which distributed spa waters throughout the world—made the area into a “center of wealth and fashion.”³¹² In 1857, *Appletons' Illustrated Hand-Book of American Travel* cited Saratoga Springs as “the most famous place of summer resort in the United

³⁰⁸Grant, Evarts, and Drexel, "Letter to George E. Jones, Esq.."

³⁰⁹New York Cancer Hospital, "Nych, Annual Report, 1886-1887," 3. Joseph Drexel died in 1888, one year after the opening of the Astor (Woman's) Pavilion at the New York Cancer Hospital.

³¹⁰Pitkin, *The Captain Departs*, 46.

³¹¹*Ibid.*

³¹²*Ibid.*

States.”³¹³ The Saratoga region in upstate New York thus had personal, fashionable, and healthful attractions for General and Mrs. Grant and their family.

Mount McGregor, “the handsomest spot...in America,”³¹⁴ surely benefited from its proximity to Saratoga Springs. It also offered the Grants additional health wise amenities. As Dr. Douglas later reported to the *Albany Evening Journal*, “I had intended to have General Grant taken to a place where the air was clear and pure and dry.”³¹⁵ Mount McGregor was that and more. Local doctors claimed that “sufferers from throat diseases...are always benefited by a sojourn there.”³¹⁶ Hotel Balmoral, a stone’s throw from the Drexel cottage on Mount McGregor, advertised itself as “No Dew, No Malaria, No Mosquitoes, Certain Relief from Hay Fever.”³¹⁷ In addition, there were stunning views of the Hudson River valley, wholesome air, and tolerable temperatures even at the height of summer—thus fulfilling the requirements of cool and dry. The quality of the air and the temperature were essential determinants of a healthful environment. *The Commercial Advertiser*, for example, concluded “the keen, bracing mountain air would have a much better effect on his health.”³¹⁸ Air quality had been an additional meteorological focus of physicians and health care reformers like Harriet Beecher Stowe for

³¹³Cited by Pitkin, *The Captain Departs*, 46.

³¹⁴Quotation from W. J. Arkell, 1881, a real-estate entrepreneur in the region, as cited by *ibid.*, 49.

³¹⁵*Ibid.*, 59.

³¹⁶The (New York) World, "Gen. Grant's Departure: Preparations for His Trip to Mount Macgregor Completed," 8:1.

³¹⁷McFeely, *Grant*, 506. The promotional literature lied. Overwhelming numbers of blood-sucking mosquitoes often drove Grant and his family inside the house. *Ibid.*, 507.

³¹⁸The Commercial Advertiser, "Strength for Gen. Grant."

decades—since the American industrial revolution began to fill factories and the atmosphere with “unnatural” chemicals.³¹⁹

It was also important that the General’s summer habitat be cool, for many physicians, including the consultants, believed excessive heat to be unhealthy for patients with cancer. Indeed, Grant’s eventual departure from New York City was to no small extent hastened by three days of intolerably hot weather that, in Dr. Douglas’ estimation, uncompromisingly “debilitated” the General.³²⁰ Cooking was a major source of heat in most homes, but those who planned the family’s excursion to Mount McGregor also foresaw and eluded this problem. Grant’s food was to be prepared at Hotel Balmoral and shuttled the short distance of three hundred feet to the cottage.³²¹ The perceived adverse effects of heat and humidity on health help explain the careful records of daily temperatures and atmospheric conditions kept by newspapers and public health bulletins for New York City and other locations throughout the nineteenth and early twentieth centuries.³²²

On the surface, Mount McGregor proved a good choice, for Grant revealed his pleasure with the climate, the weather, the atmosphere, and the accommodations. After a few days at Drexel’s cottage, he attempted to cheer up the overwrought Dr. Douglas when he told him “I

³¹⁹Harriet Beecher Stowe, "The Chimney-Corner for 1866. Vii. Bodily Religion: A Sermon on Good Health," *Atlantic Monthly*, July 1866, 85-93.

³²⁰The (New York) World, "Grant Expecting Death. He Writes Special Memoranda for His Family and Physicians. Exhausted by His Efforts of the Afternoon He Becomes Depressed--Dr. Sands Telegraphed to Come at Once--the General's Condition as Explained by Dr. Douglas," *The World*, 18 June 1885, 1:2.

³²¹"Gen. Grant's Departure: Preparations for His Trip to Mount Macgregor Completed."

³²²See, for example, the numerous “Annual Report(s) of the Board of Health of the Department of Health of the City of New York” from the 1880s.

think the chances are very decidedly in favor of your being able to keep me alive until the change of weather towards the winter.”³²³

A Most Unhealthy Journey for Health

The most optimal climate, weather, air quality, and temperature could at best merely postpone the inescapable. No reputable physician in the age of traditional cancer believed he could cure cancer—unlike claims made for the climatological treatment and possible cure of consumption and other diseases.³²⁴ Dr. Douglas, besieged incessantly by the press, related the prognosis and goals for the sojourn at Mount McGregor. “The disease is following its characteristic course,” he stated, “which is a course of steadily increasing exhaustion. We do not look for a cure from this change (to Mount McGregor). Nothing can be curative, but we do hope to prolong his life and that is the most that can be expected.”³²⁵

Meanwhile, the General continued to suffer in Manhattan as heat and humidity engulfed the city at the approach of summer in 1885. He often appeared to be near death, but recovered—as in early April—to an extent that surprised even his doctors. The number of his remaining days or months, they agreed, was limited but unpredictable. Grant directed every bit of his declining strength toward his writing. He thanked the doctors, who mercifully plied him with

³²³July 2, 1885. McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1115.

³²⁴Many physicians and others believed that a sea voyage to a temperate climate “not only to cure consumption but also to prevent it.” Sheila M. Rothman, *Living in the Shadow of Death: Tuberculosis and the Social Experience of Illness in American History* (Baltimore: The Johns Hopkins University Press, 1994), 19. The difference in the treatment and prognosis of nineteenth-century cancer and consumption is important because for most of the century lung carcinoma and tuberculosis (to use modern terms) were difficult—if not impossible—to distinguish. See Wilson I.B. Onuigbo, “The Diagnosis of Lung Cancer in the 19th Century,” *British Journal of Diseases of the Chest* 65(1971): 119-24. and “Some Nineteenth Century Ideas on Links between Tuberculosis and Cancerous Diseases of the Lung,” *British Journal of Diseases of the Chest* 69(1975): 207-10. As a result of this inability to differentiate between underlying diseases, nineteenth-century climate-based treatments were applied to medical conditions with different characteristics.

³²⁵The (New York) World, “Grant Expecting Death,” 1:2.

narcotics on a daily basis,³²⁶ for keeping him alive to continue his personal history.³²⁷ He derived some comfort from the knowledge that his family would escape the heat and humidity of New York by to the Springs area and its cool, healthy environment. The General's objective, on the other hand, was to complete his memoirs with as little suffering as possible before the inevitable.

On June 16, the Grant entourage left the East Sixty-sixth Street townhouse with great fanfare.³²⁸ William H. Vanderbilt, from whom the General had borrowed the ill-fated \$150,000 at Ferdinand Ward's request two days before the collapse of Grant & Ward, outfitted his private railcar at Grand Central "depot," barely a mile from the residence, to take the General and his family to Mount McGregor.³²⁹ The private car contained upholstered easy chairs on which Grant continued his habit of sleeping upright to minimize the risk of aspiration.³³⁰ There were also "adjustable invalid reclining chairs," forerunners of today's wheelchairs, that the General recently received as gifts from Dayton, Ohio and other locales.³³¹ No convenience was excluded.

The crowd accompanying Ulysses S. Grant, befitting the great conqueror, was large and diverse. With the General in the Vanderbilt car were Mrs. Grant, their daughter Mrs. Nellie Sartoris (who emboldened the dying Grant to live three months before), Colonel and Mrs. Fred

³²⁶Grant 3rd, "Ulysses S. Grant," 446.

³²⁷McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1115.

³²⁸The New York Times, "Gen. Grant's Summer Trip: Preparing to Start for Mount Macgregor to-Day," *The New York Times*, 16 June 1885, 5:4. and "Resting at Mt. M'gregor: Gen. Grant's Long Journey Safely Accomplished. The Old Hero Finds Relief from the Heat at Mr. Drexel's Cottage--Incidents of the Trip," *The New York Times*, 17 June 1885, 1:5-6.

³²⁹Pitkin, *The Captain Departs*, 62.

³³⁰Ibid., 62-63.

³³¹The New-York Times, "A Present for Gen. Grant," *The New York Times*, 3 June 1885, 1:6.

Grant, and, of course, the ever-present Dr. Douglas. Henry McQueeney, Grant's nurse, and Harrison Tyrrell, his steadfast personal valet, were on hand to aid the General and the doctor in any way possible. The ladies had their own attendants.³³² Cramped into the other railcar were miscellaneous items and a bevy of reporters "from almost all the metropolitan dailies."³³³ Flocks of well-wishers, alerted by the innumerable newspaper articles on the General's every move, lined each station along the way, superficially reminiscent of the black-shrouded railway catafalque that transported President Lincoln's body from Washington, D. C. to Springfield, Illinois a score of years before. Nevertheless, this was no wake. All wanted to glimpse the great man and hearten him. Except for a solemn, silent moment of respect by a troop of Grand Army of the Republic veterans at Saratoga, when "the General...looked so wan and weak that no one had the heart to cheer just then,"³³⁴ the innumerable well-wishers at each station boisterously "waved flags and cheered."³³⁵

The two-car train arrived at Mount McGregor in mid-afternoon. The trip had not been an easy one. The General, stoical but infirm, had his spirits buoyed by the cheering crowds but was physically exhausted by the time he finally reached the Drexel cottage. The trip up the mountain was particularly intolerable and suffocating for a man in Grant's enervated state. Ironically, the smoke and dust emanating from the narrow-gauge little train threw all the desirable atmospheric qualities of Saratoga and Mount McGregor to the wind. The *World* reported, "As the diminutive engine wheezed along the uneven rails up the steep grade she belched out clouds of stifling smoke which filled the car and gave the General much annoyance. Curve followed curve in

³³²Pitkin, *The Captain Departs*, 62.

³³³*Ibid.*, 63.

³³⁴The New York Times, "Resting at Mt. M'gregor," 1:6.

³³⁵*Ibid.*, 1:5.

quick succession and the car pitched from side to side like a boat in a stormy sea.”³³⁶ Grant, although much sickened by the journey, attempted to show his mettle to the adoring crowd at Mount McGregor by waving off the hospital cot waiting for him at the top and end of the line. Instead, he walked a few steps up the hill toward the Drexel cottage. However, the strain was too much and he finally yielded to the rattan chair that aides carried beside him.³³⁷ All afternoon and evening hordes of newspapermen, vacationers, G. A. R. veterans, and just about anyone else in the vicinity attempted to get close enough to the cottage to wish the General well. The protection afforded the Grant family by the New York City Police seemed a distant dream, but a G. A. R. veteran appointed himself guard of the new Grant residence. He took up a post near the cottage and warned reporters and all comers that he would maintain his watch until his commander left the mountains. As the General moved, so did the media. Mount McGregor became “the most conspicuous spot in the world.”³³⁸

Inside the Drexel cottage there was little pomp and circumstance. General Grant survived the arduous journey, but it would be his last. His physical form was worn beyond recognition. His characteristic “black Prince Albert coat hung loosely from his stooped shoulders” and the “well-worn silk hat was thrust back on his head.”³³⁹ Around his throat he wore a well-traveled white silk scarf that attempted to serve the dual function of warming his neck and hiding the monstrous cancer swelling under his right ear and neck. One reporter described him as having

³³⁶The (New York) World, "Grant at Mt. M'gregor: The Trip Made without Accident, but He Is Much Exhausted. West Point Recalls to the General's Mind Reminiscences of His Cadet Life--the Journey Causes an Increased Swelling of the Throat--Dr. Douglas Says the Relief Obtained Can Be Only Temporary," *The World*, 17 June 1885, 1:5.

³³⁷Pitkin, *The Captain Departs*, 63.

³³⁸Ishbel Ross, *The General's Wife: The Life of Mrs. Ulysses S. Grant* (New York: Dodd, Mead & Company, 1959), 304. Quoted in Pitkin, *The Captain Departs*, 65.

³³⁹The (New York) World, "Grant at Mt. M'gregor," 1:5.

the “pale, pinched features of the invalid.”³⁴⁰ The General endeavored, with all his disappearing strength, to continue to write his memoirs. That first day in the mountains he sat on the large porch with pencil and paper in hand for five hours—until the inauspicious, reportedly non-existent, mosquitoes drove him inside.³⁴¹

The Benefit of a Written History

As mosquitoes and other—more human—animals droned around him, Grant’s weeks at the Drexel cottage became more intolerable. We know this because, through one of the more silvery-lined storm clouds of history, the General left impromptu recordings of his thoughts and feelings in the form of handwritten pencil-on-paper notes intended only for their recipient during his five weeks at Mount McGregor (June 16-July 23, 1885). Those private memos grant the historian a privileged view into the normally hidden thoughts of the “Great Hero.” One of the most commonly addressed subjects was cancer and its effects on its victim because the General wrote many of the surviving notes to Dr. Douglas.

Grant’s written comments became his major method of communication on June 14, 1885, two days before the journey to Mount McGregor. The cancer probably invaded his larynx (voice box, vocal cords) and the General lost his voice—forever.³⁴² Therefore, he communicated his thoughts, emotions, pains, triumphs, hopes, and sorrows by the handwritten notes that have

³⁴⁰Ibid.

³⁴¹Ibid., 1:6. Also see Pitkin, *The Captain Departs*, 63-64.

³⁴²Shrady, *Grant's Last Days*, 64. and "Grant's Case," 123.

largely been preserved to this day.³⁴³ They afford a rare window into the identity of Ulysses S. Grant and the personal tragedy of traditional cancer.³⁴⁴

The notes reveal a frightened yet strangely impassive and accepting personality—a man of flesh and blood who presided over the Union armies and yet whose last struggles were on the battlefield within—cognitively (if not technically) out of reach of the soldiers and surgeons of the day. They highlight his fear of bodily disorder (choking, vomiting, suffocating) and they delight in—yet show realistic concerns about the completion of—his memoirs. Above all, the handwritten notes to Dr. Douglas and others show a man who accepted the finality of his diagnosis, the pronouncements of his physicians, and the futility of his treatment. Finally, he wished for a swift but non-suffering death.

By way of warning, however, it is important to remember that the notes, spontaneous as they may seem, have a self-conscious flavor about them. Early in the course of his aphonia (loss of voice and all but whispered speech), Grant noted that recipients of the scraps of paper on which he wrote his notes treated them like precious keepsakes. The sensitivity of the General to his poor spelling and grammar made him even more self-conscious of his writing. “I will have to be careful about my writing,” he scribbled to Dr. Douglas in late June. “I see ever [*sic*] person I give a piece of paper to puts it in his pocket. Some day they will be coming up against my English.”³⁴⁵ Grant was also concerned that his notes not fall into the hands of the leech-like

³⁴³Library of Congress, *Index to the Ulysses S. Grant Papers*, President's Papers Index Series (Washington, D. C.: Manuscript Division, Reference Department, Library of Congress, 1965).

³⁴⁴Much of this section is based on the section, “Notes to the Doctor,” in McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1111-21, 56-61.

³⁴⁵*Ibid.*, 1113. The spelling and grammatical errors are in the original. They occur too frequently to use [*sic*] after this first example. Ulysses S. Grant graduated West Point in 1843, but his class rank (21/39) and conduct were hardly exemplary.

press that clung to the cottage environs day and night. On July 2, for example, he begged Dr. Douglas to maintain the secrecy of his private communications.

Dr. I ask you not to show this [note] to any one, unless physicians you consult with, until the end. Particularly I want it kept from my family. If known to one man the papers will get it and they [the family] will get it. It would only distress them almost beyond endurance to know it, and, by reflex, would distress me.³⁴⁶

General Grant was not as sanguine as his consultants about the salutary nature of the Mount McGregor environment. The day after his arrival, the General alarmed Doctor Douglas by predicting his own demise.

Dr. Since coming to this beautiful climate and getting a complete rest for about ten hours, I have watched my pains and compared them with those of the past few weeks. I can feel plainly that my system is preparing for dissolution in three ways; one by hemorrhages [*sic*], one by strangulation and the third by exhaustion. The first and second are liable to come at any moment to relieve me of my earthly sufferings; the time for the arrival of the third can be computed with almost mathematical certainty.³⁴⁷

—June 17, 1885

The throat specialist, who was himself approaching a nervous breakdown,³⁴⁸ immediately telegraphed Dr. Sands to travel in haste to Mount McGregor. Grant delivered a note with similar import to Col. Grant, the General's oldest son. The Colonel drew the family together in the Drexel cottage and read the note to them. All were aghast, but Mrs. Grant was especially distraught. It was as though she accepted the finality of her husband's fatal condition for the first time. "She alone," said her son, "had been blind to the true situation of affairs."³⁴⁹ Julia's acknowledgment of the terminal nature of her husband's illness the previous October had become the same defensive denial that kept Grant from seeking medical attention sooner. The

³⁴⁶Ibid., 1115.

³⁴⁷Ibid., 1111.

³⁴⁸The (New York) World, "Grant's Physician Breaks Down. The General Evidently Enjoying About as Good Health as Dr. Douglas.," *The New York World*, 12 July 1885, 1:6.

³⁴⁹The New York Times, "Gen. Grant Much Worse: A Serious Relapse Induced by a Long Walk. Dr. Douglas and the General's Family Much Alarmed by His Condition--Dr. Sands Hastily Summoned," *The New York Times*, 18 June 1885, 1:1.

press also found out about the urgent message to Sands, but neither Douglas nor anyone else would divulge that its true basis lay in the General's prediction of his imminent passing. Grant was expressing nothing more than his belief that the end of suffering was near.

TERMINAL SUFFERING

The Quest for Palliation

Grant lived, but in life found only suffering. The cancer continued to grow and the doctors failed to control it. His notes went beyond the vivid description of his “dissolution” to highlight his own prognosis and the suffering that he would undoubtedly endure until death. “There can not be a hope of going far beyond this time,” he wrote to Dr. Douglas on June 17. “All any physician, or any number of them do for me now is to make my burden of pain as light as possible.”³⁵⁰ The General and his family believed that his medical care was the best, but he had no objection—save one—to “consultation with other professional men.”³⁵¹ He dreaded the suffering that new consultants invariably brought with them in the form of palpations, probes, and prescriptives. He was weary of the fight. “I dread them however knowing that it means another desperate effort to save me, and more suffering.”³⁵² The General most feared suffering, which to him was hemorrhage, strangulation, exhaustion, pain, and all the horror these meant after eight long months.

Suffering was inherent to the ideology of traditional cancer. The nineteenth-century belief in constitutionalism and the distrust of microscopic findings delayed diagnoses beyond hope of cure. Many physicians felt that even the possibility of surgical relief, as Dr. Gross had

³⁵⁰McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1111.

³⁵¹*Ibid.*

³⁵²*Ibid.*

so eloquently avowed in 1853, was fraudulent.³⁵³ Surgery to lighten the tumor burden, the next best hope after cure, was laden with risks. Samuel Gross and many of his colleagues believed that surgical treatment could be worse than allowing the cancer to follow its own natural course because surgical intervention might increase suffering and hasten death. This way of thinking clearly entered the thoughts of Drs. Douglas, Barker, Sands, and Shrady when they rejected surgery for Grant in March. They knew that anesthesia was problematic, analgesia of limited efficacy, and the risk of postoperative infection—if one could survive the trauma of the surgery—unacceptably high. Palliation was the best that could be hoped for in the “treatment” of most cancers. As the cancer grew and invaded the tissues under his right ear, along the jaw, and down the right neck, release from agony was the objective of the General and his consultants. For Grant, palliation came in two forms: physical and mental.

Topical treatments to the General’s cancer, systemic analgesics, and dietary changes constituted his physical palliation. The pain relievers, particularly topical cocaine and systemic morphine, helped him endure the physical suffering attending the growth and ulceration of his cancer, but they came with a stiff price—tolerance and addiction. Douglas applied cocaine in the form of a four per cent solution to the mass in his throat at least once a day. Morphine was typically administered several times a day in the form of minims (1/480 of a fluid ounce).³⁵⁴ Grant began offering the doctors ways to optimize his medication schedule, not only for his own welfare, but that, as he became more altruistic in his last weeks, “it may benefit some other fellow sufferer hereafter.”³⁵⁵ On June 27, he suggested a change in his narcotic schedule. “If

³⁵³Gross, "On the Results of Surgical Operations in Malignant Diseases," 160.

³⁵⁴Editorial and Shrady, "General Grant's Condition," 410. A minim is 1/240 of a fluid ounce. The General received four to six minims of morphine over the course of a bad day.

³⁵⁵McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1119.

this goes on I do not know but it will be best for me to take my first injection early. Three days ago I would scarcely [sic] have been able to endure the pain of to-day.”³⁵⁶ Two days later he made it clear to Dr. Douglas that he needed his morphine before retiring for the night, “not from craving,” he wrote, “but merely from a knowledge of the relief it gives. If I should go without it all night I would become restless I know, partly from the loss of it, and partly from the continuous pain I would have to endure.”³⁵⁷ On June 30, Dr. Douglas advised the General that he was receiving too much cocaine and that he should decrease the dosage in order to improve efficacy. Grant was reticent to accept any decrease in the quantity of his pain medicine, but thought it was worth the attempt in the short term if it reduced the tolerance he had developed. “It is a little hard giving up the use of cocaine [sic] when it gives so much relief,” he admitted. “But I suppose that it may be used two or three times a day, without injury, and possibly with benefit, when the overuse of it has been counteracted.”³⁵⁸ In short, Grant hoped that less frequent administration of the narcotics would make them more effective. His goal was clear. On July 2, he wrote Douglas that “I will be the happiest the most pain I can avoid.... Make me as comfortable as you can.”³⁵⁹

Other measures improved Grant’s physical comfort as well. His liquid diet, usually “a little milk and egg,” was intended to reduce the probability of nasal regurgitation, choking, and aspirating.³⁶⁰ Likewise, sleeping in one chair with his feet up on another was an attempt to forestall the pooling of secretions in his throat and the same perils. In addition, Dr. Douglas

³⁵⁶Ibid., 1111.

³⁵⁷Ibid., 1112.

³⁵⁸Ibid., 1112-3.

³⁵⁹Ibid., 1115-16.

³⁶⁰The New York Times, "Resting at Mt. McGregor," 1:5.

attempted to soothe the searing pain in his throat when he debrided the area of necrotic tissue, applied an antiseptic (usually carbolic acid) to the growth and its satellite ulcerations, and cleansed the entire tumor with a mild salt solution.³⁶¹ This treatment also reduced the risk of concurrent infection in and around the tumor mass as well as decreased the noticeable stench—so well known to the Ladies’ Board at the Woman’s Hospital and, later, the nursing staff at the New York Cancer Hospital—that accompanied the necrotic lesion and was exhaled with every breath.³⁶²

The General’s mental palliation came in two predominant forms—his family and his memoirs. Their importance to the sustenance and prolongation of his life cannot be overestimated. Grant adored his family and they seemed to love and respect him. In early April, when the footsteps of death seemed audible, the General voiced the mixed blessing of his demise. “I regret each moment I have to remain and regret leaving my family.”³⁶³ They attended him constantly and sought his counsel frequently. Nellie Grant Sartoris, his only daughter, traveled from across the Atlantic Ocean to be with him. Photographs taken of the Drexel cottage on Mount McGregor routinely picture the General in his black silk hat and well-worn coat surrounded by his children, their spouses, and their children. It was a source of great comfort to Grant to have his extended family around him. Just before his death, the General pinned a note to his clothing for Mrs. Grant. Of all the subjects he might have addressed, he singled out those two that had bolstered his identity and given meaning to his life—honor and family. “Look after our dear children,” he beseeched his wife of thirty-seven years, “and direct them in the paths of rectitude. It would distress me far more to hear that one of them could

³⁶¹Shrady, "Grant's Case," 123.

³⁶²Goldhurst, *Many Are the Hearts*, 144.

³⁶³Lorant, "Baptism of U. S. Grant," 92.

depart from an honorable, upright and virtuous life than it would to know that they were prostrated on a bed of sickness....With these few injunctions and the knowledge I have of your love and affection and the dutiful affection of all our children, I bid you a final farewell, until we meet in another and, I trust, better world.”³⁶⁴

General Grant’s memoirs kept his mind active and gave purpose to his dying days. Like his family, they sustained him through his darkest days. It has already been noted that the memoirs provided the “bread”—as Julia Dent Grant called it—to support the family monetarily after the collapse of Grant & Ward; that the memoirs became the General’s labor of love during his most trying moments; and that he envisioned this book as his legacy to the world. Not only did the memoirs nourish Grant’s soul—they also palliated his suffering and prolonged his life. Were it not for the memoirs, he admitted in early July, “life is not worth living. I am very thankful to have been spared this long because it has enabled me to practically complete the work in which I take so much interest.”³⁶⁵ He began work on the second and final volume of his memoirs in December, 1884. The newspapers claimed that at times the General wrote ten thousand words a day.³⁶⁶ He knew that the cancer could take his life at any moment, so he made sure to dictate the grand finale of the book—Lee’s surrender at Appomattox—before he transcribed the body of the corpus.³⁶⁷

By early July, he could sense the completion of the book. As with many cancer patients, the mental feeling of accomplishment rejuvenated him physically. “I feel much relieved this

³⁶⁴Ibid., 102.

³⁶⁵McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1115.

³⁶⁶Lauber, *Mark Twain*, 222-23. Would that I could write so!

³⁶⁷Ibid., 223. Ulysses S. Grant considered Robert E. Lee’s surrender at Appomattox Court House the crowning glory of Grant’s career. His autobiographic *Memoirs* end shortly thereafter, entirely excluding his Presidency and the last twenty years of his life.

morning,” he wrote on July 5. “I had begun to feel that the work of getting my book together was making but slow progress. I find it about completed, and the work now to be done is mostly after it gets back in galleys.”³⁶⁸ The first draft of the culmination of his life’s work, some dictated and some written, was almost finished. Five days later he found solace again in his memoirs. “In two weeks if they work hard they can have the second vol. copied ready to go to the printer. I will then feel that my work is done.”³⁶⁹ Grant experienced an amelioration of his physical symptoms when his writing progressed. He was particularly exhilarated as the second volume neared completion. “My breathing is less obstructed,” he noted to Dr. Douglas on the morning of July 11. “In fact my breathing is not obstructed in the least. Have used no cocaine during the night nor do I require any yet.”³⁷⁰ Later that day the General completed his revisions of the first volume and mailed them to the publisher.³⁷¹ Astoundingly, some of his lost voice returned the next day.³⁷²

Exactly one week later, Grant completed the second and final volume of his memoirs.³⁷³ His work done, his suffering worsened. “There is nothing more I should do to it now,” he confessed as he neared the end of the second volume, “and therefore I am not likely to be more ready to go than at this moment.”³⁷⁴ It is not unusual for those who are beyond death (by any

³⁶⁸McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1117.

³⁶⁹*Ibid.*, 1118.

³⁷⁰*Ibid.*, 1119.

³⁷¹The New York Times, "Faith in His Doctor's Skill," 6:2.

³⁷²McFeely, *Grant*, 515.

³⁷³McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1160. Julia Dent Grant wrote in her memoirs that her husband finished the second volume “about July the nineteenth.” Simon, *Julia Dent Grant*, 331.

³⁷⁴McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1119.

normal expectation) to live until the completion of a notable day, event, or project. The General was no exception. Ulysses S. Grant, having achieved that which sustained his life and eased his suffering, died less than five days later. At least, wrote Dr. Douglas for all in his personal record, “he had been enabled to accomplish his great desire, the completion of his Memoirs.”³⁷⁵

Futility

Fighting traditional cancer was hopeless. The patient could do little beyond denial and repression. General Grant and his family, who stated on numerous occasions that they had received the best care medicine had to offer, believed that palliation was their most realistic goal. “Mine is a different case from ordinary suffering,” Grant informed Douglas at Mount McGregor.³⁷⁶ The new cocaine, the old morphine, liquid diets of eggs and milk, and positional changes led to no permanent improvement. They only staved off the inevitable. “I know that what you are doing will be as likely to cure me as any think els,” he wrote on July 6. “All the medical skill in America...could not find a cure.”³⁷⁷

The General knew, deep within the recesses of his understanding, that even his beloved memoirs could only temporarily postpone the triumph of the cancer. As he again took up his pencil in the weeks before his death at Mount McGregor, he believed that the writing implement was in a sense digging his grave. “I said I had been adding to my book and to my coffin,” he wrote on June 23.³⁷⁸ “I presume every strain of the mind or body is one more nail in the

³⁷⁵John Hancock Douglas, "Records of the Last Days of the Magnanimous Soldier U. S. Grant," in *The Captain Departs: Ulysses S. Grant's Last Campaign*, ed. Thomas M. Pitkin (Carbondale: Southern Illinois University Press, 1885; reprint, 1973), 139.

³⁷⁶McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1113.

³⁷⁷*Ibid.*, 1117.

³⁷⁸*Ibid.*, 1111.

coffin.”³⁷⁹ The General was wrong. The memoirs, rather than hastening death, postponed it. Their completion left him no reason to live as his suffering increased. On July 7, he wrote Douglas that he “cannot endure it any longer.”³⁸⁰ “After all that however the disease is still there and must be fatal in the end,” he acknowledged on July 16.³⁸¹ “My life is precious of course to my family and would be to me if I could recover entirely.”³⁸² Nevertheless, he knew that restoring his health was a futile endeavor and that even life itself was a dead-end desire. No medicine could cure his disease and the thought of surgery had been dismissed long ago. He accepted reality and concluded “there never was one more willing to go than I am.”³⁸³

Eternal Relief

On July 18, 1885, the day that General Grant finished the literary capstone of his military achievements, he weighed less than one hundred pounds.³⁸⁴ Growth of the cancer, recurrent bleeding, nasal regurgitation, intractable hiccoughs, throat pain, and the near impossibility of sleeping upright in a chair for almost four months, took their toll on his physical frame. The last known photograph of the General, bespectacled and in the heat of summer garbed in the hat, scarf, and clothes that deceptively puffed up his emaciated body, was taken the next day.³⁸⁵ In that last picture, he is reading the newspaper—bane of his family’s existence but the greatest

³⁷⁹Ibid.

³⁸⁰Ibid., 1117.

³⁸¹Ibid., 1119.

³⁸²Ibid.

³⁸³Ibid.

³⁸⁴The New-York Times, "News of Ulysses Grant's Death," *The New York Times*, 24 July 1885, 4.

³⁸⁵McFeely, *Grant*, 516. Pitkin displayed what appears to be an insert of the identical photograph of Grant. Pitkin, though, noted in the caption that the photo was taken “three days before his death, which occurred on July 23.” Pitkin, *The Captain Departs*, 89. By my reckoning, that would be July 20 rather than the date of July 19 in the McFeely picture.

promoter of popular cancer knowledge in America during the nineteenth century. Grant's mind remained active and alert to the end—typical of a cancer that rarely metastasizes to the brain.³⁸⁶

As usual, the photograph obscured the tumorous right side of his face.

Fate played a cruel joke on the aphonic General. Accustomed to leading troops on the front lines with rallying cries and vocal orders, Grant ended his life with full mental capacity but in silence. The daily torture was unbearable. In one of the most poignant descriptions of suffering from cancer, the General—an untrained literary artist with a knack for conveying meaning through simplicity and directness—encapsulated the last months of his life to Dr. Douglas in July, 1885:

I do not sleep though I sometimes dose off a little. If up I am talked to and in my efforts to answer cause pain. The fact is I think I am a verb instead of a personal pronoun. A verb is anything that signifies to be; to do; or to suffer. I signify all three.³⁸⁷

On July 20, sensing the end, he wrote to the doctor that he wished his attendants to push him in his invalid chair to the summit of Mount McGregor. There he saw for the last time the land of his life and labor. The Hudson River valley and the Green Mountains of Vermont stretched like a phantasmagoric vision to the East. His mind sucked in all that was around him, but his body gave way. He returned to Drexel's cottage drained of his remaining strength.³⁸⁸ "The exhaustion following the excursion to the Eastern Outlook had been sudden and complete," concluded Dr. Douglas.³⁸⁹ The next day his condition deteriorated further.³⁹⁰ On the evening of July 22, he indicated with gestures—for he could no longer write or whisper—that he wanted to

³⁸⁶Douglas, "Douglas Papers," 138.

³⁸⁷McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1120.

³⁸⁸*Ibid.*, 1161.

³⁸⁹Douglas, "Douglas Papers," 139.

³⁹⁰McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1161.

be put to bed.³⁹¹ All present knew how to interpret the General's request. The physicians attempted again to ease his suffering with a hypodermic of brandy, but it did no good.³⁹²

The night was difficult. The General, surrounded by his family and Dr. Douglas, could no longer clear or expectorate his throat secretions, so they pooled and obstructed his breathing.³⁹³ However, as life slipped away, concerns of choking and suffocating disappeared. At 3 A. M. on the morning of July 23, 1885, he uttered his last word, "water." Paradoxically, he requested that which would end his life, for he drowned in his own secretions.³⁹⁴

The General's last wish was that his physicians grant him a "peaceful, painless death."³⁹⁵ The doctors obliged him with brandy, cocaine, morphine, and other anodynes. A calmer nineteenth-century death, despite the long months of pain and suffering, would be hard to imagine. *The New-York Times* reporter (perhaps the same man the General had condemned with loathing only weeks before), with a romanticized form of poetic license common during the Gilded Age, described Ulysses S. Grant's last moments shortly after 8 A. M. on the morning of July 23, 1885.

The light on the portrait of Lincoln was slowly sinking. Presently the General opened his eyes and glanced about him, looking into the faces of all. The glance lingered as it met the tender gaze of his companion [Mrs. Grant]. A startled, wavering motion at the throat, a few quiet gasps, a sigh, and the appearance of dropping into a gentle sleep followed. "At last," said Dr. Shrady, in a whisper. Dr. Douglas sighed, "It is all over."³⁹⁶

³⁹¹Grant 3rd, "Ulysses S. Grant," 450.

³⁹²Ibid.

³⁹³The New-York Times, "Grant's Death," 1.

³⁹⁴Ibid., 3.

³⁹⁵Ibid., 1. Phillippe Ariès, who has written much on the cultural history of death, named the nineteenth century "The Age of the Beautiful Death." See Philippe Aries, *The Hour of Our Death*, trans. Helen Weaver (New York: Oxford University Press, 1981; repr., 1991), 409-74. Gen. Grant's wishes were typical of those who suffered from terminal diseases like cancer, as were the depictions of the deathbed scene wherein the General lies "asleep," surrounded by family, friends, and physicians.

³⁹⁶The New-York Times, "Grant's Death," 3. The reporter, of course, was not present at the scene he described.

Apotheosis

The publicity that engulfed General Grant and his notorious cancer in life did not end with death. Despite the many consulting physicians, the multiple throat and microscopical examinations, and surely one of the most meticulously detailed documentations of the natural history of a cancer to that time, the doctors believed that the diagnosis of epithelioma remained unproven. The General's rapid deterioration and early death, they deduced, were inconsistent with epithelioma.³⁹⁷ The doctors suggested that an autopsy be performed. While the General's body was still warm they "recalled to the family the question raised in regard to the diagnosis, and asked the privilege of an autopsy."³⁹⁸ Gross, clinical examination—a method known to be fraught with inter-observer variability and inaccuracy—was the basis of the physicians' diagnosis. The microscope was distrusted and the nomenclature attached to tumors viewed through the instrument highly descriptive (rather than functional) and non-standardized. The purpose of the autopsy, they submitted, was to compare Grant's cancer with knowledge of other similar tumors gained from studies in gross pathological anatomy as least since the age of Vesalius. Nevertheless, an autopsy was not to be. The family, fresh from months of their patriarch's suffering, "would not hear of it. They were satisfied, they said, with the diagnosis."³⁹⁹ Never again was the word mentioned.

Shrady's involvement with Grant did not end at the General's death. In 1902, Shrady's son, Henry Merwin Shrady, won an architectural competition for the design of a Ulysses S. Grant memorial in Washington, D. C. The Grant memorial in Washington's Union Square was dedicated on April 27, 1922, the one-hundredth anniversary of the birth of the General. Henry Shrady, who spent decades of his life on the project, died fifteen days before its dedication.

³⁹⁷"Gen. Grant and Edwards Pierrepont," 5:1. This *Times* article quoted the March 21, 1885 edition of *The Medical News* (Philadelphia) that Grant's lifespan after diagnosis was shorter than the expected longevity of patients with epithelioma. The problem with such life expectancy "ranges" is that the time of "onset" of the cancer is quite variable. Thus life expectancies with cancer were and are approximate ranges at best.

³⁹⁸"Grant's Death," 4.

³⁹⁹*Ibid.*

In the months and years following his death, the public apotheosized General Grant—acclaimed as the most illustrious American in 1885. During life, the press used bulletins of increasing frequency to keep the nation apprised of the progress of the cancer and the deterioration of the General’s condition. Mark Twain, whose publishing house inked the contract with the General for his *Personal Memoirs* that restored the Grant family to financial health, recorded in his notebook the start of a nationwide period of mourning that began upon the death of America’s greatest hero. As the end drew near, wrote Twain, “many a person between the two oceans lay hours awake...listening for the booming of the fire bells that should speak to the nation in simultaneous voice and tell its calamity. The bell strokes are to be 30 seconds apart, and there will be 63, the General’s age. They will be striking in every town in the United States at the same moment.”⁴⁰⁰ Thomas Jefferson, who two years before Grant’s birth had likened the problem of slavery to “a fire bell in the night,” might have noted a subtle irony that the passing of the man whose battlefield exploits eliminated the problem of slavery was extolled by the striking of fire bells.⁴⁰¹

On August 4, 1885, the Rev. Dr. Newman, who sought in vain on numerous occasions to have the General take communion, delivered the Grant eulogy for over an hour on a hot day on Mount McGregor.⁴⁰² Although Newman “apostrophized Grant the warrior, Grant the President, Grant the genius, Grant the family man, Grant the Christian,”⁴⁰³ it was clear that the General,

⁴⁰⁰Lorant, "Baptism of U. S. Grant," 93.

⁴⁰¹Thomas Jefferson, Letter, 22 April 1820. Accessed August 9, 2001 at <http://www.loc.gov/exhibits/jefferson/159.html>. Jefferson’s letter was in response to the Missouri Compromise of 1820, one of many attempts before the Civil War to resolve the problem of slavery.

⁴⁰²Lorant, "Baptism of U. S. Grant," 102.

⁴⁰³Ibid.

despite his wife's urging, did not act the part of an observant Christian. He delayed baptism as long as possible, refused communion, and never comported like a choirboy. Instead, concluded Newman reverently, "he lived within himself."⁴⁰⁴ Grant was, above all, secular. He never blamed his cancer on the deity or the sinfulness of his own actions. In his silence, he knew that the end was inevitable. That attitude permeated the bulletins issued by the doctors and the family. Grant would have told the world himself, but, he wrote, he was concerned that such announcements would lead his family to despondency.⁴⁰⁵ He informed Dr. Douglas in the days before death that "he was content to await patiently the natural result of the disease."⁴⁰⁶ Nature, not ineffable powers, controlled cancer and his destiny. Herein lay the social seeds of modern cancer, for the influence of religion on the disease cancer was waning. The General epitomized the new non-religious connotation of cancer and, through the media attention he garnered, promulgated the secularization of cancer to the Nation.

Traditional Cancer Buried

Burial plans took days to arrange because the General had not specified a single site. The uncertainty of his final wishes and his popularity led several cities to suggest many "suitable locations"—reminiscent of the variety of offers he received for a summer residence months earlier. Each city, town, and village, it seemed, wanted General Grant to be buried in its back yard. As the New York Cancer Hospital was being constructed to contain the contagiousness of cancer, no one showed concern about the possible communicability of the General's life-destroying cancer. No one offered reservations about the possible sinfulness that led the victim to the horrible suffering that terminated in cancer death. On the contrary, Grant's ordeal

⁴⁰⁴Ibid.

⁴⁰⁵The New-York Times, "Grant's Death," 7.

⁴⁰⁶Ibid., 8.

endeared him further to an adoring public. The cancer added sympathy to respect. Everyone wanted his remains—like the relics of medieval European saints. Ulysses S. Grant helped turn the tide toward a new interpretation of cancer.

Grant was not oblivious to the possibility of contention over the site of his burial. A month before his death he penciled a note to Colonel Grant that “there are three places from which I wish a choice of burial place to be made.”⁴⁰⁷ West Point was his first selection, but he believed that the location was not feasible because regulations barred Mrs. Grant, whom he sorely wanted to eventually rest next to him, from burial there. Grant listed Galena, “or some other place in Illinois,” because he had received his first General’s commission there. Lastly he listed New York City, “because the people of that city befriended me in my need.”⁴⁰⁸

The thought that General Grant might be buried in their great metropolis enraptured the New York media. They immediately launched a campaign to assure that the General find his final resting-place in New York.⁴⁰⁹ *The New-York Times* headline of July 25 touted “A most fitting burial place: The Nation’s Greatest Hero should rest in the Nation’s Greatest City.”⁴¹⁰ Newspapermen interviewed scores of public officials to determine their interest in and suggestions for Grant’s burial in New York. All agreed that the General should be buried in the City, but controversy arose over the exact location. Again, no thought was given to the possibility that Grant’s cancer might be contagious, despite adumbrations at that time of germ

⁴⁰⁷The New-York Times, "Grant's Death," 6.

⁴⁰⁸Ibid.

⁴⁰⁹It is noteworthy that in 1885, "New York City," thirteen years before the consolidation of the present-day boroughs, was Manhattan and a portion of the Bronx. The family did not consider the great cemeteries of Brooklyn and Queens, like Greenwood Cemetery (which held the remains of J. Marion Sims), which were not in New York City.

⁴¹⁰The New York Times, "A Most Fitting Burial Place: The Nation's Greatest Hero Should Rest in the Nation's Greatest City," 1:4-5.

theories of cancer. On the contrary, the family and city officials selected sites with the greatest possible exposure. The majority suggested Central Park, where many of the City's citizens could conveniently pay homage to their departed leader.⁴¹¹ Mayor William R. Grace and Parks Commissioner John D. Crimmins, however, favored the increasingly popular Riverside Park, but "the family would not consider it"—at first.⁴¹² Commissioner Crimmins, in particular, urged the family to accept a site in Riverside Park near Clermont, because "at this point the surface of the plateau is 113 feet above the level of the river," which "would enable persons to see a monument for miles around."⁴¹³ Mayor W. R. Grace, founder of the company that bears his name, personally donated the land and Col. Fred and the Grant family eventually consented to the Riverside Park location.

The return of General Grant's body to New York City and subsequent memorial events reinforced his immense popularity and spread the story of his cancer far and wide. His remains lay in state in both Albany and New York's City Hall. An estimated quarter of a million mourners viewed the pale, frail corpse at the City's executive mansion.⁴¹⁴ Elaborate plans were made for the funeral procession to carry the body from City Hall up Fifth Avenue and across Fifty-seventh Street, ending on Riverside Drive just South of 125th Street.⁴¹⁵ The route passed within a few city blocks of the fledgling New York Cancer Hospital, which was still under

⁴¹¹The New-York Times, "News of Ulysses Grant's Death," *ibid.*, 24 July, 8-12. Professors Elizabeth Blackmar and Roy Rosenzweig noted that by 1865, Central Park, only six years after its public opening, had more than seven million visitors annually. Elizabeth Blackmar and Roy Rosenzweig, "Central Park," in Jackson, *Encyclopedia of New York City*, 198.

⁴¹²The New York Times, "To Rest in Central Park," *The New York Times*, 25 July 1885, 1:1. and The New-York Times, "News of Ulysses Grant's Death," *ibid.*, 24 July, 9.

⁴¹³"Grant's Death," 9.

⁴¹⁴Pitkin, *The Captain Departs*, 110.

⁴¹⁵The New York Times, "The Route of the Grant Funeral Procession Next Saturday," *The New York Times*, 5 August 1885, 1:3-5.

construction. Ironically, the Hospital, with which the General had had several indirect contacts, was only a short distance from his tomb.

The procession and burial were held on a Saturday, August 8, 1885, so that the largest number of citizens could attend. As it turned out, the number of spectators far outnumbered even the highest estimates. It was, in short, of immeasurable proportions. More than a million grieving citizens came from untold distances to stand somberly along the funeral route on that overcast and wet day. The doleful observed the once-in-a-lifetime human dirge of the General who lost his last battle to cancer.⁴¹⁶ The procession took five hours, included more than forty-two thousand marchers, and stretched seven and a half miles.⁴¹⁷ Pallbearers, selected by the President of the United States, included a “Who’s Who” of Civil War generals. Grant would have been pleased that both Union and Confederate generals were represented.⁴¹⁸ Union Generals William T. Sherman and Philip Sheridan were pallbearers, as were Confederate Generals Johnston (the Congressman who had created the highest rank in the Army for Gen. Grant) and Buckner (his old friend from West Point and opponent at Fort Donelson).⁴¹⁹ The *New York Tribune* boasted that “such a mighty outpouring of people in the streets, such a marshalling of men in one array the inhabitants of New-York never saw.”⁴²⁰ *Harper’s Weekly* noted that “the remarkable spectacle of three Presidents of the United States come to the grave of a fourth may never be seen again by the living generation, if indeed in another century. No

⁴¹⁶Harper's Weekly, "The Death of General Grant," *Harper's Weekly*, 15 August 1885.

⁴¹⁷Lorant, "Baptism of U. S. Grant," 102.

⁴¹⁸General Grant wished that his death would help heal the rift that had torn the Union asunder. Grant 3rd, "Ulysses S. Grant," 449. and Nelson, "The Victory of U. S. Grant," 435. Indeed, Mrs. Grant had requested that “if any prominent Union generals were appointed pallbearers by the President, a corresponding number of Confederate generals be appointed.” Grant 3rd, "Ulysses S. Grant," 453.

⁴¹⁹"Ulysses S. Grant," 453.

⁴²⁰August 9, 1885. Cited by Pitkin, *The Captain Departs*, 110.

similar scene has been witnessed since Jefferson, Madison and Monroe walked together in the ground of the University of Virginia.”⁴²¹ Mrs. Astor, who was stricken with cancer herself, generously opened the doors of her Fifth Avenue mansion to shop girls and others who were “prisoners in the town” as the flood of humanity passed her residence on Fifth Avenue.⁴²²

General Sherman privately wrote the widow Julia Grant, who was too heartbroken to make the trip from Mount McGregor, that “such a funeral never before occurred in America and never will again.”⁴²³ As Mrs. Grant received heart-felt condolences from the rich and famous around the world, Mrs. Hamilton Fish added convincingly that “all felt that enough could not be done to honour the greatest man of the century.”⁴²⁴

General Grant did not reach his final resting-place on August 8. He was buried in Riverside Park in a temporary brick tomb with a Roman arch and a large “G” on the ironwork gate.⁴²⁵ The Grant Monument Association, formed shortly after the General’s death, raised more than half a million dollars from over ninety thousand contributors to construct a more fitting memorial to the Nation’s glorified leader.⁴²⁶ The enormous popularity of Grant’s *Memoirs* further fueled fundraising. The architect modeled Grant’s Tomb after some of the most famous mausoleums in the world and became the largest in the United States.⁴²⁷ On a cool, dreary day

⁴²¹August 15, 1885. Cited by Grant 3rd, "Ulysses S. Grant," 452. The Presidents in attendance were Rutherford B. Hayes, Chester Arthur, and Grover Cleveland.

⁴²²Memorial Service for Mrs. John Jacob Astor, January 17, 1888. Reported in New York Cancer Hospital, "Nych, Annual Report, 1886-1887," 41.

⁴²³Ross, *The General's Wife*, 315.

⁴²⁴*Ibid.*, 316.

⁴²⁵Pitkin, *The Captain Departs*, 124.

⁴²⁶Frank Scaturro, “Grant’s Tomb,” in Jackson, *Encyclopedia of New York City*, 501.

⁴²⁷*Ibid.*, 500 and 01.

in April, 1897, almost twelve years and half a generation after the General's death, President William McKinley and Mrs. Grant dedicated the Tomb on what would have been Ulysses S. Grant's seventy-fifth birthday. The General's Tomb kept his memory fresh in the eyes of Americans for yet another generation, for it remained one of the most popular attractions in one of the most visited cities until after the First World War.⁴²⁸

Cancer Biography

The General's *Personal Memoirs*, the provident sustainer of his last months, increased universal interest in cancer through the highly publicized misfortunes of its author. The first of the two volumes was published in December, 1885; the second in March, 1886. Both were heavily subscribed. In total, Samuel Clemens' publishing house sold over 300,000 two-volume sets, making it one of the most well-known books of American literature in the nineteenth century. In the words of Ishbel Ross, one of Julia Dent Grant's biographers, the *Memoirs* "created a great sensation."⁴²⁹ In particular, noted the author, "the circumstances under which it was written gave it unique interest."⁴³⁰ It was common knowledge that the General had written his memoirs while in the throes of cancer. Indeed, had it not been for cancer, Grant may never have written his *Memoirs* at all. The memory of his slow, painful demise by cancer was rekindled when the generation of the Army of the Potomac and their children read the *Memoirs* and remembered the General and his last days. The press had made sure of that, eternally linking one of the greatest figures of America's nineteenth century with cancer. Memories of how Grant died from cancer made the *Memoirs* more celebrated, and the *Memoirs* made knowledge of cancer more widespread.

⁴²⁸Ibid., 501.

⁴²⁹Ross, *The General's Wife*, 316.

⁴³⁰Ibid.

As cancer consumed the revered General, so the continual reports on his health, his condition, and his cancer, lent social legitimacy at the end of his life and after his death to an ailment that heretofore had been treated with disdain, derision, and disgust. In his *Memoirs*, referring to another time and another place, the General wrote “wars are not always evils unmixed with some good.”⁴³¹ Ulysses S. Grant lost his war against cancer. Nevertheless, the evil of his cancer contained some good in that it brought the cancer to the forefront of the American conscience and consciousness. Consequently, it altered the way physicians and the public viewed the disease. The General and his illness thus added a critical contribution to the demise of traditional cancer and the making of modern cancer.

GENERAL OBSERVATIONS

Traditional cancer caused the suffering and death of Ulysses S. Grant. The hallmarks of the course of the General’s cancer—late diagnosis, individualism, and palliation—were common to his era and to those who endured cancer before him. The publicity surrounding the eminent warrior and his deadly disorder created a new *milieu* for the acceptance of cancer as a legitimate medical entity unencumbered by innuendo and sinister undertones. Whatever disparaging thoughts the average man and woman harbored toward cancer before Grant’s terminal illness were modified by their new conceptions of the disease afterwards. For many, the urgent bulletins penned by the physicians with Grant’s approval and the daily newspaper reports on the General’s condition were the first glimpse they ever had of the disease cancer shorn of its heavy traditional trappings of superstition, religion, and myth.⁴³² The General’s illness engendered feelings not of loathing but of compassion—and spurred efforts to attack the disease through the new technologies of scientific medicine.

⁴³¹Grant, *Personal Memoirs*, 589.

⁴³²Butler, "The Search for a Cure," 2.

Analysis of Grant's representative tumor reveals that the diagnosis and treatment of traditional cancer were more art than science. There is, of course, much art in the practice of medicine today, but theories and practices derived from the application of the scientific method to medicine form the foundation of the training of the twenty-first century physician. The medical approach to Grant's cancer, on the other hand, was highly dependent upon the subjective gross descriptive abilities of the observer and the prevalent conviction that constitutionalism explained the nature of cancer. Indeed, the theory appeared to explain much—why cancer was more frequent in certain families; why some developed cancer after “irritation” and others did not; why cancer reappeared in other parts of the body after excision from the initial site. However, it also fostered futility and hopelessness due to the inescapable implication of incurability. The General knew during the summer of 1884 that there was a dangerous condition in his throat. Many times he spoke of seeking medical attention. Nevertheless, he did not seek his physician's advice for more than four months after the onset of his symptoms. The consultative formalities of his day explain some of his procrastination, as does the universal yearning for time to heal all wounds. But Grant's prophetic words to Dr. Douglas at the time of their first consultation—“Is it cancer?”—belie the possibility that Grant postponed diagnosis because he believed the condition was trivial or benign. The assumed irremediability of cancer, spawned by constitutionalism, deterred the patient from seeking an early diagnosis. From the perspective of the practicing physician, the lack of objective, reproducible diagnostic criteria often made a verifiable cancer diagnosis less the task of the clinician than the pathologist. Occasionally only the course of the illness over time allowed the doctor to distinguish cancer from a more benign malady. The outcome, again, was delayed diagnosis.

Individualism, the second hallmark of traditional cancer, was, like delayed diagnosis, a logical derivative of constitutionalism. The belief that each cancer victim's disease was specific to him—by virtue of his background, development, and proclivities—held sway for much of the nineteenth century. The individual is, of course, indivisible (by etymology and definition) and, as such, cannot be severed into smaller parts like organs and tissues. The tenets of traditional cancer held that cancer was part of the individual and that the individual was inseparable from the cancer. The conception of an ideal, neo-platonic, disembodied epithelioma of the throat was meaningless. The consultants evaluated General Grant's epithelioma, not *an* epithelioma. Holism reigned. Treatment was complicated because the same diagnosis in different patients often led to varying prescriptives. Some nineteenth-century textbooks published attributes of generic cancer types on a gross level, but eponyms, defining characteristics, and treatments of tumors were manifold and frequently inconsistent. The individualistic nature of traditional cancer made consensual diagnosis on a gross scale difficult, thus delaying correct diagnosis, making definitive treatment unlikely, and, consequently, increasing suffering. Individualism also hampered communication between physicians and would-be specialists (i.e., practitioners with an interest in a special disease or organ). Certainly, there were studies of patients with, say, breast cancer, but the non-uniform gross descriptive terminology used to distinguish one patient from another made direct clinical application of the investigational results problematic.⁴³³ The microscope, much maligned as a medical diagnostic instrument in Grant's day, ushered in a new era of cancer definitions that resolved many of the restrictions attendant with individualism. In

⁴³³A good example is Willard Parker, M.D., *Cancer: A Study of Three Hundred and Ninety-Seven Cases of Cancer of the Female Breast with Clinical Observations* (New York: G. P. Putnam's Sons: The Knickerbocker Press, 1885)., and the correspondence from local physicians from whom he obtained much of the information for his book. See the "Williard Parker, M.D. Papers," in *Willard Parker Papers: #37-59* (New York 1884). at the Malloch Rare Book Room in the New York Academy of Medicine.

so doing, however, there was, to turn the General's phrase, some evil in the good. The microscope eliminated the human face behind the glass slide.

Constitutionalism and individualism thus effected delay and inaccuracy in the diagnosis of cancer. Further, as the narrow window of opportunity for cure closed behind the theories of traditional cancer, medical emphasis defaulted to therapy rather than diagnosis. General Grant might have been cured if Dr. Douglas suggested surgery at the time of the first consultation. The physician chose palliation, however, consonant with the teachings of the day. The benefits of palliation in the "treatment" of cancer should not be minimized.⁴³⁴ Palliation in Grant's day usually implied symptom reduction rather than surgery.⁴³⁵ Nevertheless, surgeons in the nineteenth century often caused rather than cured suffering.⁴³⁶ The General and his consultants respected this caveat. As such, palliation spared the patient the evils of nineteenth-century surgery—anaesthesia complications, intraoperative and postoperative pain, infection, bleeding, disfigurement, and death. It also saved the patient the tribulations of other, non-surgical, interventionist physicians who prodded and poked patients like General Grant endlessly. Palliation in the late nineteenth century implicitly assumed the absence or failure of definitive cancer therapy. Palliation eased death, but it did not forestall it. It was, in short, an admission of failure and hopelessness. In a pre-Darwinian Christian world ruled by a merciful God, life after death was eternal and suffering only a temporary way station on the road to endless bliss for the good—or more permanent for the well-deserved damnation of the bad. By the end of the nineteenth century, however, a more secular world found the failure implicit in palliation less

⁴³⁴I placed the word "treatment" in quotation marks because palliation does not treat the cancer. It attempts to mitigate the symptoms of cancer.

⁴³⁵It is important to keep in mind that surgery—then and now—may be undertaken for palliation as well as cure.

⁴³⁶McFeely and McFeely, *Ulysses S. Grant: Memoirs and Selected Letters*, 1111. See also Gross, "On the Results of Surgical Operations in Malignant Diseases," *passim*.

tolerable. Whether cultural imperatives lead to technological change or vice versa is debatable,⁴³⁷ but the search for remedies accelerated. Cancer medicine and surgery in the Progressive era, as a result of these efforts, were more interventionist, less risky, more successful, and more acceptable to the patient population than during the years encompassing General Grant's cancer.

Grant's therapy was also problematic. The medications and artifices he received as palliative treatment for his cancer were laden with adverse effects and unintended consequences. Barker and Douglas used morphine with care—through frequent but small doses—because it was known to be addictive. Cocaine, the new topical anodyne of the mid-1880s, was promoted as a non-addictive painkiller, but the General knew by the Spring of 1885 that this was not so. Grant, despite Dr. Douglas' assiduous direct applications of the four percent cocaine solution, suffered immeasurable pain. Skull caps, electric caps, upright positioning, and liquid diets acted as placebos or, at best, temporized the inevitable. In the end, the General knew that only death would free him from his agony.

Grant's travail transcended corporeal distress. Like the Latin etymology of the word 'travail' itself, the General suffered from 'three stakes' plunged into his psyche: his body (detailed above), his family, and his public persona as portrayed by the press. Grant's illness reunited his scattered family, but he worried incessantly about their coming to terms with the nature of his disease. After his first consultation with Dr. Douglas, he renounced the use of the word 'cancer,' choosing instead to talk of his ailment in euphemistic terms. He refused to tell his wife Julia that he had the fatal disease. She and their eldest son traveled to the physician's office to confirm their worst fears for themselves. During the course of his illness, he declined dinner

⁴³⁷Witness the debates in the 1960s and 1970s between Marshall McLuhan's technodeterminism and Raymond Williams' cultural determinism. See, for example, Raymond Williams, *Television: Technology and Cultural Form* (Hanover, N.H.: Wesleyan University Press, 1974; repr., 1992), xv-xviii.

with his family for fear that his unpredictable vomiting and nasal regurgitation would embarrass him and frighten those around him. Therefore, he reluctantly abjured the conviviality of the table—one of his favorite pastimes. He suffered in the light of his family when they refused to hear of his burial requests. Col. Grant and his siblings would brook no such discussion. Grant, practical to the end, wished to have his choices heard. Their rejection of his realistic attitude toward cancer wounded him psychologically.⁴³⁸

Finally, the General, a very private figure despite his public aura, suffered at the hands of the press. Their constant invasions of his privacy and misleading news reports unsettled his placid mien and caused him to hide behind the thin façade of home and family. The bulletins, of course, were an attempt to inject the perspective of Grant and the consultants into the newspaper reports. However, the official bulletins were only one ingredient in a roily sea of information and misinformation generated by doctors, friends, family, and other visitors with the best and worst of intentions. Ultimately, the General departed from New York City to attempt to find solace as well as a salubrious environment. Such was the power of his public persona that privacy, notwithstanding the efforts of the G. A. R. guards, was not to be.

The publicity that followed Grant and his cancer, however, opened the Nation to cancer as a medical disease worthy of succor and science. The press became more comfortable reporting on cancer after the illustrious General came down with the disease. Indeed, the media in general became more amenable to reporting on cancer-related suffering. Ultimately, the publicization of Grant's cancer brought the disease into the open and led the public to view cancer in a new light—one based in science and sympathy rather than religion and repulsion. As the new cancer hospital lent legitimacy to the disease through the éclat of the institution, so Gen.

⁴³⁸The New-York Times, "Grant's Death," 7-8.

Grant lent legitimacy to cancer through his personal stature and suffering. The General found peace only in death, but his 1868 Presidential campaign slogan, "Let us have peace," more aptly after his demise than ever before described the relationship between cancer and the people.

Chapter 4

The Reflection of Modern Cancer:

The Secret “Anxious Summer” of the President¹

General Grant’s travail and the publicity surrounding it could not fail but attract the attention of political Washington. The narrative of Grant’s appointment as General of the Army on Presidential Inauguration Day in March, 1885 has already been told. Nevertheless, there is another story, full of irony and omen, that joins traditional and modern cancer—the cancer histories of the General and the President.

Such was the nature of the acclaim for Grant in the spring and summer of 1885 that the President of the United States was constantly apprised of the vicissitudes of the General’s condition. Indeed, his first official act as the first Democratic President in a generation was the appointment of Republican Ulysses S. Grant to the newly created post of General of the Army.² In April, as Grant appeared near death, the President “deputized” a special emissary, Marshall McMichael, to express his condolences and gather unbowdlerized information on the General’s condition.³ Bulletins flowed regularly between East Sixty-Sixth Street and the White House. On July 23, the day that General Grant died, Col. Fred Grant directly informed the President of the

¹Mrs. Frances Folsom Cleveland Preston, the wife of President Grover Cleveland, used the term “that anxious summer” to describe the events of June, July, August, and September of 1893. Manuscript letter from Mrs. Cleveland Preston to Dr. W. W. Keen, 6 April 1917 in William Williams (1837-1932) Keen, compiler, “Reports, Correspondence and Clippings Relating to the Operation of President Cleveland on Board the Yacht Oneida in 1893,” in *Keen Scrap book* (Philadelphia 1893-1927). The *Scrap book* is an unpublished manuscript at the College of Physicians of Philadelphia that is mostly unpaginated.

²Thomas M. Pitkin, *The Captain Departs: Ulysses S. Grant's Last Campaign* (Carbondale: Southern Illinois University Press, 1973), 30. and Jean Edward Smith, *Grant* (New York: Simon & Schuster, 2001), 625.

³The New-York Times, “Another Uneasy Night: Gen. Grant's Rest Disturbed by Fits of Choking. The Sufferer Reported Comfortable in the Morning--His Throat Very Painful in the Afternoon,” *The New York Times*, 14 April 1885, 1:7.

death of his father.⁴ The Nation's Chief Executive expressed the sorrow of the people in his Proclamation that day, adding that "the entire country has witnessed with deep emotion his prolonged and patient struggle with painful disease, and has watched by his couch of suffering with tearful sympathy."⁵ Official Washington was draped in black for thirty days and August 8, 1885, the day of Grant's funeral, was declared a day of national mourning. The President and his entire cabinet traveled to New York, took part in the funeral procession, and witnessed the burial of Gen. Grant in the temporary tomb on the high bluff above the Hudson River.⁶ That President was Grover Cleveland. Less than eight years later, the twenty-second and twenty-fourth President of the United States was himself diagnosed with cancer.

The diagnosis and treatment of Grover Cleveland's cancer stand in sharp contrast to that of General Grant. The differences spotlight the epochal transformations that occurred in the few years separating the death of Grant and the discovery of Cleveland's tumor. The lessons learned from Grant's lost battle with cancer played a significant role in many of those changes. In sum, the history of President Cleveland's cancer illuminates the inchoate beginnings of a new perspective on the disease cancer and, in the process, reveals another critical aspect in the making of modern cancer.

STARK CONTRASTS

The Facts

In May 1893, President Grover Cleveland noted a rough spot on the roof of his mouth. A physician took a biopsy. Microscopic examination revealed malignancy. A surgeon operated

⁴The New York Times, "The President's Proclamation," *ibid.*, 24 July, 9:1.

⁵*Ibid.*

⁶Major General Ulysses S. Grant 3rd, "Grant's Last Victory," in *Ulysses S. Grant: Warrior and Statesman* (New York: William Morrow & Company, Inc., 1969), 449.

and excised the lesion. The patient was out of bed in less than two days. There was no suffering. He was fitted with an internal mouth prosthesis to restore the anatomy distorted by the surgery. Weeks later the surgeon removed additional tumorous tissue. In total, the President underwent three operations for his cancer in less than five months. No further evidence of disease was noted. Mr. Cleveland lived the remaining fifteen years of his life without recurrence of the cancer.

The story of President Grover Cleveland's cancer is more intriguing than the facts. Overall, the picture of cancer is one of significant change from the mid-1880s. Even seemingly numerous social and medical attitudes toward the disease from the 1880s to the 1890s that appear superficially similar betray subtle differences that imply how imbedded cancer was becoming in the fabric of American culture and society. The disease cancer underwent a revolution in thought and action after the death of General Grant. The history of President Cleveland's mouth cancer is a study in comparison and contrast with that of Gen. Grant. As such, it illuminates many of the differences between traditional and modern cancer.

The Panic of 1893

Cancer was the farthest thing from President Grover Cleveland's mind in the spring of 1893. Cleveland, the first Democrat in the White House since the Civil War and recently returned to the Presidency after a four-year legal career in New York City, was caught in the throes of economic and political battles not of his own making. A triple monetary whammy engulfed the nation and created a crisis of mammoth proportions. First, the value of farm produce had been declining since 1887, devastating the net worth of farmers and the fruits of their labor. A third political party rose from the agricultural ruins of the South and West—the People's Party—and the tenets of its populist appeal threatened the two established political

parties and the foundations of industrial capitalism.⁷ The producers cried out for a new egalitarian order, including cheap money. Overseas, secondly, a depression that began in Europe in 1890 endangered Eastern bankers and Southern and Western farmers alike in the increasingly global economy. Third, in the remaining solvent parts of the country, rampant speculation in railroad stocks created a credit bubble that shook Wall Street to the core.⁸ A divided Congress dealt with the uproar by appeasing the easy-money (mostly western) “silverites” with the Sherman Silver Purchase Act of 1890 in return for the passage of the McKinley Tariff Act favored by eastern businessmen. At the same time, however, countries in Europe and Asia demonetized silver. The United States was thus one of the few remaining countries that exchanged silver for gold. Monetary upheavals threatened from Wall Street to Main Street. This silver legislation, however, fulfilled the debtor’s dream because the increasing supply of silver from mining operations primarily in the West expanded the monetary supply and promised to reverse the decades-long deflation of the nineteenth century that had forced the repayment of agricultural (and other) loans in dearer dollars. The Act required the Federal government to purchase 4.5 million ounces of silver monthly, thereby increasing the demand for silver. In addition, silver was convertible into gold at a ratio of 16:1—a historical ratio that became untenable as the supply of silver from mines increased while the quantity of available gold remained relatively static. Cheap silver was exchanged for dear gold. The nation’s gold reserve plunged. Investors around the world feared that the United States “would actually leave the gold

⁷Lawrence Goodwyn, *Democratic Promise: The Populist Movement in America* (New York: Oxford University Press, 1976), 429-30.

⁸Robert C. McMath, Jr., *American Populism: A Social History 1877-1898*, ed. Eric Foner, American Century Series (New York: Hill and Wang, 1993), 181.

standard.”⁹ Anti-silver gold bugs cringed. On April 22, 1893, only weeks after Grover Cleveland reassumed the presidency, the gold reserve in the Treasury dropped below the psychologically critical \$100 million level—a level popularly regarded, as the new President wrote, “with a sort of sentimental solicitude.”¹⁰ The Democratic President, who stood for honesty and “sound” money, believed that the high tariff signed into law by his Republican predecessor combined with the dwindling supply of the auric currency essential for international trade would lead to the ruin of United States commerce. On May 5, the New York Stock Exchange perceived the crisis and the share values of stocks plummeted. The Panic of 1893 began in earnest.¹¹ That same day, President Cleveland, cigar smoker and tobacco chewer, first noted a “rough spot on the roof of his mouth.”¹²

Caveat Lector

The history of President Grover Cleveland’s cancer suffers from a problem quite different from the Ulysses S. Grant cancer story—a paucity of sources. The enormity of publicity surrounding General Grant’s cancer is legendary. President Cleveland’s cancer, ironically (for a sitting President), was shrouded in secrecy. An elaborate cover-up, spearheaded by denials and recriminations, succeeded in suppressing knowledge of the President’s cancer during the turmoil-filled years of Cleveland’s second term in office and thereafter. The whole truth was even kept

⁹Milton Friedman and Anna Jacobson Schwartz, *A Monetary History of the United States 1867-1960* (Princeton: Princeton University Press, 1963; repr., 1971), 105.

¹⁰Allan Nevins, *Grover Cleveland: A Study in Courage*, The Library of the Presidents Collector's Edition ed., 2 vols., vol. 2 (New York: Dodd, Mead & Co., 1932; repr., 1986), 525.

¹¹Gorton Carruth, *The Encyclopedia of American Facts and Dates*, ed. Raymond V. Hand, Jr. (New York: HarperCollins Publishers, 1993), 363.

¹²Nevins, *Grover Cleveland*, 2, 528.

from his wife.¹³ Amazingly, given the aggressive press coverage on the President in the 1890s, the story of the President's cancer was not officially revealed until 1917, nine years after Cleveland's death and the passing of most of the eyewitnesses.¹⁴ The *Saturday Evening Post* article that publicized the story of President Cleveland's cancer, written by Dr. William W. Keen, remains by far the major account of the history of Cleveland's cancer by a first-hand participant.¹⁵

Historiographical analysis of President Cleveland's cancer is problematic because Dr. Keen's writings and collected information hold a near monopoly over the story. Newspaper articles at the time add a different dimension, but too often they merely regurgitated what they were told by the President's dissembling henchmen. Keen made clear that he was writing the account of the President's cancer for posterity and, more importantly, to exonerate Grover Cleveland during that most dangerous era in American history. "It seems to me," he wrote Mrs. Cleveland prior to the first publication, "that there ought to be some record available to the future historian relating to Mr. Cleveland's operations and more especially to defend his memory

¹³E. J. Edwards, *Philadelphia Press*, August 3, 1893 cited in Kasson C. Gibson, "Scrapbook Relating to Operations Performed on President Cleveland," in *Presented to the New York Academy of Medicine Library by Dr. Bernhard W. Weinberger, who received the scrapbook from Mrs. Gibson. (1893-1920)*. In Malloch Rare Book Room, The New York Academy of Medicine, New York, New York. Also see Typescript letter from Dr. W. W. Keen to Mrs. Frances (Cleveland) Preston, September 25th, 1916. In Keen, *Scrap book*.

¹⁴The first non-disclaimed public admission of President Cleveland's cancer surgery that I could find appeared in *The New-York Times* obituary of Dr. Joseph D. Bryant on 8 April 1914. The *Times* reported that Bryant "was called upon to perform an operation on the President of which the public has remained in ignorance until today." In *The New York Times*, "Dr. Jos. D. Bryant, Noted Surgeon, Dies. Physician and Friend of Ex-President Cleveland Succumbs in St. Vincent's Hospital. His Many Professorships. Ex-State Commissioner of Health and Author of Medical Works--Operated on Cleveland at Sea.," *The New York Times*, 8 April 1914, 13:5.

¹⁵W. W. Keen, "The Surgical Operations on President Cleveland in 1893," *The Saturday Evening Post*, 22 September 1917, 24-5, 53, and 55. In 1928, Dr. Keen, then ninety-one years old, published an embellished version of his 1917 article. Nevertheless, the corpus is identical to the earlier *Saturday Evening Post* story. William W. Keen, "The Surgical Operations on President Cleveland in 1893," in *The Surgical Operations on President Cleveland in 1893, Together with Six Additional Papers of Reminiscences* (Philadelphia: J. B. Lippincott Company, 1928). Dr. Keen, not long before his death at age ninety-six, collected his information on Grover Cleveland's cancer in a "Scrap book" that still resides at the College of Physicians of Philadelphia.

against the vile partisan attacks that were made upon him at that time.”¹⁶ Thus Dr. Keen is hardly a neutral, objective, or nonpartisan historian. Accounts of the Cleveland cancer since Keen’s publications have done little more than mimic and distend the doctor’s notes and writings. This chapter situates the story of President Cleveland’s cancer within the socio-historical framework of the history of cancer and, in a new direction, seeks to discover within it the roots of modern cancer.

There are additional problems with Dr. Keen’s account. He wrote the 1917 synthesis twenty-four years after the events occurred. He went to great lengths, in the initial story for public consumption and again in a 1928 essay on the same subject in a more medically-oriented tome, to assure his readers that the long-belated report was accurate. He appended an “Author’s Note” to both compositions that cited the medical and personal sources from which he obtained his information.¹⁷ Some of it was contemporaneous (medical notes written after the operation) and much was not (reminiscences of the confidants).

Although Dr. Keen collected his information from many sources over the time span from the President’s secret surgery in 1893 to the 1917 article, his story suffers from those biases and peculiarities inherent in a single-witness account written years after the event. The reader must beware of Keen’s construction for at least three reasons. First, despite some timely post-surgical notes, the vicissitudes of memory blur details through the mists of time. Second, the development of new medical techniques and attitudes in the revolutionary decades between 1893 and 1917 altered the emphasis of an original observer like Keen from that of a first-hand witness to that of a historian viewing the past through the eyes of the present. Third, Dr. Keen became

¹⁶Typescript letter from Dr. W. W. Keen to Mrs. (Cleveland) Preston, February 23rd, 1916, in Keen, "Keen Scrap Book."

¹⁷Keen, "The Surgical Operations on President Cleveland." 1917, 55 and Keen, "The Surgical Operations, 1928," 76-7.

an ardent supporter of the President. Cleveland, wrote Keen, “had long had my profound respect, but he gained my affection in the very first hour I passed with him.”¹⁸ This is a further sign that his views are not unbiased and that he may have omitted unflattering information, no matter how important to Grover Cleveland’s cancer history and the history of cancer.

The few scattered contemporary private letters related to Cleveland’s cancer are insufficient to construct a meaningful history or to confirm or refute the surgeon’s story. Secondary references derive primarily from Keen. No doubt a journalist or a member of the President’s Cabinet would have written a different story. Nevertheless, given its unique position in the history of the President’s cancer, it must be the basis of this chapter section by necessity—there is no other comprehensive first-hand account.

Subsequently published sources on President Cleveland’s cancer are primarily medical, written by physicians not present at the principal operation. Unfortunately, the chief surgeon, Dr. Joseph Decatur Bryant, despite his intentions, never published an account of the Cleveland cancer.¹⁹ It should be noted that the first public notice of the President’s cancer was actually published in a Philadelphia newspaper within a month of the surgery, but the Cleveland Administration disclaimed the piece as political slander²⁰ and condemned the author as a “fakir,” “cancer fake,” and “calamity liar.”²¹ Other newspapers took the Administration’s statements at face value and supported its contention that the President had nothing more than a toothache.²²

¹⁸Keen, "The Surgical Operations on President Cleveland." 1917, 55

¹⁹Keen, "The Surgical Operations, 1928," 11.

²⁰The New York Times, "Mr. Cleveland Had a Toothache. Stories About His Ill Health Had Only One Element of Truth," *The New York Times*, 1 September 1893, 4:6.

²¹Keen, "The Surgical Operations, 1928," 13 and 17.

²²The New York Times, "Toothache," 4:6.

Can we be sure, following skepticism to its ultimate conclusion, that President Cleveland actually had cancer, and that it was removed as chronicled by Dr. Keen? Yes, physical evidence supports the existence of cancer and its excision. The surgically removed specimen, purported to be that from the President, resides in the Mütter Museum at The College of Physicians of Philadelphia, and was re-examined by contemporary pathologists.²³ The New York Academy of Medicine retains a prosthesis used to fill the gap in the President's mouth left by the excised bone and tissue. At least one author used the rubbery mass as a ball, bouncing it (to the utter horror of the curator) on the hard floors of the Academy.²⁴ Nevertheless, the full details of the history of President Cleveland's cancer and surgery must forever remain hidden.²⁵ Only Grover Cleveland and the eyewitnesses know what really happened.

If the essence of historical proof lies in the recordings of disparate—preferably disinterested—witnesses, then the reader must interpret the Cleveland cancer story with more suspicion than that of Grant. It is part of the inchoate history that surrounds the making of modern cancer. Nevertheless, the account of Keen, with its focus on political economy and surgery, is the source. However, be forewarned: Gen. Grant was an agent in the transformation of traditional to modern cancer. President Cleveland, whose cancer secret was unknown to the public until years after his death, was not an agent but rather a reflection of that change.

THE PRESIDENT'S CANCER

Diagnosis

June 25, 1893

²³John J. Brooks, Horatio T. Enterline, and Gonzalo E. Aponte, "The Final Diagnosis of President Cleveland's Lesion," *Transactions & Studies of the College of Physicians of Philadelphia* 2, no. 1 (1980): 1-25.

²⁴R. H. W. Dillard, "In Memoriam: Francelia Butler, 1913-1998," *Children's Literature* 28(2000): 182.

²⁵The Keen papers at the College of Physicians of Philadelphia contain the most complete records of Cleveland's tumor known.

Washington, D. C.

President Cleveland: What do you think it is, doctor?

Doctor Bryant: Were it in my mouth, I would have it removed at once.

The Panic of 1893, which rapidly led to the “Great Depression” of the Eighteen Nineties (long before the term was applied to the 1930s), occupied the President’s every waking moment in May and early June. Throughout these tense weeks the mouth lesion, like a persistent pest, gnawed at his palate. Cleveland initially attributed the oral irritation to an upset stomach.²⁶ In June, however, the lesion ulcerated. He now knew that he had little choice but to seek medical attention.

On June 13, Dr. Robert Maitland O’Reilly, the physician medically responsible for government officials in Washington, paid a “social call” on the White House and was “invited” to examine the President’s mouth.²⁷ The doctor recorded that “the gum had receded from the first molar and that there was a sinus opening on the palate,” but the light was too poor for a thorough inspection at that time.²⁸ The following day, Dr. O’Reilly called a dentist to examine the President’s presumed oral pathology, but the dentist concluded that neither the teeth nor tartar was the source of the lesion.²⁹ Not until the next Sunday, June 18, did O’Reilly return to further investigate the President’s mouth ulcer. What he found on the left half of Cleveland’s mouth astonished and dismayed him. “He has an ulcerative surface nearly as large as a quarter with cauliflower granulations,” wrote the White House physician, “and crater edges with at least

²⁶Francelia Butler, “President Cleveland Scoops the Press,” *The American Mercury*, January 1954, 80.

²⁷Charles L. Morreels, Jr., “New Historical Information on the Cleveland Operations,” *Surgery* 62, no. 3 (1967): 543. Dr. Morreels’ source was the *Keen Scrap Book*.

²⁸Letter of R. M. O’Reilly to J. D. Bryant, June 19, 1893. *Ibid.*

²⁹*Ibid.*

one sinus extending to the bone, which is apparently roughened.”³⁰ The President had a fungating oral mass that may have already invaded the upper left jawbone. In contradistinction to Dr. Douglas’ initial finding of a possible enlarged lymph node at the crook of General Grant’s jaw, the presence or absence of abnormal lymphatic tissue went unnoted in O’Reilly’s letter.³¹

Gross visual inspection was no longer sufficient to make a diagnosis of cancer in 1893. Confirmation by microscopic examination was mandatory. The doctor took a piece of the lesion in the brilliant light of morning. “I scraped in two places,” wrote O’Reilly, “and had a microscopical examination made by the expert at the Army Medical Museum.”³² The microscopist at the Museum (the forerunner of the Armed Forces Institute of Pathology) was not told the identity of the patient. It is not clear whether the President requested anonymity, the doctor initiated it on his own, or both simply took it for granted.³³ After all, O’Reilly knew from the gross appearance of the lesion that cancer was possible—if not probable. Regardless of the initial perpetrator, the President’s cancer remained a secret. All involved denied the identity of the cancer victim until years after President Cleveland’s death.³⁴

³⁰Ibid.

³¹Robert M. Steckler and Donald P. Shedd, "General Grant: His Physicians and His Cancer," *The American Journal of Surgery* 132(1976): 508. Dr. Douglas could not have known for sure that General Grant’s swollen gland discovered on initial examination was cancer because he did not take a biopsy. Although physicians attempt to distinguish benign from malignant lymph nodes based on “feel” (hard, rubbery, etc.), the biopsy remains the most accurate method of pathological diagnosis to this day.

³²Letter of R. M. O’Reilly to J. D. Bryant, June 19, 1893. In Morreels, "New Historical Information on the Cleveland Operations," 543.

³³More than one investigator has searched the AFIP collection for the microscopic slides used to make the diagnosis—to no avail. Brooks, Enterline, and Aponte, "The Final Diagnosis of President Cleveland’s Lesion," 9. Dr. O’Reilly wrote in his June 19 letter to Dr. Bryant that he kept the slides after the Army Medical Museum pathologist examined them. He also noted he would retain them. Morreels, "New Historical Information on the Cleveland Operations," 543. What he did with them is unknown.

³⁴Dr. Hasbrouck, as we shall see, is not an exception to this generalization. He also truthfully denied informing the press.

The pathologist's report was chilling and confirmed Dr. O'Reilly's worst suspicions. "While there are no positive proofs of malignancy," wrote the President's official physician hurriedly from the pathologist's office, "there are certain indications which make it probable that the specimens are from a case of epithelioma."³⁵ Epithelioma! General Grant had suffered and died from epithelioma within the easy memory of the doctor and everyone else. President Cleveland had even officiated at his New York City funeral less than eight years before. Moreover, both the General and the President smoked cigars and enjoyed chewing tobacco.³⁶

Unlike Grant's Dr. Douglas, Dr. O'Reilly's first reaction was to consider surgery. The report from the pathologist and other sundry material related to the President's tumor were contained in a letter written on June 19 by the government physician to Dr. Joseph Decatur Bryant, President Cleveland's good friend and the closest the Cleveland family had to a family physician.³⁷ O'Reilly had informed the President that "the bone was a little rough" and that surgery would probably be necessary.³⁸ It is not known whether the doctor used the word 'cancer' to the President. O'Reilly advised Cleveland to consult Dr. Bryant in New York with all due haste.³⁹ Secrecy, the White House physician believed, was not possible in Washington. Surgery, if necessary, would have to be performed elsewhere. The Washington press corps was simply too ubiquitous to hide something as potentially explosive as a Presidential cancer operation. The President agreed with O'Reilly's referral but, perhaps because of the escalating

³⁵Letter of R. M. O'Reilly to J. D. Bryant, June 19, 1893. Morreels, "New Historical Information on the Cleveland Operations," 543.

³⁶A. E. Bennett, "The Secret Surgical Operation on President Cleveland," *the Pharos* 38, no. 4 (1975): 160.

³⁷"Dr. Joseph D. Bryant," in Gibson, "President Cleveland Operations," 6.

³⁸Letter of R. M. O'Reilly to J. D. Bryant, June 19, 1893. Morreels, "New Historical Information on the Cleveland Operations," 543.

³⁹*Ibid.*

economic crisis or maybe because Dr. Bryant was away from New York, decided to request that his good friend travel to Washington instead.

The next day, O'Reilly took additional pieces of the oral lesion and submitted them to other pathologists in the hopes of obtaining a more definitive microscopic diagnosis.⁴⁰ At the same time, Daniel S. Lamont (1851-1905), the President's long-time personal advisor, new Secretary of War, and now confidant, was informed of the lesion in the President's mouth and the likely need for immediate surgery. While Bryant arranged the medical end of the surgery, Lamont began the non-medical preparations for Cleveland's operation.⁴¹ Bryant despised the press and public notoriety, but Lamont was an astute politician who knew they were a necessary evil—intrusive and yet essential to carrying out the agenda of the Cleveland administration. Both men hatched a plan that was complex in its details yet intriguing and compelling in its simplicity.⁴² Lamont, on his end, applied his masterful political acumen to the task of planning secret surgery on one of the most-scrutinized public figures in the world—and then keeping it hidden from the press and the public. He and Dr. Bryant, more than anyone else, were responsible for the success maintenance of this subterfuge long after the President's third and final oral cancer surgery that year.

Dr. Bryant reached Woodley, the President's suburban Washington residence, on the evening of June 24. He had received not one but two letters urging him to examine Mr. Cleveland. The first was from O'Reilly. The second was from Mrs. Frances Folsom Cleveland (1864-1947), the President's ward and now wife of seven years. She was worried that her

⁴⁰Ibid.

⁴¹Nevins, *Grover Cleveland*, 2, 529.

⁴²Nevins wrote that "Bryant took complete charge of the case," but Lamont actually worked out many of the details in Washington. Ibid.

husband's persistent complaints about his mouth were more than transient irritations. "I wish very much to speak to you," she wrote to Bryant, "about something that the President has on the roof of his mouth."⁴³ The hour of his Woodley arrival being late, he went to bed and postponed thorough examination Cleveland's oral cavity until early the next morning. Years later, Bryant described the most complete medical geography of the gross lesion.⁴⁴ He discovered "an ulcerated surface with an oval outline about the size of a quarter of a dollar extending from the inner surface of the molar teeth to within a quarter of an inch of the median line of the roof of the mouth and encroaching somewhat upon the anterior part of the soft palate."⁴⁵ In short, the mass consumed a considerable portion of the upper left quadrant of the President's mouth. Dr. Bryant had no doubt the gross appearance of the lesion was of a "malignant nature."⁴⁶ At the conclusion of the consultation the President inquired of his friend, "What do you think it is doctor?" Bryant replied that "it is a bad tenant. Were it in my mouth, I would have it removed at once. However, we will submit a portion of it to an unquestioned authority in these matters for microscopical examination before a final decision is made."⁴⁷

The "unquestioned authority" was neither a surgeon nor an internal specialist or *especialist*.⁴⁸ It was a medical microscopist—whose instrument, the microscope, had become the tool of choice for cancer diagnosis after the death of General Grant. No longer was gross visual inspection sufficient for a diagnosis of cancer. No longer were five consultants concurring on a

⁴³Morreels, "New Historical Information on the Cleveland Operations," 543.

⁴⁴Manuscript Letter of J. D. Bryant to D. S. Lamont, May 9, 1905, in Keen, "Keen Scrap Book."

⁴⁵Ibid.

⁴⁶Ibid.

⁴⁷Ibid.

⁴⁸See this dissertation Chapter 2, page 32 for a definition of an 'especialist.'

gross pathological diagnosis a match for one good microscopic examination by an experienced pathologist. The expert microscopist was probably Dr. William Henry Welch, the founder of the first pathology laboratory in America at Bellevue Hospital in New York (1878) and now professor of pathology and dean of the Johns Hopkins medical school in Baltimore.⁴⁹ Dr. Welch confirmed that the specimen was “part of an epithelial cancer.”⁵⁰ Drs. Herman M. Biggs and D. H. McAlpin also examined microscopic slides of the lesion. They agreed that the mass was a carcinoma.⁵¹ Dr. Bryant had all the verification he needed. The microscope validated Dr. Bryant’s gross diagnosis. In 1885, Drs. Barker and Douglas distrusted Dr. Elliott’s microscopic diagnosis of General Grant’s cancer. Ironically, now, in 1893, Dr. Bryant felt uncertain of his gross diagnosis until confirmed by the microscope.

Evading Disclosure and Suspicion

Dr. Bryant tolerated no delay in the removal of the President’s cancer. He wrote Secretary Lamont that postponement of surgery for even a month could result in progression of disease that might prove fatal.⁵² Bryant was sensitive to the political and economic exigencies of the day, but Grover Cleveland was not just any patient, and these were not ordinary times. The President and Dr. Bryant drove to the White House on the afternoon of June 25 to make plans for surgery with Secretary Lamont and Dr. O’Reilly.⁵³ While Dr. Bryant insisted on urgency,

⁴⁹E. Richard Brown, *Rockefeller Medicine Men: Medicine and Capitalism in America* (Berkeley: University of California Press, 1979), 72.

⁵⁰Letter of J. D. Bryant to D. S. Lamont, May 9, 1905. Cited in Morreels, "New Historical Information on the Cleveland Operations," 544; *ibid.* Note that Dr. Keen reported incorrectly that Welch concluded Cleveland had a sarcoma. Keen, "The Surgical Operations on President Cleveland," 53; *ibid.*

⁵¹Letter of J. F. Erdmann to W. W. Keen, Oct. 6, 1917. Cited in Morreels, "New Historical Information on the Cleveland Operations," 544.

⁵²Nevins, *Grover Cleveland*, 2, 529.

⁵³Brooks, Enterline, and Aponte, "The Final Diagnosis of President Cleveland's Lesion," 9.

Cleveland pressed secrecy. “The President,” Bryant reminded Lamont years later, “would not under any circumstances consent to the operative removal of the disease at a time or place that would not give the best opportunity of avoiding disclosures, and even a suspicion that anything of significance had happened to him.”⁵⁴

The Place

Cleveland agreed that Washington was no place to keep cancer surgery—or any surgery—on the President a secret, especially since the city was caught in the throes of the worst panic of the century. Indeed, he thought that none of his residences—Woodley, his summer residence Gray Gables at Buzzard’s Bay (west of Cape Cod), and certainly not the White House—was a location where a secret of this magnitude could be hidden from the press. Surgery in a hospital, far from the norm at this time for patients of means, was also out of the question if there was to be any hope of preserving the intended cover-up. After some cogitation the President, in a stroke of genius, suggested to Bryant and Lamont that the operation be performed on the *Oneida*, a substantial yacht owned by his good friend, Commodore Elias C. Benedict.⁵⁵

Cancer surgery on a yacht steaming up a river had benefits and risks. Certainly, there would be no passers-by to break the seal of secrecy. Interruptions would be minimized. The presence of the President on Commodore Benedict’s yacht, in particular, would not raise eyebrows because Cleveland and Benedict were old fishing partners who had logged more than

⁵⁴Letter of J. D. Bryant to D. S. Lamont, May 9, 1905. Cited in Morreels, "New Historical Information on the Cleveland Operations," 544.

⁵⁵Brooks, Enterline, and Aponte, "The Final Diagnosis of President Cleveland's Lesion," 2. And Leo Rosenhouse, "President Cleveland's Secret Surgery," *Private Practice* (1974): 46.

fifty thousand piscatorial miles together.⁵⁶ The press might wonder how a sitting president could relax on a fishing trip at a time of national crisis, but, if he went anyway, an absence of a few days on the Commodore's yacht during the heat of summer would be understandable. Risks, however, were substantial to both secrecy and procedure. A crewmember might recognize the President and wonder why he was below deck rather than fishing. Surgical supplies loaded onto the boat might arouse suspicion. The unpredictable motion of the ship on a potentially turbulent summer storm sea could cause an errant incision or, worse, severe an artery in the richly vascular facial area. Sterilization of equipment, an idea rather newly accepted but gaining rapidly in surgical practice, might be difficult to achieve in a ship's cabin. What if there was a complication? Whom could they call for help? What if they needed additional tools or materials? In addition, politically speaking, who would be accountable amongst this small, furtive band of operators if something went wrong? On the day of the surgery, perhaps feeling the weight of all these concerns, a nervous Dr. Bryant charged the captain, "If anything happens to the President, get your navigator to run us on the rocks and sink us all."⁵⁷

Pre-Operative Plans

While Dr. Bryant and Secretary Lamont worked out the details of the secret surgery, Dr. O'Reilly continued to tend his cancer patient. The White House physician wrote Bryant later on the twenty-fifth of June that he "penciled the jaw" with pyoktanin daily.⁵⁸ O'Reilly injected this methyl-violet aniline dye into the lesion and rubbed on additional dye to stain the diseased tissue

⁵⁶A. E. Porritt, "Some Historical Surgical Operations," *St. Mary's Hospital Gazette* 42, no. 5 and 6 (1936): 108.

⁵⁷Typescript of Keen interview with Dr. John F. Erdmann, September 13, 1916. Keen, *Scrap Book*. Keen quipped: "I have my doubts about that being said." Ibid. Fifteen years later, Dr. Erdmann communicated with Cleveland biographer Allan Nevins on November 14, 16, 1931. Erdmann reiterated Bryant's half-serious witticism to Nevins. Nevins, *Grover Cleveland*, 2, 530.

⁵⁸Morreels, "New Historical Information on the Cleveland Operations," 544.

in order to make it easier to visualize at the time of operation. The dye was also known to have antibiotic and analgesic properties. The antimicrobial aspect might reduce the risk of pre- and postoperative infections—a growing concern as germ theory gained import in surgical circles during the 1880s and 1890s. The property of analgesia mitigated the pain of the tumor and the discomfort from O'Reilly's daily oral injections. The Washington physician believed the treatment was effective. "I am decidedly of the opinion," he wrote on June 27, "that there are evidences of healing around the margin."⁵⁹

Pre-operative screening in Washington by Dr. O'Reilly revealed that the rotund President was generally in good health but noted shortness of breath upon climbing stairs. Analysis of his urine, however, gave the doctors pause and caused them to alter one of the most important components of the surgery—anesthesia. A twenty-four-hour urine collection started on June 25 revealed "beginning chronic nephritis."⁶⁰ The renal abnormality did not contraindicate surgery, but Dr. O'Reilly noted that it did "make us cautious about the administration of ether for fear of having a possible accident."⁶¹ The anesthetist would have to decrease the use ether—the anesthetic of choice due to the depth and duration of its effect. Instead, nitrous oxide, Sir Humphry Davy's laughing gas, would be administered to begin the operation and, hopefully, reduce the total amount of ether introduced into the body. Perhaps, as with General Grant, local cocaine applications could also reduce the need for general anesthesia.

The Time

⁵⁹Ibid. One would not expect an epithelioma (squamous cell carcinoma) of the mouth to heal. Brooks, Enterline, and Aponte, "The Final Diagnosis of President Cleveland's Lesion," 11. However, pyoktanin might have reduced inflammation around the tumor, leading O'Reilly to believe that the cancer was regressing.

⁶⁰Morreels, "New Historical Information on the Cleveland Operations," 545.

⁶¹Notes of R. M. O'Reilly. Keen, *Scrap book*.

President Cleveland established the parameters of the timing of the surgery. In doing so, he balanced Dr. Bryant's imperative for immediate excision of the lesion with the economic crisis of the country. "I cannot leave here before the end of the month under any circumstances," the President informed Lamont, Bryant, and O'Reilly at their White House meeting on the June 25. "Therefore, since a time must be set, I will say to you that I will be ready on the first day of July."⁶²

The next day, June 26, Dr. Bryant informed Secretary Lamont that the *Oneida* would be outfitted and ready to embark the first week of July.⁶³ Bryant was in frequent communication with the President. On June 27, Cleveland, long known for his oratorical skills and already planning to call a special session of Congress during the summer on the free silver issue,⁶⁴ thought to ask his friend and physician what effect the oral surgery would have on his speech. The doctor replied that the outward appearance of his face would be normal, but that vocalization would change.⁶⁵ Nevertheless, Bryant had a solution for this problem also.

Doctor Bryant, experienced in the ways of politics, had an additional personal concern gleaned from the annals of General Grant's cancer history.⁶⁶ What if something went wrong and the President—only months into his second four-year term—became disabled or died? Grant's apparent recovery in the spring of 1885 led myriad second-guessers to criticize both the diagnosis and treatment of the General. The burden of proof fell on Grant's consultants. Was

⁶²Morreels, "New Historical Information on the Cleveland Operations," 543.

⁶³Nevins, *Grover Cleveland*, 2, 529.

⁶⁴Cleveland intimated to a United Press International reporter on June 4 that he would call a special session of Congress. *Ibid.*, 527.

⁶⁵*Ibid.*, 529.

⁶⁶By 1893, Dr. Bryant received several medical appointments that required political ties. See biographical information below.

Bryant exposing himself to the same sorts of accusations—but now not in the case of a venerable but aging war hero, but with respect to the highest official in the United States? How could he best assure competence and a favorable result while at the same time respecting the President’s mandate for secrecy? Bryant’s solution was to assemble the best surgical-medical team possible. Short notice, however, limited the potential geographical distribution of the group. Dr. William Williams Keen, Professor of Surgery at Jefferson Medical College in Philadelphia and one of the most respected surgeons in the nation, was the farthest in distance and the first to be invited to join Bryant and O’Reilly. Keen would serve as second operator after Bryant. The President’s physician-friend then asked Dr. Janeway, a renowned New York City internist and physiologist, to examine the President pre-operatively and follow his physiological responses to the surgery. Bryant added Dr. Ferdinand Hasbrouck, a New York dentist skilled in the administration of nitrous oxide, to initiate the gaseous anesthesia as well as to remove the teeth that obstructed clear visualization of the entire oral mass. Dr. John F. Erdmann, the last of the team participants, was a young but adept surgeon who happened to be Dr. Bryant’s private practice associate.

The Panic of 1893 worsened as the medical team assembled. On June 26, global financial institutions, fearful that the success of the free silver movement would lead to a depreciation of the U. S. dollar and abandonment of the gold standard,⁶⁷ hammered down the price of a silver dollar to less than sixty cents in gold. The next day stocks fell sharply on the New York Stock Exchange. The President, who was a hands-on administrator or micromanager (depending upon your point of view), was directly involved in selling millions of dollars of government bonds to obtain gold for the Treasury in order to stabilize the economy.⁶⁸ The

⁶⁷Friedman and Schwartz, *A Monetary History of the United States*, 105.

⁶⁸Carruth, *American Facts and Dates*, 363.

planned date of the surgery could not have been worse. On June 28, Bryant, cognizant of the swirling political and economic maelstrom in Washington and around the country, insisted that a “Cabinet officer” be present on board the floating surgical suite.⁶⁹ How would the nation interpret an operative catastrophe wherein a group of physicians stole the President from Washington and hid him from the public and the press during a time of crisis? Would the nation judge the surgeons as competent operators acting for the public good, or as assassins and, possibly worse, silver fanatics? Yes, a member of the government must be in attendance—preferably an official respected by the press. There was little doubt that the representative of the Administration would be Colonel Lamont.⁷⁰

THE PRESIDENT’S TEAM

Grant’s Consultants vs. Cleveland’s Crew

President Cleveland’s surgical cancer team was a distinguished but motley crew. Bryant drew them together not only for their individual talents, but to function like the fingers of a hand. As such, they differed significantly from General Grant’s consultants. Each of the General’s physicians was a renowned expert in his field, but they worked autonomously. At times, it was not even clear which of Grant’s medical men was in charge—Barker, Douglas, or, perhaps, Shrady. Surely they worked toward a common goal—the agreed-upon palliation of the General’s cancer symptoms—but, despite the outward unanimity exhibited to the press, internal disagreements over the course of Grant’s demise from cancer are implied by the inconsistent attitude toward Dr. Elliott’s microscopic findings and the recurrent question of whether or not the General should receive operative intervention.

⁶⁹Nevins, *Grover Cleveland*, 2, 529.

⁷⁰Lamont and Bryant also had a connection. Lamont’s wife’s sister was Dr. Bryant’s wife.

Although sources are few, there is no suggestion of discord amongst Cleveland's surgical team. Certainly, the circumstances were different: Barker and Douglas brought each consultant into the Grant case at a different time and for a specific purpose—usually to answer a specific question (surgery?) or perform a specific task (clear the General's airway). Their task was more to find and fit a specific piece into the puzzle that was the General's cancer than to solve it. In contradistinction, there was no self-direction amongst the members of Cleveland's cancer team. Dr. Bryant was in charge. He handpicked each member of the group to perform a specific function. The goals were clear: successful excision of the cancer and the maintenance of secrecy. Initially, as the record will show, they achieved neither.

Part of the difference between the physicians' duties and objectives in the cases of Grant and Cleveland was attributable to the fundamental requirement for teamwork in a surgical operation. Strictly speaking, Cleveland's doctors, unlike Grant's, were not consultants. They were operators selected for their specialties to perform clear-cut assignments during and after surgery.

Enlarging the sphere of thought and history, however, suggests a greater sea change than the needs of the surgeon that put more emphasis on the team than the individual—Progressive ideology. Rare were the days when single heroic figures like Rembrandt's Dr. Tulp or Eakins' Dr. Gross could brandish a surgical knife over a motionless human figure and captivate a crowd of students or onlookers with their bravado. During the 1890s, and for almost two decades thereafter, the whole became more important than the sum of its parts. A new spirit of reform and cooperation was evident in medicine and, more specific to our purposes here, cancer research. Many believed goals more achievable through institutions than by the efforts of individuals. The objective was to function as if coordinated appendages of a body rather than as

unrelated and dismembered body parts.⁷¹ The éclat of the laboratory (and its popular successes), the acceptance of the microscope in physicians' circles, and germ theory helped put science into medicine and changed the focus of practice from therapeutics to diagnosis. General Grant's cancer occurred too early for these ideological transformations to affect his care. Cleveland's cancer, however, arose with Progressive medicine, and the President benefited greatly.

Dr. Joseph Decatur Bryant (1845-1914)

Grover Cleveland probably never knew how fortunate he was that his good friend and long-time fishing companion, Dr. Joseph D. Bryant, was the chief surgeon of his cancer team. In the medical arena of the twenty-first century, specialization and sub-(super-?)specialization are common. Patients are often referred to physicians because of their specialization and therefore aware of the specialist's expertise even before the consultation. In the late nineteenth century, however, before the pervasiveness of specialization in America,⁷² it was much less common for patients to know their doctors' interests and abilities. Experience, then as now, was the foundation of good results. In the field of medicine, there are many ways to gain experience. The most valuable for a surgeon is direct, firsthand, practical experience. Additional knowledge of the context of the operation—the patient's medical history, the surgical options, the adverse reactions, and the lessons of others—further transmutes the manual experience into surgical expertise.

Dr. Bryant was particularly well qualified to excise the President's cancer. In 1893, he was Professor of Anatomy and a Visiting Surgeon at Bellevue in New York City, where he had

⁷¹Robert H. Wiebe discussed the importance of the institutional paradigm in medicine within the Progressive framework. Robert H. Wiebe, *The Search for Order 1877-1920*, ed. David Donald, First ed., The Making of America (New York: Hill and Wang, 1967), 114-5.

⁷²Rosemary Stevens, *American Medicine and the Public Interest: A History of Specialization*, Updated with a New Introduction ed. (Berkeley: University of California Press, 1998). Part II, "Formal Recognition of the Specialties, 1900-30."

formerly been Associate Professor of Orthopedic Surgery.⁷³ This last appointment suggests that he was especially suited to remove the diseased section of the President's jawbone. His direct experience included operations personally performed on cases similar to those of the President.⁷⁴ Furthermore, he had presented a paper to the Medical Society of the State of New York on "A History of Two Hundred and Fifty Cases of Excision of the Superior Maxilla"—the most significant part of the surgery contemplated for Cleveland.⁷⁵ Research for the paper gave him context in terms of both what to do at surgery and, perhaps more important, what not to do—i.e., what surgical actions or inactions were most likely to result in complications. Awareness of bad outcomes from the experiences of others lent Bryant a knowledge of what ill effects to expect—and how best to prepare for them.

Expertise and contextual knowledge are essential ingredients for the successful cancer surgeon, but Dr. Bryant had additional qualifications that made him an ideal candidate to achieve President Cleveland's dual objectives of cancer cure and inviolable secrecy.

Dr. Bryant had a special interest in cancer that long preceded the President's operations and gave him additional advantages over other surgeons in this type of surgery. In 1889, he presented a paper to the New York State Medical Association that espoused the localistic theory of cancer origins.⁷⁶ Gone was the primary notion of cancer as a constitutional ailment—extant in Grant's final years—that predicted the futility of cancer surgery. Instead, Dr. Bryant asserted,

⁷³The National Cyclopedic of American Biography, "Bryant, Joseph Decatur," in *The National Cyclopedic of American Biography* (New York: James T. White & Company, 1933). Vol 23:31

⁷⁴Butler, "Cleveland Scoops the Press," 80.

⁷⁵Joseph D. Bryant, "A History of Two Hundred and Fifty Cases of Excision of the Superior Maxilla," *Transactions of the Medical Society of the State of New York for the Year 1890* (1890): 63-76. Bryant reported on two hundred fifty-four cases, but he only operated on two himself. *Ibid.*, 64.

⁷⁶"Malignant Neoplasmata: Read in the Discussion before the New York State Medical Association, October 10, 1888," *New York Medical Journal* 48(1888): 677-80.

cancer originates in one place in the body and, transported through the conduits of blood and lymphatic vessels, spreads over time to distant sites.⁷⁷ The cause of cancer was unsettled, he averred,⁷⁸ but much less relevant to the well being of the patient than the immediate recognition and removal of the lesion. Dr. Bryant was deeply troubled—if not angered—by cancer diagnoses made too late for surgery to cure or at least mitigate the ravages of the disease. To Bryant, the fact that the doctor was a complicit procrastinator with the patient in the failure to reach a timely diagnosis of cancer was a neglect of “his Christian and professional duties.”⁷⁹ A late or delayed cancer diagnosis was thus a moral failure on the part of the physician. There was simply no excuse for a late diagnosis of cancer, for there were many tools for making an early and accurate diagnosis. “If the physician finds himself unable to determine the nature of the growth by the means at his command,” he wrote, “the aid of the microscopist should be sought at once.”⁸⁰ In just a few years since Grant’s case, the microscope had become the major tool for the diagnosis of cancer. “The medical attendant has only to remove a small portion of the growth, if accessible, properly inclose [*sic*] it and send it by mail to the nearest recognized authority on the microscopical appearances of morbid growths, with a statement of the part of the body from which it was taken, and of his suspicions regarding it. In a few days at most the answer will be at hand.”⁸¹ Rarely, in his recent experience, had the microscope “failed to decide

⁷⁷Ibid., 678.

⁷⁸Ibid., 677.

⁷⁹Ibid., 679.

⁸⁰Ibid.

⁸¹Ibid.

the question for or against malignancy.”⁸² What a change from the skeptical attitudes of Drs. Barker and Douglas toward diagnostic microscopy in the winter of 1885.⁸³

Belief in the local theory of cancer origin combined with the new tools and techniques available to the physician/surgeon had but one objective—immediate excision of the pathologic lesion from its point of origin to prevent metastases. The clinician “should consider it a case of *emergency* in the full sense of the term” wrote Bryant⁸⁴—before the disease spread beyond the reach of the knife and all would be lost. The constitutional theory followed by Grant’s consultants and generations before them inevitably led to surgery only as a last resort. No wonder Dr. Samuel David Gross concluded in 1853 that cancer was a death sentence.⁸⁵ To physicians and surgeons like Dr. Gross in the middle of the nineteenth century, cancer was incurable and surgery a violation of the healer’s sacred oath, derived from Hippocrates, to above all, to do no harm.⁸⁶ Dr. Bryant’s conviction in the localistic theory of cancer origin led him to a very different conclusion. “The endeavors of the surgeon have been followed by a fair percentage of cures.”⁸⁷ To achieve the highest cure rate operate early and remove the lesion

⁸²Ibid.

⁸³Note also that the “game” of medical microscopy popular in Grant’s day—whereby the microscopist would be furnished with little or no information about the patient, the body site, and the presumptive clinical diagnosis prior to his rendering a pathological diagnosis that was often derided—had become an exercise in teamwork between clinician and microscopist by the late 1880s and 1890s. The duty of the clinician or surgeon, as espoused by Dr. Bryant, was to describe to the microscopist the patient, biopsy location, and clinical suspicions regarding the lesion to help achieve the most accurate pathological diagnosis.

⁸⁴Bryant, “Malignant Neoplasmata,” 679. Italics in the original.

⁸⁵S. D. Gross, M. D., “On the Results of Surgical Operations in Malignant Diseases,” *Transactions of the American Medical Association* 6(1853): 157, 61. Also on Microfilm with different pagination.

⁸⁶Ibid., 161.

⁸⁷Bryant, “Malignant Neoplasmata,” 678.

completely. His *modus operandi* was “operate first, medicate afterwards.”⁸⁸ Elaborating, he taught the members of the New York State Medical Association that “the use of the knife is the operative measure to which the patient should be subjected. The growth should be removed thoroughly by excision at the earliest possible moment after the diagnosis is made, and, if a doubt exist as to the nature of the growth, give the benefit of that doubt to the patient and remove the growth at once. The earlier the removal, the better will be the chance of preventing and limiting dissemination.”⁸⁹ In short, he concluded, “the surgeon’s watchwords ought to be, *Cut early, cut often, cut wide.*”⁹⁰

To Bryant, cancer had become a disease of different parameters—now local, circumscribed, often accessible, and, most importantly, potentially curable if excised before it spread beyond its site of origin. The magnifying ability of the microscope and the ascendancy of surgery in the pantheon of medical therapeutics helped draw this modern view of cancer. It resulted from the old constitutional theory twisted and turned on its head by cognitive reevaluations based upon new information gleaned through centuries-old processes (microscopy and surgery) now viewed through the new, young eyes of scientific medicine. Fortunately for Grover Cleveland, Dr. Bryant put local theory into practice.⁹¹

The President also gained from Dr. Bryant’s political skills. Otherwise, how was he to maintain the secrecy of the operations during the turbulent economic and social times of the

⁸⁸Ibid., 679.

⁸⁹Ibid., 679-80.

⁹⁰Ibid., 680. Italics in the original.

⁹¹Dr. Bryant delivered another paper on cancer not long after the Cleveland surgeries. Therein he reiterated many of the points he made in 1888, sometimes quoting from the earlier paper verbatim. The main point of the 1894 lecture, however, was to bring to the attention of the medical profession the startling increase in the incidence of cancer. “The Wesley M. Carpenter Lecture: Important Facts Relative to Malignant Disease,” *New York Medical Journal* (1895): 609-17.

summer and fall of 1893? Bryant was a physician unusually equipped through his life experiences in the public arena to deal adroitly with the media. He developed this expertise by holding several authoritative administrative positions over the span of his professional career. While still in his twenties, Dr. Bryant began a stint as sanitary inspector for the New York City Department of Health at a time when sanitation dominated the politics of health.⁹² During the second Grant Administration (1873-1877), he began his service as surgeon to his Seventy-first Regiment, a position that paralleled the rise and fall of the power of the Grand Army of the Republic. Grover Cleveland played no small part in the shaping of Bryant's political acumen. He was in the audience on the first day of 1883, when Grover Cleveland became Governor of the State of New York.⁹³ The two, bonded by fishing and mutual respect, became fast friends during the trials and tribulations of Cleveland's years in and out of public office. Governor Cleveland appointed him Surgeon General of the National Guard of the State of New York, a position he held with the rank of Brigadier General under three governors.⁹⁴ In 1887, Dr. Bryant vaulted to the office of Commissioner of the Department of Health for both the City and State of New York. Five years later, only months before the President's operations, he received constant attention from the press for holding ships that entered the Port of New York in quarantine until he "had assured himself that there was no cholera aboard."⁹⁵ The enmity of the merchants, who wailed publicly that he would "stop the commerce of this nation"—not to mention the incredible

⁹²The New York Times, "Dr. Joseph D. Bryant," 13:5.

⁹³Nevins, *Grover Cleveland*, 2, 109.

⁹⁴The New York Times, "Dr. Joseph D. Bryant," 13:5.

⁹⁵*Ibid.*

hardships endured by the immigrant passengers on ship⁹⁶—was assuaged only by the support he received from the native press through his appeal for the protection of the health of the many over the wealth of the few.⁹⁷ All these political posts seemed but a warm-up for the pressure he would endure in the summer and fall of 1893.

Joseph Bryant's personal friendship with Grover Cleveland led to additional familiarity with the limelight. The pretext used for the Cleveland operations—another piscatory expedition on Commodore Benedict's *Oneida*—had a chance to hide the real mission only because newspapermen knew that the President and his physician-friend frequented the shoals and depths of the waters from Washington to Buzzard's Bay and beyond in search of fishing good times. As *The New-York Times* told the oft-repeated story:

Dr. Bryant was nearly always one and often the only companion of Mr. Cleveland on pleasure trips. The two went hunting and fishing together time and again and were friendly rivals with gun and reel. Through his recreations with the President, Dr. Bryant came in contact with many newspaper men. Whenever he and Mr. Cleveland returned from a trip he was besieged by reporters eager for some incident that had occurred to Mr. Cleveland or for some expression of opinion that he had let fall. But, although Dr. Bryant was uniformly courteous to the newspapermen, he seldom told them anything of importance. His inevitable answer to their question was "I am a guest of the President's and cannot talk about his affairs."⁹⁸

Dr. Bryant gained much valuable expertise in parrying their persistent interrogations. Lessons learned bore fruit during the Presidential cover-up of 1893. Grover Cleveland was indeed most fortunate that his friend, Dr. Bryant, was in charge of his cancer. The doctor's surgical experience, professional knowledge, theoretical leanings, and political savvy made Bryant the ideal operator for the difficult task ahead.

⁹⁶Howard Markel, *Quarantine! East European Jewish Immigrants and the New York City Epidemics of 1892* (Baltimore: The Johns Hopkins University Press, 1997), 101-3.

⁹⁷The New York Times, "Dr. Joseph D. Bryant," 13:5. Bryant's well-publicized response to the cries of the merchants was "I don't give a continental." Ibid.

⁹⁸Ibid.

Dr. William W. Keen (1837-1932)

Dr. Bryant chose Dr. William Williams Keen to be second in command at the operation. Keen, as First Assistant, was a political as well as surgical asset to the team—but in a different way from the President’s fishing friend. By 1893, Keen, “the father of American surgery,” was at the pinnacle of his career and one of the most respected surgeons in the United States.⁹⁹ He had served as a physician in the Civil War and, like many American physicians of the day, continued his medical education in Europe. During his postgraduate years, he was educated in the clinics and laboratories of Rudolph Virchow in Berlin, and Theodor Billroth and Julius Cohnheim in Vienna¹⁰⁰—all of which were famed for their work on cancer. He had a particular penchant for the structure of the human body—the foundation of surgery—and received appointments in pathological anatomy at Jefferson Medical College (his alma mater), the Pennsylvania Academy of Fine Arts, and the Philadelphia School of Anatomy. His private lectures at the School of Anatomy were some of the best attended in the history of American education, an enduring testimony to his popularity.¹⁰¹ Dr. Keen was part of that new breed of anatomist-surgeons in Europe and America for whom advances in pathological anatomy during

⁹⁹“Dr. W. W. Keen Dies; Famous Surgeon: Assistant in Operation in 1893 on President Cleveland for Removal of Sarcoma. Had Served in Three Wars. Vigorous Exponent of Theory of Evolution and of Vivisection--Long Professor at Jefferson,” *The New York Times*, 8 June 1932, 19:6.

¹⁰⁰Donald C. Geist, “William Williams Keen, M.D. (1837-1932), Surgeon and Author,” *Transactions & Studies of the College of Physicians of Philadelphia* 44, no. 4 (1977): 182. By the 1860s, German universities and clinics began to supplant French medical institutions as the post-doctoral destination of well-heeled American physicians. John Harley Warner, *Against the Spirit of System: The French Impulse in Nineteenth-Century American Medicine* (Princeton: Princeton University Press, 1998), 291.

¹⁰¹The National Cyclopaedia of American Biography, “Keen, William Williams,” in *The National Cyclopaedia of American Biography* (New York: James T. White & Company, 1909), 367.

the early decades of the nineteenth century were but a means to an end—rather than an end in themselves—toward more successful surgery.¹⁰²

Bryant and Keen shared many beliefs that were controversial in their day. The President's friend may have respected Keen for the latter's early adherence to Listerism—antiseptis and its application to surgery. Keen heard Lister lecture in Philadelphia in 1876 and, purportedly related to his observations of deaths from blood poisoning during the Civil War, was immediately won over to the principles and practices of antiseptis. Indeed, he is credited as the first surgeon in Philadelphia to adopt Lister's ideas and methods.¹⁰³ "It was largely due to his battles for Listerism," lauded *The New-York Times* years later, "that the system finally became a practice in America."¹⁰⁴ As noted, Bryant had been sanitary inspector for New York City and, just the year before Cleveland's surgery, had achieved notoriety as the City's Medical Commissioner of the Health Department during the maritime cholera quarantine of 1892.¹⁰⁵ Bryant's belief in Listerism in particular and germ theory in general was revealed in his careful attention to antiseptis during surgery and by his statement to the press that if the city residents "enforce cleanliness of person" the probability of the spread of the cholera epidemic to New York would be minimized.¹⁰⁶

Keen's ambition, popularity, and love of surgery helped make him a prolific author. The year before the Cleveland surgeries he edited a major treatise on surgery, the *American Text-*

¹⁰²Drs. Bryant, Keen, and Erdmann were all expert anatomists famed for their surgical prowess. Dr. Janeway was also an experienced anatomist, but his forté was as a diagnostician.

¹⁰³Donald E. Willard, Jr., "W. W. Keen's "First Modern Brain Case"," *Transactions & Studies of the College of Physicians of Philadelphia* 26(1959): 146.

¹⁰⁴The New York Times, "Keen Dies," 19:6.

¹⁰⁵Markel, *Quarantine!*, 157.

¹⁰⁶The New York Times, "Cholera in This City. Four Deaths Announced by the Board of Health--Investigation of Other Cases Regarded as Choleraic--Reassuring Talk by Pres. Wilson and Others--No Epidemic, but Only Sporadic Instances.," *The New York Times*, 15 September 1892, 2:1.

Book of Surgery.¹⁰⁷ By the close of 1893 he had written or co-authored over one hundred and four articles in the medical literature, at least fourteen of which involved tumors.¹⁰⁸ In addition, Dr. Keen authored a markedly increased number of tumor and cancer-related publications in 1893, perhaps reflecting a quickened interest in the field because of the Cleveland surgery.¹⁰⁹ Of particular note is that Professor Keen operated on a sarcoma of the jaw in 1890,¹¹⁰ and, the same year as the operation on the President, a tumor of the hard palate¹¹¹—both surgeries akin to that on Cleveland. Last, but certainly not least, Bryant and Keen both believed in radical (aggressive) surgery. In the 1890 paper, Keen wrote that the medical profession has “no right in a case of cancer or other at present incurable diseases to set the limits and say ‘thus far shalt thou live and no farther,’ and to give one what has been properly called euthanasia, a happy, easy death. We have no right to destroy life, though we may risk life, just as a general will run great risks for victory, but we are not justified in going into absolute and certain defeat.”¹¹²

When Dr. Keen inquired of Bryant as to why he, the only non-New Yorker, was chosen for this most select surgical team, Bryant informed him that the choice was made because he was

¹⁰⁷Who Was Who in America, "Keen, William Williams," in *Who Was Who in America: A Companion Volume to Who's Who in America* (Chicago: Marquis Who's Who, 1960), 659.

¹⁰⁸Donald C. Geist, "The Writings of William Williams Keen, M.D., Hon. F.R.C.S: A Selective Annotated Bibliography," *Transactions & Studies of the College of Physicians of Philadelphia* 43, no. 4 (1976): 340-47. Several publications in Dr. Geist's extensive "selective annotated bibliography" involve tumors. These include numbers 19, 22, 29, 42, 70, 79, 81, 85, 94, 97, 98, 99, 101, 104.

¹⁰⁹*Ibid.*, 347. Cancer and tumors were the subjects of five of the nine articles published by Professor Keen in 1893—a significant increase from previous years.

¹¹⁰William W. Keen, "Sarcoma of the Cheek and Jaw," *Medical News* 56(1890): 468-9.

¹¹¹W. W. Keen, "Tumor of the Hard Palate; Removal; Recovery.," *International Clinics* 4(1893): 195-6. Also see Geist, "Geist, Keen Biography," 345, 47. The surgery on the hard palate, in particular, gave Keen added experience in the use of surgical illumination, anesthesia, respiratory support, and the risk of intra-operative hemorrhage—all of which were critical for the first Cleveland surgery.

¹¹²Keen, "Sarcoma of the Cheek and Jaw," 469.

“one of the most distinguished medical men in the United States.”¹¹³ No doubt this is true.¹¹⁴

However, when asked years later why Bryant chose Keen, Dr. Erdmann—then an elderly and eminent surgeon in his own right who had worked with Dr. Bryant for many years—remarked that Keen was selected “to assume responsibility, in part, in the event of a fatality.”¹¹⁵ If a catastrophe occurred to the President on that sea-locked yacht, Joseph Bryant wanted someone else to share the blame. Perhaps there was no more renowned potential scapegoat in the United States at that time than the celebrated Dr. William W. Keen.

Keen felt honored and thrilled to be part of the President’s surgical team. It was he, after all, who eagerly collected and retained the letters, notes, and other memorabilia related to the President’s operations.¹¹⁶ It was he who, in 1917, after most of the other participants had passed away, published the story of Cleveland’s secret surgeries. Without Keen’s writings on the Cleveland cancer case it is possible that the covert operations would remain unpublicized to this day.¹¹⁷

¹¹³Nevins, *Grover Cleveland*, 2, 529. Another connection between Keen, Bryant, and the President during the second Administration was Cleveland’s Attorney General. Richard Olney had been a classmate of Keen’s, with John Hay, in the Brown University Class of 1859. The Associated Press, “Dr. Wm. Keen Dies; Operated on Cleveland: Surgery on Yacht in East River and on Sound in 1893 Kept Secret until 1917. Served U. S. In 3 Wars. At 95, Viewed Anesthesia as Greatest Medical Gain,” *New York Herald Tribune*, 8 June 1932, 19:5.

¹¹⁴Dr. Keen must have concurred. In his will, Dr. Keen generously donated his brain to science. The New York Times, “Dr. Keen Bequeaths His Brain to Science: Brown University, Alma Mater of Philadelphia Surgeon, Gets \$100,000 for Fellowship,” *The New York Times*, 15 June 1932, 17:2.

¹¹⁵M. G. Seelig, “Cancer and Politics: The Operation on Grover Cleveland,” *Surgery, Gynecology, and Obstetrics* 85, no. 3 (1947): 376.

¹¹⁶The items in Keen’s *Scrap book* date from 1893-1927.

¹¹⁷Dr. Kasson C. Gibson also kept “a collection of newspaper clippings, pictures, letters and telegrams” related to the Cleveland cancer. Unfortunately, he did not participate in the major Cleveland surgeries. He never published his scrapbook, which resides in the Malloch Rare Book Room of the New York Academy of Medicine. Gibson, *Scrapbook*, 1893-1920.

Dr. Keen noted in his foreword to the 1928 edition of *The Surgical Operations on President Cleveland in 1893* that, at the time of publication, “Dr. Erdmann and I are the only persons [still living] who were present at both operations.” Keen, “The Surgical Operations, 1928,” 11-12. It is possible that Dr. Keen wanted to see his version of the Cleveland cancer story in print rather than that of Dr. Erdmann. Also, see Footnote 14 above on the revelation of the Cleveland cancer surgery in Dr. Bryant’s 1914 obituary.

Dr. Robert Maitland O'Reilly (1845-1912)

By 1893, Dr. Robert Maitland O'Reilly had been a friend of Grover Cleveland and his family for more than a decade.¹¹⁸ He, unlike all the other members of the surgical team, was not chosen by Bryant to tend to the President's cancer. Rather, it was his duty as White House physician. Using his tenure of experience forged under dire circumstances, he played an essential part in restoring the President to physical health.

In his role as White House physician, O'Reilly was the first to examine the Cleveland cancer. He began the diagnostic process, arranged the ineffectual dental consultation, and began sampling the pathological tissue for microscopic investigation. It was also Dr. O'Reilly who urged President Cleveland to seek Dr. Bryant's counsel¹¹⁹—relinquishing his function as the President's primary physician for the purposes of the cancer surgery. Thereafter, Dr. Joseph Bryant—the President's friend, fellow sportsman, and medical-political ally—assumed the main role in effecting the logistics of the secret surgery. Nevertheless, during the Cleveland operations O'Reilly played the important role of assistant surgeon and anesthetist. Although his personal experience with cancer as a military surgeon appears to have been minimal, Cleveland was aware of Dr. O'Reilly's contributions to his diagnosis and recovery and advanced his medical-military career.

Dr. O'Reilly's road to the cancer surgeries was geographically and occupationally circuitous. Neither luck nor connections led him to the post of White House physician. Although he and Bryant were approximately the same age,¹²⁰ the life course O'Reilly followed

¹¹⁸Garrison, Fielding H. "In Memoriam: General Robert Maitland O'Reilly, Surgeon General, United States Army, 1902-1909." *New York Medical Journal* (30 November 1912): 1126-7

¹¹⁹Porritt, "Historical Surgical Operations," 107.

¹²⁰Robert Maitland O'Reilly was born January 14, 1845; Bryant on March 12, 1845.

to reach Washington, D. C. was full of adventure and heroism rather than anatomy and politics. Indeed, his life is that rare turn of reality that makes truth look like fantasy. It is, in short, ripe for portrayal on the silver screen. Dr. O'Reilly seemed always to be in the right place at the right time—for daring or foolhardiness, depending upon your perspective on the human condition. The bravado he exhibited during his career worked to the benefit of the President in terms of the aggressive and emergent approach to cancer he shared with Dr. Bryant. Most importantly, Dr. O'Reilly never doubted that surgery was the treatment of choice for the President.¹²¹

Robert O'Reilly was part of that unique generation of medical men whose education and early training straddled the crucible of the Civil War. Drs. Bryant, Keen, Janeway, and O'Reilly all came of age as medical men during those determinative years. Indeed, it is surely no coincidence that the dual horrors of trauma and disease markedly exacerbated by the Civil War, combined with the medical advances on the Continent (especially Germany) at that time, fostered the surgical daring and attention to the application of science to medicine that characterized the new surgery of the last two decades of the nineteenth century.

The White House physician's two parallel careers, that of army officer and surgeon, began early in life. Swept into the service of the Union at the age of seventeen, he enlisted in the Military Hospital Service in 1862.¹²² Within two years, he served in the Union Army as a medical cadet. After the Civil War, he continued his medical education and received the degree

¹²¹Keen *Scrap book*: Letter of R. M. O'Reilly to J. D. Bryant, June 19, 1893. Cited in Morreels, "New Historical Information on the Cleveland Operations," 543.

¹²²My major biographical sources for Robert O'Reilly were Garrison, Fielding H. "In Memoriam: General Robert Maitland O'Reilly, Surgeon General, United States Army, 1902-1909." *New York Medical Journal* (30 November 1912): 1126-7; The National Cyclopaedia of American Biography, "O'Reilly, Robert Maitland," in *The National Cyclopaedia of American Biography* (New York: James T. White & Company, 1922); and The New York Times, "Major Gen. O'Reilly Dies in Washington: Surgeon General of the Army from 1902 until 1909--Friend of Grover Cleveland. His Anti-Typhoid Work. He Introduced the Policy of Compulsory Inoculation--Served in Indian and Spanish Wars., *The New York Times*, 4 November 1912, 11:5. In addition, personal snippets of O'Reilly's life are scattered throughout other documents of the bibliography.

of Doctor of Medicine from the University of Pennsylvania in 1866. Within a year, he was promoted to Assistant Surgeon in the U. S. Army. Lieutenant O'Reilly was shot during his Army duties in California in 1867 and disabled for months. His military career appeared to be at an end, but recovery followed and within a year he was in the field again on active scout duty in the ongoing war between the westward-migrating settlers and the Native Americans. In 1870, while serving in Colorado, he was elevated to Captain. In March, 1874, as the Sioux battled the U. S. Army to retain their western lands, Captain O'Reilly was on the scene as Chief Surgeon. Three years later he was stationed back East, caring for the sick and wounded in the strike-laden powderkegs of Baltimore and Pittsburgh. The year was 1877, a time so filled with momentous struggles between labor and capitalism that one historian has labeled it the "year of violence."¹²³ Caught up in the conflagrations, he again suffered a life-threatening injury in the line of duty. In 1880, he returned West to participate in that winter's expedition against the Sioux in South Dakota. Twice wounded, shuttled between fierce clashes in the East and West, the Army assigned Captain O'Reilly in 1882 to a relatively peaceful job in the office of the Attending Surgeon in Washington, D. C. In the autumn of 1884, when Grover Cleveland won election to his first term as President, Dr. O'Reilly received appointment as Attending Surgeon and physician to the White House.¹²⁴ He became the Democrat's "warm personal friend"¹²⁵—abetted, no doubt, by their common love of fishing¹²⁶—and served as the Clevelands' family

¹²³Robert V. Bruce, *1877: Year of Violence* (Indianapolis: Bobbs-Merrill Company, 1959; repr., 1970).

¹²⁴Grover Cleveland was not the first President to have the care of a dedicated White House physician. That honor belonged to the administration of the phlegmatic James Buchanan, fifteenth President of the United States, in 1857. Leo Rosenhouse, "White House Doctor," *Private Practice* (1972): 58.

¹²⁵Garrison, "General Robert Maitland O'Reilly," 1126.

¹²⁶Rosenhouse, "White House Doctor," 58 and 62.

physician during the first Administration.¹²⁷ Although his expertise lay in eye surgery, few conditions were so specialized as to escape his purview. This specialization within generalization was consonant with the practice of most physicians of the time. In 1890, with Cleveland out of the White House, O'Reilly returned to South Dakota as Major and full Surgeon to attend to the sick and wounded during the last Indian campaigns. O'Reilly returned to Washington with Cleveland in early 1893 and diagnosed the President's cancer barely three months into the second term. On June 30, he surreptitiously boarded Benedict's yacht, *Oneida*, in New York with his patient for the first secret cancer surgery.¹²⁸

Edward Gamaliel Janeway (1841-1911)

Dr. Edward Gamaliel Janeway was the only member of President Cleveland's surgical team who was not a surgeon.¹²⁹ Nevertheless, he was the most revered of all the physicians who took part in the cancer operations and played a vital role during the two July 1893 surgeries.

Edward Janeway was another member of the Bellevue connection that linked Bryant and Erdmann.¹³⁰ His father was a physician, and as a young man Edward may have followed him on

¹²⁷"Robert Maitland O'Reilly," *The National Cyclopaedia of American Biography*, 261.

¹²⁸Robert O'Reilly's colorful career with the U. S. Army did not end with the Cleveland cancer surgeries of 1893. In 1898, he served in the Spanish-American War as Chief Surgeon and Lieutenant Colonel for the Fourth Army Corps in Havana, Cuba. For heroism and attention to duty, Republican President Theodore Roosevelt appointed him Surgeon General of the United States Army—although they had never met—with the rank of Brigadier General. O'Reilly held the nation's top medical-military post for seven years, the remainder of President Roosevelt's administration. He retired as Major General, the first medical officer in the U. S. Army ever to attain that rank. *Ibid.*

Fielding H. Garrison, the venerable historian of medicine who wrote a laudatory obituary of Dr. O'Reilly for the *New York Medical Journal*, thanked the late Army surgeon for using a grant from the Carnegie Institution in 1903 to reinstate publication of the *Index Medicus* after a hiatus of six years. Garrison, "General Robert Maitland O'Reilly," 1126.

That same year, O'Reilly published a collaborative work on military surgery in the fourth edition of Keen's textbook, thus renewing a relationship that may have begun in their early years together in Philadelphia and again on the *Oneida* in 1893. Harper's Weekly, "The Death of General Grant," *Harper's Weekly*, 15 August 1885, 1286-307.

¹²⁹The ship's steward, who assisted the surgeons, was also, of course, not a surgeon. Unfortunately, his identity is unknown, although retrospective renditions of the *Oneida* surgery scene depict a distinctive male figure in addition to accurate portraits of the other physicians. Francelia Butler, *Cancer through the Ages: The Evolution of Hope* (Fairfax, VA: Virginia Press, 1955), 72.

his daily traveling rounds, learning the rudiments of diagnosis and developing the instincts at a tender age that later propelled him to the highest echelons of the profession. His formal higher education began at Rutgers College, from which he graduated as the voices of national dissension reached the crescendo that became the Civil War. Service as an acting medical cadet in a U. S. Army Hospital, as with so many of his colleagues, interrupted his medical education at the College of Physicians and Surgeons in New York. Nevertheless, he graduated toward the end of the War and moved to Bellevue Hospital and its Medical College in 1866, where he, like Dr. Bryant, spent most of his career.¹³¹

Drs. Bryant and Janeway were close personal friends as well as professional colleagues.¹³² Janeway was four years senior to Bryant and his mentor.¹³³ Still, the two complemented each other well and often worked together on difficult projects. Whereas Bryant was outgoing, Janeway was “reticent.”¹³⁴ Janeway was a thinker, Bryant a doer.¹³⁵ Still, Janeway’s eminence in the field of medicine—amongst his numerous achievements he succeeded Austin Flint (the founder of Bellevue Hospital Medical College) as Professor of the

¹³⁰The main sources for this focused biography are Francis ("Physician") Delafield et al., "Memorial Meeting to Edward G. Janeway, M. D., Ll. D., with Addresses by the Authors," (The New York Academy of Medicine, 1911).; The National Cyclopaedia of American Biography, "Janeway, Edward Gamaliel," in *The National Cyclopaedia of American Biography* (New York: James T. White & Company, 1906), 13:499.; and The New York Times, "Dr. E. G. Janeway, Diagnostician, Dead: Noted Specialist in Nervous Diseases Dies at His Country Home in Summit, N. J. Surgeon During Civil War. Consulting Physician to Many Hospitals in This City, and Author of Several Medical Works," *The New York Times*, 11 February 1911, 11:13.

¹³¹Dr. Janeway played a major role in the later consolidation of Bellevue and New York University Medical College in 1898. The Board rewarded him with the position of Dean of Medicine at the NYU Medical School from 1898-1905."Dr. E. G. Janeway Dead," 11:3.

¹³²Delafield et al., "Edward G. Janeway, M. D.," 16.

¹³³*Ibid.*, 2.

¹³⁴*Ibid.*, 8.

¹³⁵This over-generalized distinction between internists and surgeons persists in medical circles to this day. The old quip is that internists know everything but can’t do anything; surgeons do everything but know nothing; and pathologists know everything and do everything—but too late!

Principles and Practice of Medicine¹³⁶—pushed him reluctantly toward assignments steeped in politics. From 1875-1881, while Professor at Bellevue, he received appointment as Commissioner of Health in New York City—the same position that Bryant assumed in 1887. In 1892, the year before the Cleveland surgeries, Janeway was designated a member of the Special Advisory Committee to the New York State Chamber of Commerce during the “cholera scare”¹³⁷—along with Abraham Jacobi, Herman Biggs, Allan McLane Hamilton, Professor A. L. Loomis, and three others.¹³⁸ According to Howard Markel, they “played a widely publicized role in examining the New York quarantine station and identifying its inadequacies.”¹³⁹ Exactly how Commissioner of Health Bryant and Special Advisor Janeway interacted during those contentious times is unclear, but Bryant later wrote that Janeway “never hesitated a moment at any time to come to my support, and to remain at hand in professional emergencies.”¹⁴⁰ In addition, Bryant, only a few months after the quarantine, personally chose Janeway to play a unique role in the Cleveland surgeries. Indeed, Bryant, in a Memorial to Janeway, subtly commented that ‘professional emergencies’ in which they cooperated “weighed heavily in the balance of national affairs and of national grief.”¹⁴¹ Bryant’s veiled words, written six years before Keen’s publicization of the secret cancer surgeries, represented Bryant’s note of thanks to his old friend for Janeway’s unsung aid during the cholera scare and the *Oneida* affair.

¹³⁶Morreels, "New Historical Information on the Cleveland Operations," 545.

¹³⁷"Dr. E. G. Janeway Dead," *The New-York Times*, 11 February 1911.

¹³⁸Markel, *Quarantine!*, 158. Markel noted that Dr. Janeway was also a role model for Herman Biggs. Markel, *Quarantine!*, 243 Footnote 24. Hamilton was the grandson of Alexander Hamilton and a Renaissance man/psychiatrist. The three others were Stephen Smith, T. Mitchell Prudden, and R. H. Derby.

¹³⁹Markel, *Quarantine!*, 158.

¹⁴⁰Delafield et. al., "Edward G. Janeway, M. D.," Bryant Memorial, 16.

¹⁴¹*Ibid.*

Dr. Janeway was a diagnostician's diagnostician. "His skill as a diagnostician," wrote Bryant, "was unrivalled."¹⁴² Abraham Jacobi offered the greatest praise when he compared the cerebral Janeway to surgical and other 'specialists.' "While respecting the varied study and dexterity of specialists," concluded the father of American pediatrics, "he was superior to them because he was broader and more profound."¹⁴³ Janeway's deep knowledge and understanding of anatomy, pathology, and (what we would call) internal medicine elevated him to the rank of Professor at Bellevue when barely thirty years of age. The most difficult diagnostic dilemmas were presented to him. His expertise led him to be called "the country's foremost physiologist."¹⁴⁴ He was, in short, a doctor's doctor. It is therefore no surprise that Bryant called upon Janeway to evaluate the President pre-operatively and to monitor Cleveland's vital signs (measurements of bodily functions, such as pulse and temperature, used to gauge general well-being or deterioration) throughout the cancer operations. Indeed, it was Dr. Janeway who, with some trepidation, declared the President "fit" for surgery.¹⁴⁵ Janeway knew that one of his most delicate and yet weighty challenges lay before him.

John Frederick Erdmann (1864-1954)

Dr. John Frederick Erdmann was the youngest member of the surgical cancer team and outlived the others by decades. His medical career began in the circle of nineteenth-century traditional medicine and ended at the pinnacle of medical professionalism. Erdmann, like

¹⁴²Ibid., Bryant Memorial, 11.

¹⁴³Ibid., Jacobi Memorial, 10-11.

¹⁴⁴John Stuart Martin, "When the President Disappeared: While Panic Gripped the Nation in 1893, Grover Cleveland Suffered His Own Secret Ordeal on a Yacht in Long Island Sound," *American Heritage*, October 1957, 12.

¹⁴⁵Seelig, "Cancer and Politics," 374.

Bryant, Keen, and O'Reilly before him, was part of the band of rugged individualists who pioneered the application of scientific techniques to surgery in the late nineteenth century.

Cincinnati was the “Queen City of the West” when John Erdmann was born there in 1864. The city profited from its strategic position during the Civil War, but thereafter began to lose commerce to outlying towns, like Chicago and St. Louis, that became hubs for the nation’s westward expansion.¹⁴⁶ John apprenticed himself to a Chillicothe, Ohio physician early in 1884 to learn the basics of medicine that Janeway had learned from his father.¹⁴⁷ Like many young men at the time with an interest in medicine, his early training under the preceptor “consisted of reading medicine in all its branches under the supervision of some reliable doctor, helping to keep his books, assisting at any case which might arise, driving his horse when he went out on calls and seeing patients when he himself was too busy to go out.”¹⁴⁸ At the age of twenty, John, unlike many of his westward-moving compatriots, decided to seek his fortune back East and matriculated at Bellevue Hospital Medical College in the year Grover Cleveland was first elected President. In 1887, he graduated from Bellevue, became licensed in medicine and surgery, and caught the eye of Joseph Bryant to become part of the Bellevue connection that dominated the Cleveland surgical team. The two had many similar interests. Erdmann firmly believed in the utility of antiseptics, claiming that he had used “Lister’s spray”¹⁴⁹ in the operating room at Bellevue prior to Dr. Joseph Hunter’s brass-plaque claim at the newly-opened New York Cancer

¹⁴⁶Zane L. Miller, *Boss Cox's Cincinnati: Urban Politics in the Progressive Era* (Chicago: The University of Chicago Press, 1968), 5.

¹⁴⁷Unheralded as Chillicothe, Ohio may be today, it was the capital of the Northwest Territory in 1800 and capital of Ohio for most of its first fifteen years.

¹⁴⁸John Frederick Erdmann, “Early Surgical Experiences,” typed manuscript dated November 19, 1942, p. 1, in Memorial Hospital Archives, “New York Cancer Hospital (Old Memorial),” in *Hayes Martin Collection* (New Yorkn.d.), Record Group 500 Hayes Martin Collection, Box 5, folder 87, “Personnel Medical Staff 1915-1945.”

¹⁴⁹Carbolic acid.

Hospital that “The First Lister Spray in America was used in this Operating Room by Dr. Jos. B. Hunter, 1887.”¹⁵⁰ To Erdmann’s advantage, undoubtedly, was that he, like Bryant, was an “ardent fisherman.”¹⁵¹ The two began an association upon Erdmann’s graduation that lasted for the rest of Bryant’s professional career.

Erdmann’s career as Bryant’s associate prior to the Cleveland operations revealed no special interest in cancer or cancer surgery. However, like Bryant and Keen who had shown a proclivity toward cancer medicine, Erdmann revealed his will toward cancer surgery in his belief in localism and the aggressiveness of his procedures with Bryant. Indeed, he later served many years on the surgical staff of Memorial Hospital, the lineal descendant of the New York Cancer Hospital.¹⁵² Bryant’s protégé developed what would later become known as the “Erdmann technique.”¹⁵³ As a *TIME* magazine reporter wrote late in Dr. Erdmann’s career, “it was less a technique than an amazing speed in operating attained through practice, great anatomical knowledge and never-ending study.”¹⁵⁴ Cancer was one of many disorders to which Erdmann applied his special skills.

¹⁵⁰Martin, Hayes “Interview of Dr. John Frederick Erdmann,” in *Memorial Hospital Archives* (New York 1945). Record Group 500 Hayes Martin Collection, Box 5, folder 87, “Personnel Medical Staff 1915-1945.”

¹⁵¹The New York Times, “John F. Erdmann, Surgeon, 90, Dead: Leader in Field Was to Have Been Feted at ‘Open House’ Yesterday on Birthday. Began Practice in 1887. Taught at Post-Graduate--Had President Cleveland and Caruso as Patients,” *The New York Times*, 28 March 1954, 89:1.

¹⁵²Memorial Hospital was known as the New York Cancer Hospital from its founding in 1884 until 1899, when its name was officially changed to the General Memorial Hospital for the Treatment of Cancer and Allied Diseases in order to attract paying, non-cancer patients. In 1916, the agreement tied to a major, institution-saving donation required the name change to Memorial Hospital for the Treatment of Cancer and Allied Diseases in order to reflect a return to the focus on cancer. This third name for the old New York Cancer Hospital lasted until 1950, at which time new forces of growth based on the rise of post-war medical research and private philanthropy led the Hospital to become a Center. At the time of John Erdmann’s death in 1954, what had been the New York Cancer Hospital when he began practice was titled the Memorial Hospital Center for Cancer and Allied Diseases. The changing names of the New York Cancer Hospital over time reflect the effects of social, political, and economic forces upon its medical mission.

¹⁵³The New York Times, “John F. Erdmann, Dead,” 89:1.

¹⁵⁴*TIME* magazine, “John F. Erdmann Md,” *TIME*, 7 December 1942.

He, like his mentor Bryant, became Professor of Anatomy and Professor of Surgery at Bellevue. Erdmann, like Bryant and Keen before him, translated his anatomical skills into surgical prowess. Bryant's selection of Erdmann to become his associate and to be an integral part of the Cleveland surgical team was based upon the desire John radiated to continue learning and doing.¹⁵⁵ Bryant had seen too many others before him merely iterate stale skills and rest on their laurels as surgeons to the rich. When a *New York Times* reporter asked Erdmann on his eightieth birthday how a busy surgeon managed to keep up with new developments in his field, he answered, "a busy surgeon has to keep up or he won't be a busy surgeon."¹⁵⁶ The cancer operations on President Cleveland in 1893 formed a pivotal point in his career, and his responses to inquiries by medical historians Hayes Martin and M. G. Seelig add limited but colorful vignettes to the Keen narratives.¹⁵⁷

The Dentists

Drs. Ferdinand Hasbrouck and Kasson Church Gibson were integral members of the Cleveland cancer team. The operations were, after all, in Cleveland's mouth and the teeth in the left upper aspect of his jaw were involved with tumor. In addition, Bryant expected the cancer excision to leave a gaping hole in the President's oral cavity that would affect his facial appearance and his ability to speak intelligibly. Hasbrouck and Gibson filled the dental and prosthetic needs of the patient that the rest of the operators created with their excisions.

¹⁵⁵Dr. John F. Erdmann was appointed Professor of Surgery at Bellevue in 1893 at the age of twenty-nine—the same year he assisted at the Cleveland surgeries.

¹⁵⁶The *New York Times*, "John F. Erdmann, Dead," 89:1. Erdmann usually performed five surgical procedures daily—an amazing feat for a thoracic and/or abdominal surgeon. The *Times* estimated that he operated on more than twenty thousand patients over the expanse of his sixty-plus years in practice. At his death, colleagues called him "one of the world's most noted surgeons" and "the grand old man of New York surgery." *Ibid.*

¹⁵⁷Hayes Martin, "Interview of Dr. John Frederick Erdmann," in *Memorial Hospital Archives* (New York: 1945) and Seelig, "Cancer and Politics," 376.

Ferdinand Hasbrouck was not asked to join the surgical team for his dentosurgical dexterity, but, rather, for his expertise in the administration of nitrous oxide gas. The administration of the President's anesthesia was critical in order to achieve the proper level of sedation for the patient and allow the surgeons to speedily and accurately achieve their goals. If the anesthesia-induced relaxation was too 'light,' Cleveland would suffer unnecessary pain and, through agitation, inhibit the ability of the surgeons to visualize and excise the cancerous tissue. Too much sedation and the President could stop breathing and die. But which anesthesia? Half a century after the introduction of nitrous oxide and ether into the practice of surgery, anesthetists were still working out the details. Hasbrouck developed a reputation in New York for his painless dentistry based upon the use of 'laughing gas.' Indeed, he was one of the first in America to specialize in the use of nitrous oxide gas as an anesthetic for both tooth extractions and surgical operations.¹⁵⁸ His mastery of the use of the gas was above reproach, but, as will become clear, his ability to hold his tongue was not.

Dr. Kasson C. Gibson, another well-known New York City dentist, specialized in constructing artificial vulcanized rubber plugs to fill holes left by oral surgery. He was, in short, a prosthodontist. Dr. Bryant had warned Cleveland that the cancer surgery would alter his speech, but he did not immediately apprise the President that the operation would also change his facial appearance. Nevertheless, Bryant prepared to restore both voice and visage. In his 1890 treatise on superior maxillary excision, the Bellevue surgeon had written that "as soon as the healing is complete...the services of a dentist should be employed. The introduction of a vulcanized rubber 'plumper,' combined with an obturator, will be sufficient to remedy almost

¹⁵⁸The National Cyclopaedia of American Biography, "Hasbrouck, James Foster," in *The National Cyclopaedia of American Biography* (New York: James T. White & Company, 1950), 197.

entirely these defects.”¹⁵⁹ Gibson, although not present at the major Cleveland operations, was most important in keeping the cancer secret. Any noticeable change in the President’s appearance or voice could tip off the ubiquitous press that something was amiss. The dentist’s prosthetic devices were designed to fill out the facial depression left by the excised left jaw and plug the palatal defect, thereby restoring the fullness of the cheek and resonance of his voice.

The Others

Several others played critical roles in maintaining the secrecy and success of the cancer project, but their actions were not directly material to the surgery. Elias Cornelius Benedict (1834-1920), better known as the “Commodore,” was the lynchpin of the first two Cleveland surgeries. Bryant and his team performed the operations on his yacht, the *Oneida*. On his relationship with the President—as fellow “Piscator” or “brother of the rod”¹⁶⁰—Benedict maintained the fiction of Cleveland’s anti-neoplastic ‘fishing expedition.’ In addition, Benedict outfitted the largest room of his immense yacht for the surgery—a not insignificant task at a time when instruments and medications were much less abundant and standardized than today.

President Cleveland counted on Benedict’s aid because the two had been friends for several years and derived mutual benefits from their relationship. Benedict was one of Grover Cleveland’s inner circle of six friends who sustained him through his interregnum and helped him to regain the presidency in the election of 1892.¹⁶¹ The Commodore made his money on Wall Street, organizing a Gold Exchange Bank in the days when Gould and Fisk attempted to

¹⁵⁹Bryant, “Two Hundred Fifty Cases of Superior Maxillectomy,” 71. An obturator is a prosthetic device that closes or blocks an opening—in this case the hole left in the President’s palate after the removal of the cancer.

¹⁶⁰The New York Times, “Editorial: Commodore Benedict,” *The New York Times*, 25 November 1920, 14:3.

¹⁶¹Nevins, *Grover Cleveland*, 451-2. The others were the magazine editor Richard Watson Gilder, the actor Joseph Jefferson (another fishing buddy), Oscar Straus, the attorney Francis Lynde Stetson, and Charles S. Fairchild, Cleveland’s Secretary of the Treasury.

corner the gold market.¹⁶² Benedict continued to prosper on The Street long after the price of gold collapsed in 1869¹⁶³ and purchased one yacht after another, as he said, “to save my life.”¹⁶⁴ He believed, as did many others then (and now), that “fresh air and sunshine are important factors in the prolonging of life.”¹⁶⁵ Cleveland and Benedict shared a love of fishing and were often seen “bobbing up and down along the coast with...fishing lines trailing from their draft.”¹⁶⁶ A summer outing with the President aboard the Commodore’s yacht would hardly arouse the suspicion of the press, but what about the crew? Would the many crewmen remain silent when they espied the figure of so prominent a personage as the President of the United States looking sickly below decks rather than fishing?

If Commodore E. C. Benedict provided the logistical support for the surgical procedures, Colonel Lamont was the intermediary between the medical men and the outside world. He was well acquainted with manipulating the media and Grover Cleveland trusted him implicitly. The two met a decade earlier when Lamont was working as a journalist in Albany, New York.¹⁶⁷ In fact, Lamont originated Cleveland’s famous slogan, “public office a public trust,” which the

¹⁶² TIME magazine, "John F. Erdmann Md," 1:2.

¹⁶³The collapse of the great gold speculation occurred on September 24, 1869, a date that forever lives in financial infamy as Black Friday. Ironically, the release of Federal gold reserves into circulation by the fledgling President of the United States led to the plunge in the price of gold. Although Jay Gould and James Fisk attempted to bribe those around the new President (including his brother-in-law) to keep government gold off the market, he thwarted their efforts immediately upon discerning their scheme. That president was Ulysses S. Grant. Gould and Fisk made a fortune, but the nation sank into depression.

¹⁶⁴TIME magazine, "John F. Erdmann Md," 2:3.

¹⁶⁵Ibid.

¹⁶⁶The President’s fishing comrades considered him the expert, but none of them, reported *The New-York Times*, resembled Izaak Walton. Ibid.

¹⁶⁷The National Cyclopaedia of American Biography, "Lamont, Daniel Scott," in *The National Cyclopaedia of American Biography: Being the History of the United States* (New York: James T. White & Company, 1893), 58.

newly nominated candidate for mayor of Buffalo used on his meteoric rise to the presidency.¹⁶⁸ Governor Cleveland was so impressed with the thirty-two year old nascent political manager that he “offered him an honorary position on his military staff, which gave him the title of colonel, by which he has ever since been known.”¹⁶⁹ Upon his election to the presidency, Cleveland asked ‘Colonel’ Lamont to serve as his private secretary, a position that then involved considerable communication skills with the Cabinet, Congress, and the press. At the beginning of his second administration, Cleveland elevated Lamont to Secretary of War when the United States was embroiled in Hawaii, Cuba, and elsewhere. Lamont was the President’s clear choice to fulfill Bryant’s request that a Cabinet member be present during the secret cancer operation, for he had Cleveland’s best interests—medical and political—at heart.

Traditional Cancer Consultants vs. Modern Cancer Surgeons

The highly selected members of the President’s cancer team reflected the transformation in cancer medicine that came about during the final years of the nineteenth century. A team is no stronger than its leader, and Dr. Bryant was an exceptional surgeon and supervisor. His handpicked group of three surgeons, one internist, and two dentists mirrored his own beliefs in cancer theory and practice. General Grant’s consultants, on the other hand, constitutionalized human cancer, thereby minimizing the role of surgery in the treatment of the disease and devalorizing diagnosis at the expense of therapy. Bryant’s conviction that cancer began as a local disease, combined with the acceptance of the microscope as a trustworthy tool in the diagnosis of cancer by 1893, contribute significantly toward explaining the radically different treatments and outcomes of the General and the President.

¹⁶⁸Ibid. Cleveland transmogrified Lamont’s saying into the less poetic “public officials are the trustees of the people.”

¹⁶⁹Ibid.

The great schism in cancer theory between Grant's and Cleveland's physicians is the crux of the difference between traditional and modern cancer. Many reasons explain this divide. One is the medium of history—time. Grant's consultants and Bryant's team were of different generations. The General's consultants were all born, educated, and trained before the Civil War. Dr. Fordyce Barker was born in 1817, received his medical doctorate in 1841, and trained in Edinburgh and Paris during the 1840s.¹⁷⁰ Dr. John Hancock Douglas was born in 1824, received his M. D. from the University of Pennsylvania in 1846, and trained in Europe from 1849-1851.¹⁷¹ George F. Shrady, the youngest of the chief consultants, was born in 1837 and graduated from the College of Physicians and Surgeons in 1858. Within a year, he directly began practice at The New York Hospital, so his formative years were during the antebellum era.¹⁷² By 1893, the year of the Cleveland surgeries, Barker and Douglas were dead. Shrady, the most surgically aggressive of the three—it was he who more than once brought up the idea of operating on General Grant—gained further fame for his cross-Atlantic cable consultations with Sir Morrell Mackenzie on Prussian Emperor Frederick III's vocal cord cancer in the late 1880s.¹⁷³ He practiced for many years thereafter, but his constitutional beliefs at the time of Grant's death place him firmly in the old school of traditional cancer.

The members of Dr. Bryant's surgical team were all Civil War babies; i.e., they were all educated or trained during those watershed years. Their surgical aggressiveness, emphasis and

¹⁷⁰James R. Chadwick, "In Memoriam. Fordyce Barker, M. D., Ll. D.," *Transactions of the American Gynecological Society* 16(1891): 551-8.; Henry C. Coe, "In Memoriam. Fordyce Barker, M. D., Ll. D.," *New York Journal of Gynecology and Obstetrics* 1(1891): 112-18.; and The New York Times, "Fordyce Barker," *The New York Times*, 1 June 1891, 5:3.

¹⁷¹"Dr. J. H. Douglas," *The New York Times*, 3 October 1892, 4:7.

¹⁷²George F. Shrady, M.D., *General Grant's Last Days, with a Short Biographical Sketch of Dr. Shrady* (New York: Privately Printed, 1908; repr., One of 50 privately printed copies), 3.

¹⁷³Porritt, "Historical Surgical Operations," 92. and The New York Times, "Dr. Shrady, Dead. Distinguished Physician Was Well Known as a Consultant.," *The New York Times*, 1 December 1907, 11:5.

dependence on anesthesia and analgesia, and inclination toward the acceptance of theories of germs—all born in the trauma and diseases of the War¹⁷⁴—helped make President Cleveland the immediate surgical candidate that General Grant never was.¹⁷⁵ The personal interest Bryant and Keen exhibited in cancer also fostered a permissive effect toward more surgery. A surgeon with little or no experience in cancer might be cowed from undertaking so dangerous a mission, especially if he had been schooled in the dangers of cancer surgery expounded by Dr. Samuel Gross a few years before the Civil War.¹⁷⁶ The camaraderie of the Bryant team, based upon the Bellevue connection and fishing ties, contributed to the smooth functioning of the surgical unit. In summary, the theoretical proclivity of the Bryant team toward cancer localism rather than constitutionalism, the acceptance of the microscope in the diagnosis of malignancy, faith in surgery rather than palliation, and the advances in surgery engendered by antisepsis and anesthesia, together led O'Reilly and Bryant in June of 1893 to the ineluctable conclusion that there was only one treatment for President Cleveland's cancer—surgical excision. All that remained was to translate thought into action.

PIER A

The thirtieth of June 1893, was an unlikely day for the President to leave the embattled White House to travel to New York for cancer surgery. Just the day before, a six million-dollar infusion from clearinghouse banks in the very city to which he was traveling narrowly averted

¹⁷⁴"Keen Dies," *The New-York Times*, 8 June 1932, 19:6.

¹⁷⁵Ironically, Grover Cleveland was the first president after the Civil War not to have fought in the War. Like many others during the War, Cleveland, then an attorney in Buffalo, New York, paid \$300 to hire a substitute to fight for him. John M. Taylor, "President Grover Cleveland: Grover Cleveland and the Rebel Banners," *Cleveland Family Chronicles*, September 1994, 2. The reasons may have been altruistic (to help his mother), but his political opponents used his "avoidance" of military service against him. Nevins, *Grover Cleveland*, 51-2.

¹⁷⁶Gross, "On the Results of Surgical Operations in Malignant Diseases," 1853.

another financial panic.¹⁷⁷ The forces of silver appeared to be gaining daily and the nation's economy was sinking rapidly—according to eastern bankers and international financiers—into a soft-money abyss. Only Cleveland, a Democrat but a sound-money man, had the power to persuade members of his own party that the silver clause of the 1890 Sherman Act must be repealed.¹⁷⁸ Silverites had invaded the Democratic Party to such an extent that the President could not even count on his own Vice President, Adlai Stevenson, to lead the country in his absence back toward the gold standard that he believed offered financial stability.¹⁷⁹ Stevenson was a self-professed silverite. Thus, Cleveland insisted, even the Vice President—the official constitutionally empowered to succeed the President in the event of his death or disability—must remain uninformed of the secret cancer surgery.¹⁸⁰

In Washington, on that final day of June, Grover Cleveland acted as though it was his last. He knew that cancer surgery—or any surgery—was risky and that he might never live to see his wife, daughter, and friends again. After careful deliberation, he called a special session of Congress for August 7 to repeal the “unwise laws” that, he was certain, caused the economic crisis.¹⁸¹ The congressional meeting was more than five weeks in the future. Dr. Bryant counseled that, if all went well, a bit more than a month was enough time to recover from

¹⁷⁷Carruth, *American Facts and Dates*, 363.

¹⁷⁸Nevins, *Grover Cleveland*, 528.

¹⁷⁹*Ibid.*

¹⁸⁰The Constitution of the United States (Article II, Section I) transfers the executive power to the Vice President upon the President's “death, resignation, or inability to discharge the powers and duties of the said office.” The potential conflict of interest between President and Vice President that a catastrophic but not fatal outcome from the Cleveland cancer surgeries could have caused was not clarified until 1967, when the Twenty-Fifth Amendment (especially Sections 3 and 4) was ratified.

¹⁸¹The New York Times, “Congress to Meet Aug. 7 to Remedy Grave Perils Caused by Evil Legislation. A Proclamation Issued Last Night. The President Yields to the Pressure of the Business Men. Sherman Law Must Be Repealed.,” *The New York Times*, 1 July 1893, 1:7 and 2:1-2.

surgery. Secretary Lamont retained the President's rough draft summoning Congress and jotted down, no doubt with posterity in mind, that the message was "written the day the President left Washington on account of illness."¹⁸² In addition, Cleveland convened the Cabinet before he departed from the nation's capitol and drew up plans to deal with eventualities over the next few weeks while he embarked, as he told the press, on a "restful vacation cruise."¹⁸³ The most heart-wrenching part of his day was saying good-bye to his wife. Frances was almost seven months pregnant with Baby Ruth's first sibling and the First Family's second child.¹⁸⁴

At twenty minutes past four on that Friday afternoon, all urgent business concluded, the President, Secretary Lamont, Mrs. Lamont, and her daughter left Washington on the Pennsylvania Railroad's New York Express. Secrecy was unnecessary for this first leg, for the press, the Cabinet (except, of course, Lamont), and the nation thought the journey to New York only the beginning of Cleveland's Buzzard's Bay vacation.¹⁸⁵ Nevertheless, the President suffered no extra publicity whatsoever, so the exact travel route and time of his northward journey from Washington were unannounced. "He so carefully guarded his secret," wrote the stupefied *New York Herald*, "that no one outside the Cabinet circle knew of his intended departure."¹⁸⁶ Even at the cost of political appearances, the President avoided crowds and

¹⁸²Morreels, "New Historical Information on the Cleveland Operations," 544.

¹⁸³Rosenhouse, "White House Doctor," 58.

¹⁸⁴Grover Cleveland may have fathered a boy out of wedlock in 1874. Paternity, however, was never clearly established, so I will adhere to the "first sibling" and "second child" statements. Nevins, *Grover Cleveland*, 164-6. Nevertheless, the possible fatherhood of bachelor Cleveland led to the 1884 Republican campaign slogan: "Ma, ma, where's my Pa? Gone to the White House, ha, ha, ha!"

¹⁸⁵Rosenhouse, "President Cleveland's Secret Surgery," 45.

¹⁸⁶*New York Herald*, "Mr. Cleveland Is Off for a Rest. He Passes through This City on His Way to Gray Gables, at Buzzard's Bay. Sleeps on the Yacht Oneida. Tired out with Official Duties, He Is Preparing for the Work of the Extra Session. Dr. Joseph Bryant with Him. They Will Have a Short Cruise on E. C. Benedict's Vessel before Joining Mrs. Cleveland.," *New York Herald*, 1 July 1893, 6:4.

potentially uncomfortable interviews. Long before tunnels and bridges allowed access to the island of Manhattan, the railroad terminus for New York was located in New Jersey. Dr. Bryant's carriage met the small party as they alighted from their well-appointed private car at the Jersey City terminus.¹⁸⁷ Mr. Cleveland, according to a reporter, appeared tired and worn out.¹⁸⁸ He was definitely not in a talkative mood.¹⁸⁹ The carriage and its passengers ferried across the Hudson River to the lower end of Manhattan,¹⁹⁰ where they were met by the hulking Officer Ryan, a stentorian who guarded the President whenever he came to New York.¹⁹¹ Secrecy amongst the throngs of lower Manhattan was impossible, and none was attempted. The Officer and his army of mounted policemen cleared a path through the streets for the two carriages. The President's entourage crossed Cortland Street, rumbled down Broadway, and came to a halt at Pier A, just west of the southern tip of the Island. The parade-like ostentatiousness may have reminded the summer evening onlookers of General Grant's final journey, eight years before, from New York to Mount McGregor. Hopefully, Cleveland, who was President at the time of Grant's departure, did not have this memory of the General in mind. It would not have been a

¹⁸⁷Frank Thompson, Vice President of the Pennsylvania Railroad, placed his private rail car at the disposal of the President and his party. Rosenhouse, "President Cleveland's Secret Surgery," 43. Morreels located the New Jersey railroad terminus in Newark. Morreels, "New Historical Information on the Cleveland Operations," 545. The *New York Herald* noted that the group arrived in Jersey City. "Mr. Cleveland Is Off for a Rest."

¹⁸⁸"Mr. Cleveland Is Off for a Rest," *New York Herald*, 6:4.

¹⁸⁹The *New York Times*, "The President Seeks Rest. He Sailed on the Oneida Last Night for Buzzard's Bay.," *The New York Times*, 1 July 1893, 2:2.

¹⁹⁰The landing site abutted the contemporary location of the former Twin Towers of the World Trade Center.

¹⁹¹Rosenhouse, "President Cleveland's Secret Surgery," 43. The Secret Service did not guard the President at that time. Although Congress created the Service after Abraham Lincoln's assassination in 1865, it was not required to protect the President routinely until 1901—after President McKinley's assassination.

good omen. At forty minutes past eleven at night, the President and Lamont, with Bryant close behind, boarded the *Oneida*.¹⁹²

Drs. Keen, Janeway, O'Reilly, Erdmann, and Hasbrouck were already on board. They came from various locations quietly and independently to avoid notice. Although the President's presence on Commodore Benedict's *Oneida* might not raise eyebrows, surely this minor medical convention would. Even though the evening of this long and stressful day had long since turned to night, Cleveland, once on ship, lit "one last cigar."¹⁹³ He hardly realized—as Grant's Dr. Shrady had surmised—that cigars and chewing tobacco may have initiated the cancer that brought him to this critical juncture in his life.¹⁹⁴ The President then chatted away until bedtime, getting to know his physicians and at the same time putting them at ease. At one point, for example, he sat on a deck chair, smoking his cigar, and confided to Keen his private world of patronage-based torture: "Oh, Dr. Keen, those officeseekers! Those officeseekers! They haunt me even in my dreams!"¹⁹⁵

The night before what could be the tensest days in nineteenth-century American history passed in tranquility. Secretary Lamont and Dr. Bryant went back on shore to their New York residences so as not to arouse suspicion. The others remained on board with the preoperative

¹⁹²Morreels, "New Historical Information on the Cleveland Operations," 545 and "The President Seeks Rest," *The New-York Times*, 2:2.

¹⁹³Martin, "When the President Disappeared," 5.

¹⁹⁴In 1948, Lauren Ackerman made a relatively early statistical association between the specific type of President Cleveland's oral cancer and tobacco. See Lauren V. Ackerman, "Verrucous Carcinoma of the Oral Cavity," *Surgery* 23, no. 4 (1948): 670.

¹⁹⁵Keen, *The Surgical Operations*, 1917, 25. Keen's response was just what the nation's most prominent politician might have hoped. "I had never met him before," mused Keen years later, "but during that hour or more of conversation I was deeply impressed by his splendid personality and his lofty patriotism. I do not believe there was a more devoted patriot living." *Ibid.*

patient. The *Oneida* anchored off the Battery that balmy night, gently tethered.¹⁹⁶ It is possible, some say, to discern the level of a man's fears from his ability to sleep under trying circumstances. Whether true or not, Grover Cleveland slept well that night before surgery. He needed no tranquilizer, although he recognized that he might never leave the *Oneida* alive.¹⁹⁷

THE FATE OF A NATION IN SURGEONS' HANDS

July 1, 1893

Fortune smiled on the cancer surgical team and their prominent patient. The President, Bryant, and Lamont chose the date of the President's cancer operation, July 1, carefully. It was a Saturday and the start of the July Fourth holiday weekend. New Yorkers and, especially, the press, they reasoned, would be more interested in their personal pursuits and less concerned about the President. Even nature cooperated. The Battery and the East River were calm, the temperature was warm but not sweltering, and newspaper meteorologists forecast no rain until later in the day.¹⁹⁸ Bryant believed the clement weather augured well, for it promised smooth passage and allayed his fear that roily seas would make surgery treacherous.

As the yacht steamed up the East River the morning of first of July, Bryant's anxiety increased and his attention to every detail grew more punctilious. He became particularly concerned when the yacht passed Bellevue Bay at the foot of Twenty-Sixth Street—the home of his Bellevue Hospital. He did not want the well-known physicians on board to be noticed by those of the staff “who might be looking out,” lest the secret plot be foiled. “We went into the cabin,” recalled Dr. Erdmann, “so that we should not be recognized.”¹⁹⁹

¹⁹⁶The (New York) World, "Weather Indications," *The World*, 16 June 1885, 1:4.

¹⁹⁷Keen, *The Surgical Operations*, 1917, 25.

¹⁹⁸"Weather Indications," *The (New York) World*, 1 July 1893, 1:4.

¹⁹⁹Typescript of Keen interview with Dr. John F. Erdmann, September 13th, 1916.

The physicians permitted Mr. Cleveland less than one slice of toast and some weak coffee for breakfast at 08:30.²⁰⁰ Following the advent of surgical anesthesia in the mid-nineteenth century, food restriction before surgery was recognized to reduce the risk of intra-operative aspiration and postoperative death from pneumonia. By contrast, in 1811, Madame D'Arblay, more commonly known to posterity as Fanny Burney, was not required to fast before her mastectomy. In fact, the doctors gave her barely two hours notice before the operation and only a "wine cordial" for anesthesia.²⁰¹ Early nineteenth century knowledge of upper gastrointestinal function did not suggest the need for a pre-operative fast. In the 1820s and early 1830s, Dr. William Beaumont, the pioneering American physiologist and, like Major O'Reilly, an Army surgeon, discovered from direct observations on his reluctant patient, Alexis St. Martin, that "the *time* required for the digestion of food...is from three to three and a half hours."²⁰² This observation, coupled with the experience that deep anesthetics such as ether induced and exacerbated retching and vomiting, led to the conclusion that an empty stomach at surgery minimized complications. The President's surgeons wished to avoid ether. Nevertheless, prudence dictated preparedness. Hence Cleveland received a light breakfast and fasted pre-operatively for a Beaumont-sanctioned four hours.

Anesthesia-induced aspiration was not the surgical team's only worry. The rotund, sedentary President was an operative disaster waiting to happen. Dr. Keen, who examined

²⁰⁰Rosenhouse, "President Cleveland's Secret Surgery," 46.

²⁰¹Fanny Burney, "A Mastectomy of 30 September 1811," in *Excerpts from the Journals and Letters of Fanny Burney (Madame D'arblay. Volume Vi, France 1803-1812, Letters 550-631)*, ed. ed. Joyce Hemlow (Oxford: Oxford University Press, 1975), 610. Dr. Larrey informed his patient Ms. Burney three weeks before her surgery that she would receive only a few hours notice prior to the operation. The short notice was purposeful so that she not develop pre-operative anxiety. Not surprisingly, her anxiety mounted daily for three weeks. *Ibid.*, 606 and 08.

²⁰²William M. D. Beaumont, *Experiments and Observations on the Gastric Juice, and the Physiology of Digestion*, The Classics of Medicine Library (Plattsburgh: F. P. Allen, 1833; repr., 1980), 275. *Italics* in the original.

Cleveland for the first time that morning, noted that “the patient was 56 years of age, very corpulent, with a short thick neck, just the build and age for a possible apoplexy.”²⁰³ The President’s poor physical condition was only part of the problem. “He was also worn out mentally,” wrote Keen, “by four months of exacting labor and the officeseekers’ importunities.”²⁰⁴ Anesthesia also adversely affected the heart, lungs, and kidneys. Knowledge of the pharmacology and physiological effects of nitrous oxide and ether increased during the years after General Grant’s death, but anesthesia still significantly augmented the morbidity and mortality of surgery. The surgical team worried about the best anesthesia for the President and considered different alternatives. They considered the President high-risk.²⁰⁵ In fact, Keen was more concerned about complications related to the anesthesia than the surgery itself. “The anesthesia troubled us,” he wrote. “Our anxiety related not so much to the operation itself as to the anesthetic and its possible dangers.”²⁰⁶ Dr. Hasbrouck, whom Bryant invited to join the team for his nitrous-oxide-administering skills more than for any unique expertise in tooth extraction, averred that the gas could not sufficiently anesthetize a patient of Mr. Cleveland’s body habitus for the length of time required to perform the procedure.²⁰⁷ Thus, the team decided to begin surgery with the lighter nitrous oxide and switch to ether if or when necessary.

Dr. Janeway, the Bellevue physiologist, internist, and diagnostician, performed a formal preoperative examination on the President before the patient dressed that morning.²⁰⁸ Dr.

²⁰³Keen, *The Surgical Operations*, 1917, 53. ‘Apoplexy’ is an older term for stroke. It derives from the Greek ‘to cripple by striking.’

²⁰⁴Ibid.

²⁰⁵Ibid.

²⁰⁶Ibid.

²⁰⁷Ibid.

²⁰⁸Morreels, “New Historical Information on the Cleveland Operations,” 545.

O'Reilly recorded the findings. Surgeons had known for centuries that the success of a procedure somehow depended on the general health of the patient as well as their ability to eradicate the underlying pathology.²⁰⁹ The advent of anesthesia, which Dr. Keen called the second greatest medical achievement of the nineteenth century,²¹⁰ placed increased emphasis on knowledge of the patient's underlying physical condition, because it was discovered that anesthetics increased the risk of surgery in patients with ailments of various organ systems. Dr. Janeway obtained a "history" (i.e., a record of the patient's answers to the doctor's questions) from the President that revealed Cleveland "puffs a little in going up stairs."²¹¹ However, Janeway discovered no evidence of chest pain, shortness of breath at rest, or lightheadedness that implied heart problems. Physical examination revealed clear lungs. No heart murmur was audible, but cardiac sounds were difficult to discern—presumably because of the President's marked obesity.²¹² Janeway concluded that any weakness in "the heart muscle" did not contraindicate surgery—using the double negative that is the wont of seasoned pre-operative examiners to this day.

The President's kidneys, however, presented a potential problem. The Ancient Greeks examined urine, diagnosing diabetes mellitus by its sweet taste on their tongues. The rise of modern chemistry techniques in the early nineteenth century and their application to laboratory medicine rapidly advanced the analysis of blood and urine. The President's urine was found to

²⁰⁹Gross, *On the Results of Surgical Operations in Malignant Diseases*, 1853, Microfilm, 21.

²¹⁰The greatest medical innovation of the nineteenth century, Keen believed, was vaccination, which arguably could be dated to the eighteenth century—or before. William Williams Keen, "The Progress of Surgery in the Nineteenth Century," in *Addresses and Other Papers* (Philadelphia: W. B. Saunders & Company, 1905), 325.

²¹¹Keen, *Scrap book: Notes of R. M. O'Reilly*. Morreels, "New Historical Information on the Cleveland Operations," 545.

²¹²*Ibid.*

show evidence of “beginning chronic nephritis,” but it was mild because there was no suggestion of it “interfering with the renal function.”²¹³ Janeway’s concern was not that the early kidney disease would lead to an intraoperative or postoperative crisis. Rather, he feared that ether, which Dr. Hasbrouck predicted to be necessary to complete the planned procedure, would compromise renal function and cause “a possible accident.”²¹⁴ The operation would have to be quick and efficient in order to minimize the dose of ether administered.

Dr. Keen examined the patient next. Whereas Dr. Janeway focused on the President’s overall physical condition, Keen focused on those areas of the body most relevant to the surgery. He noted that “there were no perceptibly enlarged glands.”²¹⁵ This was an extremely important piece of information. Other than the President’s corpulence and obvious mouth cancer, it was the only part of the surgeon’s physical exam that he remarked upon in his 1917 treatise.²¹⁶ Swollen glands along the drainage route of a tumor often portend a grave prognosis. Breast cancer surgeons learned this lesson by at least the eighteenth century. Henry Francois Le Dran, a Parisian surgeon, introduced the concept in the mid-eighteenth century that malignant tumors began as local lesions that spread via the lymphatics.²¹⁷ However, the idea that cancer was local rather than constitutional defied the prevalent humoral theory and found few followers until later in the nineteenth century. Dr. Samuel Gross, whose 1853 investigation of cancer surgery for the

²¹³Ibid. Papers in the *Keen Scrap book* do not describe what was found on examination of the urine, but it may have been excess protein and certain types of white blood cells.

²¹⁴Keen, *Scrap book*: Notes of R. M. O’Reilly.

²¹⁵Keen, *The Surgical Operations*, 1917, 53.

²¹⁶Ibid., 25 and 53.

²¹⁷Mitchel D. Auerbach, *A New Concept of Cancer: With a Brief History of Changing Cancer through the Ages* (New York: Pageant Press, 1955). The practical consequence of localism theory was the exhortation by Le Dran and his colleague Jean Louis Petit to excise regional lymph nodes during breast cancer operations—more than a century before William Halstead devised the “radical” mastectomy. H. S. J. Lee, ed. *Dates in Oncology*, Landmarks in Medicine Series (Pearl River, NY: The Parthenon Publishing Group Inc., 2000), 14.

American Medical Association dominated thinking about the disease until the last years of the century, warned surgeons not to operate on patients whose cancers revealed signs of lymphatic involvement. “My observation has taught me,” wrote the esteemed Philadelphian, “that nothing but mischief is to be expected from interference when the malady has attained this crisis.”²¹⁸ Perhaps Dr. Douglas heeded Gross’ warning by not suggesting surgery to General Grant when he discovered a swollen gland under the ex-President’s right jaw during his initial examination. Perhaps not.²¹⁹ Dr. Bryant made clear in his 1888 paper on *Malignant Neoplasmata* that he was well aware of the prognostic significance of enlarged lymph nodes in cancer patients.²²⁰ It was, therefore, encouraging that Mr. Cleveland did not have palpable lymph nodes in the drainage area of his left-sided mouth tumor.

Following the meager breakfast and preoperative examinations, the President’s mouth was “repeatedly cleansed and disinfected.”²²¹ The goal of the mouthwashings was to reduce the probability of intraoperative blood poisoning (germs in the bloodstream) and postoperative infection. The concept that germs (any of various microscopic organisms that cause disease) initiate infections, including postoperative infections, gained credence in America by the 1890s. In the words of Nancy Tomes and John Harley Warner, “it is hard to think of any cognitive or technical innovation that more clearly marks a dividing line between the medicine of the mid-nineteenth century (and all that had come before) and the new medical order.”²²² Antiseptic

²¹⁸Gross, *Surgical Operations in Malignant Diseases*, 21.

²¹⁹Dr. Douglas could not have believed that Grant’s swollen gland represented an absolute contraindication to surgery. He brought up the question of surgery several times thereafter. See the discussion in Chapter 3 on “Why no surgery?”

²²⁰Bryant, “Malignant Neoplasmata,” 678.

²²¹Keen, *The Surgical Operations*, 1917, 27.

²²²Nancy J. Tomes and John Harley Warner, “Introduction to Special Issue on Rethinking the Reception of the Germ Theory of Disease: Comparative Perspectives,” *Journal of the History of Medicine* 52(1997): 7.

techniques used on General Grant bordered on the primitive compared to those used during President Cleveland's surgery—although the two were merely eight years apart. Dr. Douglas directly applied carbolic acid and salt water to the General's cancer in order to reduce inflammation around and within the cancer, but Grant's consultants stuck their hands into the General's mouth willy-nilly without so much as a handwash. The antiseptic techniques used during President Cleveland's surgery, on the other hand, were extensive. Although theories of germs were hardly new, their application to medical practice in the late nineteenth century reduced the risk of surgery and played a crucial role in the development of a new public interest in surgical solutions to medical problems.

The concept that "germs" caused disease evolved over many centuries. The medical profession in this country, however, did not embrace the concept until the late nineteenth.²²³ For medico-historical purposes, it is important not to confuse germs with contagion. Germs are infective agents; contagion is a process by which infection is transmitted from one organism to another. Thucydides knew of contagion in the fifth century BCE.²²⁴ He did not know of germs. Still, the idea that living things too small for the eye to see could cause disease began long before the invention of the microscope. Three hundred and fifty years after the Peloponnesian War, Lucretius offered a cause for contagion in his *On the Nature of the Universe*.²²⁵ "There are

²²³Phyllis Allen Richmond, "American Attitudes toward the Germ Theory of Disease (1860-1880)," *Journal of the History of Medicine and Allied Sciences* 9(1954): 428-54. and Tomes and Warner, "Rethinking Germ Theory," 7-16. The more recent analysis of Tomes and Warner reveals depth and complexity absent from Richmond's "classic" interpretation of the development of germ theory in America.

²²⁴"Mortality among the doctors was the highest of all," he noted for posterity, "since they came more frequently in contact with the sick." Thucydides knew whereof he spoke. "I had the disease myself and saw others suffering from it." Thucydides, *History of the Peloponnesian War*, trans. Rex Warner (New York: Viking Penguin, 1986), 152.

²²⁵Lucretius, *On the Nature of the Universe*, ed. E. V. Rieu, trans. Ronald Latham, The Penguin Classics (Baltimore: Penguin, 1961), 250-6.

certain atoms...flying about,” he divined, “that are pestiferous and poisonous...and upset the balance of the atmosphere.”²²⁶ Following the "discovery" of the New World by Europeans, many others, as we shall see, contributed to the notion that *contagium vivum*—contagion by (small) living things—caused disease. In the nineteenth century, Oliver Wendell Holmes (1842), Ignaz Semmelweis (1844), and, especially, Joseph Lister (1867), empirically devised methods to reduce sepsis and infections in high-risk environments. Following advances in microscopy and cellular theory, Jakob Henle (1840), Louis Pasteur (1861), and Robert Koch (1876) contributed to and proved a theory of disease causation founded upon germs. Theories of germs explained the success of these methods in minimizing surgical morbidity and mortality. These investigators all functioned within the lifetime of President Cleveland and influenced the surgical practices of Drs. Joseph Bryant, William Keen, and others who accepted this non-humoral, localistic interpretation of infection. Hence, by the early 1890s, a new standard of practice dictated that the President’s mouth be “cleaned” repeatedly before the operation.

Cancer Surgery, 1893

The *Oneida* traveled North on the East River, passed Hell’s Gate, and anchored near Plum Gut in the Long Island Sound—presumably on its way to Buzzard’s Bay.²²⁷ Although the cancer was a secret—even to the crew on the yacht (except the one steward)—the cognoscente on board were aware of the historic importance of the surgery. Indeed, it was the notoriety of the situation that drove Bryant and Keen—like Douglas and Shradly before them—to record the medical events for posterity. But, unlike Grant’s consultants, Cleveland’s surgeons could not know in 1893 if their unheralded contribution to the history of the United States would ever be

²²⁶Ibid., 250.

²²⁷Typescript of Keen interview with Dr. John F. Erdmann, September 13th, 1916. Keen, *Scrap book*.

made public—or, should a disaster occur, if they would ever want their notes to be revealed. The publication of Keen’s “Surgical Operations on President Cleveland,” in 1917, opened this chapter in the history of medicine to the world. The minute details of the first surgery are there for all to read and compare with cancer surgeries past, present, and future.²²⁸

The Operation

Drs. Bryant and Keen checked the time as the President disrobed in the Salon on that first day of July. It was 12:31. This main room of the yacht, below deck, had been furnished with the most state-of-the-art equipment available in 1893. “Oxygen, nitrous oxide, two storage batteries for the cautery and electric light, strychnia, digitaline, morphia and everything else that could by any possibility be needed” were arrayed around a large dentist’s chair that had been lashed to the mast that pierced the center of the room.²²⁹

The electric light was particularly important and noteworthy. Although Edison discovered the relatively long-lived carbonized cotton filament necessary to sustain the life of his incandescent electric “lamp” in 1879, the pervasive use of electricity to “turn night into day” took over a decade. In June 1884, Dr. Da Costa, for lack of more direct illumination, used the light of the midday sun to examine General Grant’s mouth on the porch of his summer home. Later that year and in 1885, Drs. Barker, Douglas, and Shradly visualized the General’s cancer by reflecting the light of various jerry-rigged non-electric lamps. By 1893, however, “internal” medical procedures frequently used electricity-dependent light sources.²³⁰ Dr. Keen could well

²²⁸Drs. Bryant, O’Reilly, and Keen kept surgical notes. Dr. Erdmann added to the history of the Cleveland surgeries by contributing to the publications of Keen (Interviews on September 13 and October 6, 1917), Nevins (November 14 and 16, 1931), the writings of Hayes Martin (November 19, 1942), and TIME magazine (December 7, 1942).

²²⁹Notes of W. W. Keen, 3. Keen, *Scrap Book*.

²³⁰In 1883, Newman incorporated the new Edison light bulb into a cystoscope but, as shown by the Grant case, it did not catch on immediately.

have been writing about the President's surgery when, in an article published the same year about a young man with a similarly-situated hard palate tumor, he noted the recurrent difficulty "to get good light." "I propose," he continued, "to have a mirror with a small electric light attached to my forehead, so that I can throw the light in the back of his throat."²³¹ In his *Scrap book* on President Cleveland's cancer surgery, Keen noted his gratitude that "the electric light was most useful in furnishing complete and thorough illumination of the mouth and the cavity of the antrum."²³²

The President sank into the big chair of the Salon and the operator yet again swabbed his mouth with Thiersch's antiseptic solution to reduce the number of dangerous germs. The instruments used for the surgery, in contradistinction to those used on Grant, were "scrupulously disinfected" by boiling.²³³ The physicians washed and disinfected their hands.²³⁴ They wore aprons over their street clothes.²³⁵ There were, however, no gloves, facial masks, or head coverings. These additional protections against intraoperative infection were yet to become staples of the surgical suite.²³⁶

The surgical plan was simple and straightforward. The surgeons would perform the less painful parts of the operation first, under the influence of systemic nitrous oxide gas and local

²³¹Keen, "Tumor of the Hard Palate," 196. Surgeons commonly use this equipment—with changes in magnitude rather than kind—today.

²³²Notes of W. W. Keen, 5. Keen, *Scrap Book*.

²³³Dr. John F. Erdmann Interview, TIME magazine, December 7, 1942, in *Memorial Hospital Archives*, Record Group 500, Hayes Martin Collection, Box 5, Folder 87, page 52. The quotation is from the "Notes of W. W. Keen," *Scrap book*, 3.

²³⁴Notes of W. W. Keen, *ibid*.

²³⁵Dr. John F. Erdmann Interview, TIME, 52.

²³⁶Dr. William Halsted introduced rubber gloves to the operative theater for his nurse-girl friend about 1900. Martin, "Interview of John F. Erdmann by Hayes Martin," 2.

cocaine anesthesia, in order to minimize the quantity of ether administered to the patient with the “nephritic” kidneys. Drinking (ethyl) alcohol, used as an anesthetic for Fanny Burney’s cancer surgery and General Grant’s palliation, played no role in the Cleveland operation. In addition, all surgery would be performed within the President’s mouth. There would be no external scar to expose the President’s secret. This was a critical part of the operation and, according to Dr. Keen, was made feasible by the unusual cheek retractor (a surgical instrument to hold back bodily tissues so as to better expose the operative site) he had brought back with him from Paris in 1866.²³⁷ Hence the tissues of the left cheek would first be separated from the maxilla (upper jawbone) and then the palate would be incised in an elliptical shape to remove the cancer and a wide margin of non-cancerous tissue to act as protection against local tumor recurrence. The actual exploration of the maxillary sinus (the cavity above the jawbone and below the orbit of the eye) and the removal of the deeper tissues that harbored the cancer would commence under ether. Excessive bleeding, the killer of many patients with similar surgeries in the past,²³⁸ was to be stanchd by pressure, hot water, or, if need be, the electro-cautery. If these measures failed, the operator could tie the bleeding vessel(s) with a ligature—hopefully. If that failed, Dr. Bryant would probably follow the highly risky procedure of ligating (tying off) the external carotid artery.²³⁹ There were no guarantees and it is not known if President Cleveland received what we would today call informed consent. Yes, the President knew the hoped-for results of the surgery and Bryant had briefed him on the “plug” that would be necessary to fill the gaping hole left by

²³⁷Keen, *The Surgical Operations*, 1917, 53. The unusually shaped Luer cheek retractor is part of the collection that Keen entrusted to the Mütter Museum at the College of Physicians of Philadelphia. A photograph of the instrument is part of the Keen *Scrap book* at the College. A drawing of the retractor can be found on page 60 of Keen’s 1928 *The Surgical Operations on President Cleveland in 1893*.

²³⁸Bryant, "Two Hundred Fifty Cases of Superior Maxillectomy," 65 and 66.

²³⁹*Ibid.*, 70.

the surgery. But did he know the risks he was taking? Was he aware that the anesthesia could poison his ‘weak’ kidneys or that fully one quarter of similar operations resulted in “profuse hemorrhage”?²⁴⁰ Cleveland trusted his good friend Bryant implicitly. The doctor likely shielded him from knowledge of the surgical complications as he openly sought to ‘alarm’ Mrs. Cleveland “as little as possible.”²⁴¹

Dr. Hasbrouck administered the nitrous oxide gas at 12:32.²⁴² The President rapidly fell into a swoon. Four minutes later the dentist extracted the two left upper bicuspid teeth that blocked access to the cancer. Bleeding ensued, but within another four minutes Bryant and Keen controlled it with simple pressure and hot water.²⁴³ The operator superficially swabbed cocaine, the narcotic-as-local-anesthetic that made General Grant’s miserable final months less painful, onto the President’s cancer to reduce incisional pain, but the team judged the patient too responsive to proceed with the cancer surgery. Thus at 12:47 (notice how carefully the surgeons recorded every minute!) Bryant injected five drops of 4% cocaine, the same dose often used on the General, directly along the proposed line of excision. Unfortunately, the intramucosal cocaine was also insufficient to quell the pain. Perhaps, as we now know, the quantity of narcotic was inadequate because the adipose tissue of his enormous body mass absorbed too much anesthetic, leaving too little to affect the body’s pain centers and suppress the noxious

²⁴⁰Ibid., 65.

²⁴¹Manuscript letter to Dr. Keen from Mrs. Frances F. Cleveland Preston, April 6, 1917. In Keen, *Scrap Book*. The President’s wife wrote that “I was so alarmed when I saw it [the mouth cancer] and felt that Dr. Bryant who was our dear loyal friend and guide in all things medical, should know it at once; but from that time Dr. Bryant’s effort was to alarm me as little as possible, although the nature of the trouble was told me.”

²⁴²The notes of Dr. R. M. O’Reilly and Dr. W. W. Keen document the exact times of the various stages of the operation. Ibid.

²⁴³Keen, *The Surgical Operations*, 1917, 53.

sensations. Thus, Dr. Hasbrouck readministered nitrous oxide gas, saving the potentially dangerous ether for the later.

At 12:54, the patient now adequately anesthetized, Dr. Bryant made the palatal incision that began the actual excision of the cancer.²⁴⁴ Commodore Benedict and Secretary Lamont remained on deck with most of the crew, doing what they could to make the clandestine operation a success from a logistical point of view. Dr. Bryant did not think their presence in the Salon would be helpful. He was in charge of the surgery, and only he and the other physicians—especially Keen—would shoulder the responsibility if something went wrong. Three minutes later, the surgeons divided the soft palate in the upper part of the mouth and separated the cancerous from the normal-appearing tissue.²⁴⁵ Bleeding recurred at 13:02. It was not immediately clear how much blood was lost, but pressure and hot water did not stop it initially. The electric cautery, powered by the two batteries, did the job.²⁴⁶ Nevertheless, the electricity must have irritated the President, for he required more nitrous oxide a minute and a half later.²⁴⁷ The patient then quieted enough to allow the physicians to continue the procedure.

At 13:06, Dr. O'Reilly tersely noted “incision made through gum and hard palate.”²⁴⁸ Thus, barely half an hour into the operation, the surgeons arrived at the heart of the matter. The President required more nitrous oxide a few seconds after 13:13, but it was now clear that nitrous oxide gas and local cocaine injections could not achieve the level of anesthesia necessary to complete the surgery. Thus, at 13:14, Dr. O'Reilly, who had been surprised and honored that Dr.

²⁴⁴Typescript notes of Dr. Robert M. O'Reilly. Keen, *Scrap book*, 6.

²⁴⁵Ibid.

²⁴⁶Ibid.

²⁴⁷Typescript notes of Dr. W. W. Keen. Keen, *Scrap book*.

²⁴⁸Typescript notes of Dr. Robert M. O'Reilly. Ibid.

Bryant requested his participation in the operation,²⁴⁹ began the ether. As soon as the additional anesthetic took effect the deepest and most dangerous part of the procedure commenced—the removal of the left upper jawbone. The pre-surgical plan included only partial removal of the left superior maxilla, but Dr. Bryant’s exposure of the disease site revealed that the cancer had spread farther than originally thought.²⁵⁰ The invasion of the antrum inside the jawbone and above the teeth caused the team to rethink their strategy.²⁵¹ The excision area needed to be extended, they decided, increasing the President’s risk for operative complications (including the need for more ether) and the likelihood that a change in the appearance of his face would be noticeable. Dr. Bryant, concerned but unbowed, believed that the benefits outweighed the risks. In particular, he was well aware that inadequate resection would increase the probability of local—and perhaps metastatic—cancer recurrence. He compromised, taking more tissue than originally planned, but less—as it turned out—than required. In the words of Dr. Keen, Dr. Bryant proceeded to “remove all the jaw except the floor of the orbit and the intermaxillary portion, which were clearly free from invasion.”²⁵² Still, the most essential part of the plan was preserved. No incision would pierce the skin of the President’s face, so an exceptionally fitted prosthesis could minimize distortion of his visage. Mr. Cleveland was also fortunate that the cancer had not extended into the orbit (the bone around the eye). Had the tumor spread there, necessitating removal of the floor of the orbit, the eye—the most closely observed anatomical

²⁴⁹Typescript letter from Dr. Robert M. O’Reilly to Dr. Joseph D. Bryant, June 25, 1893. In *Ibid.*

²⁵⁰There were, of course, no X-rays, CAT scans, or MRIs to pre-operatively “stage” (determine the extent of) the cancer. Drs. Bryant and Keen used clinical examination, which could be inexact, to assess how far the disease had spread. Apparently, they underestimated its dimensions.

²⁵¹The reader may virtually visualize the procedure with an anatomy textbook such as the long-popular *Gray’s Anatomy*. Henry Gray, *Anatomy Descriptive and Surgical*, The Classics of Medicine Library (London: John W. Parker and Son, West Strand, 1858; repr., 1981), 40-4.

²⁵²Typescript notes of Dr. W. W. Keen. Keen, *Scrap Book*, 6.

part of the human body—would surely appear askew. Saving the orbit might sustain the great secret.

The extended surgery proceeded well. The surgical team removed the entire left superior maxilla, cleared the antrum of all visible cancer, and left the bony support of the eye intact. Luckily, there was little additional bleeding.²⁵³ Again, Bryant disinfected the wound and then packed it with iodoform gauze to mitigate the risk of postoperative bleeding and infection.²⁵⁴ By 13:55, one hour and twenty-three minutes after Hasbrouck first administered the nitrous oxide, the operation was over.

The big man withstood the surgery with minimal apparent discomfort. The powerful triad of anesthesia, analgesia, and antisepsis that coalesced in America in the last years of the nineteenth century—after the death of General Grant—served the President well. Dr. Janeway sat at the President’s right arm throughout the procedure, monitoring his general condition as the surgeons focused on the patient’s mouth. The pulse was strong and rarely broke one hundred, an indication to the diagnostician that at least the cardiopulmonary system tolerated the procedure well. At the conclusion of the operation, Dr. Janeway noted that the pulse was a strong eighty and the temperature only slightly elevated at 100.8° F.²⁵⁵ He informed the surgical team of the excellent vital signs and the patient was put to bed. The tension felt by all in the Salon eased. “What a sigh of intense relief we surgeons breathed,” wrote a thankful Dr. Keen, “when the patient was once more safe in bed can hardly be imagined!”²⁵⁶

²⁵³Dr. Keen estimated the total blood loss at “not over six ounces” at the conclusion of the operation. This is the equivalent of three-eighths of a pint—a paltry amount for a man of Cleveland’s body mass index. Typescript notes of Dr. W. W. Keen. Ibid.

²⁵⁴Typescript notes of Dr. W. W. Keen. Ibid., 5.

²⁵⁵Typescript notes of Dr. J. D. Bryant. Ibid.

²⁵⁶Keen, *The Surgical Operations*, 1917, 53.

The operation appeared to be a success. The surgical team achieved both goals. They had removed all visible tumor and the cancer secret seemed safe. Commodore Benedict had informed his crew that the President's absence from the fishing deck was because of a tooth problem. The extractions needed to be performed on the yacht, Benedict explained, because "fresh, pure air, and disinfected quarters and skilled doctors, all had to be provided, lest blood poisoning should set in—a very serious matter when the patient was the just-inaugurated President of the United States."²⁵⁷ Thus, when the President was wheeled past the clueless crew, they were, in the words of one writer, "unaware that the important man had much of his upper left jaw gone and a large cavity in his head."²⁵⁸ Traditional cancer was a disease of accretion that added tumorous growth to the body until normal tissue was subsumed and/or consumed by the abnormal. On the other hand, modern cancer, when treated, became a disease of deletion—the removal of the abnormal to allow a return to normal.

At 14:25, exactly one-half hour after the completion of the procedure, the patient received one-sixth grain of morphine injected under his skin.²⁵⁹ It was, as Dr. Keen trumpeted to the world in his *Saturday Evening Post* exposé, "the only narcotic administered at any time."²⁶⁰ What a contrast with the treatment of General Grant! The President had surgery and required only a one-time injection of narcotic for postoperative pain. The General's palliation necessitated daily systemic and local narcotics to assuage the mounting pain. As Sir Morrel Mackenzie, the father of British laryngology, wrote in the years just prior to Grant's cancer, the

²⁵⁷Ibid.

²⁵⁸Rosenhouse, "President Cleveland's Secret Surgery," 46.

²⁵⁹Typescript notes of Dr. W. W. Keen. In Keen, *Scrap Book*. A grain is a unit of weight equivalent to 64.8 grams. Thus, 1/6th grain of morphine is a bit more than 10 milligrams or 3.52 ten-thousandths of an ounce.

²⁶⁰Keen, *The Surgical Operations*, 1917, 53.

question was not how to prevent death from throat cancer—for that was not possible in the era of traditional cancer—but how long death could be postponed.²⁶¹ By the 1890s, given the revolution in surgery fostered by the three A's—anesthesia, analgesia, and antisepsis—the pessimism of inevitable death from cancer was transformed into a beacon of hope. How long, asked the modern cancer physician, could surgery prolong the cancer victim's life? The answer, in the case of President Cleveland, was the rest of his life.²⁶²

SUCCESS?

Within days of the cancer surgery, the apparent dual successes lay in doubt. The tumor “recurred” and the secret was out.

“Tell the Truth” -Grover Cleveland, 1884

²⁶¹Sir Morrel Mackenzie, *Diseases of the Pharynx, Larynx, and Trachea* (New York: William Wood & Company, 1880), 60-1.

²⁶²Grover Cleveland's death certificate (1908) stated that he died from “heart failure complicated with Pulmonary thrombosis and Edema.” (Morreels, “New Historical Information on the Cleveland Operations,” 550) Dr. Keen's *Scrap book* contains notes from Drs. Gibson and Erdmann written in 1916 that “extensive carcinoma was found in the intestines” at postmortem. (Typescript notes of Drs. Kasson C. Gibson and John F. Erdmann, in Keen, *Scrap Book*, 9) Dr. Keen, who was unaware of this finding when he undertook his article, sought Mrs. Cleveland Preston's consent to confirm the findings with Dr. William C. Lusk, who performed the autopsy on her first husband. She refused permission and Keen denigrated the possibility that the mouth cancer could have caused abdominal cancer because of the long disease-free interval. In 1947, Dr. M. G. Seelig asked Dr. Erdmann, the last living eyewitness to the Cleveland cancer surgeries, whether the President died of cancer. Erdmann wrote back that “Mr. Cleveland died of intestinal obstruction but [he did] not know whether or not the obstruction was due to a malignant growth.” He also believed that “if the obstruction were due to a malignant growth, it must have been a second primary tumor, because it developed almost fifteen years after the removal of the jaw tumor.” (Seelig, “Cancer and Politics,” 376) In the late 1970s, the Mütter Museum gave pathologists permission to reexamine the Cleveland cancer tissue. They found it to be a verrucous carcinoma—a mouth cancer that rarely metastasizes. (John J. Brooks and Horatio T. Enterline, “The Final Diagnosis of President Cleveland's Lesion,” *Journal of the American Medical Association* 244, no. 24 (1980): 2729. Given the retrospectively-determined non-aggressive nature of the cancer and the absence of any evidence of recurrence over the fifteen year interval from the surgeries until the President's death in 1908, I agree that President Cleveland did not die from metastases from his mouth cancer.

Grover Cleveland based his political persona upon honesty and integrity.²⁶³ His three Presidential campaigns—1884, 1888, and 1892—rallied around the slogan, “Tell the Truth.” He was, after all, the son of a Protestant minister. Nevertheless, the disease, cancer, so personal and yet so potentially publicly explosive, reoriented his priorities. For several months following the July 1, 1893 cancer surgery, the Cleveland White House lived on lies and innuendoes in an attempt to hide the President’s disease. Honest men were slandered and careers foundered on the truth. President Cleveland, Secretary Lamont, Commodore Benedict, and most of the surgical team, however, believed that the end justified the means. At all cost, secrecy must be maintained for the good of the nation. Honesty and integrity were sacrificed at the altar of deceit. As Grover Cleveland was not just any patient, so cancer was not just any disease, for its legacy carried the burden of connotations that influenced the course taken by the President and, in the process, the history of the United States.²⁶⁴

The effort to maintain the secrecy of the President’s cancer, therefore, did not end with his surgery. The *Oneida*, following the Salon surgery, continued its slow course toward Buzzard’s Bay. Dr. Hasbrouck was frantic to disembark. He had agreed to administer nitrous oxide gas on July 1 to the patient of a Greenwich-based physician before Bryant called him to serve the President. He never cancelled. No one on the mainland knew where he was and Dr. Bryant at first refused to let him go ashore. It was a decision made with utmost diligence that

²⁶³A relatively recent biography of Grover Cleveland, which incorporates these generally accepted traits of the two-term President, is entitled *An Honest President*. See H. Paul Jeffers, *An Honest President: The Life and Presidencies of Grover Cleveland* (New York: William Morrow, 2000).

²⁶⁴Allan Nevins, in his comprehensive 1932 biography of Grover Cleveland, considered the President’s cancer story “one of the dramatic minor episodes of American history.” Nevins, *Grover Cleveland*, 528. Although the consequences of paths not taken can never be known, it is likely that had Mr. Cleveland’s cancer become public knowledge, or had the surgery failed, the repercussions would not have been “minor.” Hindsight, the historian’s bane, leads to judgments of degree (such as ‘minor’) that could not be appreciated by those who partook in the incident.

later returned to haunt the President, Bryant, and Lamont. Dr. Bryant knew from his extensive review of the literature that Mr. Cleveland was susceptible to postoperative bleeding and other complications that could necessitate re-operation.²⁶⁵ If so, Hasbrouck's anesthetic skills would again be required. Thus, he could not put the dentist on land immediately. Fortunately, the first postoperative night was uneventful, so Bryant allowed Dr. Hasbrouck to disembark when the *Oneida* put in at New London, Connecticut on July 2.²⁶⁶ Hasbrouck immediately telegraphed the worried Greenwich surgeon that he was in New London and would travel west forthwith. Upon arrival he blurted out the events of the past two days to the astounded surgeon, who later repeated them to the referring physician. There the secret lay—for a while.

Other circumstances conspired to reveal Mr. Cleveland's cancer secret to the world. "It would be a mistake to suppose," conceded his personal secretary, Robert L. O'Brien, "that it was an easy matter to keep this affair from the newspapers of the country, with all the light that beats on the presidential throne."²⁶⁷ Although most histories of the President's cancer surgery and the effort to preserve secrecy emphasize the exposé newspaper article published in the *Philadelphia Press* in late August, 1893, suggestions of a debilitating Presidential illness and cover-up actually began when Mr. Cleveland first set foot on land after the surgery. The actions of the immediate postoperative weeks reveal the lengths to which an individual will go to hide the fact that he has or had cancer—a subterfuge witnessed over and over again in the history of cancer.

²⁶⁵Martin, "When the President Disappeared," 11.

²⁶⁶Typescript of Dr. W. W. Keen interview with Dr. John F. Erdmann, September 13th, 1916. In Keen, *Scrap Book*.

²⁶⁷Keen, *The Surgical Operations*, 1928, 19.

The President did well postoperatively. He arose from bed on the second day after surgery and never showed signs of post-operative complications.²⁶⁸ On July 5, the fourth postoperative day, the *Oneida* quietly docked at Gray Gables late in the evening and the President returned to the lion's den. Only a few reporters were present,²⁶⁹ but, despite the holiday weekend, they had received no word as to the President's whereabouts for five nights and days—an unheard-of occurrence in peacetime.²⁷⁰ Mr. Cleveland's appearance further piqued their interest. Although Keen related that the President walked "with but little apparent effort,"²⁷¹ the press noted that something was awry. Lamont and Bryant decided on an alibi that, as in the case of General Grant's subterfuge, would stretch the truth without breaking it. The President would not talk to the press. An aide informed the press that "the President will not answer questions. He has caught a cold and is also recovering from a serious toothache."²⁷² Mrs. Cleveland added that he was also suffering from a bad case of rheumatism and therefore his mobility was severely restricted. The press, in other words, should not expect to see him any time soon.²⁷³ Soon after the *Oneida* docked they confronted Lamont, the former journalist, skeptical of official 'medical' announcements since the prevarications of President Garfield's and General Grant's doctors.²⁷⁴ In an old gray barn on the Cleveland property, he stuck to the

²⁶⁸During the three post-operative days that Dr. Janeway and the surgical team observed the President on the *Oneida* as it made its way from Long Island to Buzzard's Bay, his maximum temperature was the 100.8°F observed at the conclusion of the operation and his maximum pulse 96. Both are admirable vital signs following surgery. Typescript notes of Dr. J. D. Bryant. In Keen, *Scrap Book*.

²⁶⁹Keen, *The Surgical Operations*, 1928, 21.

²⁷⁰Martin, "When the President Disappeared," 102.

²⁷¹Keen, *The Surgical Operations*, 1928, 13.

²⁷²Rosenhouse, "President Cleveland's Secret Surgery," 46.

²⁷³Martin, "When the President Disappeared," 102.

²⁷⁴Newspaper clipping of Dr. John F. Erdmann. Keen, "Keen Scrap Book."

story. The President had been fishing and now suffered from a toothache and rheumatism. No wonder he looked unwell. The lies had just begun.

Dr. Bryant also had his hands full attempting to preserve the cover-up. On the one hand, circumstances beyond his control thrust him into the public spotlight as the President's trusted physician and reluctant medical spokesman. On the other, he sought to suppress all physician-derived avenues that could reveal the President's cancer. Indeed, he had begun the process even before the surgery by instructing the surgical team to board the *Oneida* from different places at various times. Once under way, he warned the team to stay out of view passing Bellevue Bay. After the conclusion of the operation he sought to maintain the cancer secret within the surgical team. His first strategy was to function as the sole spokesman for all medical participants. His second was to silence the team. Dr. Bryant did not perceive Drs. Janeway and Erdmann as threats, for they were in frequent contact with him as mentor and associate, respectively, through the Bellevue connection. The Commodore dealt with the steward who, despite serving at the operation merely to "fetch and carry," was witness to the entire procedure.²⁷⁵ Dr. Bryant was less certain of the silence of Drs. Keen and Hasbrouck. Bryant did not know either of them well. Certainly, he would have no direct connection or control of them after the surgery. Dr. Keen disembarked at Sag Harbor, Long Island, on July 4. Two days later, Bryant mailed Keen a letter full of praise and a not-very-subtle demand for secrecy. "I write...to thank you for your kind cooperation and support in the matter. I am convinced that my judgment regarding yourself was correctly made. Do not by word or intimation indicate the fact to anyone that you were with me, that if anyone other than your own family, even they should not know, whom you saw with

²⁷⁵Dr. Keen, in his *Saturday Evening Post* article, praised the crew of the *Oneida* and, in particular, the steward (whose identity is unknown) for their silence. "I have always thought that due credit was not given to him (the steward), and to the captain and crew, for their never betraying what had taken place." Keen, *The Surgical Operations*, 1917, 53.

me.”²⁷⁶ Should Dr. Keen not understand the message, Dr. Bryant added that “the policy of the affair will be indicated by statements of friends to the public press.”²⁷⁷ Dr. Hasbrouck, the other wild card, took his leave of the yacht two days before Keen and three days before it arrived at Buzzard’s Bay. If Bryant sent him a similar letter, it came too late.

The press was in a quandary. The President appeared ill, or at least unusually fatigued. Something was clearly wrong. Yet, his wife and trusted advisors, in an administration founded upon truth and reform, denied anything serious. Dr. Bryant, in an interview with the United Press on July 7, did not expressly deny the “rumor that the President was suffering from a cancerous growth in the mouth.”²⁷⁸ The next day, however, he publicly denounced the possibility that Mr. Cleveland had cancer. “The President,” he said with artful postoperative truthfulness after the tumor excision, “is suffering from no cancerous or malignant growth.”²⁷⁹ Again he emphasized the toothache. The press was skeptical. They wanted to know the name of the dentist and when the extractions were performed. Bryant never liked the media and usually deflected their questions,²⁸⁰ so he put off their insistent questions by refusing to acknowledge that there was a problem. It was, in his words, “too trivial” to talk about.²⁸¹ The press could not understand why the President’s doctor and advisors were minimizing his infirmity. The *Boston Herald*, in a touch of irony not lost on Lamont or Bryant, reported on July 8 that “there is no

²⁷⁶Typescript to Dr. W. W. Keen from Dr. J. D. Bryant, July 6, 1893. In Keen, *Scrap book*.

²⁷⁷*Ibid.*

²⁷⁸Keen, *The Surgical Operations*, 1928, 20.

²⁷⁹*Ibid.*

²⁸⁰The New York Times, “Dr. Joseph D. Bryant,” 13:5.

²⁸¹Keen, *The Surgical Operations*, 1928, 20.

doubt that the President, as well as Secretary Lamont and Dr. Bryant, underestimate the importance which is attached by the country to his illness.”²⁸²

Worse still, Vice President Stevenson, the Illinois silverite, heard that the President’s condition was “serious.” He immediately left Chicago for Buzzard’s Bay. Cleveland would have none of him and immediately dispatched Lamont to inform the reporters that Stevenson “was neither invited nor expected at Gray Gables.”²⁸³ The Vice President, who had never been briefed on the President’s cancer or his surgery, received Lamont’s blunt communiqué and halted his trip east in New York.²⁸⁴

The lies to perpetuate the cancer secret continued unabated. The spinmeisters of the Cleveland administration, led by the cunning Lamont and the devious Bryant, handled the press at Gray Gables and in Washington. Two days after the President landed at his summer home, Lamont was forced to hold another press conference. This time he spoke to a bevy of newspapermen who flocked to Gray Gables upon hearing the words “the President” and “cancer” in the same sentence. He elaborated on Mr. Cleveland’s rheumatism and toothache, reported *The New-York Times*, by noting that the President’s “knee is lame and his left foot swollen.”²⁸⁵ Mr. Cleveland’s natural aversion to dentistry, added Lamont (“the soul of shrewdness, diplomacy, and tactfulness”), occasioned the multi-day journey on the yacht.²⁸⁶ The President procrastinated so long, continued Lamont, that he needed to take a few days away from everyone and

²⁸²Quoted in *ibid.*, 21.

²⁸³Martin, “When the President Disappeared,” 102.

²⁸⁴Keen, *The Surgical Operations*, 1928, 31.

²⁸⁵The New York Times, “The President Improving. Dr. Bryant Expects Him to Be out of Doors Again in a Few Days,” *The New York Times*, 8 July 1893, 5:7.

²⁸⁶Lamont’s epithet is from Robert L. O’Brien, President Cleveland’s personal secretary. Keen, *The Surgical Operations*, 1928, 23.

everything to have his teeth fixed. On the yacht “he could be cool and comfortable and let the dentist make a thorough job of it.”²⁸⁷

Lamont was not alone in his prevarications. Bryant, again buttonholed about the possibility of cancer, equivocated when he informed the press that “the President is absolutely free from cancer or malignant growth of any description.” That was true, as far as the surgeon knew, after July 1. But, upon further provocation, he stated in no uncertain terms that “no operation has been performed except that a bad tooth was extracted.”²⁸⁸

The cancer lies would have shattered on the shoals of the truth were it not for the unwitting complicity of the newspapermen. They knew that too many inconsistencies conspired against Lamont’s story and Bryant’s repudiations. Why, for example, did the President call the Special Session of Congress so far in the future when the problem was now—the value of the dollar was plummeting, interest rates were soaring, and the stock market was suffering its worst decline in years?²⁸⁹ Surely exigency dictated—and modern transportation permitted—a date sooner than August 7. Why did the President insist that the planned Special Session remain unannounced until 6 P. M. on a Friday evening before the long July 4 Holiday weekend? Why did he lead the press to believe that he had just then issued the order for the Special Session when he had departed for New York hours earlier? Also, consider the late arrival of the *Oneida* at Gray Gables on July 5—too late for newspaper notices until the next afternoon. How unusual! Why go to such lengths to conceal a mere toothache? Was the President hiding something? The newspapermen were suspicious. Following Lamont’s “barn” conference they walked the mile

²⁸⁷Ibid., 24.

²⁸⁸“The President Improving,” *The New-York Times*, 8 July 1893.

²⁸⁹Friedman and Schwartz, *A Monetary History of the United States*, 109 and Keen, *The Surgical Operations*, 1928, 43.

and a half from Gray Gables to their hotel in “heated argument.”²⁹⁰ Half of them, according to Cleveland’s personal secretary O’Brien, believed Lamont. The other half did not. Nevertheless, they decided to present a single story to the nation, perhaps because it is safer to be wrong with a crowd than right on your own. They conferenced at the hotel that night. The next morning the newspapermen, including those representing the press associations, unanimously presented Lamont’s version of the story to the world. Bryant and Lamont had saved the cancer secret—at least temporarily.

In perpetuating falsehoods, often your friends present more of a danger than your enemies for exposing the truth. The fact that Lamont was the only member of the President’s Cabinet who knew of the cancer and the surgery is a case in point. As the rumors flew that “Mr. Cleveland is a sick man,” the Secretary of War tried to assuage the Cabinet’s “uneasiness” in a telegram to Secretary of State Walter Gresham on July 7.²⁹¹ “Rheumatism in his knee and foot,” assured Lamont, was the problem and only a temporary one at that.²⁹² Telegrams, however, were inadequate to conduct the business of the Executive branch. Richard Olney, the Attorney General, requested an urgent tête-à-tête with the President over the upcoming Congressional silver debate. After several unsuccessful attempts to meet with Mr. Cleveland (for Lamont and Bryant feared that anyone—friend or foe—could leak the true reason for the President’s incapacitation), he was finally allowed to converse with the President on July 8.²⁹³ The Attorney General, as he noted in his unpublished autobiography, was aghast at what he saw.

²⁹⁰Keen, *The Surgical Operations*, 1928, 25.

²⁹¹*Boston Herald*, July 8, 1893. Cited in *ibid.*, 19.

²⁹²Keen, *The Surgical Operations*, 1928, 20-21.

²⁹³The New York Times, “The President Is All Right. Alarming Stories of His Illness without Foundation,” *The New York Times*, 9 July 1893, 5:5.

Mr. Cleveland did not at all look the same as he did a few weeks before. He had lost much weight and antiseptic pads filled his mouth.²⁹⁴ Olney was unaware of the true cause of the President's metamorphosis. All he heard was the President's nearly unintelligible speech. Mr. Cleveland, after several attempts to be understood, said something that the Attorney General interpreted as "My God, Olney, they nearly killed me!"²⁹⁵ Whom Olney told of his observations is unknown, but the risk of public exposure was there. Charles S. Hamlin, the Assistant Secretary of the Treasury, personally delivered statistics relevant to the silver question to the President about three weeks after the surgery and two weeks before the special Congressional session. In his diary, Hamlin recorded that "Cleveland appeared not well at all. Had his mouth packed with some kind of bandage. Could not speak distinctly. C. S. Hamlin thinks he had some serious trouble with his mouth. Cleveland looks thoroughly tired out."²⁹⁶ Neither Hamlin nor Olney passed the damning information to the press. The cancer secret endured the threat of friendly fire.

The greatest public threat to the President's cancer secret came from the pen of Mr. E. J. Edwards, the New York correspondent for the *Philadelphia Press*. Edwards' quest to reveal the cancer truth is a bitter story with repercussions that tainted the remainder of the newspaperman's life. He was, in his own words, "very greatly abused."²⁹⁷ Indeed, Dr. Keen's guilt over his personal role in denouncing Edwards' honest revelation led the physician to go out of his way to

²⁹⁴The surgeons used the soaked pads to reduce the chance of Bryant's second greatest post-operative fear—infection—as well as to allow early detection of rebleeding from the operative site.

²⁹⁵Richard Olney Papers. Quoted in Nevins, *Grover Cleveland*, 532. Olney's recollections are another reason to question Keen's near-monopoly history of the Cleveland cancer. Keen wrote that the President went into the Gray Gables cottage on the evening of July 5 "with but little apparent effort." Keen, *The Surgical Operations*, 1917, 53. A week after the surgery, as Olney's personal papers reveal, the President was still recovering. Keen also offered nothing about the newspapermen's dilemma until 1928—and never mentioned Richard Olney at all.

²⁹⁶Nevins, *Grover Cleveland*, 532.

²⁹⁷Manuscript letter from E. J. Edwards to Dr. W. W. Keen, September 12, 1917, 2. In Keen, *Scrap Book*.

exonerate—if not extol—the journalist in his 1917 and 1928 versions of *The Surgical Operations*.²⁹⁸ The history of Edwards' exposé reveals the extent to which the President and those closest to him went in order to prevent the public from learning of his cancer.

Dr. Hasbrouck's candid explanation to the Greenwich surgeon for his absence from the July 1 operation was nothing more than instinctive self-protection. Whether Hasbrouck requested a vow of silence from the physician is unknown. Nevertheless, the Connecticut surgeon passed the story to Dr. Leander P. Jones, a medical man with many influential connections. Jones had no reason to conceal Mr. Cleveland's cancer and surely had not been asked to do so. Indeed, he concluded, the public would know of the President's disease forthwith—if not from him, than from someone else.²⁹⁹ Dr. Jones related Hasbrouck's story verbatim to his friend and patient E. J. Edwards. The journalist, known better by his *nom de plume* "Holland," attempted to reveal the President's cancer to the world on August 3—four days before the epochal Congressional battle on the silver standard. However, given the import of the narrative, he sought confirmation. First he confronted Hasbrouck. Edwards even asked him if "the President's affliction is much of the same character as that from which General Grant suffered."³⁰⁰ After hearing Edwards' presentation of the *Oneida* affair, the dentist, with profound consternation, admitted that the story was substantially correct but denied responsibility for it. "Some of the Physicians who were aboard the yacht must have told you that

²⁹⁸Keen, *The Surgical Operations*, 1917, 24 and Keen, *The Surgical Operations*, 1928, 13-14.

²⁹⁹Typescript letter from E. J. Edwards to Dr. W. W. Keen, received October 3, 1916. In Keen, *Scrap Book*.

³⁰⁰Dr. Hasbrouck allegedly answered that the General and the President had different cancers because a "jagged tooth" caused Grant's cancer, as fellow dentist Dr. Abbott argued nine years before. Gibson, "President Cleveland Operations."

story,” he argued in self-defense. “You could not have obtained it in another way.”³⁰¹ Next, the conscientious Edwards questioned Drs. Bryant, Keen, and Lamont. All lied. No, there was no cancer. No, there was no problem but a toothache and some rheumatism. The *Press* would not publish Holland’s story.³⁰²

By the end of August, Cleveland and his comrades could no longer suppress the cancer story. Edwards suspected that some of his sources were lying. Many newspapermen at Gray Gables agreed with him. The *Philadelphia Press* finally published the article in the form of a correspondent’s letter on August 29, 1893. The timing favored Cleveland in some ways, but not in others. The House of Representatives, despite a three-hour harangue from young Democratic Congressman William Jennings Bryan, voted to repeal the silver purchase Act the day before.³⁰³ The President’s eloquent tones had long since returned to the Capitol for all to hear. Nevertheless, the Senate had not yet voted on the repeal and “Holland’s” published report created an uproar. Newspapermen besieged the White House. Again, administration spokesmen denied all links between the President and cancer. The media, however, no longer accepted the denials of Lamont and Bryant without confirmation. Therefore, the War Secretary called in his friends and members of Mr. Cleveland’s inner circle. L. Clarke Davis, a member of the President’s small group and the respected newspaper editor of the *Public Ledger*, was widely quoted as saying that Edwards’ revelation “has a real basis in a toothache.” In addition, if there was a more serious medical condition, “Mr. Cleveland’s closest friends do not know it.”³⁰⁴ Dr.

³⁰¹From *The New York Evening Mail*, October 6, 1917. Quoted by Morreels, "New Historical Information on the Cleveland Operations," 549.

³⁰²I have been unable to determine if the White House exerted pressure on the editors and/or publisher of the *Press* not to print the cancer story on August 3.

³⁰³Nevins, *Grover Cleveland*, 540.

³⁰⁴*Ibid.*, 533.

Erdmann, intensely interrogated by the press after the “Holland” publication, summed up the efforts of the cancer team on the President’s behalf when he revealed that he then “did more lying than in all the rest of his life put together.”³⁰⁵

Given the President’s healthy appearance, the lack of a facial scar, his resonant voice, and the persistent denials from his closest friends, *The New-York Times* and other influential newspapers denounced Edwards’ story.³⁰⁶ The correspondent for the *Philadelphia Press* was labeled a “fakir,” “cancer fake,” and “calamity liar.”³⁰⁷ Edwards, because the publication appeared timed to do Cleveland political damage in the Senate, was considered nothing more than a tool of the Republican Party. (*Philadelphia Times* cartoon) His career, with his reputation pulverized, changed forever. The cancer secret, however, was preserved. In 1917, Robert O’Brien, then editor of the *Boston Herald*, noted that “one can but marvel at the completeness with which an event of such magnitude—aside from sporadic leaks which were soon arrested—escaped the scrutiny of the press, and has remained a secret until this late date.”³⁰⁸

Cancer Surgery—Again—and Again

Ironically, “Holland” was not aware that Mr. Cleveland underwent a second cancer operation on July 17, more than a month before the publication of his exposé of the President’s initial shipboard surgery. Although the circumstances mimicked the first procedure, they were sufficiently different to reinforce the momentous cognitive change in the notion of the surgical

³⁰⁵Ibid. Bellevue promoted Dr. Erdmann to Clinical Professor of Surgery that year.

³⁰⁶“Toothache,” *The New-York Times*, 1 September 1893, 4:6.

³⁰⁷Philadelphia Times, “The Calamity Liar,” *The Philadelphia Times*, 1 September 1893. The *Philadelphia Times* competed with the *Press* for readership.

³⁰⁸Robert L. O’Brien, *Boston Herald*, 30 September 1917. Quoted in Keen, *The Surgical Operations*, 1928, 32.

treatment of cancer that had occurred since Grant's palliative therapy. In particular, the second operation, even more than the first, showcased the extent to which localistic theory replaced the constitutional concept of cancer.

On Friday, July 7, as Bryant and Lamont denied the Cleveland cancer, Dr. Kasson C. Gibson arrived in Gray Gables. Gibson was a New York prosthodontist sent to fashion a plug for the large defect in the President's mouth that resulted from the first cancer surgery.³⁰⁹ Dr. Bryant, exhausted "physically and mentally" by the press and his constant ministrations to Mr. Cleveland, envisioned his return home.³¹⁰ Dr. Gibson set up a small dental laboratory on the premises of Gray Gables.³¹¹ With the help of measurements taken inside the mouth and basic trial and error, he was able to fit the President with a vulcanized rubber prosthesis within a few days.³¹² Mr. Cleveland found it difficult to adjust to the rubber plug (it was two and a half inches long and just shy of an inch wide), but it allowed him to speak without major recognizable impediments despite a left-deviated uvula.³¹³

Dr. Bryant, though temporarily absent during most of the fitting process, had planned the prosthodontist's work carefully. Three years before, in his article on maxillary surgery, Dr. Bryant noted that "the introduction of a vulcanized rubber 'plumper,' combined with an

³⁰⁹Martin, "When the President Disappeared," 102.

³¹⁰Typescript of Dr. W. W. Keen interview with Dr. Kasson C. Gibson, New York, September 14, 1916. In Keen, *Scrap Book*.

³¹¹*Ibid.*

³¹²Attorney-General Olney, who reviewed the Silver speech with the President on July 8, interviewed Mr. Cleveland before the first prosthesis was constructed.

³¹³Typescript of Dr. W. W. Keen interview with Dr. Kasson C. Gibson, New York, September 14, 1916. In Keen, *Scrap Book*. Researchers may view some of the casts made by Dr. Kasson to fashion prostheses for the President at the New York Academy of Medicine. The College of Physicians of Philadelphia holds other casts. Dr. Keen's *Scrap book* also contains photographs of casts. See Keen, *Scrap Book* and Morreels, "New Historical Information on the Cleveland Operations," 548, 549, and 550.

obturator, will be sufficient to remedy almost entirely these defects.”³¹⁴ And so it was. When the President met Congress on August 7, no one noted an alteration in his facial appearance or a deficiency in his speech.³¹⁵ His presentation was convincing but not immediately effective. The cancer secret seemed safe, but months passed before both houses of Congress repealed the silver Act.³¹⁶

All the more amazing, given the normal countenance and voice in early August, was that Mr. Cleveland had survived a second cancer operation less than three weeks prior to the Special Session of Congress. Dr. Bryant, who provided the sole postoperative surgical care for the President, noted in mid-July that a “suspicious-looking growth” was present at “the inner margin of the wound.”³¹⁷ The cancer returned at the site of excision. On the other hand, had it been there all along? The difference between recurrent and residual cancer was significant for diagnosis, therapy, and prognosis. Bryant realized that the small operative field occasioned by the necessity to perform the entire operation within the mouth for the sake of secrecy meant that it was possible the first surgery had not allowed complete visualization and removal of all the cancerous tissue. Thus the cancer could be residual. If it was, excision of the remaining tumor could be curative. On the other hand, if the growth was new, the cancer could return again and the President’s prognosis was poor. Bryant had no method to determine the difference. He

³¹⁴Bryant, "Two Hundred Fifty Cases of Superior Maxillectomy," 71.

³¹⁵Keen, *Scrap Book*.

³¹⁶The House passed the Wilson repeal bill of the Silver Act on August 28. The Senate, delayed by filibusters against repeal, did not pass the bill until October 30. The Senate vote for repeal (48-37) was much closer than that of the House (239-108). Nevins, *Grover Cleveland*, 540 and 547.

³¹⁷Typescript letter from Dr. J. D. Bryant to Col. Daniel S. Lamont, May 9th, 1905. Keen, *Scrap Book*. Dr. Gibson may have made Dr. Bryant aware of the previously unseen cancer, for Dr. Bryant did not explicitly note that he discovered the growth.

pondered the dilemma and concluded that the growth “should be removed for sake of giving the patient the benefit of every doubt.”³¹⁸

On July 17, 1893, the President and Dr. Bryant quietly boarded the *Oneida* at Gray Gables. This second operation was less major than the first, so Bryant deemed a separate dentist-anesthetist unnecessary.³¹⁹ Drs. Janeway, Keen, and Erdmann, already on board, assisted Bryant in curetting (scraping away) the visible cancer and, as a further precaution, seared “the entire surface of the wound with galvano-cautery.”³²⁰ The patient was observed overnight, suffered no complications, and returned to Gray Gables the next night. The President recovered his sense of well being faster than after the first, more extensive, operation and outwardly returned to his summer schedule of fishing and visiting the local village.³²¹

Will the cancer return?

Sages have written that it is not given to man to know his future—probably, they add, for the better. The President had no way of knowing whether his mouth cancer would recur yet again. That summer, therefore, he developed worsening anxiety about the cancer he knew could terminate his life.³²² Neither he nor Dr. Bryant could predict the course the disease would take.

³¹⁸Typescript letter from Dr. J. D. Bryant to Col. Daniel S. Lamont, May 9th, 1905. Ibid.

³¹⁹Dr. Hasbrouck was definitely not present at the second operation. Keen believed that Major O'Reilly attended, but neither his notes nor those of Dr. Bryant confirm this. Keen, *The Surgical Operations*, 1928, 64.

³²⁰Typescript letter from Dr. J. D. Bryant to Col. Daniel S. Lamont, May 9th, 1905. Keen, *Scrap book*, 7. The use of an electricity-based cautery became commonplace in the late 1880s. See Charles E. Sajous, *Lectures on the Diseases of the Nose and Throat, Delivered During the Spring Session of Jefferson Medical College* (Philadelphia: F. A. Davis, Att'y, 1886), 276. Crown Prince Friedrich's German physicians applied the electrocautery to his vocal cord lesion in the Spring of 1887. See this dissertation, Chapter 6.

³²¹The New York Times, "The President's Vacation Over. Restored in Health and Well Rested, He Starts for Washington," *The New York Times*, 31 August 1893, 5:3.

³²²As a patient, President Grover Cleveland, according to Dr. Keen, was “dutiful,” “most docile,” “courageous,” and obedient. Keen, *The Surgical Operations*, 1917, 55. Again, the evidence questions Keen's filiopietistic interpretation. On multiple occasions, the President wrote that Dr. Bryant chided him for not following instructions. Bryant complained to Lamont that the President was not doing as told and growled at him when he offered medical advice Cleveland did not like. All this occurred despite the President's admiration and appreciation

Twentieth-century oncologists expended much effort to divine a cancer patient's future based upon the microscopic appearance and extent of the tumor. Unfortunately, these techniques were not available to allay the President's unease. Dr. Bryant's instinct led him to cut widely around the tumor, but there was no definite tumor-free "margin of resection" to act as a safety cushion. The acceptance of "frozen sections" for intra-operative determination of the reach of a cancer was more than a decade away.³²³ Even the idea of "staging" a cancer (the determination of the extent of disease to determine prognosis) lay in the century after the President's surgery.³²⁴

These quasi-predictive attributes of modern cancer, derived directly from the work of pathologists and surgeons in the late nineteenth century, were not available to Cleveland and Bryant in 1893. Would the two cancer operations save the President to continue the work for which he earnestly believed the people of the United States put him in the White House? Or was "the coming night"—his term for death—near at hand?³²⁵ Cleveland did not know, but he feared the worst. When Stephen Grover Cleveland was a youth, few doubted that a diagnosis of cancer was a death sentence. Surgery, Dr. Samuel Gross warned, often made the suffering worse. Palliation offered minimal respite. General Grant's case proved that to the world.

for Dr. Bryant's ministrations. For a life-long summary of Cleveland's feelings about Bryant, see "Letter from Grover Cleveland to E. C. Benedict, Princeton, January 2, 1907," Allan Nevins, ed. *Letters of Grover Cleveland 1850-1908* (Boston: Houghton Mifflin Company, 1933), 611.

The literature on cancer and depression is extensive. For a relatively recent example, see William Breitbart et al., "Depression, Hopelessness, and Desire for Hastened Death in Terminally Ill Patients with Cancer," *Journal of the American Medical Association* 284, no. 22 (2000): 2907-11.

³²³James R. Wright, Jr., "The Development of the Frozen Section Technique, the Evolution of Surgical Biopsy, and the Origins of Surgical Pathology," *Bulletin of the History of Medicine* 59, no. 3 (1985): 297 and 302.

³²⁴Dr. Cushman Haagensen, a Depression-era physician and medical historian, credited Borst with the idea of staging cancer around the year 1900. Microscopic pathology formed the basis for Borst's early twentieth-century concept. Cushman D. Haagensen, "An Exhibit of Important Books, Papers, and Memorabilia Illustrating the Evolution of the Knowledge of Cancer," *The American Journal of Cancer* 18(1933): 45. P. F. Denoix, of the Institut Gustav-Roussy in France, proposed the current TNM (Tumor—Node—Metastasis) classification of cancer in 1944. Lee, *Dates in Oncology*, 104.

³²⁵Letter from Grover Cleveland to Thomas F. Bayard, Washington, September 11, 1893. Nevins, ed., *Letters of Grover Cleveland*, 334.

After the second surgery, the President went into relative seclusion at Gray Gables. To Mrs. Cleveland fell the task to explain to a friend that the President, who penned volumes of letters and documents in his lifetime, “has not been writing at all.”³²⁶ Later that same day a depressed Mr. Cleveland wrote his friend Joseph Jefferson that while all around him remarked on how good he looked, he did not feel that way. “I wish I were in better condition to return to my work.”³²⁷

The depression associated with his cancer worry continued through the summer. Wife and friends sought to distract him from his fears by means of jaunts and jollies, but, as has been true of the human reaction to cancer through the centuries, their efforts were minimally successful. “Every day is an anxious one for me,” wrote the President, “fearing that something may occur to distract time and attention from the [silver] topic.”³²⁸ Near the end of August, as the vote to repeal the silver Act approached, Cleveland wrote to another friend and colleague that “this and other things have perplexed me almost to death.”³²⁹ In October, with the debate over the repeal of the silver Act still raging in the Senate, the President became increasingly concerned with his physical condition—a not-unusual consequence of depression. To Dr. Gibson, who had just sent him a new mouth prosthesis to replace the old uncomfortable one, Mr. Cleveland wrote that he was still suffering from problems with his “strength and hearing.”³³⁰

The Third Operation

³²⁶Letter from Frances F. Cleveland to Governor William E. Russell, Gray Gables, July 31, 1893. *Ibid.*, 329.

³²⁷Letter from President Cleveland to Joseph Jefferson, Gray Gables, July 31, 1893. *Ibid.*

³²⁸Letter from President Cleveland to Thomas F. Bayard, Washington, September 11, 1893. *Ibid.*, 334.

³²⁹Letter from President Cleveland to Don M. Dickinson, Gray Gables, August 25, 1893. *Ibid.*, 332.

³³⁰Letter from President Cleveland to Dr. Kasson C. Gibson, Washington, October 14, 1893. *Ibid.*, 338.

The hearing difficulty continued throughout October and into November. Dr. Bryant feared that recurrent cancer explained this new postoperative symptom, but he could not be certain without re-exploration. In mid-November the President traveled to New York to (as he predicted to Gibson a month earlier) “spend a day among the doctors.”³³¹ Drs. Albert H. Buck, with whom Bryant co-authored an eight-volume text on the *American System of Surgery*,³³² and Robert Lewis, Jr.—both otologists (ear and hearing specialists)—operated on the President with Bryant. The physicians involved never published information on this third cancer surgery, though Dr. Keen (who was not present at the procedure) included some post hoc newspaper clippings on the operation in his private *Scrap Book*.³³³

Dr. Gibson’s *Scrapbook*, however, is a better source for the President’s last known cancer operation. It contains more details of the procedure than the Keen *Scrap book*, perhaps because the New York prosthodontist was elated that Dr. Bryant invited him for the first time to partake directly in this third Cleveland operation. Dr. Bryant ostracized Dr. Hasbrouck from the cancer team when he discovered that the dentist leaked the story of the first operation to the newspapers (or so thought Bryant).³³⁴ Dr. Gibson, on the other hand, had a reputation as “a dentist whom [Bryant] considered impervious to the questions of newspaper men.”³³⁵

Thus for the third time in less than five months a cancer that would have been managed with palliation and hopeless expectation in Grant’s year of decline less than a decade before was

³³¹Ibid.

³³²“Dr. Joseph D. Bryant,” *The New-York Times*, 8 April 1914, 13:5.

³³³Keen, *Scrap Book*.

³³⁴Dr. Bryant was so furious at Hasbrouck that he sent his \$250 fee by messenger and vowed never to work with him again. Brooks, Enterline, and Aponte, “The Final Diagnosis of President Cleveland’s Lesion,” 3. The leak resulted in J. E. Edwards’ exposure of the President’s cancer in the *Philadelphia Press* on August 29, 1893.

³³⁵From newspaper clipping, “Cleveland’s Jaw,” *New Jersey Recorder*, December 9, 1893. In Gibson, “President Cleveland Operations.”

treated by surgery.³³⁶ The *New Jersey Recorder*, in a clipping from the *Gibson Scrapbook*, reported that the undisclosed cancer operation on the President occurred on November 15.³³⁷ The *Recorder* did not expose the source of the information, but it was probably not the surgeons. The New Jersey newspaper went out of its way to note that “none of the physicians concerned will discuss the case, on the ground that to do so would be a gross violation of professional etiquette.”³³⁸ Hasbrouck’s fate provided a lesson for all. Dr. Bryant was again the chief operator, assisted by Drs. Buck and Lewis. Dr. Gibson served as the anesthetist, but he did not list the anesthesia administered.³³⁹

Little is known about the actual procedure, but the operators apparently resected additional tissue from the original operative site. They also excised more bone “from the edges of the opening” that remained after the first and second surgeries.³⁴⁰ The results of the pathological examination on the removed tissue are unknown.

Ironically, newspapermen interviewed Dr. Hasbrouck as to the nature of the President’s disease. He sheepishly deferred to Bryant. The dentist admitted that cancer was possible, but, he

³³⁶Morell Mackenzie, *A Manual of Diseases of the Throat and Nose Including the Pharynx, Larynx, Trachea, Oesophagus, Nasal Cavities, and Neck*, vol. 1 (London: J. & A. Churchill, 1880), 82.

³³⁷From newspaper clipping, “Cleveland’s Jaw,” *New Jersey Recorder*, December 9, 1893. In Gibson, “President Cleveland Operations.”

³³⁸*Ibid.*

³³⁹Adverse reactions to anesthesia attained greater importance as the number of operations for cancer increased late in the nineteenth century. Drs. Janeway and O’Reilly feared that ether would weaken the President’s already-compromised kidneys. Ether was probably not utilized for the second and third operations because they were relatively brief, but Grover Cleveland did suffer from renal failure as he aged. Nevins, *Grover Cleveland*, 763 and Seelig, “Cancer and Politics,” 374.

³⁴⁰“Cleveland’s Jaw,” *New Jersey Recorder*, December 9, 1893. In Gibson, “President Cleveland Operations.” The size of the opening naturally decreased over time as granulation tissue grew into the surgical wound over the four or more years that Dr. Gibson constructed prostheses for the President. Morreels, “New Historical Information on the Cleveland Operations,” 548 and 550.

noted, “it is for Dr. Bryant to say whether or not the disease is cancer.”³⁴¹ Hasbrouck learned his lesson in patient-doctor confidentiality and medical professionalism—but too late. His final comment, though, accentuates the basis of modern cancer. When asked how the diagnosis would be determined, he unhesitatingly replied that “the fact can only be determined by the microscope.”³⁴² The microscopic world of modern cancer diagnosis supplanted the macroscopic world of traditional cancer diagnosis, bringing with it a whole new language and conceptualization of the disease. By the 1890s, this transition was completed.

The Mental Toll of Cancer

In certain ways, the President never really recovered from the cancer surgeries. Physically, he tolerated the third operation well, but his hearing deficit persisted. Mentally, doubt and anxiety continued to plague him. To be sure, Cleveland had many worries. The repeal of the silver Act lasted several months and consumed so much political capital that his desire for tariff reform became an unreachable dream. The silver issue also split his Democratic Party and he knew that Party members would hold him responsible.³⁴³ His Vice President was an unpredictable silverite who could overthrow Cleveland’s policies if illness forced the President to withdraw from office. In addition, already on the horizon, was a major battle over

³⁴¹“Cleveland’s Jaw,” *New Jersey Recorder*. In Gibson, “President Cleveland Operations.”

³⁴²*Ibid.*

³⁴³Cleveland was well aware that the silver issue destroyed the unity of the Democratic Party he helped to forge. In a letter written three weeks prior to the repeal of the silver act by the Senate, the President wrote “I am looking full in the face a loss of popular trust in the Democratic party which means its relegation to the rear again for many years if not its disruption.” Letter to Don M. Dickinson, Woodley, October 9, 1893, in Nevins, ed., *Letters of Grover Cleveland*, 337.

The banner of the Democratic silver crusaders, waved most noticeably by William Jennings Bryan, helped exclude the Democrats from the Presidency for twenty years. Indeed, Republicans ruled the Executive branch for the remainder of Cleveland’s life. The next Democrat to win the presidency was Woodrow Wilson in the three-party election of 1912—four years after Cleveland’s death.

America's role as a nascent international power and, indeed, the very essence of the United States that played out on a small island in the Pacific known as Hawaii.

Fear of cancer and the anxiety it created, however, were the paramount causes of what had become the President's depression. Shortly after the third surgery, the press again documented Cleveland's mental anguish over his health. "People who are close to the President," noted the *New Jersey Recorder*, "say that he dreads ill-health more than anything else in the world, and that he will cheerfully undergo any amount of physical torture, in the hope of being cured. The slightest ailment always causes deep mental depression."³⁴⁴

The President had not been sensitive to his physical condition prior to the discovery of his cancer and the subsequent operations. On the contrary, he had prided himself on his rugged body habitus and strong nature. Cancer, however, forced him to re-evaluate his life and his physical condition. In a revealing letter written after the second cancer surgery to Thomas Bayard, Secretary of State during his first administration, the President disclosed that he "turned the corner to the stage of enforced care-taking almost in a day. And this must be hereafter the condition on which will depend my health and life."³⁴⁵ The uncertainty of his future changed his outlook on life. No longer full of energy and boundless optimism, he projected his dimmed hopes when he concluded with thinly veiled pessimism "I believe the chances in my favor are at least even."³⁴⁶ One of his earliest biographers added that Cleveland believed himself under "the shadow of death."³⁴⁷

³⁴⁴"Cleveland's Jaw," *New Jersey Recorder*. In Gibson, *The Surgical Operations*, 4.

³⁴⁵Letter from President Grover Cleveland to Thomas F. Bayard, Washington, September 11, 1893, in Nevins, ed., *Letters of Grover Cleveland*, 334.

³⁴⁶*Ibid.*

³⁴⁷Robert McElroy, *Grover Cleveland: The Man and the Statesman (an Authorized Biography)*, 2 vols., vol. 2 (New York: Harper & Brothers, 1923), 30.

In early October, Cleveland wrote a close friend “I am very much depressed.”³⁴⁸ The day before he had dejectedly complained “I am suffering many perplexities and troubles and this term of the Presidency has cost me so much health and vigor that I have sometimes doubted if I could carry the burden to the end. My determination,” he added with more faith than reason, “is to live.”³⁴⁹ As the months passed after the third cancer surgery, the minister’s son sought solace in the two-edged religiosity that earlier in the century had made cancer a sin. “I know, too, there is a God, but I do not know His purposes, nor when their results will appear. I know the clouds will roll away, but I do not know who, before that time, will be drowned in their floods.”³⁵⁰ More than five years after the last surgery, Grover Cleveland battled the demons of cancer past. At that time, former Secretary Lamont requested that the ex-President sit for a formal portrait. At first, Mr. Cleveland was nonplussed. “I cannot see,” he wrote to Lamont with the glimmer of relief evinced by a man tired of years in the public spotlight, “why even you should want it.”³⁵¹ After he regained composure he struggled to find a metaphor to connect the sitting to the worst situation possible. It was, he concluded, like “asking me to sit in a dentist’s chair and be operated upon”—exactly where he had been five and a half years earlier under Dr. Bryant’s knife.³⁵² The memory of those cancer-ridden months lingered. As the years rolled by, he exposed the mental anguish that the disease had perpetrated upon his psyche. “I am trying to

³⁴⁸Letter from President Grover Cleveland to Don M. Dickinson, Woodley, Washington, October 9, 1893, in Nevins, ed., *Letters of Grover Cleveland*, 337.

³⁴⁹Letter from President Grover Cleveland to Richard Watson Gilder, Washington, October 8, 1893. Ibid.

³⁵⁰Letter from President Grover Cleveland to Richard Watson Gilder, Gray Gables, October 12, 1894. Ibid., 370.

³⁵¹Letter from Grover Cleveland to Daniel S. Lamont, Princeton, December 31, 1898. Ibid., 507.

³⁵²Ibid., 507-8.

keep a little quiet,” he wrote in 1904, “to fret as little as possible.”³⁵³ Outside his immediate family and close-knit circle of friends, he never mentioned the word ‘cancer.’ Adding to the weight on his soul was that even after he left the Presidency, this man, who based his entire identity—both public and private—upon honesty, never revealed his lie to the public.

SECRECY

The Rationale and Value of Secrecy

Why secrecy? Why did a man believed by many to be the embodiment of truth risk the hallmark of his image for a cancer lie? What was so important about his disease that he overturned the mottoes of his life—“Tell the Truth,” “Public office a Public Trust,” and others—to perpetrate a fraud against journalist E. J. Edwards, the media, and the people of the United States?

Grover Cleveland never answered these questions to the public. Nevertheless, the heavy toll he paid in the form of postoperative depression and lingering melancholia implies that their significance was not lost on him.

Dr. Keen never doubted that the silver crisis occasioned and sustained the cancer lie. His 1917 *Saturday Evening Post* article is replete with explanations of the enormity of the early 1890s silver issue to an incredulous First World War readership that had lived on only the gold standard for over a generation. Keen believed that “great destinies hung by a thread,” and that the solitary but unwavering hand of the President firmly tethered that thread.³⁵⁴ “To Mr. Cleveland—and we might say to Mr. Cleveland alone—belongs the honor of securing the passage of the Repeal Bill,” quoted Keen from a contemporary issue of *The Nation* to mirror his

³⁵³Letter from Grover Cleveland to Daniel S. Lamont, Princeton, October 27, 1904. *Ibid.*, 590.

³⁵⁴Keen, *The Surgical Operations*, 1917, 24.

own feeling.³⁵⁵ Indeed, the Philadelphia surgeon began his *Post* article with several pages justifying secrecy (some said *too many* pages) based on the economic crisis of the day before he even described the President's cancer.³⁵⁶

The President hid the true nature of his disease from the press and the public for several reasons, according to Dr. Keen. However, they all revolved, as he later wrote in a belated apology to Edwards, around the instability of the “political and financial conditions” of the nation.³⁵⁷

Politically, repeal of the silver Act necessitated the full support and power of the President. “The whole country,” summarized Keen, “felt that our future were staked on a single life”—that of Grover Cleveland.³⁵⁸ The publication of “Holland's” cancer exposé on August 29, 1893 came so soon following the House repeal of the silver Act. Had the Philadelphia paper published the article a few days earlier, the outcome of the repeal bill in the House would have been in doubt. Further, had the conspirators not immediately quashed the veracity of the exposé, the Senate at the end of October might have reversed the favorable vote Cleveland so much desired. Keen believed that a force higher than man had intervened on the nation's behalf: “It was most fortunate, in fact providential for this whole country that the information did not leak out until the Silver Clause had been repealed by the House and the knowledge of the operation

³⁵⁵October 26, 1893. Ibid.

³⁵⁶James Ford Rhodes, the historian whom Keen consulted when writing his 1917 article, criticized Keen's lengthy description of the 1893 economy. “The account of the financial situation is disproportionately long,” he wrote. Letter from James Ford Rhodes to Dr. W. W. Keen, February 21, 1917, in Keen, *Scrap book*.

³⁵⁷Typescript letter from W. W. Keen to Mr. E. J. Edwards, Union League, NYC, September 10th, 1917. Ibid.

³⁵⁸Typescript letter from W. W. Keen to Mr. Greenslet, February 19th, 1917. Ibid.

did not prevent its being passed by the Senate.”³⁵⁹ In addition, Keen wrote to the historian James Ford Rhodes, the succession of silverite Vice President Stevenson to the Presidency in Cleveland’s absence would have cast a long shadow over the entire repeal process. At best, Stevenson’s actions on silver repeal as President would have been unpredictable. Many thought he would have postponed repeal—perhaps indefinitely. The Vice President had already surrounded himself with a group of free-silver men who the press designated the “Stevenson Cabinet.”³⁶⁰

Financially, Keen envisioned the United States in economic ruin if President Cleveland was unable to exert himself in favor of repeal. The nation had already suffered several crises in the few months he had been President before the first cancer surgery. Investors exchanged silver for gold daily and, sensing the collapse of the dollar, foreigners hastily repatriated their American investments, thereby magnifying the domestic difficulties. In July 1893, shortly after the first surgery, the Erie Railroad went into receivership and the stock market suffered its worst decline of the year.³⁶¹ Not until September—after Cleveland secured the repeal of the silver Act in the House, Edwards’ cancer revelation was branded a hoax, and Stevenson seemed unlikely to assume the reins of government—did massive gold imports begin to reverse the flight of capital from the United States.³⁶² Dr. Keen, however, knew the truth of the President’s medical condition. “Had the fact of his operation been known,” he wrote to Cleveland’s widow in 1916, “in view of the Vice-President’s advocacy of silver it is quite sure I think that the country would

³⁵⁹Typescript letter from W. W. Keen to Mr. E. J. Edwards, Union League, NYC, September 10th, 1917. Ibid.

³⁶⁰Nevins, ed., *Letters of Grover Cleveland*, 370 Footnote 1.

³⁶¹Friedman and Schwartz, *A Monetary History of the United States*, 109.

³⁶²Ibid., 110.

have suffered from a panic worse than any we have ever seen. The politicians would have regarded Mr. Cleveland as the setting sun and Adlai Stevenson as the rising sun and the panic would have been upon us very shortly thereafter.”³⁶³

Others corroborated Dr. Keen’s arguments. No one—Democrat or Republican—doubted that the repeal of the silver Act could have transpired without the all-out effort of the President and his staff. The newspapers of the day (especially in the East) sang his virtues after Congress voted to rescind the act. “Praise is due first,” wrote Joseph Pulitzer’s *New York World*, “to the Administration of Grover Cleveland, which has stood like a rock for unconditional repeal.”³⁶⁴ Even *The New-York Times* lifted its glass to toast the President’s selfless and even self-sacrificing achievement. History, they predicted, would judge that the 1893 silver crisis failed to destroy the United States of America because “at that moment, as often before, between the lasting interests of the nation and the cowardice of some, the craft of others, in his own party, the sole barrier was the enlightened conscience and the iron firmness of Mr. Cleveland.”³⁶⁵ The repeal of the Sherman Act, they concluded, would never have occurred if the President’s political and economic opponents perceived him as riddled by cancer.

“Without Equal as A Dissembler”

Those who instituted and maintained the cancer secret rationalized their lie based on current events. Nevertheless, their falsehoods did not go undiscovered. How, then, did secrecy prevail despite the most visible public office in the nation? The answer lies in the prevailing conception of the nature of cancer in the late nineteenth century.

³⁶³Typescript letter from Dr. W. W. Keen to Mrs. Frances Folsom (Cleveland) Preston, February 23rd, 1916. Keen, *Scrap book*, n.p.

³⁶⁴Quoted by Nevins, *Grover Cleveland*, 548.

³⁶⁵*Ibid.*

The unsuccessful prevarication of General Grant and his consultants in their attempt to hide knowledge of his cancer from the public is an instructive counterpoint to the case of President Cleveland. Two months after Dr. Douglas' initial cancer diagnosis, the General unwittingly revealed his malady to Mr. E. F. Beale. The Philadelphian alerted the press, but Grant's doctors repeatedly denied the story of malignancy. Before another two months passed, however, Barker and Douglas could no longer suppress the cancer secret. The newspaper frenzy began and, once in force, the media withheld no occurrence in the General's life, no matter how trivial, from the demanding masses. How did President Cleveland succeed where General Grant failed?

The late-nineteenth-century public and, to a large extent, physicians, perceived cancer as a debilitating, painful, disfiguring, and, inevitably, fatal condition. In December 1884, when Grant scribbled his note of apology to Beale for breaking off the speaking engagement, the General experienced pain and difficulty swallowing. These are internal symptoms not readily apparent to friends and relatives—or the press. Thus, Grant's physicians could initially suppress the rumor that he suffered from cancer because there was no overt evidence to corroborate Beale's revelation. In addition, the still-respected physician-consultants repudiated the idea. By February 1885, however, the General had lost significant weight, his head was disfigured by lymphadenopathy (cancer-swollen lymph glands), and, despite his best efforts to the contrary, he seemed to visitors (and ever-snooping reporters) to be in distress. Grant then fit the preconceived notion of the appearance of a man with cancer and the secret became unsustainable.

President Cleveland suffered no such fate. Pathologically, his mouth cancer lay anterior (closer to the front) and superior (above) to Grant's. When discovered it had not reached the site

where it could directly impair swallowing. In addition, Cleveland did not procrastinate as long as Grant in seeking medical attention after the first onset of symptoms,³⁶⁶ although it is not possible to determine which lesion was more advanced when initially examined by Dr. O'Reilly and Dr. Douglas, respectively.³⁶⁷ Most importantly, of course, the President's cancer was treated by surgery rather than palliation, thereby preventing further growth of the mass to the point where it would lead to the state of enervation and obvious infirmity suffered by the General. Dr. Bryant prepared for surgical eventualities and complications through his extensive study of the relevant surgical literature and his own personal experience. Because he knew that the extent of disease found at the time of operation might differ from his pre-operative suppositions, and that therefore the exact procedure and its complications could not be predicted beforehand, he enlisted the most elite cancer surgical team he could muster on short notice. The surgery concluded without major adverse reactions, but Bryant was not successful in removing all the cancerous tissue. Nor could he assure Cleveland that he had excised all the offensive tissue. Hence the two subsequent secret cancer operations in 1893 and the President's resultant melancholy. Nevertheless, external signs of disease were absent and the cancer remained successfully hidden from all but those who had to know about it.

³⁶⁶Grant waited more than four and a half months between Dr. Da Costa's urging to seek further medical attention and his October visit to Dr. Barker. Cleveland's interval from initial symptoms to diagnosis was six weeks—about one third as long. Given a solid tumor doubling time in the order of months, this is a significant difference. Of course, tumor location is also critical. Skin cancers are often detected early in their natural history, whereas tumors deep within the abdomen are frequently more advanced when diagnosed. Hence the high fatality rate and short-lived prognosis of most pancreatic and ovarian cancers.

Parenthetically, both wives prodded their husbands to visit their physicians shortly after each man first noted symptoms. Mrs. Cleveland was the more successful of the two.

³⁶⁷“Advanced” is a tricky medical term that seeks to predict prognosis based on the characteristics of the tumor under the microscope, degree of tissue invasion (including lymph node infiltration), and the general condition of the patient. Since Grant's cancer was not biopsied until several months after discovery, and concepts of anaplasia [reversion of cells to a less “developed” or “mature” form] were relatively primitive, it is impossible to accurately gauge the level of “advancement”.

Still, the surgery itself posed problems that threatened to unravel the cancer secret that General Grant did not face. The press could see that the President was unwell immediately upon his disembarkation at Gray Gables four days following the first cancer surgery. Lamont sensed that he could not deny some form of illness, so he fabricated the untruth about rheumatism and a toothache to protect the cover-up. He did not choose those disorders at random. Although appearing robust, Cleveland's massive corpus stressed his fifty-six-year-old joints to the point where musculoskeletal symptoms would surprise few and unsteadiness of gait was understandable. In addition, who could not relate to a toothache? The President appealed to the common sense of the public when the papers reported that "toothache was the one pain which even his rugged frame could not endure."³⁶⁸ All had experienced the gnawing aggravation broken only by sharp pangs. Oral surgery for a dental disorder could surely hide a multitude of oral problems—including the iodoform- and blood-soaked mouth gauze introduced as postoperative packing. Lamont's intent was clear: create a plausible explanation of the obvious debility that would not conjure thoughts of incapacity. No one believed that rheumatism or toothache would permanently devitalize the President. Cancer, in the eyes of the public, was a disease of progressive enfeeblement and death.

The incessant repetition of the rheumatism-toothache fiction by the unimpugnable Mrs. Cleveland, the accessible Lamont, and the protective Bryant deflected the press from their scrupulous pursuit of the true facts. In addition, the President's conspirators sequestered him from the media for most of July as he recovered from the surgical procedures. They allowed only his family, doctor, and closest friend to see him. Reporters could not romance chambermaids across from the President's study to glimpse him in travail and seemingly had no

³⁶⁸"Toothache," *The New-York Times*, 1 September 1893.

reason to bribe house servants for more information, so his true condition remained unknown to the press. Further, when Edwards exposed the truth to the world, Cleveland's supporters denigrated its veracity as nothing more than partisan politics and sensationalism to sell newspapers. As the *Times* noted in July, "a certain line of competition in the newspaper business demands that all such reports shall be magnified, and not corrected or stopped."³⁶⁹ The reputation of the man whose health was in question, however, was the most important psychological bulwark contributing to the success of the cover-up. And Cleveland (ab)used the image of honesty he had constructed over the previous decade to abate suspicion. *The New-York Times* quoted a friend of the President as saying that if Mr. Cleveland had surgery, "he is simply without equal as a dissembler."³⁷⁰

In the final analysis, the restoration of the President's healthy appearance and vibrant voice protected and preserved the secret of his cancer. Specifically, the lack of postoperative complications, absence of external disfigurement, relatively rapid recovery from the operations, Dr. Gibson's oral prosthesis, and the eventual eradication of the cancer by the surgeons saved Cleveland from Grant's doom.³⁷¹ Dr. Bryant and his team, through careful preparation, skill, and, undoubtedly, luck, effected no major surgical complications upon the President during the three operations.³⁷² Thanks to Keen's Luer cheek retractor and Bryant's preparations, none of

³⁶⁹"The President Is All Right," *The New-York Times*, 9 July 1893, 5:5.

³⁷⁰The New York Times, "Mr. Cleveland Not a Sick Man. The Story That He Is, Laughed at by His Friends in Washington," *The New York Times*, 30 August 1893, 5:2.

³⁷¹Part of Grant's fame after his death rested upon his cancer martyrdom. Had Grover Cleveland suffered a similar fate while in office—his term ended nearly four years after the surgeries in March 1897—historians might judge him differently in the pantheon of Presidents. No Chief Executive has died from cancer in office.

³⁷²The hearing impairment may have been a complication of the first operation rather than a sign of cancer recurrence, but not enough evidence is available to support either conclusion.

the procedures required a facial scar or resulted in a dropped eyeball or other noticeable deformity.³⁷³

The President recuperated within a month of the first and most extensive cancer surgery. He wrote letters, accepted visitors, and interacted with the locals as though nothing had changed. The salubrious sea breeze and relative quiet of Gray Gables contributed to his rehabilitation, but Mr. Cleveland ascribed his physical improvement to his savior Bryant.³⁷⁴ Dr. Gibson's prostheses restored the President's voice and lifted the jawbone-less left cheek to its normal position. Legislators who spoke with Cleveland after his well-conceived message to the Special Session of Congress on August 8 did not detect any impairment in his speech.³⁷⁵ On September 5, a week after the *Philadelphia Press* broke Edwards' revelations, Grover Cleveland's voice rang out at the First Pan-American Medical Congress in a way that was "even clearer and more resonant," wrote Keen, than he projected at his second inaugural, four months before the first cancer surgery.³⁷⁶ *The New-York Times* concurred. The next morning it reported that "he looks

³⁷³The change in appearance that Attorney-General Olney noted at Gray Gables in July was temporary. McElroy, *Grover Cleveland*, 31.

³⁷⁴The year before his death, Cleveland wrote to Commodore Benedict that he must "acknowledge a debt of gratitude to [Dr. Bryant] which no length of years would allow time enough to repay." Letter from Grover Cleveland to E. C. Benedict, Princeton, January 2, 1907. In Nevins, ed., *Letters of Grover Cleveland*, 611. The ex-President's letter included a little poem that urged the seventy-two year-old Benedict to seek Bryant's medical advice:

Friday sorry
Yet defiant;
Next day send for
Doctor Bryant.

³⁷⁵Ironically, Grover Cleveland's life-and-death message to Congress urging repeal of the silver Act to revive the moribund economy was promulgated eight years to the day after he attended General Grant's enormous New York funeral.

³⁷⁶Keen, *The Surgical Operations*, 1928, 15.

well and walked with a firm step and spoke with a clear resonant voice.”³⁷⁷ The public was reassured and, from that time on, no serious challenge to the President’s cancer secret was mounted. Without the restitution of voice and cheek by Gibson’s prosthesis, however, the preservation of the secret would have been untenable. Of course, the greatest advantage the President enjoyed for the maintenance of the secret was that his cancer did not recur or metastasize. Outwardly, unlike the long-suffering General Grant, he appeared healthy for the remainder of his Presidency. Mr. Cleveland simply did not fit the image of the “desperate invalid” that cancer connoted in the contemporary mind.³⁷⁸

Cancer: Beyond Truth

The culture of cancer in 1893 was too deeply ingrained within the national psyche to ascribe the President’s secret solely to the silver crisis. Grover Cleveland’s disease was not just any medical condition—it was cancer. By the late nineteenth century, popular culture had long established the tumorous disorder as a disease apart with special meanings and implications.³⁷⁹ No doubt the panics of 1893 and the perceived urgency to repeal the silver act provided an

³⁷⁷Quoted by Morreels, "New Historical Information on the Cleveland Operations," 550. The similarity of language between Keen and the *Times* may imply that Keen was not present at the event and merely rehashed the newspaper accounts.

³⁷⁸The quotation is from "Mr. Cleveland Not a Sick Man," *The New-York Times*, 30 August 1893, 5:2.

³⁷⁹Susan Sontag, in her brief, rich, and insightful book, *Illness as Metaphor*, wrote “it was not possible definitively to separate cancer from TB until after 1882, when tuberculosis was discovered to be a bacterial infection.” Susan Sontag, *Illness as Metaphor* (New York: Vintage Books, 1977), 10. Her focus on cancer as twentieth-century metaphor does the history of cancer a disservice. Hers is a very modern, ahistorical conception of cancer. Although the two diseases may not have been diagnostically distinct until then, cancer as metaphor extends centuries into the past.

The diagnosis of “cancer” has been made since ancient times. However, such a designation does not mean that a disease accepted as cancer then would be sustained with equivalent accuracy and connotations in modern times—any more than tuberculosis or menstruation provoke the same thoughts in the mind of today’s physician as in that of a nineteenth-century physician. Nevertheless, diagnostic accuracy in contemporary eyes is irrelevant for the purpose of metaphor synthesis. It is the image of the disease *at the time in question*, regardless of our thoughts and feelings today, that matters historically and semantically. Not until the late nineteenth century did a conception of cancer arise that physicians of the early twenty-first century would recognize as cancer—hence the distinction I have drawn between traditional and modern cancer. Nevertheless, by the nineteenth century the disease named ‘cancer’ had stirred emotions and excited layers of meaning for centuries, if not millennia.

immediate cloak for the reasons for secrecy. No doubt the power base Cleveland established to push through repeal would have eroded if foes perceived him as vulnerable due to a significant health problem. No doubt the probability of repeal would have diminished if silverite Vice-President Stevenson had replaced an ailing President Cleveland. Nevertheless, why did *An Honest President*, as a recent Cleveland biography is entitled,³⁸⁰ never reveal the truth about his disease and his surgeries? Not after Congress repealed the silver act. Not after the battles over the tariff, Hawaii, and other issues. Not after his Presidency. Not before his death. Not ever.

A historian may consider the silver crisis a necessary reason for short-term secrecy, but it was not sufficient to explain the President's life-long suppression of the truth. It was, rather, more an expedient than a definitive justification. Some questioned whether Vice President Stevenson would have reversed Cleveland's hard-money position.³⁸¹ Indeed, the President himself joked about the "Stevenson Cabinet," albeit after the repeal of the silver Act.³⁸² Cleveland's rapid recovery from the first surgery, overnight return from the second, and "day among the doctors" for the third, proved that any debilitation was minor. In fact, he barely missed a beat composing his hard-wrought message to the August Special Session—despite Richard Olney's alarming recollections.³⁸³ Certainly, the mental consequences of the cancer were a force with which the President struggled for years, but he kept them invisible to critics and adversaries. The same factors that permitted Cleveland and his confreres to preserve the cancer secret—no facial scar or deformity, resonant voice, rapid return to the duties of office

³⁸⁰Jeffers, *An Honest President*.

³⁸¹Letter to Dr. W. W. Keen from James Ford Rhodes, 392 Beacon Street, Boston, February 21, 1917. Keen, *Scrap book*.

³⁸²Letter from President Grover Cleveland to Richard Watson Gilder, Gray Gables, October 12, 1894. Nevins, ed., *Letters of Grover Cleveland*, 370.

³⁸³McElroy, *Grover Cleveland*, 31.

(and the short memory of the public)—also augured well for the President’s ability to rebuff opponents who would claim that cancer prevented him from doing his job. Counterfactualization aside,³⁸⁴ the evidence shows that cancer had a minimal impact on his ability to function after his speedy recovery from the first *Oneida* operation. Had his disease not been cancer, he could have revealed it by August.

Instead, personal and psychological reasons for cancer secrecy displaced the President’s political and economic rationalizations shortly after the surgeries. The political and economic became personal. Mr. Cleveland had moved beyond truth. This is not surprising. The connotative social construction of cancer in the late nineteenth century changed little from earlier decades. In essence, the cultural image of cancer as a disease associated with shame and blame (embarrassment and stigmatization) traversed the entire century. This common notion of cancer crossed the cognitive and temporal boundaries between traditional and modern cancer. Indeed, to some extent these cultural constructions exist today. It is in the realm of the body (medicine)—not the mind (psychology)—that technological advances in the late nineteenth century served to transform traditional into modern cancer. Grover Cleveland, therefore, was caught in a whirlwind of a disease changing rapidly in some aspects—diagnosis and treatment—but glacially in others. These others, founded in fears that extended back in time, perhaps, to the birth of mankind as a sentient species, possessed the President for the remainder of his life and imposed a lock on his cancer secret for what was for him forever.

The Cost of Secrecy: Opportunity Lost

³⁸⁴David Brion Davis defined ‘counterfactual’ as a “disciplined fantasy—disciplined because its plausibility and ultimate value depend on reasoned inferences and analogies based on empirical knowledge, and a fantasy because it departs from reality and arbitrarily assumes that certain events could have been different without altering every other variable.” David Brion Davis, “American Slavery and the American Revolution,” in *Slavery and Freedom in the Age of the American Revolution*, ed. Ira Berlin and Ronald Hoffman, *Blacks in the New World* (Urbana: University of Illinois Press, 1983; reprint, 1986), 262-3.

A certain amount of innocent mendacity was required to keep news of Cleveland's actual condition from reaching the public.

—Allan Nevins, *Letters of Grover Cleveland*³⁸⁵

Late in life, Grover Cleveland summed up the aura of truthfulness for which he had become famous when he related to his friends that “it is no credit to me to do right. I am never under any temptation to do wrong!”³⁸⁶ His last words, as he lay dying, were “I have tried so hard to do right.”³⁸⁷ One can only surmise why a man whose soul was commonly believed to be haloed in rectitude would focus on that for which he was so well known with words that would stand as his final testament. General Grant's last utterance, as he lay stuporous near death from his palliative drugs, requested liquid refreshment to quench the thirst he sensed to the end. Others who die in peace and old age, if conscious, speak of love and thankfulness. Some curse their lives. Many pray. However, few concentrate on their purported achievements on earth—unless, perhaps, Grover Cleveland fixated on deeds undone.

Everything has its cost. The price of successfully keeping a secret is no exception. Some consequences of falsehoods are immediate. Others are latent. The consternation of the press in early July 1893 concerning the apparent contradictions between Cleveland's appearance and Lamont's story led immediately to a new pursuit “from which it is doubtful any President will ever find it possible to again escape”—closer surveillance of the Chief Executive by the press than ever before. From that time forth, they vowed, neither the location nor the health of the President would be in doubt. And, with rare exceptions, it has been so.³⁸⁸

³⁸⁵Nevins, ed., *Letters of Grover Cleveland*, 329 Footnote.

³⁸⁶Nevins, *Grover Cleveland*, 765.

³⁸⁷“Collector's Notes.” In *Ibid.*

³⁸⁸Martin, “When the President Disappeared,” 103. Most of the exceptions occur during wartime or the semblance of war—as with Franklin Roosevelt's secret rendezvous with Churchill in the Atlantic in August 1941.

History may be a compilation of lies; nevertheless, it contains a few truths, and they are the only guides we have for the future.

—Emma Goldman, *The Traffic in Women*

In the end, the success of the preservation of Mr. Cleveland's secret represented a lost opportunity in the history of cancer. General Grant sought unsuccessfully to hide his cancer. In its revelation, however, the public became more cognizant of the disease than ever before. The tight-budgeted New York Cancer Hospital, for example, took advantage of the rise of Victorian advertising and the intensified public awareness of cancer after the General's death to reap increased donations through newspaper announcements, magazine articles, and private fund-raising efforts.³⁸⁹ The perseverance of the Hospital through the dark days of the late 1880s and depression-filled 1890s is a tribute to their success—aided to no small extent by popular sympathy for the plight of cancer victims generated by Grant's legacy.³⁹⁰

President Cleveland's cancer contributed nothing to medical, institutional, and public health efforts to deal with the rising incidence of cancer in the late nineteenth and early twentieth centuries. The success of his secret was a loss for science and society. Had the medical establishment and the public perceived the true nature of his malady, it is likely that such knowledge would have thrust the disease cancer into the limelight even more than did General Grant. The confluence of a nation more educated in the ways of cancer through the publicization of a sitting President's malignancy, combined with new forms of diagnosis, treatment, and the technological transformations in cancer medicine of the day, may have altered the psychological

³⁸⁹For a brief overview of Victorian advertising, see Thomas J. Schlereth, *Victorian America: Transformations in Everyday Life, 1876-1915*, ed. Richard Balkin, The Everyday Life in America Series (New York: HarperPerennial, 1991; repr., 1992), xiii.

³⁹⁰See, for example, B. Farquhar Curtis and William T. Bull, "The Treatment of Cancers and Other Tumors," *Harper's New Monthly Magazine*, November 1891, 923. The purpose of Curtis and Bull's popular monthly magazine article, they stated, was "to call...the attention of the public to [the New York Cancer Hospital], which is striving with inadequate means to do the great work for which it was founded." *Ibid.*

legacies of traditional cancer as early as the waning years of the nineteenth century. The vestige of shame and blame would have encountered a formidable foe if the common man had been privy to the successful cure of a President who harbored a disease widely assumed to be debilitating, incurable, and fatal. Perhaps patients fearful of cancerous lumps and bumps would have come forth earlier to be diagnosed and treated at the hands of modern surgeons like Dr. Bryant rather than procrastinating until their fear became reality.

Perhaps more physicians would have become interested in the study of the nature and treatment of cancer—a disease that was rapidly rising in prevalence in the hierarchy of mortal afflictions in the United States. For doctors, also subsumed by the culture of cancer, oftentimes confused objectivity with subjectivity and sometimes still shied away from the aggressive early treatment of tumors. Perhaps knowledge of Mr. Cleveland's cancer would have fueled the laboratory investigation of the disease sooner through private philanthropy and the approving nod of a federalized government that saw its role at the time as caretaker rather than promoter.³⁹¹

The newspaper frenzy that accompanied Grant's cancer began a process that carried the disease to the front page of every newspaper in the country. Public knowledge of Cleveland's cancer might have propelled cancer education, practice, and research into the national consciousness just as seminal discoveries in cancer medicine took root. Grover Cleveland saved his secret, but the nation lost a great opportunity.

³⁹¹The first laboratory for cancer research in the United States was founded in Buffalo in 1898 as the New York State Pathological Laboratory. Harold Rusch, "The Beginnings of Cancer Research in the United States," *Journal of the National Cancer Institute* 74, no. 2 (1985): 391. Money legislated reluctantly by New York State founded and maintained the Pathological Laboratory. The name of this and many other cancer institutions changed over the course of the twentieth century as the culture of cancer responded to its contemporary historical context. Today it is called the Roswell Park Cancer Institute.

Chapter 5

From Grant to Cleveland: Small Steps and Giant Leaps

Grover Cleveland lived a normal lifespan after the discovery and treatment of his cancer. Ulysses S. Grant did not. This was one of many distinctions between them. Some social and medical aspects of their diseases were closely aligned. Others were not. Similarities and differences illuminate the heart of the transformation from traditional to modern cancer at the end of the nineteenth century. This chapter compares and contrasts the case studies of the General and the President in the light of traditional and modern cancer.

Is it fair to compare?

Is it right and proper to compare and contrast the case studies of Grant and Cleveland? Alternatively, was the General simply the victim of incompetent physicians and the President blessed with such luck that the passage of time between the two cancers contributed nothing to his more felicitous course? Indeed, the patients, doctors, and foundations of their respective therapies were remarkably alike.

General Grant and President Cleveland were both middle-aged, overweight cigar smokers.¹ They had poor dentition and noted their initial cancer symptoms while eating. Although born in different sections of the country, both men lived in New York City in the years just preceding their cancer diagnoses.² Their wives both instigated them early in their symptomatology to seek medical advice. Both men knew that something was terribly wrong,

¹Although both smoked cigars, Grover Cleveland consumed more chewing tobacco than did the General. Chewing tobacco is a high-risk activity for verrucous tumor of the mouth—Cleveland's cancer. Also, see Chapter 4, Footnote 195.

²Grant was born in Ohio; Grover Cleveland in New Jersey. Grant settled into his East Sixty-Sixth Street townhouse in New York City in 1881, shortly after completing his twenty-eight month world tour. Philip R. Moran, ed., *Ulysses S. Grant 1822-1885: Chronology--Documents--Bibliographical Aids* (Dobbs Ferry, NY: Oceana Publications, Inc., 1968), 16. Between his two presidencies, Cleveland lived at 816 Madison Avenue (68th Street)—a stone's throw from Grant's Manhattan home. Jackson, ed., *Encyclopedia of NYC*, 244. Geographical location became a risk factor under the germ theory of cancer.

and both surmised that the diagnosis was cancer. From a medical perspective, different physicians diagnosed both men not only with oral cancers, but also specifically with epitheliomas. Both patients sought to hide their diagnoses, initially from those close to them as well as the public. Both explicitly followed their doctors' treatment suggestions and neither significantly criticized his care. They both believed they had benefited from the best that medicine had to offer.

The most renowned physicians in the United States at the time attended the General and the President. Although Grant's consultants and Cleveland's surgical team were drawn locally rather than nationally—they primarily hailed from the Northeast, especially New York City—the physicians and the City were at the forefront of cancer medicine.³ The two leaders retained physicians who followed the most advanced prescriptions and proscriptions of the era. Both patients had known their primary care physicians (Barker and Bryant) for some time. These doctors (and not their celebrated patients) chose their collaborating colleagues based on prowess, skills, and achievements. In addition, both sets of physicians tacitly supported their principal's desire for secrecy—with the exception of harried Hasbrouck.

General Grant and President Cleveland received the most current, consensual diagnostic and treatment modalities available. Sir Morrell Mackenzie's 1880 textbook on *Diseases of the Throat*, the ENT bible of the early 1880s, emphasized the inevitably fatal character of cancers in this part of the body and urged palliation. "The only doubt which can exist in the prognosis," advised the knighted Englishman, "relates to the question as to how soon the malady may be

³Such a claim is always open to question. Nevertheless, the origin of the first cancer-only institution in New York City and the publication of so many of the medical newsletters and journals of the day in the City support my contention.

expected to prove fatal.”⁴ He concluded that “palliative measures alone can be adopted.”⁵ The General’s palliative therapy centered on local cocaine applications that had been in clinical use as a topical anesthetic for barely a year. Clearly, cocaine represented the most advanced pharmacotherapy of its day.⁶

President Cleveland also received the best treatment of his day. The President’s physicians likewise went by the book—but what a difference a decade made! “It is possible,” wrote Dr. Francis de Havilland Hall about epitheliomas, “to extirpate the growth completely”—especially with careful attention to antisepsis and anesthesia.⁷ Dr. O’Reilly diagnosed Mr. Cleveland early in the course of his cancer with the aid of the microscope and, shortly thereafter, the President underwent his first surgery. Had Grant’s cancer been discovered in the 1890s rather than the 1880s, it is likely that he too would have received operative intervention.⁸ Thus, in many important ways, the patients, their physicians, and the contemporary nature of their treatments were comparable. The critical differences in the diagnosis and treatment of Grant and Cleveland resulted from new methods of seeing and doing that developed over the passage of time.

SIMILITUDES

Transition from the old disease cancer to the new, which began in the late nineteenth century, occurred unequally for different aspects of the disease. The culture of cancer, in

⁴Mackenzie, Morell Mackenzie, *A Manual of Diseases of the Throat and Nose Including the Pharynx, Larynx, Trachea, Oesophagus, Nasal Cavities, and Neck*, Vol. 1, (London: J. & A. Churchill, 1880), 82.

⁵*Ibid.*, 82-3.

⁶John Walton, Paul B. Beeson, and Ronald Bodley Scott, eds., *The Oxford Companion to Medicine*, 2 vols., Vol. 1. (Oxford: Oxford University Press, 1986; reprint, Gryphon Editions, Inc., 1988), 48-9.

⁷Francis de Havilland Hall, *Diseases of the Nose and Throat* (Philadelphia: P. Blakiston, Son & Co., 1894), 193.

⁸Compare the Mackenzie, 82-3 with Hall, 193.

particular, was slow to change. The connotations and denotations with which the two men viewed their disease were more similar than different. Cultural transformations often lag technological and intellectual advances, like a truck driven with the brakes on. Both men, for example, sought to suppress medical evaluation of the symptoms they knew could represent cancer. Both feared the disease, accepting the common knowledge that cancer was fatal. Both believed in the new science of medicine and exhibited faith in the pronouncements of their physicians. Both were severely affected by the *sub rosa* implications of their disease. Grant carried the marks of cancer—figuratively and literally—to his grave. Cleveland bore them psychologically into old age. Moreover, both strove mightily to hide their cancers from the public, their friends, and, initially, their families.

The fact that one failed to hide the truth and the other succeeded does not lessen the message of the attempt. All presidents are not equal. The vagaries of time trump the Constitutional similarities of the office. General Grant had been out of the presidency the better part of a decade when cancer struck. President Cleveland had just begun his second term. By the year of his cancer travail, 1884-5, the General was a venerated Civil War hero—indeed, perhaps, *the* War hero. The public brooked little criticism of his person. The President, on the other hand, found himself in a political and economic maelstrom unrivalled in recent memory. Attacks on his politics, economics, and personality were predictable but still gushed like a torrential downpour. Remarkably, though, General Grant's strength became his weakness as veneration led to an insatiable thirst for the revelation of his true ailment. President Cleveland's weakness became his strength as Lamont and Bryant knew what to expect from the media and others and successfully obfuscated the truth through the force of their offices and reputations. Grant's failure was Cleveland's success, and the publicization of the General's cancer in 1885

aided the transformation toward the modern conception of cancer that the diagnosis and treatment of the President's secret cancer reflected eight years later.

The General and the President similarly derived disadvantages and advantages from the assumptions of the code of professional conduct extant in the late nineteenth century. The import of this code should not be denigrated. Grant lost more than four precious months before the initiation of his cancer treatment because Dr. Da Costa would not minister to the General's oral lesion without Dr. Barker's explicit request or consent. Dr. O'Reilly immediately engaged the President's friend, Dr. Bryant, upon discovering the mouth cancer. Nevertheless, he, likewise, would not consider treating Mr. Cleveland himself, although such care was legally his responsibility. Further, the White House doctor was even surprised that chief surgeon Bryant included him on the surgical team. Dr. Da Costa's code of secrecy also prevented him from informing the General of his differential diagnosis (diagnostic possibilities). Had Da Costa told Grant on June 2, 1884 that the mouth pain might be caused by cancer, the General may have sought medical consultation sooner rather than waiting for Dr. Barker's return from his annual European vacation. Although Dr. O'Reilly was the first to examine the President's oral tumor, obtain biopsies for microscopic examination, and retrieve the pathological results, he told Mr. and Mrs. Cleveland nothing of his findings. Only Dr. Bryant, under the same code of secrecy, could do so. The rule of patient-physician privilege, codified in most states to this day,⁹ gave both leaders control over whether their physicians could divulge their private medical information to family, friends, or the public. Only the patient, as permitted by statute, could waive this right to confidentiality. Grant eventually did so. Cleveland did not, making Dr.

⁹Henry Campbell Black, Joseph R. Nolan, and Jacqueline M. Nolan-Haley, *Black's Law Dictionary: Definitions of the Terms and Phrases of American and English Jurisprudence, Ancient and Modern*, Sixth ed. (St. Paul, Minn.: West Publishing Co., 1990), 1126-7.

Hasbrouck's presumed divulgence, in the President's words, "a most astounding breach of professional duty on the part of a medical man."¹⁰ In both cases, the press, well acquainted with the rights of the privilege of confidentiality and the negative implications of a diagnosis of cancer, vigilantly endeavored to uncover the true nature of each man's disorder. They held the physicians' pronouncements suspect because of the lessons learned from those who preceded them in prevarication—Garfield's doctors for Grant and Grant's for Cleveland.¹¹ The equilibrium between the privacy of the individual and the state-condoned protection of the press through the First Amendment was tenuous. The culture of cancer, ultimately derived from the interplay of the one and the many, hung in the balance. Grant, through his reluctant openness, contributed to its slow but inexorable transformation. Cleveland, whose individual mastery overpowered the scrutiny of the press, used the cloak of medical professionalism to suppress public knowledge of his plight and, thereby, denied himself an immediate (although unwanted) role in the changing culture of cancer.

The human toll of cancer devastated both men. The ordinarily poker-faced General, as impassive on his horse in the midst of battle as on the dying-porch at Mount McGregor, cried out months before his death that the pain was killing him.¹² His deepest wish was to die without pain.¹³ The General's outward exclamations, as his silent communiqués revealed, mirrored the

¹⁰Letter from Grover Cleveland to Thomas F. Bayard, Washington, September 11, 1893. In Allan Nevins, ed., *Letters of Grover Cleveland 1850-1908* (Boston: Houghton Mifflin Company, 1933), 334.

¹¹George F. Shrady, M.D. *General Grant's Last Days, with a Short Biographical Sketch of Dr. Shrady* (New York: Privately Printed, 1908), 53, and "Illnesses of Grant and Blaine and denials recalled," from the *Washington Dispatch*, August 18th (1893?), clippings of Dr. John F. Erdmann. In Keen, *Scrap Book*.

¹²Stefan Lorant, "Baptism of U. S. Grant: Newly Discovered Diary of a Minister Tells the Intimate Story of the Spiritual Battle the General Waged in His Dying Days," *LIFE*, 26 March 1951, 92.

¹³Mary Drake McFeely and William S. McFeely, "Notes to the Doctor," in *Ulysses S. Grant: Memoirs and Selected Letters; Personal Memoirs of U. S. Grant, Selected Letters 1839-1865, The Library of America* (New York: Penguin Books USA Inc., 1990), 1111.

inner turmoil that riled his being. President Cleveland also suffered the cycle of repression and depression that engulfed the General. The haste to surgery and success of the operations telescoped the physical pain, but the mental anguish lingered. Mr. Cleveland paid the price of cancer, bedeviled the rest of his life with thoughts of recurrent disease although—as he could not know at the time—the surgical team had extirpated the ill-starred malady in 1893.

Common to both, of course, was their gender. This is not a trivial observation. In Victorian America, the boundaries between men and women transcended biology in cancer connotations as in socioeconomics. Had they been women, and particularly if their cancers had been of the sexually-linked breast or cervicouterus, the weight of Victorian judgment would have come down heavily upon them. For as Elizabeth Hamilton Cullum, Charlotte Astor, and their supporters at the Woman's Hospital were forced to realize in 1883, oppression and exclusion of the cancerous woman was a prejudice woven deep into the fabric of society. Gender became less of an issue in the conception of cancer only in the twentieth century, as the disparagement of Victorian women and the disease cancer slowly dissipated. General Grant and President Cleveland were fortunate not to have to endure the double burden of womanhood and cancer.

Subtler were the modes by which the disease cancer evinced its effect on the ways the General and the President portrayed themselves to the public. Grant's tumor involved the right side of his throat. It grew inexorably to encompass the right jaw and neck. Photographs and drawings from his last months reveal his neck covered with a ubiquitous white scarf. Sometimes a blanket draped the mass—even in summer.¹⁴ The right side of his face was rarely shown, except perhaps in pictures that portrayed him writing on the Mount McGregor porch. However, even these images mask his lesions, for photographers captured these likenesses at long

¹⁴See, for example, Pitkin, *The Captain Departs*, 74, 77, 83, 89.

distances. The grotesque bulges are not visible.¹⁵ Close-up shots exposed only the left—unaffected—side of his face,¹⁶ although his younger military and presidential portraits routinely showed him obliquely from the right—as do his representation on the Grant presidential medal and the current fifty dollar bill.¹⁷ Cleveland, whose cancer, surgery, and prosthesis involved the left side of his face, displayed the right side of his face and neck in posed pictures.¹⁸ Although informed that his visage appeared normal, he would take no chances. His presidential medal and engraved portrait on the now-retired one thousand-dollar bill are three-quarter right-sided depictions.¹⁹ As both men sought to suppress public knowledge of their diseases, so both men concealed images of the disfigurement—external and internal—wrought by their cancers.

Institutional attitudes gleaned from the behavior of the two men betray the long-harbored prejudice against hospitals for most of the nineteenth century by those atop the social hierarchy. Physicians treated neither the General nor the President in the once-charitable houses of medical care and social conformity. Grant's family, physicians, and friends attended him until his end within walls of close familiarity. During his final months, he never entered a hospital. Fears of germs in the years after the General's death slowly but relentlessly shifted the site of surgery to institutional operating suites mindful of antisepsis. Nevertheless, the secrecy demanded by the President precluded a standing hospital as the locus for his cancer excision. Instead, he

¹⁵ As Grant struggled to walk the short distance from Lexington Avenue and Forty-fifth Street into Grand Central Depot on his final journey from New York to Mount McGregor, his scarf momentarily loosened, exposing the “ominous swelling”—as *The New-York Times* called it—for all to see. “Resting at Mt. M'gregor,” 1:5. He never allowed the public to see his uncovered neck thereafter.

¹⁶McFeely, *Grant*, 510.

¹⁷*Ibid.*, frontispiece. The medal and currency are standard products of the United States Treasury.

¹⁸Note, for example, the five later photographs of Grover Cleveland at <http://www.loc.gov>.

¹⁹The only photograph I could find of Mr. Cleveland showing the left side of his face after 1893 is an unposed picture of him in old age. Surely there are others, but, unless probability is stacked against me, the point appears valid. Nevins, ed., *Letters of Grover Cleveland*, frontispiece.

condoned the construction of a makeshift surgical suite in the Salon of the *Oneida* for the first two operations. The third and last known cancer operation on Mr. Cleveland took place in the doctors' office. The familial home was the exclusive setting for postoperative care. Thus important cultural and institutional similarities bound the General and the President together in the ways of traditional cancer—but others, of a more modern nature, tore them apart.

The Peach: Differences within Similarities

General Grant's painful downfall to cancer began with his eating of a peach.²⁰ President Cleveland was also fond of the succulent summer fruit, but followed a very different path after he too ate the fruit at a critical time. In mid-summer 1893, within weeks of his two major cancer operations, the President could not resist the temptation to eat a peach. Mrs. Cleveland, in a letter to her friend, Mrs. Joseph Jefferson, revealed her astonishment at her husband's foolishness. "This morning when no one noticed he got a peach and ate it. Wouldn't you think a *child*," she continued, "would have more sense after the narrow escape he had?"²¹ Did Mrs. Cleveland know that General Grant's travail, with which she and her husband were so familiar, began with a peach? Unlike the General, however, the President continued to recover and, by the end of the summer, had returned, as judged by the hoodwinked press and the public, to his pre-operative functional level. Despite the cancer gloom that clouded his remaining years, the President lived to eat many more peaches. No historian can overlook the irony of the peach. For General Grant the peach was the beginning of the end. For President Cleveland the peach, unbeknownst to him, was the end of the beginning of one of the most fearful episodes in his life.

²⁰Simon, ed., *Julia Dent Grant*, 329.

²¹McElroy, *Grover Cleveland*, 29. Italics in the original.

DISSIMILITUDES

General Grant did not have surgery and wasted away as cancer consumed his being. President Cleveland had surgery and survived. Why he, and not General Grant, underwent surgery speaks to the theoretical and practical differences that revolutionized cancer medicine in the last two decades of the nineteenth century.

Theory and Practice

Theory is the foundation of practice. Medical theories, like the physicians who consciously or subconsciously apply their concepts to everyday patient care, are part and parcel of the society wherein they exist. They are, in other words, *of* society as well as *in* it. One of the ideational revolutions of the nineteenth century was the belief that man is an agent unto himself—the so-called secularization of society. The decline in the belief that supernatural forces ruled mankind gave rise to new ways of thinking about the human body and disease. The sacrosanct human form became workable and even modifiable. Secularization melded with the impulses of the industrial revolution (also a nineteenth-century phenomenon in the United States) to valorize the systematic methodology of science. In the process, it reduced the landscape of the body from a constituted whole to a mechanistic consolidation of parts open to the analysis of medical scientists.

From Whole to Parts

The transformation of the anatomical, physiological, and pathological human from whole to parts subsumed cancer medicine. Cancer, traditionally conceptualized as a humoral imbalance or an ingrained, inevitable, recurring constitutional catastrophe, became a disease of the microscope, measurement, and melioration. It was also interpreted as a local pathology confined (at least in its early stages) to a limited and therefore potentially remediable region of the body.

As localism became generally accepted, cancer nomenclature changed from a basis in gross descriptive terms to a terminology founded on cells, tissues, and organs. Hence, *epithelioma* became *squamous-celled carcinoma*.²² Surgery had been useless for the cure of systemically-conceived diseases like traditional cancer. Nevertheless, it became the treatment of choice for modern cancer because it was perfectly suited for the excision of local diseases. The fact that parallel developments in chemistry and bacteriology helped surgery achieve a level of safety and success unwitnessed in human history dynamically hastened the conceptual conversion from constitutional to local cancer. Surgery offered the patient benefits that palliation never could. Cancer, once believed invariably fatal, became treatable and possibly, as in President Cleveland's case, curable. Bryant's mantra—"cut early, cut often, cut wide"²³—became the slogan for the treatment of the new modern cancer.²⁴

From Specific to General

As the transition from constitutionalism toward localism and the breaking down of the human body into smaller parts continued, a conjoined movement shifted medical emphasis from the specific to the general. These were not contradictory tendencies, for the blindered gaze lost sight of the whole. Cancer in the body part of one person became indistinguishable from a cancer in the same part of another. Traditional cancer was a disease of and in individuals. Modern cancer was no longer a disease specific to *a* human body. It was standardized and

²²Today *squamous cell carcinoma* is the (perhaps grammatically incorrect) term.

²³Joseph D. Bryant, "Malignant Neoplasmata: Read in the Discussion before the New York State Medical Association, October 10, 1888." *New York Medical Journal* 48 (1888): 680.

²⁴Not all cancers—then and now—are amenable to surgery. Early solid tumors—i.e., non-hematogenous cancers that had not spread beyond their points of origin—were and are most likely to be ameliorated or cured by surgery. The recognition that the earlier the diagnosis, the more likely the cure, was a major impetus for the formation of the education-oriented American Society for the Control of Cancer in 1913, the forerunner of the American Cancer Society.

generalized. General Grant's traditional tumor was specific to General Grant. He and his cancer were literally and figuratively inseparable. Although others might develop epitheliomas, physicians (and the public) thought each case to be individualized, independent, and non-interchangeable. Physicians recognized some commonalities between same-site tumors, but cancer was specific to the whole.

President Cleveland, on the other hand, was merely another patient with an epithelioma of the mouth.²⁵ Like others with similar lesions, his pathology was amenable to surgery if treated early. This shift in focus from the specific to the general permitted nascent epidemiologists and others with a demographic inclination to compile more detailed cancer statistics than ever before. In turn, these particulars revealed trends that had been indeterminable during the era of individualized cancers. The individual as a distinct whole lost importance. Medical emphasis shifted from the patient who had cancer within to the cancer within the patient.

Out of Many, One

Review of the medical literature for the period provides evidence for this change in focus. Prior to the 1880s, cancer entries in journals such as the *New York Medical Journal* and *The Boston Medical and Surgical Journal* typically described individual patients and their clinical courses. These published reports highlighted the surgical since cancer operations were noteworthy at the time and palliative treatment (or no therapy) was not. Gross pathology was included, but microscopic findings were not routine until the late 1880s and 1890s.

Compilations and reviews of the literature—such as Dr. Samuel Gross's 1853 study to survey the

²⁵The temporal transition from *epithelioma* (etymologically 'on top of the nipple') to *squamous cell carcinoma* (named after the transformed microscopically visualized cell type) began in the late 1880s to 1890s. The 1894 text of F. de H. Hall explicitly juxtaposes the two terms: "epithelioma (squamous-celled carcinoma)." Francis de Havilland Hall, *Diseases of the Nose and Throat* (Philadelphia: P. Blakiston, Son & Co., 1894), 191.

results of cancer surgery at home and abroad (specially commissioned by the American Medical Association)²⁶—were rare.

During the last two decades of the nineteenth century, however, medical articles analyzing more than a single patient with the same cancer diagnosis became more commonplace. These were primarily simple collections of characteristics statistically formulated to reach general conclusions. In contradistinction to earlier clinical reports, however, they focused on groups of patients rather than individuals. At first these new cluster studies appeared as monographs,²⁷ but in the last decade of the century journal articles appeared that evaluated large numbers of cancer patients with the same organ involvement. More often than not, microscopical examination, rather than gross pathology, was now the key to diagnosis. Dr. Bryant's 1890 literature review of two hundred and fifty-four cases of superior maxillectomy, most of which were performed for cancer excision, is representative of many examples from the era.²⁸ The old fixation on the one patient became a new focus on the many: *e unum pluribus*.²⁹

From Therapy to Diagnosis: The Fruits of Quantification

²⁶Samuel D. Gross, M. D., "On the Results of Surgical Operations in Malignant Diseases," *Transactions of the American Medical Association* 6 (1853): 153-313.

²⁷A typical example of a cancer monograph from the early 1880s is Willard Parker, M.D., *Cancer: A Study of Three Hundred and Ninety-Seven Cases of Cancer of the Female Breast with Clinical Observations*, 1st ed. (New York: G. P. Putnam's Sons: The Knickerbocker Press, 1885).

²⁸Joseph D. Bryant, "A History of Two Hundred and Fifty Cases of Excision of the Superior Maxilla." *Transactions of the Medical Society of the State of New York for the Year 1890* (1890): 63-76. Microscopical results are given on p. 72.

²⁹Literally, out of one—many. The refocus from the one to the many was hardly restricted to cancer medicine. The "golden age of public health" during these years was a much broader consequence of this ideological shift.

As constitutionalism yielded to localism and individuation to generalization, doctrinal medical emphasis shifted from therapy to diagnosis.³⁰ During the 1830s and 1840s, the Frenchman P. Ch. A. Louis (1787-1872) applied the scientific method of Francis Bacon to medicine. His “Numerical Method” fostered the transition from therapeutic hegemony to the avoidance of unproven therapies and, in the process, elevated the status of diagnosis.³¹ Louis’ collection and observation techniques recorded and interpreted large numbers of patients, their treatments, and their outcomes.³² He countered the subjective, anecdotal tendencies of clinical impressions by enumerating data and basing his results thereon. Many hallowed therapies, like bloodletting, fell into disrepute as Louis’ figures revealed their fruitlessness and, frequently, their harmfulness. He received credit as the founder of medical statistics and became a driving force in the birth of scientific medicine later in the century.³³

Physicians in the United States were slow to adopt Louis’ quantification system. Some American medical pioneers, like Dr. Samuel Gross, applied Louis’ method to the analysis of cancer surgery outcomes in mid-century.³⁴ However, his belief that “if then there is a means of

³⁰Paul Starr, among others, alludes to this transformation in his discussion of public health at the turn into the twentieth century. Paul Starr, *The Social Transformation of American Medicine: The Rise of a Sovereign Profession and the Making of a Vast Industry* (New York: Basic Books, Inc., 1982), 192.

³¹See, for example, Pierre-Charles-Alexander Louis, *Researches on the Effects of Bloodletting in Some Inflammatory Diseases*, trans. C. G. Putnam (Boston: Hilliard, Gray, & Company, 1836), Pierre-Charles-Alexander Louis, *Researches on Phthisis: Anatomical, Pathological and Therapeutical*, trans. Walter Hayle Walshe (London: The Sydenham Society, 1844). His early statistical collections on the effects of bloodletting revealed the treatment much less effective than previously thought. The recognition of Louis’ work was a major factor, along with the criticisms hurled by the “irregular” medical sects in the middle decades of the nineteenth century, in the decline of the use of venesection.

³²His motto was *ars medica tota in observationibus*.

³³P. Ch. A. Louis, in the language of the twenty-first century, may also be called the father of evidence-based medicine.

³⁴Gross, "On the Results of Surgical Operations in Malignant Diseases," 1853.

embodying the experience of ages, it is the numerical method,”³⁵ did not hold sway in America until later in the nineteenth century. By the late 1880s and 1890s, as the passion to count consumed Progressive America,³⁶ quantification of the results of cancer therapies, including palliatives, began to replace the older descriptive medicine. In the process, cancer treatments touted by “practitioners” from William Avery Rockefeller to Grant’s consultants were assessed and found wanting. Dr. William Osler, physician in chief at Johns Hopkins in Baltimore from 1889-1905, was a leader in the movement toward proof of therapeutic efficacy.³⁷ Osler recognized a kindred spirit in P. Ch. A. Louis and lauded him for his seminal role in the development of scientific medicine and, in particular, re-evaluating old therapies, by substituting “observation and method” for “speculation and theory.”³⁸

Therapeutic Nihilism

The tenet that no therapy is better than an ineffective or baneful treatment—therapeutic nihilism—was a direct outgrowth of this new method of analyzing the results of treatments. Therapeutic nihilism, concomitant with the rise of the microscope as the instrument of choice for cancer diagnosis, helped transform the focus of analysis from treatment to diagnosis. Statistical results of therapies applied to numbers of similarly diagnosed cancer patients objectified what case reports of improvements and cures never could. By means of Louis’ methodology, medical

³⁵Louis, *Researches on the Effects of Bloodletting*, 69.

³⁶Thomas J. Schlereth, *Victorian America: Transformations in Everyday Life, 1876-1915*, Richard Balkin, ed., *The Everyday Life in America Series* (New York: HarperPerennial, 1991. Reprint, 1992), 3.

³⁷Sir Osler furthered the emphasis on diagnosis by going so far as to employ therapy to confirm diagnosis (therapeutic trial). In his groundbreaking textbook, first published in 1892, Osler suggested that physicians treat difficult-to-diagnose ulcers of the pharynx with mercury and iodide of potassium in order to differentiate malignant from syphilitic ulcers. If the ulcer healed with potassium therapy the diagnosis of cancer was unlikely. William Osler, *The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine* (New York: D. Appleton and Company, 1892; reprint, 1978), 331.

³⁸William Osler, "The Influence of Louis on American Medicine," *The Johns Hopkins Hospital Bulletin* 77-78 (1897): 190.

practice returned to its ancient roots embodied by the Hippocratic aphorism *primum non nocere*—above all, do no harm.³⁹ In 1913, Samuel Hopkins Adams, a muckraking journalist of the early twentieth century famous for his exposés on patent drugs, looked back on medical progress in the late nineteenth century. He informed his readers in the *Ladies Home Journal* that the foundation of the triumph of laboratory and clinical medicine was the elimination of ineffectual and harmful treatments from the arsenal of cancer therapies.⁴⁰

General Grant's consultants in the mid-1880s preferred therapy over diagnosis. Microscopic confirmation of Dr. Douglas' initial gross diagnostic impression of the General's cancer was a mere afterthought, consistent with the notion of the cell-and-tissue magnifier as a "toy."⁴¹ Douglas and colleagues used multiple drugs, as needs dictated, to palliate Grant's tumor. They administered many of the treatments systemically. President Cleveland's physicians, on the other hand, used every means at their disposal, including immediate biopsy and microscopical analysis, to quickly and accurately diagnose their patient's tumor. Diagnosis led to surgical therapy. Cleveland's doctors opted for surgery without dissent once the diagnosis, confirmed by the microscope, was deemed irrefutable. Bryant's studies of "malignant

³⁹An interesting consequence of therapeutic nihilism reveals another interpretation of the reinstatement of state licensure laws in the 1880s and 1890s. Paul Starr and others suggested that re-licensure resulted from the agency of regular physicians and their "consolidation of authority" as a consequence of the rise of scientific medicine. Starr, *The Social Transformation of American Medicine*, 102-06.

I would add that therapeutic nihilism and the principle of *primum non nocere* obviated the perceived public need to continue to hold the practice of medicine open to all. 'Regular' physicians in the Jacksonian era, many of whom held to the phlebotomy-driven treatments of Benjamin Rush, witnessed the loss of their state-sanctioned exclusivity as 'irregulars' like Thomsonians and other empirics treated patients with less harmful therapies. The public outcry against the regulars resulted in the denunciation of licensure as the privilege of aristocrats in a democratic society. As 'heroic' therapies like bloodletting were found to yield poor results and abandoned, the public applauded the more salutary treatments that regulars had in part co-opted from irregulars, appreciated the results of the new scientific medicine, and lauded the principles of therapeutic nihilism. The pendulum swung and state legislatures reinstated medical licensure laws by the end of the century as most believed that it was more dangerous to the public to keep access to the profession open than to restrict it.

⁴⁰Samuel Hopkins Adams, "What Can We Do About Cancer?," *Ladies Home Journal*, May 1913, 21.

⁴¹Robert M. Steckler and Donald P. Shedd, "General Grant: His Physicians and His Cancer," *The American Journal of Surgery* 132 (1976): 510.

neoplasmata” and superior maxillectomy assumed a level of diagnostic accuracy that was not possible just a few years earlier. The President, in contradistinction to the General, received only minimal postoperative medication. Therapy bowed to diagnosis.

Et causæ quoque estimatio sæpe morbum solvit.

—Celsus⁴²

Another conceptual transformation bears mention, although it will be more fully explored in a later chapter. It is the change from internal to external cancer causation that washed over the United States between the death of Grant and the cancer of Cleveland. The perceived cause of cancer is of enormous importance, for, as Celsus wrote, the determination of the cause of a disease often leads to its remedy. For most of the nineteenth century, popular and medical lore held that the cause of cancer was something within the body itself—that it was part of one’s constitution. “Exciting” causes like Grant’s cigars could irritate the membranes and hasten the onset of cancer, but the cause was, in essence, inside the body. By the last years of the century, however, as localism, generalization, and diagnostics came to dominate cancer medicine, many medical researchers and clinicians became convinced that agents external to the body caused cancer. The microscope, coupled with the statistical investigations of P. Ch. A. Louis’ intellectual descendants, exposed these agents to be germs.⁴³ Dr. Bryant the surgeon was not immune to this change in thought. In his 1888 article on malignant neoplasmata, Bryant listed the most likely causes of cancer. The last and, presumably, most recent was “that malignant

⁴²“To determine the cause of a disease often leads to the remedy.” Translation by William Osler, *The Evolution of Modern Medicine: A Series of Lectures Delivered at Yale University on the Silliman Foundation in April, 1913* (New Haven: Yale University Press, 1921), 214.

⁴³Oliver Wendell Holmes was a student of both the microscope (figuratively) and P. Ch. A. Louis (literally). Not surprisingly, he became an exponent of extrinsic disease causation, as witnessed by his attack on puerperal fever in 1842, two years before Semmelweis’ frustrated efforts.

growths are of an entirely local origin, dependent on a specific virus, endowed with characteristic bacilli.”⁴⁴

Conclusion and Prologue: Microscopes, Malignancies, and Microbes

The consequences of this cognitive transformation from internal to external cancer causation were far-reaching. Discover germs with the microscope. Discern which cause cancer. Prevent them from invading the body and forestall cancer. Excise the germ-infested tissue and cure the cancer. Kill the germs and kill the cancer. Although philosophers and dreamers postulated germs for millennia, these methods of dealing with cancer began in the late nineteenth century and carried into the twentieth. The germ theory of cancer causation, reified in the architecture of newly-constructed modern cancer institutions like the New York Cancer Hospital, replaced the perennial pessimism of cancer treatment with newfound hope. Here was a cause of cancer that lent itself to models of prevention and treatment during the boom years of public health. Physicians like Bryant, Keen, Janeway, O’Reilly, and Erdmann now had a rational basis on which to believe that removing cancerous tissue initiated by germs could thwart the disease and prevent its recurrence.

By contrast, General Grant’s consultants bore no such optimism. Cancer, to them, was of the body as well as in the body. Excision promised nothing more than a futile endeavor rife with potential disaster. The confluence of the microscope, surgery, and this new view of the body and malignancy struck at the heart of traditional cancer. How these major forces of causation, diagnosis, and treatment came together in the final years of the century is a matter of great import. Momentous in and of themselves, they also set the stage for a new epistemology of cancer and novel techniques that characterized cancer medicine in the twentieth century.

⁴⁴Bryant, "Malignant Neoplasms," 677.

In the 1890s, the future of cancer lay not in a play-toy for the naturalist or partygoer, but through the lens of a new medical instrument called the microscope; not in a dangerous intervention that increased suffering and shortened life, but in the knife of a surgeon who believed extirpation could cure the disease. The cancer histories of General Grant and President Cleveland illustrate traditional and modern cancer—although in transitional and nascent form—respectively.

The final section of the dissertation will focus on the tangible and the conceptual—the microscope and cancer therapeutics. These defined modern cancer at its outset. Specifically, I shall explore the forces that confluenced at the end of the nineteenth century to render the diagnosis and treatment of President Cleveland's cancer so different from that of General Grant. The microscope and the "golden age of surgery" made modern cancer "modern."

SECTION III
MODERN CANCER

Introduction to Section III

Scientific Cancer

**The theory was of the cell,
The practice through the ‘scope;
Like hand in glove they fit so well
To expunge the cancer’s swell.**

Section I explored medical, societal, and institutional aspects of traditional cancer, primarily in the early-to-mid-nineteenth century, through the thoughts and actions of its major participants: pathologists, patients, patrons, and practitioners. Chapter 1 focused on the culture of cancer for the beginning of the century through the explorations of those who most strove to understand the nature of the disease—pathologists. Chapter 2 contextualized and analyzed the cultural and societal underpinnings of the founding of the first major cancer institution in the Western hemisphere—the New York Cancer Hospital. Thus, Section I established “Traditional Cancer.”

Section II analyzed the transition from traditional to modern cancer through the personal travail and medical diagnosis and treatment of the cancers of two celebrated figures—General Ulysses S. Grant and President Grover Cleveland. Although barely separated in space and time, major changes in the visualization, treatment, and conceptualization of the disease in the 1880s and early 1890s led to two very different approaches to their neoplasias—and two very different outcomes.

If Section I emphasized the “what” of traditional cancer, and Section II the “how,” then Section III seeks to analyze the “why” of the great cancer revolution of the late nineteenth

century.¹ The scientificization of medicine, though incubating in the United States and especially Europe for decades prior to the end of the nineteenth century, supplanted the didacticism and empiricism of early and mid-century practitioners in the final years of the century and replaced them with a more measured, analytical approach toward patients with cancer. Three tandems in particular—the microscope and cancer, surgery and cancer, new theories and cancer—transformed traditional into modern cancer – a set of thoughts and actions very much congruent with the diagnosis and treatment of the disease today. These interactive pairings of cancer with technology, treatment, and etiology bear much of the responsibility for the “why.” Thus, Section III explores the making of modern cancer by attempting to answer the question: Why modern cancer?

¹The “who, “when,” and “where” are detailed throughout these histories.

Chapter 6

New Visions, Newer Insights: The Birth of Medical Microscopy and The Rise of Modern Cancer

**“Faith” is a fine invention
When Gentlemen can *see* –
But *Microscopes* are prudent
In an Emergency.**

-Emily Dickinson

Today, cancer medicine and the microscope are inseparable.² Cancer diagnosis, treatment, prognosis, and research are highly dependent upon a scientific instrument that has become an icon of modern medicine as well as the neoplastic diseases.³ The interpretation of the microscopic image of a surgically-obtained specimen or “biopsy”—a term from the late nineteenth century that is derived from the phrase “an autopsy of the living”⁴—extracted from a “suspicious” lesion is the touchstone of cancer diagnosis. The microscopic diagnosis, in conjunction with the extent of disease “work-up,” determines treatment.⁵ At the time of surgery,

²In contemporary medicine, there are different types of microscopes based upon varying properties of the electromagnetic spectrum—the light microscope, phase-contrast microscope, electron microscope (of which there are two sub-types, scanning and transmission), etc. In the nineteenth century, *the* microscope was the optical microscope, commonly referred to as the light microscope. Thus, the focus of this chapter is on the light microscope. All references to “microscope” should be interpreted as “light microscope” unless otherwise noted.

³The other two great pictorial icons of medicine—the stethoscope and the white laboratory coat—are less specific to cancer, but—consonant with the age of the rise of modern medicine—also date from the nineteenth century.

A neoplasm is an abnormal new growth of tissue that is usually synonymous with ‘tumor’—benign or malignant.

⁴Credit for the origination of the term ‘biopsy’ is generally given to the French dermatologist Ernest Besnier for his work in the last years of the nineteenth century. He defined it in his 1900 text, *La Pratique Dermatologique*, as “une sorted’ ‘autopsie’ sur le vivant.” See James R. Wright, Jr., “The Development of the Frozen Section Technique, the Evolution of Surgical Biopsy, and the Origins of Surgical Pathology,” *Bulletin of the History of Medicine* 59, no. 3 (1985): 317.

⁵The “extent of disease” is usually determined by preoperative imaging procedures such as X-rays, ultrasounds, CT scans, and MRIs. In addition to these indirect representations of the “inside” of the body, biopsy tissue samples may reveal microscopic evidence of the invasion of structures adjacent to the tumor that may directly influence diagnosis, treatment, and prognosis.

a biopsy rapidly frozen and sectioned (thinly sliced) for microscopic analysis may yield information about the patient's type of cancer as well as the stage (i.e., degree of tumor spread) attained by the pathological growth. Such knowledge guides the mind of the oncologist to map out a treatment plan and, if amenable to extirpation, the mind and hand of the surgeon to execute an operation to achieve the desired result ("cure") with the least harm. The microscopic interpretation of the ominous tissue also predicts—within the limits of current medical science—a future of health or illness through the determinism implied by prognosis.

To many laymen (especially those untouched by cancer), however, the diagnostic, therapeutic, and prognostic roles the microscope plays in cancer medicine form merely a backdrop to the protagonistic function of the instrument in research. It is impossible, for example, to imagine the foundational cancer research of the German pathologist Rudolf Virchow (1821-1902), whose three-volume treatise on the disease inspired and incited more than a generation of cancer investigators, and the American Francis Peyton Rous (1879-1970), who showed in the first years of the twentieth century that cancer could be transmitted in chickens through a contagious element, without envisioning a microscope.⁶

Indeed, the microscope was the technology that opened cancer to science and abetted the cultural drift of the popular conception of cancer away from the shame and blame of sin with which it was earlier invested. Nevertheless, although cancer today is a peculiarly microscopic disease, it was not always so. Prior to the last years of the nineteenth century, practitioners hotly debated the clinical value of cancer microscopy—and its parent, medical microscopy—with feud and acrimony.

⁶Rudolf Virchow, *Die krankhaften Geschwülste. Dreissig Vorlesungen gehalten während des Wintersemesters 1862-1863 an der Universität zu Berlin* (Berlin, 1863-67); Peyton Rous, "A Sarcoma of the Fowl Transmissible by an Agent Separable from the Tumor Cells," *Journal of Experimental Medicine* 13 (1911): 397-411.

Most medical practitioners in the United States at the beginning of the last quarter of the nineteenth century—separated from Virchow (pronounced fear-c(h)ow) in space and Rous in time—did not embrace the microscope as a tool of medicine. Unquestionably, German, French, and British cancer researchers accepted medical microscopy earlier in the century,⁷ as did many American researchers.⁸ Nonetheless, American clinicians—those on the front lines who every day made life-determining decisions for their cancer patients—eschewed medical microscopy until the final years of the century. General Grant’s physicians exemplified this stance. Their standards for diagnosis, therapeutics, and prognosis excluded the microscope in favor of the trained hand and the experienced, unaided eye of the clinician. So it had been for centuries. And so it might have continued had not a confluence of cultural, societal, technologic, and medical transformations thrust the microscope into the limelight of the new scientific medicine during the last two decades of the nineteenth century. The very different attitude toward the use of the microscope in medicine assumed by President Cleveland’s medical team only a few years after the death of the General reflected this radical new position. This chapter investigates those changes, the instrument (or, properly, instruments) that inspired them, and the unique contribution of the microscope to the development of modern cancer.

I scarce know one improvement in the history of medicine, which has not met with a strong opposition. It is a melancholy reflection, that a man should incur the displeasure of the members of his profession, for those very inventions which merit the approbation of all mankind.

-Dr. William Rowley to Dr. William Hunter,
1774

⁷See, for example, the case study of L. S. Jacyna, "a Host of Experienced Microscopists: The Establishment of Histology in Nineteenth-Century Edinburgh," *Bulletin of the History of Medicine* 75, no. 2 (2001): 226., as well as the work of Johannes Müller discussed below.

⁸Deborah Jean Warner, "The Campaign for Medical Microscopy in Antebellum America," *Bulletin of the History of Medicine* 69 (1995).

I will call attention to one fact apparent to anyone familiar with the history of medical discoveries, that the relative value of such discoveries bears not the slightest relation to the rapidity of acceptance by the medical profession.

-Dr. William Bradley Coley (1862-1936)

To write a history of cancer and the microscope is to relate only part of a larger but contemporaneous saga of the development of medical microscopy. This more encompassing tale, filled with genius, technological wizardry, acrimonious backstabbing, and, ultimately, the triumph of the scientific method in medicine, furnishes an essential backdrop for cancer and the microscope during the nineteenth century. From a tool of cancer researchers for most of the century, the microscope transcended optical, interpretative, and cultural obstacles to play a growing role in the diagnosis of cancer as the methodology of medicine transitioned from didacticism to science. To understand the function of the microscope in the history of cancer, therefore, it is necessary to comprehend a more general outline of the evolution of medical microscopy.

Distrust and Contempt

At the beginning of the nineteenth century, practicing physicians ridiculed and eschewed the microscope as a medical instrument. This exclusion of the microscope from clinical medicine for most of the century was the consequence of neither oversight nor passive neglect. American practitioners during the opening decades of the century actively avoided the magnifying machine. Indeed, they were quite skeptical—even derisive—of its application to the art and practice of medicine. Oliver Wendell Holmes, Sr., the *Autocrat of the Breakfast Table* and father of the famed jurist, taught one of the first American medical microscopy courses in 1851 at the Tremont Street Medical School in Boston. He noted that as a student the textbooks of his “medical pupilage treated the microscope and the results obtained by the use of it with

distrust and even with contempt.”⁹ This anti-microscopy mindset prevailed among practitioners for more than a generation thereafter.

Skepticism, derision, distrust, and contempt toward the use of the microscope in cancer medicine were justifiable. Clinicians deemed cancer a disease best diagnosed by physicians, not microscopists. Both theory and practice supported this point of view. If the diagnosis of cancer could not be made until it invaded adjacent tissue or spread far and wide throughout the body (invasion or metastasis)¹⁰—both observable in later stages of the disease with the naked eye—well, what was the need to visualize cells? In addition, the microscopic diagnosis of cancer for the majority of the nineteenth century was fraught with error. The optics of the microscope well into the nineteenth century left much to be desired and slide preparation was variable and even capricious. Further, different observers of the same microscopic preparations rendered dissimilar diagnoses. Even if two or more microscopists concurred that the lesion was a tumor, they might not agree whether the pathology was benign or malignant.¹¹ Upon this critical distinction rested the fateful decision to subject the patient to operation. What was the practitioner—responsible to the patient for a verdict in the here and now—to do? Perhaps, many concluded, it was better to avoid microscopy and its inconstant histologic interpretation altogether. Traditional cancer excluded the microscope.

The common impression is that these investigations into the minute structure and habits of tumours are more interesting than useful, and that they are not calculated to throw much light upon the question of treatment. -H. Arnott, 1872

⁹Oliver Wendell Holmes, "An Address Delivered at the Annual Meeting of the Boston Microscopical Society." *Boston Medical and Surgical Journal* 96, no. 21 (1877): 602. Microscopy was not taught at Harvard until 1855. Nevertheless, even this seemingly late date was many years before medical microscopy under the title of histology became a regular part of the curriculum in most American medical schools. See Thomas E. Hunt and Eleanor A. Hunt, "Dr. Oliver Wendell Holmes: Teacher and Microscopist," *The Alabama Journal of Medical Sciences* 3, no. 1 (1966): 78.

¹⁰Wright, "Surgical Pathology," 318.

¹¹Warner, "Antebellum Medical Microscopy," 382.

Not surprisingly, the majority of practitioners who treated cancer patients avoided the microscope as late as the 1870s. In 1878, the New York microscopist C. Heitzman, a great proponent of medical microscopy, related an anecdote before the New York County Medical Society. “A few months since I had a conversation with a renowned physician in this city...about the great value of the microscope, especially in the practice of medicine. The physician laughed at me, and asserted the science of microscopy to be good for nothing.”¹² In 1885, despite the promising microscopical findings of Louis Pasteur, Robert Koch, and other microbiologists in the intervening years, General Grant’s doctors belatedly used the microscope to secondarily support rather than determine his diagnosis and treatment. The microscope merely validated their gross impression and plan of treatment months after Drs. Barker and Douglas reached their original diagnosis on the basis of plain visual inspection. Dr. Elliott, the microscopist, merely dreamed of using the microscope to reach scientific conclusions for the diagnosis, treatment, and prognosis of the General and others with the disease.

It takes fifty years from the discovery of a principle in medicine to its adoption in practice.

-Martin H. Fischer (1879-1962)¹³

By 1893, however, a major change in thought and process had occurred. Cleveland’s physicians determined his diagnosis, therapy, and prognosis entirely upon their interpretation of microscopic findings. Dr. Robert O’Reilly, the first physician to note Grover Cleveland’s oral anomaly, sent a specimen of the President’s tissue biopsy for microscopic examination and diagnosis even before informing the President’s long-time friend and trusted family physician, Dr. Joseph D. Bryant, that something was amiss. The importance of the patient mandated

¹²C. Heitzmann, "The Aid Which Medical Diagnosis Receives from Recent Discoveries in Microscopy," *Archives of Medicine* I (1879): 44.

¹³Jess M. Brallier, *Medical Wit and Wisdom: The Best Medical Quotations from Hippocrates to Groucho Marx* (Philadelphia: Running Press, 1993), 260.

corroborative opinions from Dr. William Henry Welch and others, but once confirmed no doubts remained and the microscopic diagnosis of cancer immediately set the wheels of treatment into motion. Bryant scheduled surgery forthwith.

So rapidly did the microscope transmute from pariah to icon that by 1896 a vocal but minority group of physicians (presaging declamations a century later) rebuked practitioners for placing too much emphasis on the microscope and too little on the individual and physical diagnosis. “Our eyes and our minds are rather apt in consequence to dwell too much on our detailed notes and manifold instrumental aids, and too little on the patient,” Sir Dyce Duckworth wrote that year. The English clinician concluded: “We must, if we are to be great in medicine, sometimes lift our eyes from the microscope.”¹⁴ Thus, to the dismay of some, the microscope, within a score of years, became an integral and essential component of clinical medicine and cancer. The explanation for this transformation transcends the advent of scientific medicine in America and reveals the potent force that the microscope represented in the rise of modern cancer.

A Brief History of the History of Microscopy

The tenor of historical writings on cancer and the microscope have changed with the times. In the final years of the nineteenth century, when the profession of history flourished and books rife with optimism by Lord Acton and others predicted that all the facts of history would soon be known (thus heralding the end of history), the history of microscopy adorned introductory sections and first chapters in medical textbooks and articles on the microscope.

¹⁴Sir Dyce Duckworth, “The Prognosis of Disease,” *British Medical Journal* 2 (1896): 251-2. Duckworth’s article was cited by Stanley Joel Reiser, *Medicine and the Reign of Technology* (Cambridge, England: Cambridge University Press, 1978), 90FN74.

Even then, however, chapters on tumors within more general medical and surgical texts, often buried near the end of the work, were not so inclusive.

Modern historians of medicine and the microscope locate the acceptance of the instrument for research in the mid-nineteenth century.¹⁵ On the other hand, the microscope remained unwelcome within the offices of most clinicians for many years thereafter. With few exceptions, I have found that practitioners did not acquiesce to the virtues of the microscope until the second half of the 1880s. Even the most forward-looking clinicians, like William Williams Keen of Philadelphia, did not embrace the microscope as a tool of patient care until the last quarter of the century.¹⁶ John Harley Warner appears to agree that the advent of clinical microscopy, unlike research microscopy, did not occur until well into the 1880s. Prior to that time, Warner noted, microscopists castigated physicians for their “lamentable ignorance concerning the microscope.”¹⁷ Medical microscopy did not flourish until germ theory, in this view, revolutionized the way the average doctor thought about health and disease.

For the first six decades of the twentieth century, histories of cancer microscopy focused primarily upon technical and illustrational challenges. Description held sway over analysis. These consolidating years of scientific medicine sought methodological precision, focusing upon the cancer cell and its environment to the exclusion of the world (i.e., tissues) around it.

The social and cultural revolution of the 1960s affected the approach to the history of medical microscopy as well as most other sections of historical analysis—albeit seemingly more

¹⁵Examples include James H. Cassedy, "The Microscope in American Medical Science, 1840-1860," *ISIS* 67 (1976), Warner, "Antebellum Medical Microscopy."

¹⁶Drs. William Henry Welch and William Osler were of a later generation. They, like Dr. Oliver Wendell Holmes, learned the value of the microscope during their years of European post-graduate training and incorporated it into their notions of a new paradigm of patient care grounded in scientific investigation.

¹⁷John Harley Warner, "'Exploring the Inner Labyrinths of Creation': Popular Microscopy in Nineteenth-Century America," *Journal of the History of Medicine and Allied Sciences* 37 (1982): 19.

slowly. Perhaps reactionary forces were greater than in other historical specialties. Perhaps the need to challenge the establishment lacked the immediacy felt in other fields. Nevertheless, by the 1970s the focus of history of medicine writing shifted from the physician to the patient and from the individual to the system, consonant with the general tendency away from Carlyle's "great (white) men" (usually white male physicians) and toward those excluded from prior discourse.¹⁸ Writings on the microscope and medicine, such as those by Stanley Joel Reiser, faithfully chronologized individual contributions to the history of the medical microscope while at the same time emphasized the schism between patient and physician to which many believed the instrument contributed.¹⁹

By the 1980s, castigation of the "good ol' boys" networks in medical offices and hospitals reached its height. Paul Starr and others cynically interpreted patient care as physician care.²⁰ The microscope became a weapon of medicalization, professionalization, and exclusion—separating the ranks of doctors and the new medical scientists from everyone else and raising their status (and income) in the process. Revisionist history transmogrified age-old altruism into self-interest. At the same time, medical texts (written by physicians for physicians), ostensibly oblivious to the revolution in historical emphasis, continued to teach the development of the microscope as a product of heroic protagonists as well as its essential role of the microscope in cancer medicine. The two streams in the history of medicine—academic and medical—paralleled each other with very different audiences and motives.

¹⁸Of examples too numerous to mention, two of my favorites are Ivan Illich, *Medical Nemesis: The Expropriation of Health*, First American ed. (New York: Pantheon Books, 1976), Lloyd G. Stevenson, Manuscript rejection letter, 4 June 1973.

¹⁹Stanley Joel Reiser, "The Microscope and the Revelation of a Cellular Universe," in *Medicine and the Reign of Technology* (Cambridge, England: Cambridge University Press, 1978), 90.

²⁰Paul Starr, *The Social Transformation of American Medicine: The Rise of a Sovereign Profession and the Making of a Vast Industry* (New York: Basic Books, Inc., 1982).

The final years of the twentieth century witnessed a sometimes uneasy rapprochement as physicians, many now trained in departments of history as well as medical schools and hospitals, combined with doctors of a more philosophical nature to create works of context and conciliation. Others continued to delve deep into periods past with questions and methodologies aimed at syntheses that kindled further interest in the history of mankind's eternal quest for health.

Today, in the early twenty-first century, the history of the microscope—like that of cancer specifically and medicine generally—resides in context, free to boast its hopes and blessings while at the same time provoking criticisms and inquiries of the what, where, who, when, and, most interesting, the why of its development over time. Not far from the surface lies the ever-present academic question: what could have been if the microscope had....

The Microscope Evolved

All of human history, adequately examined, in the end is the history of better tools.

—Ernst Kapp, 1877

The micro-scope, literally “to observe the very small,” was not the same device in the seventeenth, eighteenth, and opening years of the nineteenth centuries that it became later in the nineteenth. In its more than five-hundred-year history it has undergone, in the words of the late Stephen Jay Gould, a series of punctuated equilibria. As a testament to the insufficiency, inaccuracy, and history of language, it is regrettable that the same term for Galileo's seventeenth-century magnifier of nature is applied to the late-nineteenth century instrument used by William Henry Welch to scrutinize President Cleveland's biopsy tissue. Although fixed in a foundation of lenses and objects, the two “microscopes” were quite different.

Further, the culture of the microscope—like that of cancer—changed over time. It was an instrument of spectacle, society, and even science long before it became a tool of medicine.

The optical modifications and historical evolutions that transformed the microscope and its imagery in society help explain why American cancer practitioners of the 1870s shunned the microscope as “little better than a scientific toy”—as Baron Lister recalled²¹—whereas these same practitioners adopted it as an indispensable instrument of modern medicine by the 1890s. To understand the great transmutation of the microscope in the diagnosis and study of cancer requires a knowledge of these technological and cultural changes.

The Lens

A lens, the principal element of the microscope, is a ground or naturally formed piece of glass or other transparent material with its two opposite surfaces either curved or straight.²² The power of the magnifying lens rests in the ability of transparent materials of varying densities to bend light differentially. This process is called refraction. Optics (derived from the Greek word ‘to see’) is the science of that portion of the electromagnetic spectrum visible to the unaided eye. Refraction magnifies (or minifies) objects. A microscope may have one lens (a ‘simple’ microscope) or many (a ‘compound’ microscope). Today, unlike the seventeenth century, single lenses are often simply called magnifiers. The term ‘microscope’—usually understood to be a compound microscope—is usually reserved for a series of lenses that transmit lit images through otherwise dark tubes. The microscope, then, is the conceptual product of the knowledge of optics and the properties of refractive lenses.

The key element in the first microscope was the discovery of glass with acceptable refractivity. No one knows when the first lens was found or invented. Archeologists unearthed

²¹Joseph Baron Lister, *The Collected Papers of Joseph, Baron Lister*, 2 vols., vol. 2 (Oxford: Clarendon Press, 1909; reprint, 1979), 515.

²²The word ‘lens’ is derived from the Latin for ‘lentil,’ a small seed with a biconvex shape.

evidence of glass manufacturing as early as the third millennium BCE.²³ They have also uncovered crystal and glass that have the ability to magnify images at the eight-century (BCE) palace of Nimrud in Assyria,²⁴ but their possible use to enlarge the appearance of objects is unconfirmed. There is no evidence that they were employed to examine the human body or tumors.

As with so many other discoveries, the magnifying lens evolved through the principle that “necessity is the mother of invention.” The first extant record of the use of a magnifying lens (but not to increase image size) is found in Aristophanes’ *The Clouds* (423 BCE). Therein the Greek playwright of wit and wisdom wrote of “burning glasses”—lenses that concentrated light on a single area to start a fire. It is likely, therefore, that the Ancients noted the ability of glass to concentrate light into heat and, through extension, magnify small into large. Indeed, the Sicilian polis of Syracuse deployed such lenses to burn the attacking Roman fleet in 250 BCE.²⁵ Seneca, Roman statesman, Stoic philosopher, and—to his great misfortune—tutor to Nero, writing in *Questiones Naturales* during the first century CE, left the first explicit record of the magnification of objects by a lens. He noted that globules of transparent water, serving as tiny convex lenses (characterized by an outward bulge of both sides of the lens), enlarged objects seen through them.²⁶ Thus, the cradle of microscopy lay in war and observation.

²³Corinne Jacker, *Window on the Unknown: A History of the Microscope* (New York: Charles Scribner's Sons, 1966), 171.

²⁴J. H. Wilson, "The History of the Microscope," *International Journal of Microscopy and Natural Science* Third ser., vol. 1 (Old ser. vol. 10) (1891): 169.

²⁵Ibid.

²⁶Ibid., 170.

The so-called Dark Ages, so crucial for the development of post-Roman culture in the West, shed no known light in Christian Europe on microscopy.²⁷ Muslim science, however, continued to explore the science of optics. In 1039, Abu'Ali al-Hasan (Alhazen) wrote *Kitab al-Manazir*, a seminal treatise on optics.²⁸ Therein he discoursed on the optics of refraction. Roger Bacon, the English friar-philosopher who argued that Christianity should embrace science, included a tract on optical studies in his *Opus Majus* (1268). Adhering to the empirical tradition of medieval Scholastic Aristotelianism, Witelo Ciolek of Poland translated Alhazen's findings into Latin less than a decade later.

The initial application of such studies, however, was not the microscope. Around 1290, Salvino D'Armato degli Armati invented spectacles.²⁹ Bacon had described aids to vision earlier, but Armati is given credit for the creation that Benjamin Franklin would improve almost half a millennium later. Like the microscope, "eyeglasses,"³⁰ as we now call them, refract incoming light in series with the lens of the human eye so as to bring it to convergence on the retina. In consequence, the visual cortex at the posterior aspect of the brain receives a neurologic transmission of a clear, sharp image. The mental perception is that the cerebral representation of the exterior image is 'focused.'

Spectacles and the microscope are conceptually and lineally related. They both depend upon precision lens grinding to transmit an image with minimal distortion. Spectacles do not

²⁷Nevertheless, the "Dark Ages" were anything but intellectually dark. I use the term because most late nineteenth-century writers used it. A more appropriate description would be the "Early Middle Ages," encompassing approximately the sixth through tenth centuries.

²⁸Wilson, "The History of the Microscope," 170.

²⁹Jacker, *History of the Microscope*, 171.

³⁰Note the subtle change in language from spectacles—instruments of seeing—to eyeglasses—aids to the eye. During the Renaissance, agency shifted from the tool to the sensory organ, a transformation toward Man that emphasized the vision rather than the tool that improved it.

significantly alter the image size. Microscopes (and telescopes) do. By the middle of the fifteenth century, single-lens magnifiers were in use.³¹ In the sixteenth century, Daniello Barbaro (1568) and Giovanni Battista della Porta (1589) magnified images visible to the eye with single convex lenses in a dark chamber.³²

An ideational leap in optics occurred toward the end of the fifteenth century. Rather than enlarge objects normally visible to the naked eye to unnaturally large proportions (as in a *camera obscura* with a convex lens), natural philosophers used such lenses to make the invisible microscopic world visible to the natural eye. The reification of this conceptual change was the microscope. Three hundred years after the initial production of spectacles, the first lens pairing that could reasonably be called a compound microscope was constructed in the lens-grinding capitol of Europe—Holland. Around 1590, in the small town of Middelburg (in southwest Netherlands today), three spectacle makers magnified objects by pairing two convex lenses in series in a tube.³³ Hans Janssen, his son Zacharias, and Hans Lippershey produced this first compound microscope.³⁴ Galileo Galilei, who used both microscopes and telescopes in the first decade of the seventeenth century, also attributed the creation of the original multi-lens microscope to the Dutch.³⁵ Not to be outdone, however, he built his own compound microscope

³¹John Walton, Paul B. Beeson, and Ronald Bodley Scott, eds., *The Oxford Companion to Medicine*, 2 vols., vol. 1 (Oxford: Oxford University Press, 1986; reprint, Gryphon Editions, Inc., 1988), 787.

³²Jacker, *History of the Microscope*, 172.

³³E. M. Nelson, "Historic Microscopy," *Journal of the Quekett Microscopical Club Ser. 2*, vol. 2 (1885): 222.

³⁴In 1880, Joseph Janvier Woodward wrote that Lippershey invented the first microscope in 1609. See J. J. Woodward, "Riddell's Binocular Microscopes: An Historical Notice," *The American Monthly Microscopical Journal* I, no. 12 (1880): 230. Most scholars today favor the earlier date, as per S. Bradbury, *The Evolution of the Microscope* (Oxford: Pergamon Press, 1967), 21, Jacker, *History of the Microscope*, 172.

³⁵Wilson, "The History of the Microscope," 170. Interestingly, Galileo, who accepted credit for the idea of the telescope that he did not conceive, made no such claim for the microscope.

in 1611.³⁶ True to the early scientific interest of his time in the natural world, the object of his microscopic studies was the insect, not human anatomy or disease.³⁷

Precocious Newborn: Seventeenth-Century Microscopy

Microscopy has had two periods of brilliant achievement in the course of its history: the seventeenth century and the latter half of the nineteenth century.

—E. Nordenskjold (1928)³⁸

The seventeenth century was a time of vibrant theoretical and practical growth in the microscopy of nature, but not in cancer microscopy. The focus of the microscope aimed at the natural world. The arena of disease—an unnatural and unbalanced phenomenon to the physicians of the era—lay outside the sphere of microscopical attraction. The French rationalist philosopher, René Descartes, applied his genius in analytic geometry to optics. In the process, he added to the theoretical underpinnings of optics through his belief in mind-body dualism and mathematics, but others—more practical than theoretical—guided the microscope toward the study of life.³⁹

³⁶The microscope and the telescope are both grounded in the physics of refraction. Thus they are more similar than at first meets the eye. Galileo's account of the construction of his first telescope, about a year before he produced his first microscope, is instructive for insight into the fabrication of both instruments. After learning that a "Dutchman" (Hans Lippershey) had built a telescope (thus Galileo, in his own writings, confirmed that he *did not* invent the telescope), Galileo "determined...to give myself up first to inquire into the principle of the telescope, and then to consider the means by which I might compass the invention of a similar instrument, which after a little while I succeeded in doing, through deep study of the theory of refraction; and I prepared a tube, at first of lead, in the ends of which I fitted two glass lenses, both plane on one side, but on the other side one spherically convex and the other concave. Then, bringing my eye to the concave lens, I saw objects satisfactorily large and near, for they appeared one third of the distance off and nine times larger than when they are seen with the natural eye alone." Quotation from Forest Ray Moulton and Justus J. Schifferes, eds., *The Autobiography of Science*, Second edition, revised and enlarged ed. (Garden City, NY: Doubleday & Company, Inc., 1960), 67.

³⁷Walton, Beeson, and Scott, eds., *Oxford Companion to Medicine*, 787.

³⁸Quotation from Freda Gray and Peter Gray, "History of Microtechnique and Microtomy," in *The Encyclopedia of Microscopy and Microtechnique*, ed. Peter Gray (New York: Van Nostrand Reinhold Company, 1973), 260. The Grays took the quotation from E. Nordenskjold, *The History of Biology* (New York: Tudor, 1928).

³⁹In 1637, Descartes published the first line drawing of the optical physics of a simple convex lens. Bradbury, *Evolution of the Microscope*, 19.

By the help of Microscopes, there is nothing so small, as to escape our inquiry;
hence there is a new visible World discovered to the understanding.

-Robert Hooke, *Micrographia* (1665)

The great pentumvirate of early microscopists—Marcello Malpighi, Robert Hooke, Nehemiah Grew, Jan Swammerdam, and Anton von Leeuwenhoek—opened a new window onto the world of microscopic images of plants and animals to the delight of the invigorated minds of the Scientific Revolution.⁴⁰ Nevertheless, physicians at the time continued to diagnose and treat cancers as they had for millennia—through sight, feel, and, sometimes, smell. Unfortunately, these giants of early microscopy left but faint footsteps for the generations of scientists and

⁴⁰Marcello Malpighi (1628-1694), the father of microscopic anatomy, worked with a simple (single-lens) microscope. The “fantastic red network” he described in lung tissue he described in *De Pulmonibus* (1661) shattered the prevalent notion that blood poured from arteries into open spaces before returning to the heart along the venous system. For more detail, see Catherine Wilson, *The Invisible World: Early Modern Philosophy and the Invention of the Microscope*, ed. M. A. Stewart and David Fate Norton, *Studies in Intellectual History and the History of Philosophy* (Princeton: Princeton University Press, 1995; reprint, 1997), 67. Thus, Malpighi’s discovery of the capillary circulation closed William Harvey’s loop of internal blood circulation (as set forth by him in *Exercitatio anatomica du motu cordis et circulatione sanguinis in animalibus*, known concisely as *Du Motu Cordis*, and published 1628) and provided additional proof for the value of microscopy in the natural sciences.

Robert Hooke (1625-1703), whose inventive genius drove him to ideas of steam engines and astrophysics long before their times, used the term ‘cell’ to describe the “great many little Boxes” he observed with his microscope in a slice of cork. See Robert Hooke, *Micrographia: Or Some Physiological Descriptions of Minute Bodie Made by Magnifying Glasses with Observations and Inquiries Thereupon* (London: Jo. Martyn and Ja. Allestry, 1665; reprint, The Classics of Medicine Library, 1996), 113. Also note his remarkable drawing opposite page 115.

Nehemiah Grew (1641-1712), an English botanist, extended Hooke’s concept of ‘little Boxes’ from lifeless cork to living plants in his 1672 publication, *Anatomy of Vegetables Begun*.

Jan Swammerdam (1637-1680) used his Dutch lens-grinding and microscope-manufacturing skills to become the first to describe red blood cells in 1658. He was twenty years old at the time. Ironically, his masterpiece, *Bybel der Natuure (The Bible of Nature)* was not published until 1737-1738, decades after his untimely death.

Antoni van Leeuwenhoek (1632-1723) was a cloth maker from Delft, Holland who ground his own lenses. He was the most famous of the pentumvirate from the perspective of microscopy. Leeuwenhoek augmented studies of the microscopists before him and visualized many of the tiny creatures (“animalcules”) of nature—bacteria, amoebae, spermatozoa—for the first time. (Henry E. Sigerist, “The Great Doctors: A Biographical History of Medicine,” (1933; reprint, 1975), 350.) Although Leeuwenhoek never published a book on the results of his observations, his correspondence (especially to the Royal Society of England) documents the astounding character of his discoveries. (Steven I. Hajdu, “Cytology from Antiquity to Papanicolau,” *Acta Cytologica* 21, no. 5 (1977): 688.) Amazingly, Leeuwenhoek’s method was to manufacture one (simple) microscope per specimen. Many of these optical marvels magnified the object up to 300X, a remarkable power of magnification for a simple lens system. Many of these microscope-specimen combinations still exist. I had the good fortune to ogle one (owned by Bill Gates of Microsoft) at the American Museum of Natural History.

For a beautifully written, perceptive analysis of the microscope in the context of the seventeenth century, see Wilson, *Invisible World*..

medical men who followed them. By 1692, Hooke bemoaned the fact that “Mr. Leeuwenhoek seems to be the principal Person left that cultivates those (microscopic) Enquiries” and offered his own explanation for the decline in interest in the microscope. It “is not for Want of considerable materials to be discovered,” he suggested, “but for Want of the inquisitive Genius of the Present Age.”⁴¹

Modern writers offer different perspectives for the apparent dearth of microscopical investigations from the late seventeenth until the nineteenth century. In 1961, David Wolfe speculated that the “intellectual resistance” of influential English empiricists like Thomas Sydenham and John Locke thwarted a budding interest in natural and medical microscopy.⁴² In 1978, Stanley Joel Reiser, reviewing Wolfe’s article in his own text on medicine and technology, added that the British empiricists saw no pragmatic connection between the microscopic image and the diagnostic and therapeutic care of the patient.⁴³ Perhaps the images themselves disarmed and dissuaded.⁴⁴ Perhaps the world of medicine was ill-prepared for visions and insights of such a radical nature. That which is not comprehensible is easier to avoid than analyze.⁴⁵

As the leading lights of medicine tackled questions of anatomy and nosology from the sixteenth century on, microscopists began the long process of displacing received wisdom with notions of science: valorizing observation and experience in the present over the authority of the

⁴¹Quoted by Bradbury, *Evolution of the Microscope*, 77.

⁴²David E. Wolfe, "Sydenham and Locke on the Limits of Anatomy," *Bulletin of the History of Medicine* 35, no. 3 (1961): 211. Quotation from Wolfe, "Sydenham and Locke on Anatomy," 193.

⁴³Reiser, *Medicine and Technology*, 73.

⁴⁴See the section on “Aberrations” below.

⁴⁵In addition, future historical research may discover that the “curious decline of significant microscopic inquiry during the eighteenth century (that) has been noted repeatedly by historians of medicine and biology” simply reflects a gap in present knowledge. Perhaps the ‘dark ages’ were not so dark after all—as has been revealed in other fields of history.

past; inductive over deductive reasoning; and the seemingly unconnected discoveries of the new natural “science” against the age-old explanations of syncretic theology. Only slowly from the seventeenth to the nineteenth century did physicians adopt these revolutionary tenets. The seductive theoretical framework that undergird the microscope from the time of its earliest imagery initially affected medicine and cancer much less than the blurred visions that dissuaded physicians from its application to clinical medicine.

During the eighteenth century, the microscope was as much vilified for its failings as it was beatified for the insight it proffered that there was much more to the world than was visible to the naked eye. As anatomists and physiologists of the era disdained the microscope for its limitations,⁴⁶ others sought to improve its optical systems and microtechnique (the preparation of the object for examination by the microscopist). Problems predominated.

Problems with Early Microscopes⁴⁷

The microscope did not spring fully formed like Athena from the forehead of Zeus. The multi-lens compound microscope, whose nature changed most over time, projected images in the seventeenth and eighteenth centuries that were blurry, especially around the periphery, and included a kaleidoscope of changing shapes and colors. Such visual artifacts, which transformed

⁴⁶See Brian Bracegirdle, "J. J. Lister and the Establishment of Histology," *Medical History* 21 (1977): 187, L. J. Rather, Patricia Rather, and John B. Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, trans. L. J. Rather (Canton, MA: Science History Publications, 1986), 7.

⁴⁷I define “early microscopes” as those manufactured before the 1820s, when microscopists corrected many of the optical aberrations. Thus early microscopes are also “uncorrected” (to use an anachronistic but easy-to-understand term). Early, uncorrected microscopes include those manufactured in the sixteenth, seventeenth, eighteenth, and early nineteenth centuries. Many survive in the United States, England, and on the Continent. See Major General Joe M. Blumberg, Captain Bruce H. Smith, and Colonel Claude K. Leeper, *The Billings Microscope Collection of the Medical Museum, Armed Forces Institute of Pathology*, Copy #548/1000 ed. (Washington, D. C.: The American Registry of Pathology, 1967), Gerard L'E Turner, *The Great Age of the Microscope: The Collection of the Royal Microscopical Society through 150 Years* (Bristol: Adam Hilger, 1989).

the image with the slightest movement of the microscope stage, slide, or focus wheel, made uniform interpretation of tumors and other specimens virtually impossible.⁴⁸

The single-lens simple microscope, in contradistinction to the compound microscope, did not project such blurs, comet-tailed “globules,” or shifting colors. However, its power of magnification was limited compared to the multi-lens microscope. Leeuwenhoek may have constructed single-lens microscopes in the seventeenth and early eighteenth centuries that approached the image-enlarging abilities of compound scopes, but the development of medical microscopy in the late nineteenth century depended upon the perfection of an instrument that could visualize to the level of the cell. Only the compound microscope could consistently achieve that.⁴⁹

Aberrations

In the language of optics, microscopists found that the compound microscope image was distorted by “aberrations.” These misleading projections of the slide specimen included spherical aberration, coma, and chromatic aberration. Hardly anachronistic fabrications, naturalists first recognized these deceptive distractions at the dawn of microscopy in the

⁴⁸In 1973, Majno and Joris demonstrated some of these artifacts when they used an eighteenth-century Culpeper-type microscope to examine “known” inflamed tissue (as diagnosed by contemporary standards with modern instruments) that was “fresh, unfixated and unstained.” See Guido Majno and Isabelle Joris, “The Microscope in the History of Pathology: With a Note on the Pathology of Fat Cells,” *Virchows Arch. Abt. A Path. Anat.* 360, no. 4 (1973): 273, 80. Such an analysis is, of course, fallacious because it applies presentist knowledge and ideas to a situation that microscopists of more than two centuries ago could not have imagined. The image remains the same; the interpretation differs. On the other hand, the view through what the authors termed the “ancient microscope” did yield an image of what was seen by those early microscopists that could never be adequately described in words. Perhaps the use of “sliders” from those early years in the history of microscopy reviewed by twentieth-century authors offered a vision more akin to that seen by eighteenth-century microscopists.

⁴⁹A single-lens microscope may permit magnification into the low hundred Xs (e.g., 100X-200X), but the smaller and smaller lenses necessary to achieve such high curvatures refract little light to illuminate the object for the eye of the spectator. Leeuwenhoek’s lens-grinding abilities were exceptional. As Harold Malkin noted, “Only Antony van Leeuwenhoek (1632-1728), who was a man of infinite patience and was able to grind lenses as small as a grain of sand, was successful in making major observations” with these exquisite, simple lenses. See Harold M. Malkin, *Out of the Mist: The Foundation of Modern Pathology and Medicine During the Nineteenth Century* (Berkeley: Vesalius Books, 1993; reprint, 1995), 129-30. Nevertheless, Leeuwenhoek’s simple microscopes, which magnified up to 300X, still fell short of the magnification level of most nineteenth-century compound microscopes.

sixteenth century.⁵⁰ Their importance to the history of microscopy as an explanation for the belated acceptance of the microscope in American medicine fully three centuries after its invention cannot be overstated. According to Gerard L'E. Turner, a leading scholar on the history of microscopes and microscopy, the aberrations were so crucial that "the history of the development of the microscope is of attempts to banish these defects."⁵¹

Spherical aberration is a consequence of the nature of light and the physics of the lens. When light from a single source, such as a medical specimen on a slide, hits a non-planar (curved) lens, more refraction occurs at the ends of the lens (top and bottom) than through the center. Thus the light refracted from the periphery of the lens will converge at a focal point proximal to (in front of) that of a centrally-transmitted light. The second lens of the compound microscope amplifies the distortion of the image of the first lens. The human mind perceives different focal points as a blur, especially around the periphery of the image where the unrefracted central light is absent.

Single-lens microscopes essentially eliminate this aberration, but their powers of magnification are too weak to clearly visualize the pathological foundation of cancer medicine—the cancer cell.⁵² Thus simple microscopes predominated until Dr. Smith of Cambridge and many others solved the problem of spherical aberration in the eighteenth and early nineteenth

⁵⁰Franciscus Maurolycus first noted spherical aberration in 1575. Jacker, *History of the Microscope*, 50.

⁵¹Robert Bud and Deborah Jean Warner, eds., *Instruments of Science: An Historical Encyclopedia*, vol. 2, *Garland Encyclopedias in the History of Science* (New York: Garland Publishing, Inc., 1998), 387. Aberrations are not defects in lenses. They are consequences of the physics of the lens, as described below.

⁵²Robert Hooke, the first to describe the 'cell,' used a compound microscope to limn the cork latticework. Hooke, *Micrographia*, 112-13. This is not to say that Hooke understood the concept of the cell—only its external architecture. The modern idea of the cell as a unit of life stems from the early nineteenth century. See Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 4.

centuries by using the second lens of the compound microscope to correct the aberration produced by the first lens.⁵³

Coma is a consequence of spherical aberration.⁵⁴ The magnification of a point by a simple microscope produces a clean, unblurred image. The same object illuminated through an uncorrected compound microscope yields a smeared image with a central concentration and a “tail” that trails off away from the center—similar to a comet. Hence early microscopists spied globules, indistinct smears, and hairy comet tails⁵⁵ where single-lens microscopes transmitted distinct dots of light and thus clearer images.

Chromatic aberration represented a more complex problem that turned out to be more difficult to rectify than the other two aberrations. It stems from the fact that white light and sunlight (which is really white—not yellow—light) are composites of radiations of many wavelengths.⁵⁶ Scientists call these energy emissions the visible portion of the electromagnetic spectrum. Others call them colors. In 1665, when Isaac Newton (at the age of 23) retreated to the family farm at Woolsthorpe to escape plague-shuttered Cambridge, he passed a solitary beam of white light through a prism in an otherwise dark room. The solid glass triangle dispersed the single light into its component colors—from red to violet.⁵⁷

The lenses of most seventeenth- and eighteenth-century compound microscopes likewise created a dazzling display of colored fringes around the magnified image as though split by a

⁵³Nelson, "Historic Microscopy," 224.

⁵⁴Bracegirdle, "J. J. Lister," 188.

⁵⁵Coma and comet are derived from the Greek word ‘coma,’ meaning ‘hair.’ To visualize this aberration, imagine strands of long hair blown by the wind.

⁵⁶Bracegirdle, "J. J. Lister," 189, Jacker, *History of the Microscope*, 51.

⁵⁷The story of Isaac Newton and the prismatic dispersion of white light that explained chromatic aberration is drawn with grace and detail by Gale E. Christianson in Chapter 4, “A Movable Feast,” *In the Presence of the Creator: Isaac Newton and His Times* (New York: The Free Press, 1984; reprint, the Easton Press, 1989).

prism. Worse, the colors moved as the focus shifted. The higher the magnification, the more pronounced the chromatic aberration. The first achromatic lens system may have been constructed by Chester Moor Hall in 1733,⁵⁸ but it was not until nearly a century later that innovative combinations of lenses eliminated the distractive kaleidoscope. In the decades between, the interpretation of compound microscope images of tumors and other human pathologies remained laden with uncertainty, confusion, and error.

Aberrational Consequences: The Father of Histology *sans* Microscope

The three deceptive aberrations discouraged would-be medical microscopists in many fields, foremost among them pathological anatomists. Some, like Marie-François-Xavier Bichat (1771-1802), often considered the “father of histology,” gave up the instrument entirely.⁵⁹ “Our microscopic instruments,” he wrote in 1800, “(are) a species of agents from which physiology and anatomy, do not seem to me, besides ever to have derived any great assistance, because when we view an object obscurely, *every one sees in his own way*, and according as he is affected.”⁶⁰ Another nineteenth-century physician wryly commented that the accuracy of the microscopic diagnosis of cancer depended upon the “cerebral tissue *behind* the visual organ of

⁵⁸Jacker, *History of the Microscope*, 173.

⁵⁹Dr. Leland J. Rather recorded that Bichat “made no use of the microscope” in his classical work, *General Anatomy Applied to Physiology and Medicine (Anatomie générale appliquée à la physiologie et à la médecine*, 1801). See L. J. Rather, *The Genesis of Cancer: A Study in the History of Ideas* (Baltimore: The Johns Hopkins University Press, 1978), 55.

⁶⁰My *italics*. Noted by Ibid. The translation used here, slightly different from that of Dr. Rather, is taken from the 1813 English version of Bichat’s *Traité des membranes* (1800). See Xav. Bichat, *A Treatise on the Membranes in General, and on Different Membranes in Particular*, trans. John G. Coffin, A New ed. (Boston: Cummings and Hilliard, 1802; reprint, The Classics of Medicine Library, 1987), 42. Bichat provided numerous examples of contradictory results through deceptive microscopic images. See, for example, the experiments of Leiberkuhn, Hunter, Cruikshank, and Hewson on page 41.

Ironically, historians have labeled Bichat the “father of microscopic anatomy” and the “father of histology.” As Rather correctly pointed out, Bichat was no such thing. See Rather, *The Genesis of Cancer*, 55. As noted above, Marcello Malpighi, who saw red blood cells through his microscope in the seventeenth century, is a more plausible candidate for those appellations.

the observer.”⁶¹ Some, he believed, never got it right. Henri Milne-Edwards was so convinced of the veracity of what he saw through the microscope in 1823 that he concluded the structure of all tissue was globular.⁶² Optical distortions enhanced viewer bias, giving full rein to fantasy. Thus Bichat and other researchers ceased microscopical investigations in the early nineteenth century in frustration. The faulty images cast doubts on the fidelity of the magnified objects to their underlying nature in the minds of microscopists and those interpreting their findings.⁶³

The optical aberrations of early microscopes contributed mightily to its disavowal by medical practitioners before the late nineteenth century. But optical distortions were not the only problems with early microscopes. Practical limitations abounded. Many were massive, intricate, and expensive. In an oft-quoted address to the Boston Microscopical Society in 1877, Oliver Wendell Holmes quipped that even early nineteenth century microscopes were “nearly as big as a funeral casket, and it almost requires an undertaker to lay it out after one has done with it.”⁶⁴ Despite their bulk, however, they were unstable. In bustling nineteenth-century cities like London and New York, “where no throughfare is exempt from the rattle of passing vehicles” and “vibrations were even imparted by people walking about in the room,” even slight movements of

⁶¹Edwd. M. Schaeffer, "On the Microscopical Diagnosis of Cancer," *Journal of the American Medical Association* 12, no. 12 (1889): 444. Italics in the original.

⁶²Bracegirdle, "J. J. Lister," 187. The globular appearance was an aberrational distortion.

⁶³In retrospect, Stanley Joel Reiser noted that “a current evaluation of the optical performance of seven compound microscopes built between 1690 and 1790 reveals an average image distortion of 19%, while a microscope designed in 1838 which used (lenses that minimized spherical and chromatic aberration) had a distortion of only 3%.” Reiser, *Medicine and Technology*, 76.

⁶⁴Oliver Wendell Holmes, "An Address Delivered at the Annual Meeting of the Boston Microscopical Society," *Boston Medical and Surgical Journal* 96, no. 21 (1877): 604.

the microscope caused shifting images.⁶⁵ At high magnification even minimally shifted images felt like the effects of an earthquake thrown across the field of vision.⁶⁶

Nor were microscopes easy to acquire. As late as the 1850s, the instruments and their necessary accessories cost US\$360, a small fortune at a time when the average workman earned less than a dollar a day.⁶⁷ Only well-endowed schools and the wealthy could afford such a device. Harvard acquired the first microscope in British America in 1732; Yale the second in 1734; and Brown the third in 1769.⁶⁸ Not surprisingly, high prices fostered minimal demand and slight supply. In 1850, only one American company manufactured microscopes and it produced only a few dozen annually for the entire United States.⁶⁹ Hence individually-owned microscopes were rare well into the second half of the nineteenth century.⁷⁰ All in all, the recognized shortcomings of the microscope severely reduced its acceptance by mainstream medicine.

Problems with Early Microscopical Preparations

⁶⁵Turner, *Great Age of the Microscope*, 11. Turner cited the first quotation from Andrew Ross, "Microscope," *The Penny Cyclopaedia of the Society for the Diffusion of Useful Knowledge* xv (London, 1839) 177-88.

⁶⁶Ibid., 10.

⁶⁷Donald L. Padgitt, *A Short History of the Early American Microscopes* (London: Microscope Publications Ltd., 1975), 17.

⁶⁸Ibid., 3. To avoid the three Gorgons of aberration, these were simple microscopes.

Consonant with the general theme of this chapter that the general acceptance of the microscope for medical diagnostic purposes was a process that stumbled along for centuries until it reached its culmination in the late 19th century, Harvard Medical School did not initiate microscopic instruction until 1855. Dr. Oliver Wendell Holmes was the first instructor. See Warner, "Antebellum Medical Microscopy," 374. The first mention of a microscope in the HMS catalogue did not occur until 1869. See Abraham Flexner, *Medical Education in the United States and Canada: A Report to the Carnegie Foundation for the Advancement of Teaching* (Boston: The Merrymount Press, 1910; reprint, 1990), 8-9.

⁶⁹Turner, *Great Age of the Microscope*, 13.

⁷⁰Harold M. Malkin, "History of Pathology: Comparison of the Use of the Microscope in Pathology in Germany and the United States During the Nineteenth Century," *Annals of Diagnostic Pathology* 2, no. 1 (1998): 84.

The problems with early microscopes do not entirely explain the calculated reluctance of medical practitioners to use the instrument for medical purposes prior to the last years of the nineteenth century. There was also the matter of specimen preparation—otherwise known as microtechnique.⁷¹

Any specimen obtained for microscopic analysis—a flea, a drop of water, a tumor—must be readied for examination. Intact samples cannot simply be placed under the lens of the microscope because they are generally too thick, difficult to illuminate (since what is seen depends upon the light that reaches the eye after it passes through the object), and degenerate rapidly as a result of atmospheric processes (e.g., evaporation) and saprophytes. Thus a specimen required adequate preparation for advantageous viewing.

In contrast to many modern preparative techniques that are automated and—often—hardly given a second thought, specimen preparation before the late nineteenth century was laborious and inconsistent. A series of steps evolved over two centuries or more after the advent of the first microscopes to improve preservation of the specimen, visualization, and uniformity. These processes are called sectioning, fixation, embedding, mounting, and staining. The development of each signaled a problem in specimen preparation that had to be overcome with improved microtechnique.

Specimen Preservation

The seventeenth-century giants of microscopy collected diverse specimens from nature for microscopic viewing. They faced many of the same difficulties with specimen preservation and preparation that plagued their descendants two centuries later. In general, early

⁷¹Comprehensive histories of microtechnique may be found in Brian Bracegirdle, *A History of Microtechnique* (Ithaca: Cornell University Press, 1978), George Clark and Frederick H. Kasten, *History of Staining*, Third ed. (Baltimore: Williams & Wilkins, 1983). Gray provides a brief but engaging summary of the same. See Gray and Gray, "History of Microtechnique and Microtomy."

microscopists did little to emphasize the elements of the specimen other than fixing it to a relatively stationary device. Robert Hooke, in preparation for the examination of the oak bark that would forever link his name to the discovery of the cell, took a “good clear piece of Cork, and with a Pen-knife sharpen’d as keen as a Razor, I cut a piece of it off, and thereby left the surface of it exceeding smooth.”⁷² The basics of early microtechnique were there—a good specimen sectioned to a thin slice. Antoni van Leeuwenhoek, who was less descriptive of his methodology than Hooke,⁷³ mounted his solid specimens (hair, teeth, muscle) to his lens apparatus on the point of a pin with glue. He smeared liquid specimens like spermatozoa and blood on thin glass that was subsequently secured to the needle-like spit. Indeed, he was probably the first to spread a liquid specimen on a glass slide, a common practice to this day.⁷⁴

Knife slices and glue did more to exacerbate problems of sectioning and fixation than solve them. The ideas were clear—specimens must be thinly cut so as to allow light to pass through them to reach the eye of the microscopist; they must be treated so as to minimize change over time—but the methods were faulty. Cutting with a hand-held blade created sections of variable thickness. Glue cracked and discolored after short periods. Good quality “sliders,” as early multiple-specimen mounts were called, commanded respect, attractive prices, and often accompanied the purchase of a microscope.⁷⁵

In addition, contrasting elements of the specimen were difficult to discern. Even red blood cells, one of the earliest components of the human body to be seen through the

⁷²Hooke, *Micrographia*, 112.

⁷³Bracegirdle claimed that Leeuwenhoek was “secretive” about his specimen preparation. See Bracegirdle, *A History of Microtechnique*, 9.

⁷⁴*Ibid.*

⁷⁵*Ibid.*, 18.

microscope, appeared quite pale and undifferentiated through early instruments.⁷⁶ Various attempts to add natural stains and artificial chemicals to the object foundered in a sea of bewildering lights, darks, and colors.

One of the more frustrating problems was the durable preservation of the specimen. Organic material naturally dried, cracked, and decayed within days of accession. Early microscopists used glue, alcohol, and ice to allay the inevitable deterioration by physical forces, but none were satisfactory. The preservatives merely evaporated. The solution lay in the form of a material that both covered the specimen and transmitted light. Nevertheless, the seemingly lowly cover slip—a thin transparent material barely an inch long that protects the prepared specimen on the glass slide—was not described until late in the eighteenth century. Even then, it did not become a staple of microtechnique until decades later.⁷⁷ Thus both the microscope and its associated processes failed to fulfill their intended purpose to transmit a clear, accurate image of the specimen.

Problems with Early Microscopy

More than technical deficiencies hampered the potential utility of the microscope to medicine. Improvements in optics and microtechnique found limited dissemination prior to the nineteenth century. Malpighi, Hooke, Grew, and Swammerdam publicized their optical systems and preparative techniques in their treatises, but Leeuwenhoek and others did not. The Royal

⁷⁶Thomas Hodgkin and Joseph Jackson Lister, "Notice of Some Microscopic Observations of the Blood and Animal Tissues," *Philosophical Magazine* ns2 (1827). Lack of color and contrast probably contributed to the lively debate Thomas Hodgkin and Joseph Jackson Lister fostered when they (correctly) claimed that the (mature) human red blood cell did not have a nucleus. Most investigators at the time saw a nucleus. The Englishmen were vindicated, but not until fourteen years later. Bracegirdle, *A History of Microtechnique*, 309-10.

⁷⁷Jan Ingen-Housz first used a cover slip, also known as a cover glass, in 1789. He limned it clearly in his 1789 text, *Nouvelles experiences et observations sur divers objets de physique*, Paris: Barrois, vol. 2. For further information on the cover glass, see Hebbel E. Hoff, "Jan Ingen-Housz and the Cover-Slip," *Bulletin of the History of Medicine* 36 (1962). Also cited in Bracegirdle, *A History of Microtechnique*, 23, 113. The cover slip was "reinvented" as a "revolutionary material" by the Chance Brothers of Birmingham, England in 1839. Gray and Gray, "History of Microtechnique and Microtomy," 260.

Society of London and the Paris Academy published the first scientific and medical journals in the seventeenth century, but periodicals expressly devoted to microscopy did not appear until the microscopical societies that founded and maintained them were established in the nineteenth century. The Microscopical Society of London came together in 1839.⁷⁸ The *Journal of the Royal Microscopical Society*, one of the best sources for studies on the history of the microscope and microscopy, commenced publication in 1840.⁷⁹ John Quekett, one of the most celebrated English microscopists of the nineteenth century,⁸⁰ printed *A practical treatise on the use of the microscope* in 1848. This work, published almost exactly two hundred and fifty years after the invention of the compound microscope, was the first major textual treatment of microtechnique.⁸¹

American interest in scientific microscopy during the nineteenth century lagged that of England and the Continent. Indeed, had United States medical graduates like Oliver Wendell Holmes not furthered their graduate education in the universities and clinics of Europe, the development of medical microscopy in America might have come even later than the closing years of the century. Into the 1870s and beyond, training in the use of the microscope and microtechnique in the colleges and medical schools of this country was rare. C. H. Stowell, who headed microscopy at the University of Michigan, boasted in 1883 with only a modicum of boosterism that his school had two microscopy courses (although only the more advanced dealt

⁷⁸Warner, "Popular Microscopy," 8.

⁷⁹Bracegirdle, *A History of Microtechnique*, 3-4. The *Journal of the Royal Microscopical Society* was originally a quarterly journal.

⁸⁰The Quekett Microscopical Club, which also published its own journal, was founded in honor of John Quekett.

⁸¹The full citation is John Quekett, *A practical treatise on the use of the microscope* (London: Bailliere, 1848).

with issues of slide preparation) and “offers far greater advantages, for general microscopical work, than any other institution of learning in this country.”⁸² A decade later, Jacob D. Cox, president of the American Microscopical Society, urged his constituents to advocate the teaching of microscopy at the University level so as to dispel “the doubt, the error, and the cost through which we ourselves have had to make our way.”⁸³ Education was the cornerstone of microscopy. In the United States, at least, that foundation had to wait until late in the nineteenth century.

At first little better than a mere toy, the delight of the dilettanti, kindling wonder and exciting curiosity....

-J. H. Wilson, 1891⁸⁴

Cultural inattention to the microscope as a tool of science supplemented the technical and educational deficiencies of microscopy for most of the nineteenth century.⁸⁵ Europeans and Americans considered the microscope a diversion on par with a parlor game. Beginning with the age of Enlightenment, well-heeled gentlemen (and sometimes ladies) would retire to the drawing room after sumptuous gatherings to spy the otherwise invisible, small world laid bare by the microscope. The return to nature fostered by the Romantic movement of the late eighteenth and early nineteenth centuries added impetus to the popular diversions occasioned by microscopy. What, after all, did the toy offer if not nature on a slide?

⁸²C. H. Stowell, "Microscopy in the University of Michigan," *The Microscope and Its Relation to Medicine and Pharmacy* 3, no. 2 (1883): 68.

⁸³Jacob D. Cox, "Address of the President: A Plea for Systematic Instruction in the Technique of the Microscope at the University," *Proceedings of the American Microscopical Society* 15 (1893): 16.

⁸⁴Wilson, "The History of the Microscope," 215.

⁸⁵Warner, "Popular Microscopy." is an excellent source on the microscope as an icon of popular rather than medical culture in the United States prior to the end of the nineteenth century. Nevertheless, the focus of much of his article is an analysis of the decline of public microscopy and the rise of the science-related microscopy.

Naturalists promulgated the value of microscopy for the study of biology, but the images and drawings of fleas and flies stimulated little interest among physicians. Indeed, as late as the 1882, after the advent of a number of American microscopical clubs and dedicated journals, cognescenti castigated physicians for their “lamentable ignorance concerning the microscope.”⁸⁶ Within a few years, as illustrated by comparison of the case studies of General Grant and President Cleveland, the practitioner’s attitude toward the microscope and its perceived value to the practice of medicine in general and cancer in particular underwent a radical change. The toy spurned by traditional medicine became the scientific instrument of modern cancer medicine. In 1894, James Reeves asserted in no uncertain terms that “microscopy is the key to open up the way to rational and successful treatment. It is the foundation of therapeutic deduction; and without its proper study and acquaintance, the Practice of Medicine and Surgery would be but little better than guesswork and a dangerous play with human life.”⁸⁷ The transition of the microscope from traditional to modern cancer—despite its long incubation period from a medical perspective—was swift and complete, but the roots of this revolutionary change ran deep.

Optical *perfectionnement*: Joseph Jackson Lister

Well into the late nineteenth century, physicians diagnosed cancer solely on the basis of clinical findings. Cancer researchers in Europe and then the United States, however, gained new insights into the structure and function of cancer following improvements to the optical system of the microscope that culminated in the 1820s. The betterment of the microscope lens system, the result of more than a century of intense efforts by microscopists of many countries, owes a debt in particular to one man who, as “an occasional object of (his) leisure,” combined “the zeal

⁸⁶“Physicians as microscopists,” *Am. Mon. microsc. J.*, 1882, 3, 136. Cited by Warner, “Popular Microscopy,” 19 Footnote 46.

⁸⁷James E. Reeves, *A Hand-Book of Medical Microscopy for Students and General Practitioners, Including Chapters on Bacteriology, Neoplasms, and Urinary Examinations* (Philadelphia: P. Blakiston, Son & Co., 1894), 19.

of the amateur with the skill of the superior artist”—Joseph Jackson Lister.⁸⁸ Nevertheless, Lister, like scientists and physicians through time, owed a great debt to those who preceded his success.

The problems of spherical aberration, coma, and chromatic aberration were sometimes circumvented through the inventive genius of Europeans in the eighteenth and early nineteenth centuries. The blurred, kaleidoscopic images of seventeenth-century compound microscopes became clear, delineated images at magnifications in excess of 200X, the level at which the aberrations began to dominate earlier uncorrected lens systems. Chester Hall and John Dolland of England noted in the middle of the eighteenth century that the right combination of different-shaped lenses could virtually purge the image of chromatic aberration.⁸⁹ François Beeldsnijder, with a long heritage of superior Dutch lens grinders behind him, used flint and crown glass lenses (lenses with very different refractive properties from common glass lenses) to construct the first achromatic microscope in 1791.⁹⁰ Although the instrument virtually eliminated color fringes, persistent spherical aberration limited higher magnifications. Indeed, despite the achromatic lens, the greater the magnification the more the spherical distortion.

The Napoleonic Wars temporarily halted further development of non-aberrational lens systems. Thereafter, a burst of industrial innovation followed the European peace of Metternich. The improvement of the microscope was part and parcel of this unroofed creativity. The Italian mathematician and botanist Giovanni Battista Amici made lenses of concave mirrors to avoid

⁸⁸Joseph Jackson Lister, "Xiii. On Some Properties in Achromatic Object-Glasses Applicable to the Improvement of the Microscope," *Philosophical Transactions of the Royal Society of London* 30, no. Part I. (1830): 187, 200.

⁸⁹Dolland constructed an achromatic lens system in 1758, but he incorporated it into the telescope—not the microscope. Jacker, *History of the Microscope*, 174.

⁹⁰Bracegirdle, "J. J. Lister," 188.

refractive errors, as Isaac Newton had suggested in the seventeenth century. Unfortunately, they were not practical.⁹¹

In the early 1820s, the problem of reducing or, preferably, eradicating spherical along with chromatic aberration was attacked on many geographical fronts. Amici continued his efforts in Modena. Joseph von Fraunhofer, physicist and optician, investigated glasses with different refractive indices in Munich. Nevertheless, it was M. Selligie of Paris who reaped the credit for the first combination of sequential achromatic lenses to reduce aberrations.⁹² An English contemporary credited him with taking the achromatic lenses to the next level in the construction of the first truly achromatic microscope.⁹³ Unhappily, the placement of the lenses, although they virtually eliminated chromatic error, still tended to aggravate spherical error. Vincent Chevalier, scion of a long line of distinguished instrument makers and manufacturer of microscopes prized to this day, noted the poor orientation of the lens that faced toward the object, reversed it, and found that he could reduce spherical aberration.⁹⁴ Chevalier called the product of his insight the *Microscope Achromatique Perfectionne*.⁹⁵

The greatest invention of the nineteenth century was the invention of the method of invention.

—Alfred North Whitehead⁹⁶

⁹¹Turner, *Great Age of the Microscope*, 8. Ironically, Isaac Newton believed that the eradication of chromatic aberration from refractive lenses was impossible. Hence his interest in concave reflective telescope mirrors that would not be subject to the aberrations of refractive lenses. He based this conclusion on calculations that others later found to be erroneous. See Andrew D. Booth, "Microscope History: The Aperture Question," *Journal of the Royal Microscopical Society* 83 (1964): 119.

⁹²John Jr. Mayall, "Cantor Lectures on the Microscope" (paper presented at the Cantor Lectures, London, 23, 30 November and 7, 14, 21 December 1885), 62.

⁹³Lister, "On Some Properties in Achromatic Object-Glasses," 188.

⁹⁴Nelson, "Historic Microscopy," 228.

⁹⁵H. R. Purtle, "History of the Microscope," in *The Encyclopedia of Microscopy and Microtechnique*, ed. Peter Gray (New York: Van Nostrand Reinhold Company, 1973), 256.

⁹⁶Alfred North Whitehead, *Science and the Modern World--Lowell Lectures, 1925* (New York: The Free Press, 1925; reprint, 1967), 96.

Despite international efforts to correct these long-known aberrations, the greatest *perfectionnement* of the microscope in the first half of the nineteenth century was actually achieved by a Quaker wine merchant who dabbled in the improvement of microscope lenses for—as noted above—his “leisure.” Joseph Jackson Lister, father of the knighted antiseptist, was a paragon of Whitehead’s epigraph. Methodically, he tested different combinations of lenses—convex, concave, planar—in an attempt to discover a lens system that would permanently eradicate all the aberrations of the compound microscope. In the process he converted a centuries-old empiricism seeking optimal lens combinations and placements into a theoretical paradigm that could be used to fashion microscopes that relayed undistorted images to the eye.

In 1825, Lister came upon a combination of three lenses that, in the opinion of another nineteenth-century Englishman, has “never been exceeded by any similar combination for accurate correction throughout the field.”⁹⁷ Lister discovered that the placement of three crown-flint planoconvex achromatic doublets (two lenses combined) at specific locations (aplanatic foci) along the barrel of the microscope virtually eliminated all major aberrations. His “Law of Aplanatic Foci,” described with historical detail and scientific prowess in his seminal article of 1830, “On some properties in achromatic object-glasses applicable to the improvement of the microscope,” established a process for the routine construction of microscopes with accurate magnifications to 300X and more⁹⁸—enough to see the fine details of tissues and their

⁹⁷The quotation is from Andrew Ross as cited by Nelson, “Historic Microscopy,” 228.

⁹⁸The pathologist Harold M. Malkin wrote that microscopes that followed Lister’s design “could separate points only one micron apart.” Malkin, *Out of the Mist*, 133. A micron is one millionth of a meter or one ten-thousandth of a centimeter.

components.⁹⁹ He also suggested a microscope with greater stability to reduce image movement, thus complementing his achievement of undistorted images at high magnifications.¹⁰⁰ This work, rewarded with fellowship in the Royal Society, has been eulogized by a twentieth-century medical historian as “the most important ever published on microscopy.”¹⁰¹

The Modern Microscope before the 1880s:

Scientists—Yea, Clinicians—Nay

During the early part of the 19th century, progress in histology and cytology occurred hand in hand with the availability of better achromatic microscopes.

-George Clark & Frederick H. Kasten¹⁰²

Lister’s optical theory and the microscope manufacturing process it set in motion began the modern age of the microscope—but not medical microscopy. Not until more than two generations later did American practitioners embrace microscopes that descended from Lister’s lenses and, in the process, herald the age of modern cancer. In the interim, medical scientists in Europe (and some in the United States) utilized the improved microscope to offer fresh concepts of disease mechanisms based upon the now-clearer optical imagery. In short, the Listerian microscope was a catalyst for novel thoughts on human science. New visions led to new insights, one of the greatest of which was direct support for cell theory and its impact on the making of modern cancer.

CELL THEORY

⁹⁹Lister, "On Some Properties in Achromatic Object-Glasses." Joseph Jackson Lister’s 1830 article is beautifully written in clear prose, but readers who desire a more modern explanation of the physics of his optical system—with excellent diagrams—should consult Bracegirdle, "J. J. Lister."

¹⁰⁰Turner, *Great Age of the Microscope*, 10.

¹⁰¹Roderick E. McGrew and with the collaboration of Margaret P. McGrew, "Microscopy: Microscope," in *Encyclopedia of Medical History* (New York: McGraw-Hill Book Company, 1985), 202.

¹⁰²Clark and Kasten, *History of Staining*, 201.

People have absolutely no conception of the progress made by the natural sciences in the last thirty years. For physiology the decisive factors have been, firstly the tremendous development of organic chemistry, and secondly, the microscope, which has been properly used only for the last twenty years....The main thing which has revolutionised the whole of physiology and for the first time made comparative physiology possible is the discovery of the cell—in plants by Schleiden and in animals by Schwann. Everything is a cell.

-Friedrich Engels to Karl Marx, July 14, 1858¹⁰³

The structural and functional idea of the cell was the theoretical foundation for the development of modern cancer. Cell theory, nurtured by the post-Listerian microscope, helped convert medicine from an empirical series of observations into a scientific investigation of human form and action. The physiological cell, as well as its pathological anomaly, fostered new methods of thinking about disease in general and cancer specifically. In addition, the theory of the cell emphasized a localistic view of disease, hastening the demise of constitutionalism and radically altering the practitioner's conception of cancer. Archaic methods for the inspection of the human body and its diseases tended to favor notions of constitutionalism; cell-based microscopy boosted ideas of localism. The microscope revealed, as in other aspects of life, that the devil was in the details.

Joseph Jackson Lister was the first to apply the fruits of his idle hours with microscope optics to the study of the body. In 1827, one year after James Smith constructed a microscope to Lister's specifications,¹⁰⁴ Lister and a young physician at Guy's Hospital, Thomas Hodgkin, published their observations on "blood and animal tissues."¹⁰⁵ Their findings on (unstained) muscle and, especially, red blood cells were considered fantastic. Received wisdom held that

¹⁰³*Marx-Engels Selected Correspondence*, tr. I. Lasker (Moscow: Progress Publishers, 1955; 3rd rev. ed., 1975), 101; and cited by Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*.

¹⁰⁴James Smith built a microscope to Lister's specifications in 1826. This instrument of beauty and precision, number 234/1949 of the Wellcome Institute for the History of Medicine microscope collection, is pictured in Plate I of Bracegirdle's article. Bracegirdle, "J. J. Lister." Plate following page 188.

¹⁰⁵Hodgkin and Lister, "Notice of Some Microscopic Observations of the Blood and Animal Tissues."

blood corpuscles—symbols of life and spirit from at least the days of the ancient Hebrews—had nuclei. Hodgkin and Lister claimed they did not.¹⁰⁶ The vehemence against their reputed discovery was such that opponents blamed Lister’s microscope for its inability to allow visualization of the red blood cell nucleus. Not until fourteen years later, in 1841, did medical consensus accept the idea of the enucleated mature red blood cell.¹⁰⁷ Hodgkin and Lister’s 1827 article, with its more accurate depiction of the microscopic anatomy of animal tissues, was a harbinger of the tensions and controversies that followed the introduction of the corrected light microscope.

Histology, the study of tissues under the microscope, properly began with the Hodgkin-Lister paper.¹⁰⁸ The Frenchman Bichat, who spent his short adult life studying anatomic tissues, eschewed the microscope. Nevertheless, his discoveries, rather than being hampered by his reluctance to use the microscope of his time, set the stage for the explosion in microscopic anatomy that followed the advent of the Listerian microscope.

In 1819, prior to the invention of the achromatic, aspherical microscope, the German August F. J. K. Mayer built upon Bichat’s foundational studies to coin the term ‘histology’ and to systematize the classification of tissues.¹⁰⁹ His pamphlet, circulated throughout Europe during the spirit of Metternichian rapprochement that followed the defeat of Napoleon I, especially

¹⁰⁶Early, progenitor forms of human red blood cells, which do not normally circulate in the bloodstream, do have nuclei. As noted, mature, circulating red corpuscles does not.

¹⁰⁷Bracegirdle, *A History of Microtechnique*, 309-10. The confirmatory paper, as cited by Bracegirdle, was E. H. Weber’s “Über menschliches Blut,” *Deutsch. Naturf. Verslamml. Bericht*, 1841: 93-94.

¹⁰⁸Bracegirdle, "J. J. Lister," 190. has also come to this conclusion.

¹⁰⁹Cited by Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 7. Mayer’s original work is August Franz Joseph Karl Mayer, *Über Histologie und eine neue Eintheilung der Gewebe des menschlichen Körpers bei Gelegenheit der Eröffnung seiner Vorlesungen über Anatomie* (Bonn: A. Marcus, 1819). In English: *On Histology and a New Classification of the Tissues of the Human Body*.

piqued the interest of one of his young pupils, Johannes Peter Müller. The German physiologist, Müller, and his future renowned students, built upon cell theory and ideas of histopathology to revolutionize the theory and practice of medicine and cancer on both sides of the Atlantic.

Müllerian Contributions

The cell is by far the most common element in tumors.

—Johannes Peter Müller, 1838¹¹⁰

Müller's influence on the development of modern cancer cannot be overstated. Born in Koblenz, Germany, in 1801, Müller was a child of the romantic period and a student of early industrialism. Influenced by his philosophy of mechanical naturalism, he applied the new microscope to the study of human form, function, and disease.¹¹¹ Indeed, according to medical historian Henry Sigerist, he "insisted" that investigators use the microscope for the study of human pathology.¹¹² In the process, Müller created a new perception of cancer that, years and many technological innovations later, aroused practitioners in the United States to adopt the microscope in the modern era as the primary tool for the diagnosis and prognosis of tumors of all kinds.

Müller transformed the definition of tumors from the clinical to the anatomical. His great perception was that the microscope and its revelations could yield unfathomable insights into the study of cancer. He built upon the cell-constructed histology of his student-colleagues, Matthias

¹¹⁰Johannes Müller, "Über Den Feinern Bau Und Die Formen Der Krankhaften Geschwulste (on the Finer Structure and the Forms of Morbid Tumors)," in *Johannes Müller and the Nineteenth-Century Origins of Tumor Cell Theory* (Canton, MA: Watson Publishing International (Science History Publications, U.S.A.), 1838; reprint, 1986), 63.

¹¹¹Henry E. Sigerist, *The Great Doctors: A Biographical History of Medicine*, trans. Eden and Cedar Paul (Garden City, NY: Doubleday & Company, Inc., 1933; reprint, 1958), 306-07.

¹¹²Sigerist claimed that Müller's insistence on the use of the microscope was his greatest achievement. *Ibid.*, 310. As will be shown, I believe Müller's greatest achievement was his application of cell theory to the study of cancer. Nonetheless, without the microscope, of course, Müller would not have been able to investigate the cellular aspects of tumors.

Jakob Schleiden and Theodor Schwann, to envision cancer microscopically rather than macroscopically. He opened a new window onto the structure, composition, and development of cancer that engendered novel ways of addressing the ancient problem of the nature of tumors. In the process, he suggested untried avenues of research and practice that transformed cancer medicine from the traditional world of symptoms and signs to the modern world of microanatomical structure and function.

Nevertheless, Professor Müller, for all his impact on the future of medical education and practice, was not of modern cancer. He was a brilliant educator of the early nineteenth century who applied a new tool to an old disease. His findings revised and expanded upon what had been seen with uncorrected compound microscopes, but ultimately his system of tumor classification was securely rooted in traditional cancer.¹¹³ With a firm grounding in the traditional gross pathology of cancer, he described cancer under the microscope as an abnormal cell and (in the best German romantic tradition of Hegel, von Ranke, Marx, and others) classified tumors accordingly. Thus his discoveries and methodology were new, but his assumptions were solidly pre-Listerian. After years of the deep study of neoplasms, he concluded in a now-famous prediction that while microscopy and chemistry might be great aids to cancer research, the

¹¹³Dr. Leland Rather wrote that Müller's classification "contains little that is new." (Ironically, Müller noted that although some progress had been made in the elucidation of tumors over the centuries, "the method of description employed still remains...almost at the level of a Marcus Aurelius Severinus," who published *De Recondita Abscessum (The Obscure Nature of Tumors)* in 1632. Müller, "Müller, Morbid Tumors," 59. See Josiah C. Trent, "Five Letters of Marcus Aurelius Severinus to 'the Very Honourable English Physician, John Houghton'," *Bulletin of the History of Medicine* 15 (1944): 311-12.) Indeed, Rather believed that Müller's clinical classification of tumors was no different from that of the sixteenth-century anatomist, Gabriele Fallopio. See Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 29. As will be shown, I do not completely agree with this conclusion, but the basic point is valid. Müller was a pioneer who applied a new tool to an old problem.

microscope and chemical analysis can never become a means of surgical diagnosis for malignant growths; it were ridiculous to desire it, or to suppose it practicable.”¹¹⁴

The Life and Times of the Father of Cancer Microscopy

Johannes Müller, not long after the final defeat of Napoleon I, came to the vibrant city of Berlin. He was one of many intellectuals with varied interests to gravitate to the capital city of Prussia. Several, like Müller, hailed from Bonn—Schwann, Jakob Henle, and the sharp-witted Karl Marx.¹¹⁵ Müller and his circle went to study medicine and, in particular, anatomy. Pathological anatomy, as noted in Chapter 1, was the brightest star of medicine, and Berlin had become the center of the pathological universe. Two inventions—one technological, the other conceptual—propelled Müller and his famous students into the forefront of medical history. The first was the development of the aspherical, achromatic compound lens system by Joseph Jackson Lister and others. The second was the advance of cell theory.

Cell theory—the idea that the anatomical, functional, and reproductive unit of the organism is a cell—was not invented or discovered by Schleiden or Schwann. Robert Hooke’s seventeenth-century anatomical box-like ‘cell’ was the first credited description of the cell, but it

¹¹⁴Johannes Müller, *On the Finer Structure and the Forms of Morbid Tumors*, 1838, as translated by Howard W. Haggard and G. M. Smith, "Johannes Muller and the Modern Conception of Cancer," *Yale Journal of Biology and Medicine* 10, no. 5 (1938): 432, Müller, "Müller, Morbid Tumors," 58.

Rarely do critics acknowledge that the isolated condemnatory phrase can hide what should be high praise for the depth of understanding that engendered that phrase. An example does not a proof make.

¹¹⁵Although Marx went to Berlin to study law and philosophy, he was a keen observer of the medical crowd. In an 1837 poem, he noted the power of anatomy among physicians:

Damned philistino-medico-student crew
The whole world’s just a bag of bones to you.

See Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 46FN52.

lacked an understanding of cell functionality.¹¹⁶ By the early nineteenth century, however, years before the seminal papers of Schleiden and Schwann in the late 1830s,¹¹⁷ the cell, now imbued with traces of function, began to replace the tissue as the physiological entity of health and the pathological unit of disease. Thus, as L. J. Rather documented, the modern notion of the cell preceded the Berlin circle of Schleiden, Schwann, and Müller by decades—if not longer.¹¹⁸ Imaginative conceptions of structure and function based upon sightings through aberrated microscopes notwithstanding, cell theory would have remained an architectural honey-comb of limited actions without the corrected microscope. The achromatic, aspherical microscope was the *sine qua non* of modern cell theory, for it allowed the naturalist *qua* biologist to clearly visualize individual cells and demonstrate their importance. Schleiden, who worked with plants, and Schwann, who investigated animals, revealed their inner mechanisms by means of the microscope. Without this “new” (and improved) instrument of science, it is unlikely that cell theory would have sustained its meteoric rise in the 1830s and 1840s.

¹¹⁶Indeed, Hooke’s first reference to the cork cell was even more metaphorical than descriptive—like a miniature beehive too tiny for the naked eye to see. In his own words, he noted that “me thought I could perceive it to appear a little porous.” Upon thinner sectioning, further microscopical investigation revealed “I could exceeding plainly perceive it to be all perforated and porous, much like a Honey-comb, but that the pores of it were not regular; yet it was not unlike a Honey-comb in these particulars.” Further, “these pores, or cells (with “thin” “partitions” between them), were not very deep, but consisted of a great many little Boxes, separated out of one continued long pore.” Hooke realized that his visual discovery was momentous for he exclaimed that these “were indeed the first *microscopical* pores I ever saw, and perhaps, that were ever seen, for I had not met with any Writer or Person, that had made any mention of them before this.” Hooke, *Micrographia*, 112-13.

¹¹⁷Matthias Schleiden, “Beiträge zur Phytogenese,” *Müller’s Arch.*, Berlin, 1838; Theodor Schwann, “Über die analogie in der Structur und dem Wachstume der Thiere und Pflanzen,” (“On the Analogy in Structure and Growth of Animals and Plants”) *Neue Notizen aus dem Gebiete der Natur- und Heilkunde*, Berlin, January 1838: 33-36; “Fortsetzung der Untersuchungen über die Übereinstimmung in der Structur der Thiere und Pflanzen,” (“Continuation of the Studies on the Correspondence in Structure of Animals and Plants”) *Neue Notizen*, February 1838: 225-229; and “Nachtrag zu den Untersuchungen über die Übereinstimmung in der Structur der Thiere und Pflanzen,” (“Addendum to the Studies on the Correspondence in Structure of Animals and Plants”) *Neue Notizen*, April 1838: 21-23.

¹¹⁸See Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, v and ff.

Müller, with a microscope far superior to that of Bichat, accepted the microscope into his laboratory like a new love.¹¹⁹ He received his first microscope, of English origin, as a gift from his professor in 1824.¹²⁰ By 1830, when Sir Everard Home, the English surgeon and brother-in-law of John Hunter, published the first report of cancer ‘lymph globules’ seen through the microscope,¹²¹ Müller was already insisting that the corrected microscope was essential to the study of pathology. With the aid of his new tool, Müller transformed the cancer ‘globules’ of Home into the cancer ‘cells’ on which the modern science of oncology is based. Further, the initial volume of his magnum opus, *Handbuch der Physiologie des Menschen (Manual of Human Physiology)*, published in 1833, marked Müller’s transition from the deductive book-begotten natural philosophy of his romantic forebears to the *a posteriori* inductive empiricism of the modern life sciences. Had his cancer research and celebrated students not left their mark on the history of medicine, this ideological contribution alone would have assured his position as a leading light of mid-nineteenth-century European medicine. Müller’s 1833 text also facilitated his ascendancy to the chair of anatomy at Friedrich Wilhelm University in Berlin following the death of Karl Asmund Rudolphi—the teacher who had given him his first microscope a decade earlier.

Throughout his career, Müller applied the new microscope to a host of organs, tissues, and cell types. His goal was nothing less than to attain understanding of the structure and

¹¹⁹Indeed, Müller may never have developed an interest in pathology and the microscope had it not been for two life-changing events early in his career. After obtaining his medical degree in the early 1820s, he practiced privately in Bonn. The death of a friend under his care, however, dissuaded him from pursuing a clinical career as a medical practitioner or “people doctor.” Around this time, he married Anna Zeiler, the daughter of a man of property, thereby giving him the means to undertake the poorly-recompensed specialty of medical professor. See Haggard and Smith, “Johannes Muller and the Modern Conception of Cancer,” 429.

¹²⁰Ibid.

¹²¹Sir Everard Home, *A Short Tract on the Formation of Tumours, and the Peculiarities that are met with in the Structure of those that have become Cancerous; with their Mode of Treatment* (London, 1830). Home’s cancer cells, unlike those described in Müller’s 1838 work, are labeled “lymph globules.”

function of life. He investigated nerves, retinal cells, blood, lymph, chyle, heart tissue, and embryonic forms. The fetal protonephric “Müllerian” ducts are named in his honor. He was a diligent researcher and charismatic mentor whose impromptu lunches in slovenly quarters with students and colleagues were most inspiring and illuminating. In substance, they represented the birth of modern biology.

In the 1830s, as the idea of the cell swept into the consciousness of philosophers and pathologists, the nature of tumors captivated Müller above all else. Tumors defied definition. Tumors defied unified description. Tumors defied cure. To him they presented an enticing and fundamental challenge. Perhaps the new microscope could solve the problem of cancer. Surely it would allow elucidation of heretofore unknown anatomic, physiologic, and evolutionary features of the disease. In the mid-1830s, Müller determined to investigate every and any tumor he could find.

By 1836, Johannes Müller was deeply involved in the microscopical and chemical study of tumors.¹²² Although the chemistry of cancer is not the focus of this chapter, it should be noted that the application of chemistry to biology arose in Europe alongside microscopy during the second quarter of the nineteenth century. As such, chemical principles generated another mode of investigation that held promise for the determination of the nature of neoplasms.¹²³

Unfortunately, Müller found that “little does carcinoma have chemical constituents peculiar to it alone.” Thus he concluded that he could not differentiate tumors on the basis of their chemical

¹²²Müller probably began his study of tumors in 1834, shortly after assuming the chair of anatomy in Berlin. Evidence for this derives from his 1838 work *On the Finer Structure*, wherein he noted that “in four years I have seen more than thirty fresh cases” of breast cancer. Müller, “Müller, Morbid Tumors,” 77. The high prevalence of breast cancer and its frequent diagnosis long before the advent of internal imaging techniques make it likely, due to the relatively superficial location of many breast tumors, that cancer of the breast would have been one of the first and most frequent tumors that Müller studied.

¹²³I will revisit the application of chemical techniques to cancer research through cell-component staining later in this chapter.

properties.¹²⁴ On the other hand, the microscopic nature of cancer quickly garnered a plethora of sensational (and controversial) perceptions.

On the Finer Structure and the Forms of Morbid Tumors

—Johannes Müller, 1838

Müller's chief contribution toward an understanding of the nature of tumors was the application of new tools—the post-Listerian microscope and chemical analyses—within the framework of cell theory to cancer medicine. As such, he established an anatomical, physiological, and developmental basis for the investigation of the disease. Müller's major work on tumors, which propounded this new *modus operandi*, was his 1838 technical publication entitled *Über den feinern Bau und die Formen der krankhaften Geschwülste (On the Finer Structure and the Forms of Morbid Tumors)*.¹²⁵

Like Galileo's report of his original experiments with motion and Newton's observations on mechanics and optics, Müller pointed to the groundbreaking nature of his studies with the first words of his monograph. "The pathologic anatomy of morbid tumors and funguses is still in its first childhood," he began. "The classification of tumors is based on their external form and consistency, and on differences visible to the naked eye on section; it has, in contrast, kept at a distance from chemical tests and the microscopic study of structural elements."¹²⁶ Müller

¹²⁴His evidence can be found in Müller, "Müller, Morbid Tumors," 91-93. The quotation and his conclusion are on page 95.

¹²⁵Berlin: G. Reimer, 1838. Hereafter cited as *On the Finer Structure*.

¹²⁶*On the Finer Structure*, 56. All quotations from Leland J. Rather's translation of Müller, "Müller, Morbid Tumors."

'Fungus' was one of the descriptive terms for cancers that resembled in gross appearance the colonies of achlorophyllic, often filamented organisms to which the term is commonly applied today. The expression was usually 'medullary fungus' because of its soft texture.

Due to the efforts of Müller, Virchow, and other microscopists of the nineteenth century, the 'fungal' description of cancer had essentially (and somewhat grudgingly) disappeared from the cancer lexicon by the turn into the twentieth century.

significantly narrowed the cognitive distance between the microscopic and chemical characteristics of tumors and their nomenclature. His work served as a bridge from the traditional gross pathology of tumors to the microscopic emphasis of modern cancer.

Of Benign and Malignant

Müller discovered early in his investigations that tumors with similar macroscopic appearances were not necessarily the same when viewed microscopically. At a time when the diagnosis of ‘tumor’ could imply any swelling from a sebaceous cyst to a metastasized malignancy, Müller applied the new microscope and cell theory to the crucial problem of distinguishing benign and malignant growths. This differentiation was both essential and practical. Caustics and other “medical” (non-surgical) treatments for cancer were painful and often disfiguring. Surgical remedies were fraught with danger unto death. Indeed, Müller considered this “better distinction of such tumors” as his primary goal.¹²⁷ Experience taught him that manifestations visible to the naked eye could deceive. “Innocent tumors,” he noted, “take on, as a result of surface growth, the mere appearance of malignancy.”¹²⁸ Surgical extirpation of such benign tumors could lead to complications and unnecessary death.

Müller’s solution to the problem of differentiating benign from malignant tumors was a new taxonomy based upon their microscopical and chemical properties. He was not the first to classify tumors, but he was the first to create a classification based upon the technology of the corrected microscope and the idea of cell theory. True to his personal and professional heritage in a rapidly changing world, however, the result of his labors was a systematized list that straddled old and new—traditional gross anatomy and modern microscopy.

¹²⁷*On the Finer Structure*, 57. “The practical aim of our studies urges us in any case to separate tumors of...malignant and benign nature.” *Ibid.*, 69.

¹²⁸*On the Finer Structure*, 57.

Tumor Pathology circa 1838

The title of his monograph divulges his mentalité. *The Finer Structure* is at once antiquated and pioneering. It promises something previously unseen while assuring that the new detail is predicated upon a known edifice. What of *The Forms of Morbid Tumors*? He celebrated form—not function; form—not development. Form is grounded in the anatomic, the hallmark of his predecessors, not the physiologic or ontogenic. Morbid tumors cause disease. Yet Müller included in his treatise extended discussions of growths that did not cause illness, albeit only for the purpose of differentiating them from harmful neoplasms. Characterize the benign and the malignant would stand out—and vice versa. To achieve this goal, Müller meticulously examined any and all tumors he could find for examination. His thorough microscopic examination of tumors extended the time-honored methodology of inductive empiricism (many examples, some interpretations) to tumors and set the stage for one of the pillars of modern cancer.

Because Professor Müller was not a clinician, he had no direct access to patient's tumors. Nor could he obtain surgical specimens from pathology laboratories attached to hospitals, as might an investigator today. Such laboratories simply did not exist.¹²⁹ Thus, he actively sought tumors from those who had them in Germany, France, and Great Britain—practitioners and museums.¹³⁰

Although Müller, by his own estimation, examined “a very large number of cancerous tumors,” actual quantities pale in comparison to the number of cancers studied in most modern-

¹²⁹George Dock, "Clinical Pathology in the Eighties and Nineties," *American Journal of Clinical Pathology* 16 (1946): 671.

¹³⁰Müller noted, for example, that he was “indebted to the generous support of Messrs. von Gräfe and Dieffenbach” for the breast cancer specimens he examined. *The Finer Structure*, 77.

day monographs.¹³¹ He perused only a few dozen cases over the course of four years, far short of the number a twenty-first century pathologist at an academic center might scrutinize in a week. In addition, Müller's tumor examinations occurred under conditions of primitive microtechnique. Tissue staining, though initiated by Hooke in the seventeenth century and Leeuwenhoek and Sir John Hill in the eighteenth,¹³² was rare prior to the second half of the nineteenth century. Sectioning, performed by the inconsistent hand, was also problematic. The medical microtome lay in the future.¹³³ Given the available microtechniques of his time, Müller's achievement of the microscopic characterization of tumor types was remarkable.

Müller's initial analysis of cancerous growths was firmly rooted in traditional pathology. "Every tumor," he explained, "that breaks up the natural structure of any tissue, that is constitutional from the beginning or regularly becomes so in its natural course of development, and that, having become constitutional, regularly recurs after extirpation and leads to the certain downfall of the individual concerned, may be called cancerous."¹³⁴ His definition of cancer could have been glyphed by a surgeon of the seventeenth century.

Nonetheless, he quickly superseded his vintage definition of cancer with a new awareness gleaned from the microscope. "Aside from capillaries, the finer microscopic elements of tumors are fibers, granules, nucleated and non-nucleated cells, tailed or spindle-shaped corpuscles, and

¹³¹*The Finer Structure*, 68. Nevertheless, Müller probably examined more tumors than other pathologists of his day. Busy surgeons like J. Marion Sims, however, undoubtedly handled many more gross tumor specimens than did pathologists, because surgeons, at least in the United States, did not routinely involve pathologists in tumor analysis (surgical pathology) until well into the twentieth century. See Wright, "Surgical Pathology," 324-25.

¹³²Clark and Kasten, *History of Staining*, 35.

¹³³ Jan Evangelista Purkinjê, who lent his name to the Purkinjê cells in the cerebellar cortex, the cardiac muscle ventricular conduction system, and also recognized fingerprints as unique identifiers, proposed the medical microtome in 1839. Müller had published his treatise on *die krankhaften Geschwülste* (not to be confused with Virchow's treatise of the 1860s) the previous year. Hajdu, "Cytology," 670. John Hill invented a microtome in 1770 that could be used for the same purpose, but its use was not widespread. See Bracegirdle, *A History of Microtechnique*, 117.

¹³⁴*The Finer Structure*, 69.

vessels.”¹³⁵ The microscope clearly revealed that tumors consisted of the organic elements listed and one inorganic element—crystals.¹³⁶ As advanced and complete as this schema appeared, humility prevailed. Müller did not claim to have seen all there was to see despite his certainty that he had seen more than those before him. Thus he modestly added that “I have *as yet* found no other elements in tumors.”¹³⁷

Reconstructing Assumed Wisdom

As with many revolutionary approaches, Müller’s earliest discoveries with the corrected microscope stirred controversy because they contradicted long-held knowledge. Some of these time-honored myths were specific; others general. Observation verified specific queries into the nature of cancer, but general attacks on traditional wisdom were often synthetic, less easy to verify, and thus more contentious. Science was and is inertial. Prone like all society to fads and fallacies, the untrue, misleading, and incomplete eventually fall to hypotheses that better explain and illuminate observations. But only with the passage of time. Deficient concepts fail the hallmark of scientific proof—testability and falsifiability.¹³⁸ The microscope offered Müller and cancer investigators after him the tool for testing, verifying, and refuting.

Müller’s study of breast tumors, then as now one of the most prevalent of all pathologic growths, created the opportunity for his decrial of specific cancer myths. In its advanced state, the most common stage available to Müller, breast cancer is usually a solid, dense lesion. Based on its macroscopic appearance, early nineteenth-century pathologists and practitioners thought

¹³⁵*The Finer Structure*, 63.

¹³⁶Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 26-27.

¹³⁷*Ibid.* My italics.

¹³⁸Karl Popper was a major exponent of this philosophical analysis of science. See Karl Popper, *The Logic of Scientific Discovery*, 1959.

the scirrhus (hard) tumor amorphous and bloodless on the inside, yet covered with veins resembling the legs of a crab on the outside.¹³⁹ The detailed resolution possible with Müller's corrected scope revealed the ridiculousness of this presumed organic architecture. "The notion that scirrhus is unorganized and contains no vessels is absurd....Tumors appear to consist of nothing but vessels."¹⁴⁰

Traditional belief also held that the veins overlying the tumor, so prominent as to lend name (cancer) to imagination (crab's legs), were pathognomonic for cancer. Müller quickly found that "dilated veins...are a(n) unreliable sign of malignancy."¹⁴¹ On the contrary, he noted that prominent vasculature appeared omnipresent among cancers. This finding stimulated great hope—and concern—for the investigation of cancerous diseases. On a positive note, enlarged vessels served as two-way conduits that could reveal the source of tumor growth through the pathways of its nourishment. On the other hand, great vessels could facilitate metastasis through distal spread.

Müller crushed several general myths with his new juggernaut of microscopic discovery. Bichat, who propelled the study of medicine and tumors from organs to tissues, taught that tissues were the fundamental units of structure and function in the organism. Pre-Listerian microscopes could not resolve tumors to the cellular level, so tissues were thought to be the dominant structural element in tumors. As late as 1836, Müller reported that the dominant elements of tumors were fibers, a major constituent of tissues.¹⁴² Müller, building on the work of Schleiden and Schwann, then found that Bichat's findings were macroscopically valid but

¹³⁹Hence the reason for the association between 'cancer' the crab and 'cancer' the disease.

¹⁴⁰*The Finer Structure*, 63.

¹⁴¹*The Finer Structure*, 70.

¹⁴²Rather, *The Genesis of Cancer*, 196FN9, 97FN28.

microscopically inaccurate. Like an explorer mining an old cave with new tools for the first time, Müller saw tumors in a new light. “I carried out a search for cells in all tumors where no cells had as yet been found,” he wrote in 1838. “In several tumors where I had previously found no cells, I now found them at higher magnification.”¹⁴³ Müller discovered that cell theory even applied to these growths that were “contrary to nature.”¹⁴⁴ “Schwann’s observations on the development and growth of normal tissues have been confirmed, even in these pathologic formations.”¹⁴⁵ Müller discovered that cells, not tissues or fibers, were the dominant architectural feature of tumors.

The Origin of Tumors

The microscope, Müller believed, would also settle the eternally divisive question of the cause of tumors—a query rooted so deeply in the history of medicine that it might be called tumor creationism. Although hypotheses as to the cause of cancer proliferated at least since the ancient Greeks, the major controversy in early nineteenth-century swirled around whether dangerous growths began in the same tissue in which they were found (homologous tumor development) or in tissues other than their site of diagnosis (heterologous tumor development). The dispute was not settled until after Müller’s death, but he was prescient in predicting that the answer was unknowable in his time but ultimately amenable to the microscopical analysis. “A separation of pathologic tissues into homologous and heterologous forms cannot be carried out. That classification is based on blind, risky assumption, in the absence of any understanding of tumor structure. The structure of the most benign tumor does not differ at all, with respect to its

¹⁴³*The Finer Structure*, 60.

¹⁴⁴The phrase is from Galen.

¹⁴⁵*The Finer Structure*, 60.

genesis and finest elements, from cancer.” In short, “neither anatomist nor pathologist has been remotely able to define tissue heterology.”¹⁴⁶ Even the corrected microscope had its limitations.

By the time of the publication of *The Finer Structure* in 1838, Müller surmised by the indirect process of elimination that tumor development was most likely homologous—i.e. that growths originated in their home tissues. “The structure of carcinoma shows nothing that is at all heterologous or that is foreign to normal organization.”¹⁴⁷ Cancer, he concluded, arose in the tissue in which it was found.¹⁴⁸ Although tumor growth might be provoked by extracellular substances carried to the vulnerable site from elsewhere by the bloodstream,¹⁴⁹ malignancies, opined Müller, did not begin in extraneous tissues and secondarily transmogrify normal tissue into cancer. No, cancer originated in normal tissues gone bad. Breast tissue begat breast cancer; prostate tissue, prostate cancer. Thus Müller’s science of cancer, though founded upon traditional notions of tumor origin and spread, indirectly addressed the issue of constitutionalism dominant in his day and found it wanting. If tumor development was homologous, localism was a reasonable hypothesis for tumor origin and extirpation possible. A decade and a half before the prominent American surgeon Samuel David Gross advised the futility of cancer surgery, the German pathophysiological Müller laid the conceptual framework for the operative cure of cancer as a result of his studies with the post-Listerian microscope.¹⁵⁰

¹⁴⁶*The Finer Structure*, 68.

¹⁴⁷*The Finer Structure*, 71. Also see Conclusion III. on page 95.

¹⁴⁸Metastases confounded this judgment, for pathologists, surgeons, and practitioners could not always differentiate primary (original) and secondary (metastases) tumors.

¹⁴⁹I am here referring to the “amorphous cytoblastema” that incited such rancor among European scientists in the mid-nineteenth century.

¹⁵⁰The controversy over the heterologous vs. homologous development of tumors did not end with Müller. Rudolf Virchow, his most famous student, promulgated his unrecanted belief in 1858 that cancer arose in connective tissue. See Rudolf Virchow, *Cellular Pathology as Based Upon Physiological and Pathological Histology: Twenty Lectures Delivered in the Pathological Institute of Berlin During the Months of February, March, and April, 1858*,

A New Classification of Tumors

In no disease was the advantage of the microscope illustrated better than in cancer.

-Stanley Joel Reiser¹⁵¹

Beyond microscopic evidence for the homologous tissue origin of cancer, the presence of cells in tumors allowed Müller to see patterns that none before him had found. He was “unable to understand” how his predecessors classified tumors solely on the basis of their “anatomic features.”¹⁵² Macroscopic structural characteristics were subjective and lacked reproducibility. He delighted in finding microscopic tumor patterns—the essence of “the Forms of Morbid Tumors”—that consistently identified individual cancers. “I was always most pleased when I would again meet up with something familiar; this gave me faith that there exist invariable distinctions, which can be recognized again with certainty, in these structures.”¹⁵³ Müller’s drive to classify tumors was part and parcel of the early nineteenth century endeavor to list and categorize nature through recognized commonalities. The improved microscope empowered him with the technical ability to construct a whole new set of criteria for classification. Previously unrecognized patterns based upon those criteria led to new insights. Without the new microscope, he realized, such observations would have been impossible.¹⁵⁴ Forms and patterns

trans. Frank Chance, 2nd ed. (London: John Churchill, 1860; reprint, The Classics of Medicine Library, 1980), Lecture XIX, April 24, 1858, 442-461. Karl Thiersch, who was not one of Müller’s students, debunked the heterologous theory—including Virchow’s connective tissue hypothesis—in 1865 by showing that epithelial tumors arose from endothelial tissue, not connective tissue. (See Thiersch’s *Der Epithelialkrebs, namentlich der Haut: eine anatomisch-klinische Untersuchung/mit einem Atlas mikroskopischer Abbildungen*, Leipzig: W. Engelmann, 1865.)

Today the battle for the origin of cancer continues with the major focus on the DNA molecule, thought to be anatomically identical while functionally different in (almost) all cells. The fundamental question that Müller, Virchow, and Thiersch grappled with during the nineteenth century remains; viz. why do some cells develop into cancer?

¹⁵¹Reiser, "Medicine and Technology," 77.

¹⁵²*The Finer Structure*, 59.

¹⁵³*Ibid.*, 59.

¹⁵⁴*Ibid.*, 59.

implied type-specific characteristics and the possibility of distinguishing one tumor from another. Perhaps he could reliably and consistently separate the benign from the malignant. Müller leaped at the opportunity to classify tumors on the rational basis of the configurations he saw through the microscope in his mind's eye.

Prior to Müller, a panoply of names and terms greeted the would-be student and practitioner of neoplasms. Often, they described, in Latin, the appearance of tumors to the naked eye. Sometimes they bore eponyms that honored those deemed to have discovered this or that reputed characteristic. The array of nomenclature baffled learners and made comparative tumor pathology nearly impossible. Müller, on the other hand, used his microscope to assert that “understanding of the forms of cancer is possible.”¹⁵⁵ Further, he asserted that gross appearances could be deceiving, for “there are forms that lack striking external characteristics and that can be confused with each other.”¹⁵⁶ Thus anyone who concluded that tumor pathology grounded in gross observation could be clear, distinct, accurate, and reproducible between observers was mistaken. Hence Müller saw the need for a new nosology of tumors based upon microscopy.

The Prussian Academy Presentation (1836)

Müller's classification of tumors, though derived from the greater detail afforded by the high-resolution microscope, betrayed his background in traditional tumor pathology. Nevertheless, it also looked forward to the solution of the problem of the differentiation of benign from malignant tumors. As early as 1836, Müller divided tumors into those curable and those not.¹⁵⁷ To the young professor, this was the hallmark of benignity or malignancy,

¹⁵⁵Ibid., 69.

¹⁵⁶Ibid., 69.

¹⁵⁷Müller read “Über den feinern Bau der krankhaften Geschwülste” before the Royal Prussian Academy of Sciences on December 8, 1836.

respectively. The distinction was critical, for common wisdom acknowledged that malignancies were incurable. The idea that tumor microscopy could predict prognosis lay in the future. For Müller, the great step forward was to be able to inform pathologists and practitioners whether the patient's tumor was benign or malignant.

Leland J. Rather, Patricia Rather, and John B. Frerichs, in their text *Johannes Müller and the Nineteenth-Century Origins of Tumor Cell Theory*, tabulated Müller's 1836 classification of anomalous growths.¹⁵⁸ Müller, true to his heritage, rooted his terminology firmly in traditional tumor pathology. Surgically curable (and therefore benign) tumors included fatty tumors (lipomas), myxoid tumors, albuminoid tumors, sinewy fibrous tumors, enchondromas, and telangiectasias (dilated groups of blood vessels that produce raised red skin blotches). Incurable malignancies included reticular carcinomas (such as the common breast cancer), fibrous carcinomas (including scirrhus), alveolar carcinomas (such as in the stomach), medullary carcinomas, hyaline carcinomas, phyllode (leaf-like) carcinomas, and melanotic carcinomas (highly pigmented neoplasms, like melanoma). Müller advanced no consideration for the possibility of cure by non-surgical means.

The microscope played an essential role in Müller's further characterization of the different tumors. He divided them on the basis of their microscopic fibers, globules, corpuscles, and cells. Nevertheless, his nomenclature was reductive and retrospective. Many of the names derive from features visible to the unaided eye and palpable to the hand—visible networks (reticulate), hardness (fibrous/scirrhus) or softness (medullary), translucency (hyaline), and pigmentation (melanotic).

Über den feinern Bau, 1838

¹⁵⁸Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 13-14.

Professor Müller's 1838 monograph on *The Finer Structure*, which added *Forms of Morbid Tumors* to the title from his paper of two years earlier, elaborated a difference of degree rather than kind in his classification of tumors. The prime objective remained—derive for the practitioner, often a surgeon, a straightforward and simple method to differentiate benign and malignant tumors. Though he expanded the microscopic and chemical details, his terminology remained essentially unchanged from 1836.

After a panegyric on the importance of the microscope to cancer research, Müller enumerated his six main types of malignancy: scirrhus or carcinoma simplex; carcinoma reticulare; carcinoma alveolare; carcinoma melanodes; carcinoma medullare; carcinoma fasciculatum (formerly hyaline).¹⁵⁹ The monograph added to the 1836 work discourses on the development of carcinoma, the chemical characteristics of tumors, and an illuminative summary entitled the “nature of cancer.”

The Nature of Cancer

Johannes Müller's ten-part “nature of cancer” served as a valedictory to his application of the microscope to an understanding of tumors, for his future investigative endeavors lay elsewhere. His findings crowned the thoughts and labors of a mature natural scientist over many years. They reveal a struggle to fathom the unfathomable; an attempt to reconcile the traditional macroscopic tumor pathology of the clinic and dispensary with the new microscopic pathology of the laboratory. Further reflection discloses that Müller achieved remarkable insights as a result of the application of a new tool to an old disease. Despite a superficial resemblance to the 13 Queries of the 1802 Edinburgh Society for Investigating the Nature and Cure of Cancer,¹⁶⁰

¹⁵⁹See Müller, “Müller, Morbid Tumors,” 72-89. and Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 27-28.

Müller's approach attacked the question of cancer from radically different perspectives—technical and analytic rather than sensorial and demographic. His conclusions serve as both tribute to and confirmation of the role of the microscope in the investigation of cancer. As such, they are nothing short of a *tour de force* in the history and understanding of cancer.

I. *Carcinoma differs from simple induration both in structure and intrinsic nature.*

Müller tackled the question of the diagnosis of cancer directly. Many practitioners of his era believed that hardened tissue (induration) was cancer until proven otherwise. Some extrapolated the process backwards to claim that inflammation-generated induration (a not uncommon circumstance) was the root of all cancer. Müller disagreed. His microscopic studies revealed that soft, non-indurated lesions could be cancerous and that hard, indurated growths might not be. The hallmark was change over time—the biologic history of the tumor. Inflammatory states healed or caused death with relative rapidity; cancerous conditions were chronic and continued toward their natural end. “Microscopic studies fully bear out this view,” he stated.¹⁶¹ One thought, based upon his microscopic investigations into the nature of cancer, corrected the confusion of centuries.

II. *Carcinoma also differs essentially from ulceration of indurated parts.*

A chronic, non-healing ulcer had been a hallmark of cancer for centuries. How many women over countless generations suffered from hard tumors in their breasts that degenerated into ulcerated masses! How many men since the 1496, when Columbus first introduced tobacco

¹⁶⁰The Medical Committee of the Society for Investigating the Nature and Cure of Cancer, "Thirteen Queries," *Edinburgh Medical and Surgical Journal* 2 (1806).

¹⁶¹Müller, "Müller, Morbid Tumors," 93-94.

from the New World to Europe for its “medicinal value,” developed ulcerated sores on their pipe-accustomed lips—ulcers that ate into their flesh and caused a rank discharge! Nineteenth-century texts are rife with such illustrations.¹⁶² One need not be a blueblood to see the logic (or desire for sensorial harmony) that led the Ladies’ Board of the Woman’s Hospital to deny admission to Dr. Sims’ malodorous ulcer-ridden cancer patients. Müller, presciently, discovered decades before the clash between Sims and the Ladies’ Board that not all ulcerated masses are cancer.

Unsatisfied that the micropathological distinction between inflammatory and malignant processes was known only to himself and his students, Müller sought to highlight the differences for the entire community of pathologists. One of his students, Jakob Henle,¹⁶³ concluded that the microscopic response of the body to inflammation (such as after an injury) consists “of cells like those found in embryonic structures.” Müller confirmed Henle’s microscopic finding and promulgated the idea that the microscope revealed distinctive cells that could diagnose different pathological processes.

At a deeper level, an offshoot of this groundbreaking association between cell types and functions was that similarities existed between wound healing and embryonic development at the microscopic level—a rare insight that is still being explored in cancer genetic laboratories today. Cancer in Müller’s day was linked to wound healing through the prevalent notion that chronic

¹⁶²Such pictures are abundant in the literature. A text that shocks the senses but easily serves the purpose is George M. Gould and Walter L. Pyle, *Anomalies and Curiosities of Medicine* (New York: W. B. Saunders, 1896; reprint, 1956), Chapter XV. Most illustrated surgical texts of the nineteenth century would do.

¹⁶³Jakob Henle was a fascinating character in his own right. Not only was he credited with the discovery of a major anatomic and physiologic component of the kidney’s basic unit, the nephron—called the loop of Henle to this day—but he was also a political activist like Rudolf Virchow, another Müller student. Even greater acclaim lay in his conceptual collaboration with Robert Koch that led to the Henle-Koch postulates that established the notion of “proof” for the causative agents of infectious diseases.

Coincidentally, Henle, whose name shall forever be linked with the kidney, died of a renal sarcoma. See Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 39.

irritation caused cancer. Microscopy offered a rationale for this causal interrelationship wherein both processes shared common cell types. These new concepts antedated the work of Gregor Mendel in the 1860s and the early twentieth-century geneticists who found that heritable particles (called genes) governed both the development and maturation of living organisms as well as their ability to cope with environmental flux over time.¹⁶⁴

Müller recognized that, unfortunately, cell types did not always clearly separate benign and malignant tumors, for both could contain early cell forms. He cautioned that “this finding cannot be cited in support of the similarity of carcinoma to ulcers in indurated parts, for most benign tumors too consists (sic) of embryonic cells.”¹⁶⁵ If the same cell types could sometimes be found in both, how was the pathologist to differentiate benign from malignant? Time and the microscope offered the best chance of differentiation, for, as Müller wrote, “only in carcinoma do the various tissue formations of the parts undergo metamorphosis into the underlying carcinomatous mass.”¹⁶⁶ Microscopic findings preceded macroscopic changes and predicted them more accurately. Again, Müller’s discoveries challenged traditional wisdom and found that the pathologist’s microscope offered the best available method to achieve the earliest and most precise diagnosis of cancer.

III. *Carcinoma is not a heterologous tissue, and the finest components of its tissue are not essentially different from the tissue components of benign tumors and of primitive embryonic tissues.*

¹⁶⁴Gregor Johann Mendel's publication on hereditary “elements,” “Versuche über Pflanzenhybriden” in *Verh. Naturforsch. ver. Brunn* 4 (1866): 3-47, was rediscovered by Hugo de Vries (Holland), Carl Correns (Germany), and Erich Tschermak (Austria) around 1900.

¹⁶⁵Müller, “Müller, Morbid Tumors,” 95.

¹⁶⁶*Ibid.*

Müller's microscopic findings revealed that too much overlap occurred between the cells of immature tissues, benign growths, and malignant tumors to identify significant extracellular influences in the development of carcinoma. Microscopic "granules," "tailed bodies," and "fibers" could be found in both.¹⁶⁷ The naked eye saw none of these structures. Time and tissue architecture—chronicity and patterns—on the microscopic level provided the main modes for tumor differentiation.

IV. *Just as little does carcinoma have chemical constituents peculiar to it alone (leaving putrefaction aside).*

The chemistry of Müller's era yielded no telltale differences between the compounds found in benign and malignant tumors. Common to both were "albumin, gelatin, casein, a substance related to salivary matter (ptyalin?—LK), and fats, including cholesterin."¹⁶⁸ In the mid-nineteenth century, the microscope afforded greater discernment of tumor type than chemical analysis.

V. *The peculiar productive and destructive activity of carcinoma nevertheless does give rise to general anatomical features, which are recognizable even with the naked eye in many if not most instances of carcinoma.*

Unfortunately, few physicians had the experience to examine for such characteristics and fewer still were capable of discerning them. Müller showed that chemical tests could not divide harmless from dangerous growths. Visual inspection could—earlier with the microscope, later

¹⁶⁷Müller, "Müller, Morbid Tumors," 95.

¹⁶⁸Ibid.

with the naked eye. The clinic appeared the best location for making both determinations.

Improbably, the father of cancer microscopy believed that the microscope could *not* be used as a bedside discriminator. Something else was necessary. Perhaps, he reasoned, knowledge of the ontogeny¹⁶⁹ of tumors could provide this information. Thus the next several conclusions address the question of the nature of cancer from the perspective of their origin and development.

VI. Proper to the development of cancer is a general disturbance that tends to become generalized.

Constitutionalism was so well accepted during the first half or more of the nineteenth century that Müller asserted “this statement requires no proof. The natural history of cancerous diseases confirms it in thousands and thousands of cases.”¹⁷⁰ Further, “the most experienced surgeons assume a constitutional disposition of cancer to be present in a large majority of cases, if not all.” Müller, however, did not reach this conclusion from personal experience or investigation, for he was himself “a stranger to the practice of medicine.” Instead, he relied upon “the abundant experience of my honored colleagues.”¹⁷¹ Assumption of the time-honored concept of constitutionalism rooted Müller firmly in traditional cancer even as his avant-garde microscopical investigations opened new insights into the pathology and pathogenesis of cancer. Indeed, decades passed before the optical tool that Müller introduced into cancer medicine illuminated the way toward confirmation of the non-constitutional, localistic nature of malignancy.

¹⁶⁹Origin and development of an organism or pathological entity such as a tumor/cancer.

¹⁷⁰Müller, "Müller, Morbid Tumors," 96.

¹⁷¹Ibid.

Constitutionalism cast such a wide net over theories of cancer ontogeny in Müller's era that alternate concepts were difficult to sustain. The longevity of constitutionalism in light of the microscopic discoveries of Müller and others is disturbing, for it reveals the tenacious hold upon the scientist of an idea whose time has passed. Müller's affirmation of homologous tumor development clearly implied a local basis for tumor development. Another notion, however, less obvious to the practitioner than constitutionalism, preserved the idea of general tendency for tumor development long after accumulated evidence pointed against it.¹⁷² That concept assumed a substance from the blood that effected cancer development—the “amorphous cytoblastema.” Müller, like many histologists and cancer investigators from the late 1830s through the early 1850s, embraced the idea of this formless, blood-derived tumor-cell promoter.

VII. *Although in most cases a general carcinomatous disposition is already present when a carcinoma arises locally, it must nevertheless be admitted that carcinoma can also form on the basis of a local disposition that develops into a general disposition only later in its course; this local disposition can demonstrably be caused by certain agencies.*

As Müller depended more upon his own studies, and less on the assumptions of others, he realized that tumors could indeed develop locally. Nevertheless, overcoming the inertia of the tradition of constitutionalism was difficult and he sought compromise within the prevalent idea of generalization.

¹⁷²Derivative notions of constitutionalism survive today. Nor shouldn't they, for current theories of cancer formation invoke induced transformations of DNA that potentially affect any and every cell in the body. Nevertheless, the idea that the entire body has a tendency to promote tumorous growths that just happen to appear in this or that organ, recur willy-nilly, and/or grow as a consequence of the influence of an amorphous cytoblastema, have passed.

The problem, shared by all pathologists in Müller's day, was that a microscopist could not see change over time. At best, the histopathologist viewed individual specimens taken at different sittings that implied discrete temporal changes.¹⁷³ Nineteenth-century microscopy was not a moving picture. Microtechnique fixed slide specimens in time and place. As in the study of evolution, the steps and processes that led from one static image (e.g., a fossil) to the next had to be inferred. How, then, could the investigator decide whether there was a "general disposition" to cancer or a local one? Surgeons and other practitioners, who had the ability to evaluate patients' with tumors over time, reached what was to them the obvious conclusion that malignancy involved the entire body. Removal of one cancerous lesion eventually engendered another elsewhere. Just as the wisest savant and the greatest fool could see that the sun revolved around the earth, so the entire body appeared to have a constitutional proclivity for cancer. However, just as Galileo utilized the telescope to show that Copernicus's solar-centered universe provided a more accurate reflection of instrument-based measurements of the heavens than the time-tested notion of earth centricity, so Müller intuited through microscopy the possibility that cancer originated locally. Tumor cells surrounded by normal cells in the same tissue suggested a local origin of disease, but Müller still required a leap of faith—the temporal transition imagined by evolutionists—to preference localism over constitutionalism.

Not surprisingly, Müller remained unsettled over the question of the constitutional vs. the local onset of cancer. The transitional nature of his thinking seems clear from his acceptance of the eventual predominance of the "general disposition" while propounding a localistic theory. What was his evidence for localism? Some "true carcinomas," he noted with an emphasis on

¹⁷³Biopsies excised from the same patient at lengthy intervals were probably rare in the nineteenth century, for each biopsy conferred intra-operative and post-operative risks for the patient.

‘true,’ “have been healed by extirpation.”¹⁷⁴ Who was to judge a true cancer, for ‘false’ cancers (especially inflammatory lesions) skewed outcomes? Müller was well aware that “everything imaginable has been extirpated in the name of scirrhus and cancer.”¹⁷⁵ No matter, for, as he noted with an intellectual pride that would make a twentieth-century philosopher of science beam with admiration, “the existence of even a single verified case of carcinoma cured by extirpation demonstrates the possibility of an at first merely local disposition, which, after removal of the affected part, cannot become generalized.”¹⁷⁶

Müller was aware of successful cancer removal in at least two such cases—chimney sweeper’s malignancy of the testicle (where the ‘agent’ was thought to be soot) and cancer of the lip. On the basis of such studies he asserted that “a general disposition is not necessary for its origin.”¹⁷⁷ Indeed, case studies of locally cured cancers led him subtly to alter the meaning of “constitutional” to include changes in the body that occurred *after* the development of a malignancy, for, he concluded, “the disease becomes constitutional after it has persisted for some period of time.”¹⁷⁸ How could this be? Müller did not know. He acknowledged that “the way in which a carcinomatous dyscrasia develops from a mere local disposition escapes our further studies.”¹⁷⁹ Less than a decade after J. C. A. Recamier speculated that widespread cancers merely represented distant travels of an originally localized malignancy (hence he coined the

¹⁷⁴Müller, "Müller, Morbid Tumors," 96.

¹⁷⁵*Ibid.*, 97.

¹⁷⁶*Ibid.*

¹⁷⁷*Ibid.*

¹⁷⁸*Ibid.*

¹⁷⁹*Ibid.*, 98. A dyscrasia is an abnormal condition within the body, usually implying an “imbalance” or (etymologically) “bad mixture” of fluids—especially blood. During the nineteenth century, the term was used more commonly than today.

term ‘metastasis’ for ‘change in place’), Müller noted that the “germ-nuclei” of cancer journeyed via the bloodstream to fall on “soil suitable for their development.”¹⁸⁰

VIII. *Certain tumors, in themselves not cancerous, and whose nature it is to remain completely local, can rather easily give rise under appropriate conditions to a local cancerous disposition.*

Each generation of physicians construes its own cancer etiology. Chronic or “continuous” (to use Müller’s word) irritation predominated as the proximate cause of cancer throughout the nineteenth and early twentieth centuries. Simple observation supported this viewpoint, for patients and doctors invariably discovered malignancies after the bruising of a breast or, as in General Grant’s case, persistent buccal inflammation from a deformed tooth.¹⁸¹ Müller cited telangiectasias (dilated blood vessels visible as red blotches—LK) and nevi (congenital skin patches—LK) as examples, but these hardly proved his point. Once again, examples culled from the beliefs of others contained less truth than those derived from his own experience.¹⁸² In the end, he did not or could not explain the “appropriate conditions” that gave rise to the local cancer propensity.

¹⁸⁰Ibid. Joseph C.A. Recamier (1774-1852) published *Recherches sur le Traitement du Cancer, par la compression Méthodique simple ou Combinée, et sur l’Histoire Generale de la Même Maladie* in 1829. The term ‘metastasis’ is found in Vol. 2, page 110, lines 3-7. Recamier was a French gynecologist and obstetrician. See H. S. J. Lee, ed., *Dates in Oncology, Landmarks in Medicine Series* (Pearl River, NY: The Parthenon Publishing Group Inc., 2000).

¹⁸¹Today, physicians would likely implicate smoking as the proximate cause of General Grant’s and President Cleveland’s tumors. As noted in previous chapters, however, the relationship between smoking and cancer was controversial in the late nineteenth century.

¹⁸²Müller, “Müller, Morbid Tumors,” 99. The great fallacy of the irritation hypothesis—*post hoc ergo propter hoc*—implied that because the subsequent event (cancer) occurred after the first event (irritation), the first caused the second.

IX. *In contrast, many non-cancerous tumors have no tendency to develop a cancerous disposition even after repeated mistreatment, or, more correctly, their tendency toward a cancerous disposition is at least no greater than that of other healthy tissues.*

Müller found that some tumors, no matter how ‘mistreated’ (i.e., irritated or partially excised), did not develop into cancers. This finding must have disturbed Müller, for it upset his dominant notion of proximate causation. He gave no explanation for the discrepancy. Instead, he used it as a foil for his then radical claim that total extirpation of a tumor could permanently prevent recurrence. Cure by extirpation is an incongruous conclusion at this point in Müller’s treatise because the issue at hand was carcinogenesis rather than the justification of tumor excision. Vindication of the non-intuitive, contrary theory of localism weighed heavily upon him as he reached his tenth and final conclusion.¹⁸³

X. *Every form of cancer appears to occur at all times of life and in all organs, but at certain times of life some organs are more prone to cancer than others.*

This last conclusion could have been the first, for it is an epidemiological statement that lays the groundwork for all the others. Nevertheless, the placement of this proposition as the last conclusion is consonant with Müller’s interest in the aftermath of the (clinical) diagnosis of tumors and their differentiation into benign and malignant lesions. Although some cancers were known to be associated with specific organs in special populations (breast cancer and nuns¹⁸⁴; scrotal cancer and chimney-sweepers¹⁸⁵), most were not. Müller, the tumor microscopist, sought

¹⁸³Ibid.

¹⁸⁴Bernardino Ramazzini, *Diseases of Workers (De Morbis Artificum Diatriba)*, trans. Wilmer Cave Wright (Chicago: The University of Chicago Press, 1713; reprint, 1983). Ramazzini, justly titled the Father of Occupational Medicine, associated dozens of occupations with diseases to which their laborers were prone.

a method—the algorithm of today—to aid the practitioner. The microscope was the instrument of that method, but Müller’s romantic mind was the synthesizer.

The Berlin professor of anatomy had come full circle. After contrasting the microscopic characteristics of benign and malignant tumors, he elucidated the origin of tumors in an attempt to rationalize their differences. Why does cancer show a predilection for some parts of the body rather than others? Why do certain cancers tend to occur more frequently at some ages than others? Interestingly, Müller did not state—as others would after him—that the female organs showed a special predilection to malignancy around menopause. Neither did he emphasize that the incidence of cancer increases with age. On the contrary, he specifically maintained that cancer occurred “in all organs” and “at all times of life.”¹⁸⁶ But just which cancer occurred in this organ or at that age? Müller found that the old terminology of tumor origin and differentiation learned during his school years made little sense in light of his microscopical investigations. The problem with terminology again reared its ugly head, for the classical Latin nomenclature of ‘soft,’ ‘hard,’ ‘reticulated,’ and ‘brain-like’ was insufficient to the task.

Benign growths: “Tumors That Can be Confused With Cancer”

Müller’s “nature of cancer,” explicated by his ten conclusions, marked only the half-way point of his journey toward an understanding of pathological growths. To this point he had collected his thoughts on the microscopic structure of morbid tumors, their chemical composition, their development, and their nature. In the process, Müller demonstrated how the

¹⁸⁵Percival Pott, *The Chirurgical Works of Percivall Pott*, 2 vols. (Dublin: James Williams, 1778; reprint, 1985), vol. II, 403-06. Pott pays homage to Ramazzini in his late eighteenth-century treatise on surgical diseases, but noted that although the Professor of Medicine at Padua described many occupational diseases with which “every body is acquainted,” “there is a disease as peculiar to a certain set of people, which has not, at least to my knowledge, been publicly noticed; I mean the chimney-sweeper’s cancer.” (Ibid. 403) It is likely that Pott’ London had many more chimney sweeps than Ramazzini’s Padua.

¹⁸⁶Müller, “Müller, Morbid Tumors,” 99.

pathologist could use his conclusions to critically differentiate benign and malignant lesions. He then turned his focus to a deeper analysis of benign tumors.

Müller added the insights of the microscope and the new chemistry to the investigation of the structure and composition of non-malignant growths. To view him solely as the father of cancer microscopy is to miss his contribution to the pathology of benign tumors.¹⁸⁷ The enchondroma—a benign bone growth that literally means ‘tumor in cartilage’—confused clinicians seeking to discern benign from malignant lesions for centuries. Surgeons amputated many otherwise healthy limbs that actually harbored a benign enchondroma in the name of cancer. The fact that the excision “cured” the “cancer” was not surprising. Within the classical framework of his analysis, Müller teased apart the nature of enchondromas to show that they were not malignancies; that they could be differentiated from other tumors of bone—especially with the aid of the microscope; and that complete surgical removal (whether necessary or not) led to permanent cure. Likewise he attacked the problematic nature of other benign growths that many before (and even after) him removed in the name of cancer: fatty tumors (“cholesteatomas”), cystic tumors (“cystosarcomas”), and tumors of connective tissues (“tumor fibrosus s. desmoides”).

In his analysis of each growth, Müller combined traditional methodology with the new tools of microscopy and chemistry to make his case for benignity. General descriptions of the tumor at the macroscopic level began his presentation. Questions related to its origin and development followed. The crux of his argument focused on microscopic and chemical studies that revealed, for example, how enchondromas were similar to normal cartilage, but not to other

¹⁸⁷An analogy would be the clinician is deficient who knows not normal. Dr. Elliot Hochman, my first clinical instructor in physical diagnosis, taught that the hardest diagnosis to make is ‘normal.’

cancers.¹⁸⁸ Indeed, he showed that “the (microscopic) developmental history of enchondroma is exactly that of primitive chondrogenesis.” The microscope made clear that this common lesion of bone was not cancer.

The microscopic findings also allowed the investigator to differentiate the enchondroma from other bone growths—benign as well as malignant.¹⁸⁹ Müller followed the conformist tradition of rationalistic medicine and the etiquette of empiricism to connect the findings of those who preceded him—that which he entitled “the history of observations bearing on enchondroma.”¹⁹⁰ Finally, he described the known specimens (he called them ‘cases’) of enchondromas in museums throughout England and the Continent, beginning (nationalistically) with those in Germany. Similar but less detailed analyses followed on the other benign tumors. Throughout his analysis he sought completeness, for in his philosophy the key to understanding tumors was universal knowledge of the subject.

Müller Unbound

Müller, who, despite his pioneering valorization of the role of both cell and microscope in cancer, concluded that it was “ridiculous” to think that the instrument could be useful for the clinical (bedside) diagnosis of cancer. Nevertheless, he endeavored to create a means to reliably differentiate malignancies from other growths based upon that selfsame cell and microscope. The microscope was still a rare medical instrument in the 1830s and Müller could not foresee the day that every medical student (including future surgeons) would become familiar with its workings and teachings.

¹⁸⁸*The Finer Structure*, 106-114.

¹⁸⁹*Ibid.*, 120-122.

¹⁹⁰*Ibid.*, 122-128.

The microscope afforded Müller the ability to seek empirical, reproducible answers to critical questions where previously only hypothetical or untestable answers had been possible. Further, the science of the tumor microanatomy evolved over a much shorter period of time than the development of gross anatomy, thus lending a measure of uniformity to the thought and language of the microscopic aspects of the disease that the passage of time would otherwise have dissipated. In essence, the new microscope contributed toward the scientization of medicine.

Professor Müller's quest to create a reliable method to differentiate benign and malignant growths near the bedside (but not *at* the bedside!) remained largely unfulfilled throughout his life. Nevertheless, his investigations into the nature of cancer fired his students to continue the research he began toward an explanation of the origin and development of cancer. His seeming shortsightedness in declaring futile the use of the microscope for surgical diagnosis venerated a too-deep contemporary perception of the inability of practitioners to adapt new methods to old problems. Until late in the nineteenth century, he was largely correct. Indeed, long after his death in 1858, Müller's prediction that the microscope would play no role in the everyday diagnosis and treatment of cancer patients held true in the United States. The case of General Grant reveals the marginal use of the microscope in cancer diagnosis into the 1880s. Cell theory and the application of the instrument to pathological research sowed the seeds of modern cancer, but the further development of microtechnique and surgical advances that made tumor biopsy safe and reliable sparked the enduring role of the microscope in cancer medicine.

The Modernization of Cancer Microtechnique

Improving the Slide

The microscope was there; the microscope slide was not.

-Freda and Peter Gray¹⁹¹

¹⁹¹Gray and Gray, "History of Microtechnique and Microtomy," 260.

In 1838, the year of the publication of Müller's *Finer Structure*, most specimens for microscopic viewing were poorly prepared, inadequately fixed, and typically unstained. Practitioners, generally unfamiliar with the importance of microtechnique for slide interpretation, could not abide the all-to-often erroneous micropathological diagnoses offered them by histopathologists who examined their patient's specimens. By the time of Grover Cleveland's secret cancer surgery in 1893, however, slide preparation had progressed to a level not greatly below the microtechnique of today. Microscope-based diagnoses became less problematic. In 1889, merely four years after General Grant's peripheral brush with medical microscopy, Edward Schaeffer could write in truth that the microscope "enabled (the clinician) to make a correct diagnosis when other signs fail."¹⁹² What a turnaround! Only then did American clinicians consistently begin to rely on microscopic cancer diagnoses. Theories of the cell and improved microscope optics generated a decades-long flurry of activity toward the betterment of specimen preparation. The goal was clear: to see what was there (true positive) but not what was not there (false positive);¹⁹³ i.e., to eliminate the errors of pre-Listerian microscopy.

Medical Non-Microscopy in the United States

Here was a new field for the American student because the techniques of section cutting and the staining and mounting of histological preparations were practically unknown in our medical curriculum. In the United States the value of the microscope in medicine was regarded as a matter still to be proven, and by many this apparatus was looked upon goodhumouredly as a fad for the idealist rather than a useful tool of the teacher or practitioner.

-J. Collins Warren (1842-1927)¹⁹⁴

¹⁹²Schaeffer, "On the Microscopical Diagnosis of Cancer," 403.

¹⁹³I do not wish to give the reader the impression that the microscope and microtechnique had reached a state of perfection by 1893. On the contrary, the battle over cancer germs that will be addressed in a later chapter strongly suggests that optical artifacts persisted well into the 1890s and beyond. Nonetheless, microtechnique was not responsible for all the visualized 'artifacts.' Some were constructions of the mind's eye.

¹⁹⁴Cited by Malkin, "Comparison of the Use of the Microscope in Pathology in Germany and the United States During the Nineteenth Century," 82.

The United States was ill-prepared to further the development of microtechnique in the mid-nineteenth century. As late as June, 1875, Dr. William Henry Welch, a recent graduate of Columbia's College of Physicians and Surgeons, penned a letter to his father decrying his lack of education in microscopy. "I understand pretty well the lesions visible to the naked eye," he allowed, "but I know nothing about the microscopical appearances. I am sorry I have not yet been able to study with the microscope."¹⁹⁵ A generation later, lack of familiarity with microscopy would be unusual among medical graduates in the United States (thanks in no small part to pathologists like Dr. Welch), just as such inexperience was already unusual in graduates of German medical colleges when Welch complained to his father.¹⁹⁶ Later that year, Welch, like many other American physicians after the Civil War, set off to study in Germany—the mecca of scientific medicine and medical microscopy.¹⁹⁷

Science builds upon itself. That which comes before provides an ever-expansive latticework for new ideas and constructions that come to fruition after. Like an organism that requires the proper environment to thrive, Germany constituted a fertile soil for the growth of medical research in general and cancer investigation in particular. The United States did not. It

¹⁹⁵Simon Flexner and James Thomas Flexner, *William Henry Welch and the Heroic Age of American Medicine* (New York: Viking Press, 1941; reprint, The Johns Hopkins University Press, 1993), 70-71. Nevertheless, Welch recognized the value of microscopy, for he proceeded to explain to his father that the microscope "is very important." *Ibid.*, 71.

¹⁹⁶The valorization of microscopy was a German—not a Continental—endeavor. James Cassedy labeled the French disdain for microscopy "anti-microscopism" and added that the importation of this sentiment by American medical graduates who furthered their medical training in Paris during the early decades of the nineteenth century also served to fan the fires against medical microscopy in the United States. See Cassedy, "The Microscope in American Medical Science," 79. Brian Bracegirdle noted that as late as 1869 a Parisian medical group asserted that "the microscope's place in medicine...was not only valueless but actually detrimental." See Bracegirdle, *A History of Microtechnique*, 339 Footnote 60.

¹⁹⁷Kenneth M. Ludmerer, *Learning to Heal: The Development of American Medical Education* (New York: Basic Books, Inc., 1985), 32.

is therefore no surprise that Germany contributed most to the advancement of microtechnique in the mid-nineteenth century.

The Fatherland, Young America, and the Science of Medicine

The unification of Germany between 1849-1871 coincided with the institutionalization of medical inquiry. The Johns Hopkins model that Abraham Flexner proposed for the reform of American medical education in his influential 1910 Carnegie Foundation report had its roots in the state-supported academic institutions of Germany.¹⁹⁸ Johannes Müller, Rudolf Virchow, Robert Koch, their students, and their students' students were all part of a system that combined medical teaching and research. Status within the German medical community derived from productivity, and productivity depended upon research (especially through experimentation), teaching affiliations, and publications.¹⁹⁹

Medical education in America, at least until the twentieth century, laid emphasis elsewhere. As the policy of laissez-faire dominated the economics of the nation, so it also transfixed health care and medicine.²⁰⁰ Antebellum "physicians," in a land with lax or absent

¹⁹⁸Flexner, *Medical Education in the United States and Canada*.

¹⁹⁹Theodor Billroth, *The Medical Sciences in the German Universities: A Study in the History of Civilization*, ed. John K. Crellin Morton D. Bogdonoff, Robert A. Good, Ferenc Gyorgyey, John P. McGovern, Sherwin B. Nuland, Eugene A. Stead, Jr., Frank Vellios, Richard J. Wolfe, Norman R. Zinner, trans. William H. Welch, Intro., *The Classics of Medicine Library* (New York: The Macmillan Company, 1924; reprint, 1998). A contemporary source is the incomparable nineteenth-century Austrian surgeon, Professor Theodor Billroth, who was another famous student of Johannes Müller. William Welch, who transplanted the German system of medical education to the United States after his post-graduate studies on the Continent, wrote the introduction to the 1924 English translation of Billroth's work. Welch noted that *The Medical Sciences*, which probably influenced Flexner's 1910 study, stressed that "the importance of a liberal and scientific training in preparation for the study of medicine, has struck the balance more justly between the functions of the University as Schola and as Academia, has described more eloquently the personal tradition, influence and significance of the great university teacher, has dwelt more forcibly upon the importance of maintaining the integrity of the great, central clinical departments, has pointed out more convincingly the dangers of inbreeding, or has condemned more unsparingly the substitution of superficial routine for thorough grounding in sound methods and scientific principles in the training of medical students." See Welch's Introduction to Billroth, *The Medical Sciences in the German Universities*, viii.

²⁰⁰Lawrence Koblenz, "Medicine, God, and Belief Schisms: The Evolution of Fever Causation and Treatment in the Antebellum United States," (New York: Columbia University, 1996). Unpublished paper.

requirements for the practice of medicine (many states abandoned medical licensure in Jacksonian America), were often nothing more than those who called themselves so. Physicians labeled “regulars” and “sectarians” battled for dominance in an increasingly health-conscious populace. The Civil War thrust medicine and especially surgery into the public limelight. Nevertheless, it was not until the valorization of science in the popular imagination that the old regulars came to peace with their sectarian rivals, adopted or co-opted many of the sectarians’ patient-friendly prescriptives, and laid aside their frightening lancets to adopt a new “scientific” (and less “heroic”) medicine. In medical circles, as noted by Nathan and Ida H. Reingold, “echoes of Jacksonian rhetoric...persisted into the Progressive era.”²⁰¹

In 1878, Dr. Welch bemoaned the paucity of rigorous investigation in American medicine. During his Continental training, his German colleagues inquired why “no scientific work in medicine,” including the use of the microscope, was performed in the United States. Welch responded that “there is no opportunity for, no appreciation of, no demand for that kind of work here.”²⁰² Neither would there be, until the last years of the century, when improvements in European microscopy and microtechnique catapulted medicine and the study of cancer from the realm of popular wonder to medical science. In consequence, the microscope became *de rigueur* in cancer research and practice from the *fin de siècle* to the present. What were those advances, and how did they come to pass?

Microtechniques 1838-1858

²⁰¹Nathan Reingold and Ida H. Reingold, eds., *Science in America: A Documentary History 1900-1939*, 1st ed., *The Chicago History of Science and Medicine* (Chicago: The University of Chicago Press, 1981), 168.

²⁰²Quoted by Malkin, *Out of the Mist*, 343. Reasons for the belated development of scientific medicine in the United States are beyond the scope of this work, but explanations are abundant. For different perspectives, see, for example, Ludmerer, *Learning to Heal*, Chapters 1 and 2.; Phyllis Allen, "Etiological Theory in America Prior to the Civil War," *Journal of the History of Medicine and Allied Sciences* 2 (1947): 518-19.; and Cassedy, "The Microscope in American Medical Science," 79-80.

In the years surrounding the publication of Müller's seminal 1838 work on cancer microscopy, researchers discovered that microtechnique revealed deficiencies related to individual dexterity. Shortcomings led to difficult-to-reproduce or even irreproducible results. Proficiency and imagination fostered new ways of addressing inadequacies. Just as necessity is the mother of invention, so need is driven by awareness of deficiency. The corrected microscope magnified the failings of eighteenth- and early nineteenth-century microtechnique. In turn, it prodded those whose professional stature depended upon productivity to transmute natural specimens on sliders into microscopic slides that took advantage of the detail and richness that the new lens combinations could illuminate.

Microtechnique is as much art as science, for the goal is to create a slide that best manifests the pathological anatomy of the original specimen. The art derives from the choice among different methods—some better than others—to reach the objective. Following the introduction and acceptance of the aspherical, achromatic microscope, however, the trend decidedly favored science over art.²⁰³

The Specimen—Microscopy's Beginning

Cellular decomposition commences immediately upon tissue death. Specimens excised from the body are cut off from their sustenance and thus die. The microscopist seeks to preserve the characteristics of the living tissue as much as possible, because, the truer the slide, the closer the resemblance to the pathology of the living—and the greater the likelihood of an accurate diagnosis. Conservation of cellular characteristics is especially important for cancer specimens because the distortion of normal architecture by malignant growths is enough to dismay any

²⁰³The microtechnique that evolved over the previous century and one-half before the advent of the post-Listerian microscope was not the only procedure that converted elements of medicine requiring considerable individual skill and expertise for accuracy into routine, standardized, everyday undertakings. The same may be said of medicine in general as lab tests, imaging techniques, and clinical procedures scientificized patient diagnosis and management. Practice guidelines later codified objectification.

physician unaccustomed to such pathology. Obvious as the decomposition that death brings may be, such knowledge seems to have been unacknowledged until the nineteenth century.

Microscopists left tissues lying idle, oblivious to the fact that time alters the dead as well as the living.²⁰⁴ Artifacts that arose from poor specimen preparation aggravated the falsity of the image and increased diagnostic error. Therefore it should come as no surprise that microscopic depictions of cancer prior to the second quarter of the nineteenth century contained findings that could best be described in present parlance as “science” fiction—a problem that was partially (but not entirely) solved with improvements in microtechnique.

To Preserve the Appearance of the Living

The more rapid the “kill,” the greater the likelihood of accurate specimen preservation. Hence animal specimens from “fresh” tissue yielded better specimen preparations than those from human postmortems, which were typically obtained hours to days after death. Cancer, with its natural history of prolonged *in vivo* solid tumor decomposition (as in the cases of General Grant and President Cleveland), produced perhaps the least true-to-form specimens. Not until the development of the surgical biopsy in the latter half of the nineteenth century did procurement and preservation techniques offer the cancer investigator specimens that maximized true viewing of the patient’s underlying micropathology.

Microscopists of the seventeenth century and thereafter were aware that atmospheric forces adversely affected non-living specimens, but the corrected microscopes of the late 1820s and thereafter made the problem more acute. Low humidity, for example, dried nature’s samples rapidly. Dessicated organisms shrunk and distorted tissue architecture. Researchers sought

²⁰⁴Bracegirdle, *A History of Microtechnique*, 59.

methods to “fix” tissues as close as possible to their natural state. “Fixatives” preserved and hardened specimens for microscopical examination.

Robert Hooke’s 1665 answer to the problem of fixation—glue—was inadequate to the task. In 1833, as chemistry became the fashion of science, J. Jacobson, one of a long string of innovative German microscopists, suggested that chromic acid could be used for such purpose.²⁰⁵ This chemical was one of the first to harden and preserve the tissue without destroying its natural detail. In 1840, A. Hannover discovered another fixative in the form of chromium trioxide.²⁰⁶ The slow dissemination of scientific information among microscopists in those years hampered the general use of these improved preservatives, so that it was not until the late 1870s that they became widespread.²⁰⁷

Chemists and microscopists tested other chemical fixatives over the intervening decades, but not until 1892 did J. A. Trillat and, the next year, F. Blum hit upon formaldehyde as an excellent preservative.²⁰⁸ Today formaldehyde, a simple molecule, is the most common constituent of fixatives. The finding of this enduring fixative, however, did not come easily or methodically. As so often occurs with scientific discoveries, Blum’s application of the chemical as a fixative was serendipitous. One night he accidentally failed to remove an anthrax-infected mouse from a weak solution of formaldehyde. The next day, to his surprise and delight, he returned to find the murine tissues firm and well-preserved.²⁰⁹ The recent discovery of

²⁰⁵“Versuche über technische und medicinische Anwendung der Chromoxyde und der Chromsalze,” *Liebig, Annal.*, 1833, 7: 329-331. Cited by Bracegirdle, *A History of Microtechnique*, 97FN16.

²⁰⁶“Die Chromsäure, ein vorzügliches Mittel bei mikroskopischen Untersuchungen,” *Müller’s Archiv*, 1840: 549-558. Cited by *Ibid.*, 97FN19.

²⁰⁷*Ibid.*, 60.

²⁰⁸Cited by *Ibid.*, 62 and 98FN53 and 54. Formaldehyde, or HCHO, was also found to be an excellent disinfectant, thus serving a double duty in the quest to preserve the microscopic specimen.

formaldehyde for tissue preservation and fixation make it unlikely that the pathologist at the Army Medical Museum used it to prepare President Cleveland's tumor biopsy submitted by Dr. O'Reilly in June 1893, but the records do not reveal the fixative.²¹⁰

The Scientific Slice: Microtomes and More

An accurate microscopical diagnosis depends upon good tissue, preparation, and interpretation. Nevertheless, no matter how good the interpreter, poor tissue and/or preparation will thwart an accurate diagnosis. Thus, good preparation is essential. Following procurement, preservation, and fixation, the specimen must be cut or "sectioned" for examination under the microscope. Since the optical cortex of the human brain "sees" images based upon light from the subject that strikes the retina, too thick a specimen creates many layers through which transmitted light must pass. Limited light reaches the retina and confusion reigns in the mind's eye. For centuries, those who would examine the creatures of nature under the microscope sought effective, reliable, and reproducible methods to pare specimens for optimal viewing.

Cancerous tissue was particularly difficult to cut, for tumors often had soft, liquified centers that made clean cuts through superficially solid masses nearly impossible. Even scirrhous lesions ulcerated, yielding the malodorous discontent that so offended the Ladies' Board at Dr. Sims' Woman's Hospital, and at the same time making sectioning problematic. Fixatives added little in such situations. Hence diagnosticians often obtained specimens from the firmer periphery of growths, hopeful that the outer cells would accurately represent the whole and portray an image sufficient to yield a correct diagnosis. The specimens Dr. Riley excised

²⁰⁹Ibid., 62.

²¹⁰Microscopists have employed many other chemical and physical fixative agents since the second third of the nineteenth century. Freezing and drying the specimen, two of the earliest physical methods, found renewed life with the electron microscope in the twentieth century.

from General Grant (“small pea” from the edge of an ulcer) and Dr. O’Reilly from President Cleveland (“scrapings”) were of this ilk.

The earliest microscopical specimens were uncut. In the late seventeenth and early eighteenth centuries, Leeuwenhoek’s simple-lens instruments contained a pin that skewered the object, rendering it fixed (in position, not time) rather than preserved. Higher powers of magnification required not only the marvelous lens-grinding abilities of the Dutch microscopist, but also a thinner piece of specimen through which light could be transmitted rather than reflected. Hence was born a tool for cutting small—the microtome.²¹¹

The knife and razor were the first tools used to slice tissue specimens.²¹² The vagaries of hand-cut preparations, however, wreaked interpretive havoc on interpretation due to the dimensional vagaries of the slice. In 1770, the Englishman John Hill addressed the problem with the construction of what was arguably the first mechanical microtome.²¹³ It was an elegant affair—practical and clearly a product of the nascent industrial revolution in England.²¹⁴ Unfortunately, it did not always function as intended, for animal tissues in general and cancerous tumors in particular, lacking the stiffening cell walls of plants, rolled under the blade and curled like soft wood under a whittling knife, whereas microscopists demanded flattened shavings for easy layout on a slider. Nevertheless, the seed had been sown and others, as we shall see, later improved on the idea.

²¹¹The microtome is misnamed. The emphasis is on thin slices rather than small slices. Although contemporary sections may be cut so small that they can be visualized only with a light microscope or even an electron microscope, tissue sections in the nineteenth century were thin rather than too small. A Latin construction for ‘thin cutter’ might be ‘ten tome.’ Better to embrace ‘microtome.’

²¹²Hunt and Hunt, "Dr. Oliver Wendell Holmes," 83.

²¹³Bracegirdle, *A History of Microtechnique*, 12.

²¹⁴Hill microtomes are still extant. Bracegirdle provides several photographic plates of the original machines with an explanation of their mechanisms. *Ibid.*, 152, Plates 2, 3, and 4.

Myriad advances in microtechnique helped transform the microscope from a dilettante's playtoy to a medical instrument over the course of the nineteenth century. Embedding the specimen in a substance to facilitate preservation and sectioning was one.²¹⁵ Mounting—the act of placing the specimen on top of a slide for viewing—was another. Lighting, which took a giant leap forward with the advent of electrical illumination (again in the 1880s)—was a third.²¹⁶ All added parts to a whole, the objective of which was perception of nature and nature's diseases as they actually were.²¹⁷

The work of Schleiden, Schwann, and Müller laid the foundation for European improvements in thin sectioning and other aspects of microtechnique. In 1839, for example, Johannes Evangelista von Purkinje (1787-1869) of Prague, friend of Goethe and originator of the term 'protoplasm,' first applied the microtome to medical microscopy.²¹⁸ In fact, the word 'microtome' was initially used that year—by a Frenchman—although, ironically, he meant it to signify a hand-held knife rather than a mechanized device.²¹⁹ Thus, although Johannes Müller's "microtome" was a sharp knife, mechanical devices dominated in the years to come.

²¹⁵Edwin Klebs began the modern technique of embedding in paraffin in 1869, but it was not widely practiced in the United States until the early twentieth century. See William Derek Foster, *A Short History of Clinical Pathology* (Edinburgh: E. & S. Livingstone Ltd., 1961), 18, 19.

²¹⁶In the space of a decade, from the 1880s to the 1890s in New York and other municipalities, microscopical illumination advanced from the reflected light of the sun or candle to the "anytime, anywhere," less combustible opportunities afforded by electric lighting.

²¹⁷With apologies to Leopold von Ranke, who wrote of capturing the historical past "wee as eigentlich war"—as it actually was.

²¹⁸Hajdu, "Cytology," 670.

²¹⁹The neologist was C. Chevalier, who noted "un nouveau microtome de l'invention de M. Valentin." The original use of the word 'microtome' is in Chevalier's *Des microscopes et de leur usage* (Paris: Crochard, 1839), 192, as noted by Bracegirdle, *A History of Microtechnique*, 47, 117, 281FN17. 'Microtomy,' the expression used for the preparation of specimens with a microtome, was not found in print until 1884, the year of General Grant's cancer diagnosis. J. A. Ryder, who noted the word for the first time in his *American Monthly Microscopical Journal* article, "On some points in microtomy (5: 190-191)," called it "a new art." See Bracegirdle, *A History of Microtechnique*, 281FN17.

New methods of specimen presentation, developed from the 1830s to the 1880s, were forged by the industrial revolution, impelled by scientific inquiry, augmented by German medical institutionalism, shaped by the rise of cell theory, and made possible by the theory's required tool of the trade—the corrected microscope. All this being said, the aspect of microtechnique that caught the attention of the scientific community and best allowed easier slide viewing, better comparison between specimens, and the teaching of microscopy—was staining.

The Marriage of Chemistry and Microscopy

Staining is a biochemical process.²²⁰ Colored chemicals flood the microtomed, fixed specimen and are “taken up” differentially by various tissues, cells, and organelles. Chemical reactions that bind the dye to the biological specimen occur at the nano-level. If the wavelength of the light reflected from this union lies within the visible spectrum, the viewer perceives color. Stains vivify the drab colors and amorphous shapes of unstained preparations. Poorly-seen microanatomical features stand out as never before. Although some human tissues, like striated muscle and nerve cells, have distinctive markings or contours that distinguish them from others, stains make conspicuous otherwise hard-to-see somatic components. The greater detail visualized through the high-magnification compound microscope of the 1830s and thereafter, coupled with the rise of chemistry, brought forth a marriage of opportunity that served to propel microscopy—and medicine—from passive didacticism to active science. The study of cancer benefited more than most other disciplines, because highlighting stains revealed that the secret of cancer lay concealed in the subvisible world of the microscopic.

²²⁰The works of Clark and Kasten, *History of Staining*. and Bracegirdle, *A History of Microtechnique*., provide great detail on the history of staining but few specifics related to neoplasms.

Staining is an offshoot of dyeing, a process at least as old as the Ancient Egyptians, Persians, and Chinese. Staining and dyeing both alter the natural color of substances. Although ‘stain’ retains a somewhat negative meaning today, that connotation is absent from the field of microscopy, possibly because of the essential role staining played in the advancement of medical science through the elucidation of histologic features.

Nineteenth-century microscopists were not the first to realize the value of stained specimens. There is some debate as to whether Hooke or Leeuwenhoek used “the first stain,” but the argument is more semantic than substantial.²²¹ Hooke’s *Micrographia* (1665) illustrated both unstained and stained hair and wool.²²² In 1714, Leeuwenhoek colored muscle fibers with the natural dye saffron in spirit.²²³ Both recognized the need to highlight organic structures in order to differentiate them under the microscope. Injections of hued materials like cinnabar (bright red) into the vessels of animals followed, but these outlined the anatomy more than spotlighted its components. In 1735, Belchier serendipitously discovered the first intra-vital stain—a finding made more important to modern cancer diagnosis since the advent of endoscopic and most other *in vivo* tests in the twentieth century. He found that animals fed with madder, a yellow-flowered plant with red roots, stained the bones of the living creature red.²²⁴

²²¹Bracegirdle wrote that “Leeuwenhoek used the first true stain.” Bracegirdle, *A History of Microtechnique*, 67. Clark and Kasten claimed that the Englishman Hooke, not the Dutchman, was “the first to describe the microscopic appearance of a stained object.” See Clark and Kasten, *History of Staining*, 35. Although the two statements are not mutually exclusive, the import denotes historians’ conflicting views between the timing of advances made by the older Englishman and the younger Dutchman.

²²²Clark and Kasten, *History of Staining*, 35.

²²³Bracegirdle, *A History of Microtechnique*, 67.

²²⁴Hajdu, “Cytology,” 669. The scientific name of madder is *Rubia tinctorum*—or, etymologically, ‘red dye.’

The importance of staining technology to cancer medicine can be illustrated with a brief note on the history of lung cancer diagnosis by means of expectorated sputum examination. In 1821, Andral presciently conceived that sputum coughed up by a patient with abnormal pulmonary findings on physical exam might reveal the cause of the problem. Poor staining made his quest for the validation of this new diagnostic technique unattainable. In 1887, however, Hampeln, utilizing techniques and stains developed after the advent of the achromatic, aspherical microscope, achieved the sputum diagnosis of lung cancer via the microscopic examination of stained cells—the accomplishment that eluded Andral for lack of staining.

The first wave of scientific discovery often results from the union of new thoughts with old methods or new techniques with old ideas. Rarely do novel concepts and innovative techniques come together simultaneously to foster fresh discoveries. The development of staining during the nineteenth century, however, represented one of those unusual instances when two originalities combined—in this case the cognitive powers of chemistry with the physics of microscopy.

The Problem with Natural Dyes

Although weavers had used natural plant and animal dyes for millennia, the small number of dyes, limited color spectrum, and scant availability largely restricted their use to enterprises with more profit potential than histology.²²⁵ Nevertheless, natural dyes served an important function in the development of medical and cancer microscopy because during the 1850s, when microscopic staining became prevalent for the first time, such dyes revealed their value for histology and propelled the quest for new stains.²²⁶

²²⁵Clark and Kasten, *History of Staining*, 203.

²²⁶Malkin, *Out of the Mist*, 136.

Carmine was the most frequently used natural dye prior to the second half of the 1850s. Although carmine's rich history reveals that John Hill used it in 1770,²²⁷ Göppert and Cohn reiterated its use in 1849,²²⁸ and Hartig boosted all staining and carmine in particular beginning in 1854,²²⁹ J. von Gerlach made it so popular in 1858 that he is often falsely credited with its discovery.²³⁰ A long tradition of intermittently-used staining with natural dyes worked in tandem with the improved microscope and the impetus of cell theory to usher in an augmented interest in histopathology in general and cancer micropathology in particular.

The catalyst for this first wave of cancer-cell staining in the 1850s was none other than Rudolf Virchow, the father of cell pathology. Nevertheless, staining was a mere tool for Virchow. His contributions to the history of cancer lay elsewhere. Thus, the man and his work shall be explored prior to returning to the discipline of staining later in the nineteenth century under one of the greatest medical chemists of all time.

Rudolf Virchow

One generation passeth away, and another cometh: but the earth abideth for ever.
—Ecclesiastes 1:4

Rudolf Virchow reached the height of his medical prowess in the late 1850s with his work on cellular and cancer pathology.²³¹ At about the same time Johannes Müller, whom Virchow admired, died tragically—the likely consequence of an opium overdose after years of self-medication for depression.²³²

²²⁷Clark and Kasten, *History of Staining*, 44.

²²⁸*Ibid.*, 202.

²²⁹Bracegirdle, *A History of Microtechnique*, 67.

²³⁰Clark and Kasten, *History of Staining*, 202.

²³¹The tomes by Virchow are *Cellular Pathology* and *Die krankhaften Geschwülste*.

Virchow, Müller's most famous student, was a Renaissance man with a fascination for *die krankhaften Geschwülste*—morbid tumors. Born in 1821, one year before Ulysses Grant, he played a role during his life of more than eight decades in many of the great movements of the nineteenth century—from the anti-capitalist revolts that fanned the fires of 1848 to the reformist liberalism of Bismarck's German empire to the founding of modern medicine. Even more than “doctor, statesman, anthropologist,” to quote the muted subtitle of Erwin Ackerknecht's 1953 biography,²³³ gadfly Virchow sought to right wrongs wherever he found them—from the elimination of poverty (and the maladies it engendered) to the accurate attribution of eponymic diseases.

As a youth of 18, the young Prussian declared the desideratum of his life to be “all-round knowledge of nature from the Deity down to the stone.”²³⁴ Virchow studied with Müller during the latter's most productive years and earned his medical degree from the University of Berlin in 1843 at the age of 22. His academic record qualified him for a post-graduate position at the Berlin Charité, where his fledgling interest in cell theory was whetted by one of his hospital colleagues at the hospital—Theodor Schwann. Thus, before his twenty-fourth birthday, Rudolf Virchow's passion for knowledge was quickened for cell theory, microscopic pathology, and cancer by those on the cutting edge of what was becoming medical *science*.

²³²Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 33. Eighteen fifty-eight was the year of Virchow's triumph and Müller's demise. Müller died on April 28, 1858. Virchow dated the preface to the first edition of *Die Cellularpathologie* August 20th. Both events occurred in Berlin.

At his teacher's eulogy, Virchow noted that “there was something supernatural about Müller, for his whole appearance bore the stamp of the uncommon; and that his commanding influence did not wholly depend on his extraordinary original endowments, is certain from what we know of the history of his mental greatness.” (Cited by Malkin, *Out of the Mist*, 136. from R. Virchow, *Johannes Müller, the Physiologist*, tr. By A. M. Adam, *Edin. Med. J.* 1858, 452 and 527, tribute delivered at the University of Berlin.)

²³³Erwin H. Ackerknecht, *Rudolf Virchow: Doctor, Statesman, Anthropologist* (Madison, WS: The University of Wisconsin Press, 1953).

²³⁴Jessica Bendiner and Elmer Bendiner, *Biographical Dictionary of Medicine, Facts on File* (New York: Facts on File, Inc., 1990), 248.

Virchow manifested no reticence in furthering the application of empiricism to pathology. Gone was the natural philosophy that introduced Müller to medicine a generation before. Instead, the mechanistic view of physiology and pathology that subsumed Müller in his mature years dominated the thought of his student Virchow. At the age of twenty-six, while advocating “democracy, education, freedom, and prosperity” as the cure for epidemics (and social injustice),²³⁵ he co-founded the influential *Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* (*Archives for Pathological Anatomy and Clinical Medicine*).²³⁶ This journal, still published today under the title *Virchows Archiv*, promoted his plea for scientific medicine.²³⁷ The goal of the publication, as stated in the first issue, is well worth noting, for it established the foundation of Virchow’s relentless pursuit of cell pathology, including the cancer cell. As translated by Henry Sigerist, Virchow wrote:

The standpoint we propose to adopt and which is already manifested in this first issue is simply that of natural science. Practical medicine as applied theoretical medicine, and theoretical medicine as an embodiment of pathological physiology, are the ideals towards which we shall strive so far as lies within the scope of our powers. Pathological anatomy and clinical work, although we fully recognize their justification and their independence, are both mainly regarded as the sources of new problems whose answers must be supplied by pathological physiology. Since, however, these problems must for the most part be formulated by means of a laborious and comprehensive study of detailed phenomena in the sick and upon the post-mortem table, we maintain that a precise and purposive development of anatomical and clinical experiences is the first and most important requisite of the day. Through an empiricism of this sort there will gradually be brought into being a genuine theory of medicine, a pathological physiology.²³⁸

²³⁵Ibid., 249.

²³⁶To reach a wider audience, Virchow established his *Archiv* with his friend and fellow pathologist, Benno Reinhardt. Virchow enlisted the aid of Reinhardt, at least in part, because not everyone (to put it mildly) appreciated Virchow’s dogmatic views. He continued to use the *Archiv* as his main organ of pathological expression until his death in 1902. See Malkin, *Out of the Mist*, 145.

²³⁷In 1994, *Virchows Archiv A* (pathological anatomy and histopathology) merged with *Virchows Archiv B* (cell and molecular biology) to create *Virchows Archiv—An International Journal of Pathology*.

²³⁸Sigerist, *The Great Doctors*, 319-20.

Thus, instead of the venerable model of natural philosophy, Johannes Müller's beliefs in natural science colored Virchow's framework for understanding the structure and function of disease. Observation trumped theory, but theory persisted as both mother and child of empiricism. Nevertheless, the student of the master directed his effort not only toward the description of observations, but to process—not merely toward the anatomy of disease, but toward a knowledge of “pathological physiology.”²³⁹

Omnis cellula a cellula.

—Rudolf Virchow, 1855

The microscope had afforded Müller the opportunity to achieve a novel view of cancer. Virchow carried his mentor's methodology farther to answer not only the “what” about cancer but also the “how.” Müller had characterized the microscopic appearance of cancer cells. Virchow further posited that the essence of the structure and function of the disease lay within the tumor cell. As the keystone of his work in pathology, he wrote in the transitional German-Latin of his day that “Ich formulire die Lehre von der pathologischen Generation, von der Neoplasie im Sinne der Cellular-pathologie einfach: Omnis cellula a cellula.”²⁴⁰ All cells out of cells. The origin of cells—diseased or healthy, cancerous or not—is from prior cells. Cells do not appear *de novo*. Cell theory displaced the time-honored belief in spontaneous generation.²⁴¹

²³⁹The resemblance of Virchow's emphasis on process to Georg Wilhelm Friedrich Hegel's (1770-1831) dialectical process of history and philosophy is striking. Hegel, a contemporary of Müller in Berlin, died when Virchow was a boy, but his influence on German thinking, as evidenced by the ideas of Marx and the Positivists, was far-reaching.

²⁴⁰Rudolf Virchow, “Cellular-Pathologie,” *Arch. path. Anat. Phys. klin. Med.* 8 (1855): 7.

E. H. Ackerknecht noted that the concept that all cells derived from prior cells had been put forth by Raspail in 1825, Goodsir in 1845, and Remak in 1852. See Ackerknecht, *Rudolf Virchow*, 74-76. Virchow, however, made it famous. See Bracegirdle, *A History of Microtechnique*, 318 and 39 Footnotes 68-71.

²⁴¹The term ‘spontaneous generation’ can be confusing. In the nineteenth century, spontaneous generation referred not to the creation of new cells by self-induction or self-generation without external instigation (as one might conclude from a strict interpretation of the two words), but rather to the genesis of life from non-life—like maggots from meat. To this day, cell division, the process of new cell formation from old cells, is thought to occur

Simply put, the cells of life do not generate from non-life. The cell was the epicenter of Virchow's physiological and pathological universe.

Nature's Crayons: Carmine, Iodine, Acetic and Sulfuric Acids

Virchow used natural dyes to enhance visualization and interpretation of microscopic pathology. Just as the achromatic, aspherical microscope energized the development of cell theory, so the application of colors to the specimen slide furthered cancer histopathology. Johannes Müller's 1838 treatise on unstained cancer cells represented a beginning—a recognition—of the importance of the microscope for cancer pathology. Virchow's use of natural stains to highlight tissue elements provided him with the ability to differentiate structures and cellular patterns unknown to his teacher. The tinted actors were clear and distinct: carmine stained red; iodine pale blue or blue-gray; acetic acid decolorized and enhanced nuclear detail; and sulfuric acid turned iodine's light blue to violet.²⁴²

Virchow's forte for slide preparation aided his prowess in pathology. Staining was an integral part of that special ability. His carefully prepared slides allowed him and his students to grasp the intricacies of tumor morphology. George Dock, the eminent American clinical pathologist, penned a glimpse of Virchow's *modus operandi* in his description of the summer course he attended under the tutelage of the renowned Herr Professor as a post-graduate student in mid-1880s Berlin.²⁴³ With his own microscope accessories in hand, he “took a course on autopsies, pathologic anatomy and microscopy under Virchow from seven to nine A. M., three times a week. In this course, the microscopes, with slides clamped on them, were moved along

from forces inside the cell; i.e., ‘spontaneously’ (although extracellular factors, like hormones, promote cell cycle progression). A better term for spontaneous generation might have been ‘abiogenesis.’

²⁴²Virchow, *Cellular Pathology*. See especially pages 371, 372, and 430 for Virchow's application of (natural) stains to his pathological specimens.

²⁴³Dock, "Clinical Pathology in the Eighties and Nineties."

three sides of a large room on a miniature railway. Gross specimens were sent around on trays and the sections taken from them were unstained or treated with acetic acid or iodine.”²⁴⁴

Unstained or treated with natural chemicals. Virchow’s extensive investigation of cancers, published in the final chapter (“Lecture XX”) of his famous *Die Cellularpathologie* (1858) and expanded upon in his 1800-page never-finished opus, *Die krankhaften Geschwülste* (1863-1867), matched a keen intellect with acute powers of observation—enhanced by slides stained with natural dyes.

Observations versus Conclusions

The stained tumor slides viewed by Virchow helped him to advance cancer pathology to new levels of theory and empiricism. Although of great relevance in his day, it matters less at present that many of his conclusions as to the origin and development of cancer were later shown to be wanting. Indeed, Virchow’s formulations as to the etiology of cancer—some of his most controversial ideas—could not even be verified by the microscope. Despite Müller’s admonition to the contrary,²⁴⁵ Virchow maintained that chronic irritation caused cancer²⁴⁶ (the most prevalent theory of cancer causation in the nineteenth century), that “cancer juice” was carcinogenic (a bow to the reign of chemistry),²⁴⁷ and that cancer developed from heterologous tissue.²⁴⁸

²⁴⁴Ibid., 672.

²⁴⁵Müller, "Müller, Morbid Tumors." on “The Nature of Cancer,” IX.

²⁴⁶Virchow, *Cellular Pathology*, 462.

²⁴⁷Ibid., 485 and 87.

²⁴⁸Ibid., 403 and 62. German pathologists in the Müller-Virchow heritage appear notorious for not following their teacher’s ideation. As Virchow disavowed Müller’s warning that ‘mistreated’ (irritated) growths rarely change into cancer and heterology is impossible to prove, so Julius Cohnheim, Virchow’s most famous student (and William Henry Welch’s most influential post-graduate European mentor), disputed the chronic irritation hypothesis to put forth his ‘embryonal rest’ theory of cancer formation.

Microscopy could confirm none of these findings because each required the ability to observe cellular transformation over time. In Virchow's day, however, microscopy was static—one slide preserved cells from one moment in time. No microscopist-pathologist could observe a direct carcinogenic effect from chronic irritation because that was a transformation that occurred over days, weeks, months, or years—depending upon the circumstances. No microscopist-pathologist could follow the transmogrification of connective (heterologous) tissue cells into epithelial cancer cells for the same reason. Nevertheless, absence of proof was not proof of absence, so Virchow's observations did not preclude theorizing.²⁴⁹

Interestingly, Virchow recognized the atemporal nature of his pathological studies. He even protested against the “ontologizing” of disease—the creation of distinct pathological entities from transient states in the natural development of the disease.²⁵⁰ Ironically, he was himself guilty of leaps of the imagination when he unscientifically adopted chronic irritation, cancer fluid, and heterology as the mainstays of cancer causation. Had he avowed only that which he personally observed rather than that which others professed—also a criticism of his mentor Müller—his conclusions might have been different. Such deracination of thought, however, was nearly impossible in a scientific community that prided itself—moreso, was founded upon—the free exchange of ideas.

Cellular Pathology as Based upon Physiological and Pathological Histology

Lecture XX.

“Form and Nature of Pathological New-Formations”

²⁴⁹Virchow, in his defense, believed that the time-frozen specimens he viewed under the microscope did reveal pathological change over time. See, for example, his analysis of tubercle formation, at *Ibid.*, 476.

²⁵⁰Rather, *The Genesis of Cancer*, 101.

April 27, 1858

The essence of Virchow's contribution of cellular pathology to cancer medicine in his classic mid-nineteenth-century tome can be distilled from his insistence on the application of microscopically-derived names to "new-formations"—a term that can be rendered more clearly as neoplasms.²⁵¹ In his twentieth lecture, he applied his understanding of the nature of the cell to the unsettled question of the origin of the cancer cell. He asserted that physiological and pathological histology, as the sub-title of the work implies, must be applied to tumors as well as other lesions. Cancer was part and parcel of human pathology, not something from the outside that invaded the host. The best example of such a new-formation, according to Virchow, was the tubercle (a pathological expression of what is now called tuberculosis), an entity then believed to be malignant and impossible to clinically differentiate from cancer.²⁵² New-formations, consonant with the broad definition of 'tumor' commonly held at that time, thus included all growths—benign, malignant, infectious, and otherwise.

True Names

"We must consider the histological point of view as the true one," he demanded.²⁵³ Thus the microscopic is the perspective from which all perceptions—and thus names—must originate.

²⁵¹Webster's Ninth New Collegiate Dictionary notes that 'neoplasm,' an internationally recognized word, was first used in 1864—six years after the initial publication of *Die Cellularpathologie*. See Frederick C. Mish, ed., *Webster's Ninth New Collegiate Dictionary* (Springfield, MA: Merriam-Webster Inc., 1991), 792. Webster's notwithstanding, Virchow used the word "neoplasie" in the preamble to his famous 1855 quotation, 'omnis cellula e cellula.'

I believe 'new-formation' is unfortunate language because it recapitulates the problem of tumor definition in the nineteenth century—viz. the incorporation of inflammatory as well as benign and malignant neoplastic lesions into the meaning of tumor. Granulation tissue that leads from wound to scar, for example, can be conceived, technically, as a 'new-formation.'

²⁵²Wilson I.B. Onuigbo, "The Diagnosis of Lung Cancer in the 19th Century," *British Journal of Diseases of the Chest* 65 (1971). Consumption, the term for the disease that became tuberculosis at the end of the nineteenth century, and cancer had many similarities. For most of the century, practitioners and pathologists believed both to be hereditary and to have several common micropathological features. See Wilson I.B. Onuigbo, "Some Nineteenth Century Ideas on Links between Tuberculous and Cancerous Diseases of the Lung," *British Journal of Diseases of the Chest* 69 (1975).

If the proper study of man is by man, then the proper study of cancer is by the microscope. And just as God gave man the gift of naming the beasts and fowl of the Earth,²⁵⁴ so man should name tumors on the basis of their histological attributes and not follow the haphazard naming procedures of an ill-ordered past. Names of new-formations had “been based pretty much upon accidental peculiarities, and not so very unfrequently (sic) selected in quite an arbitrary manner.”²⁵⁵ Even the most valiant efforts at systematized nomenclature “were really only based upon the consistence of tumors”—the hard, soft, and gelatinous textures well known to Müller.²⁵⁶ “It is self-evident,” Virchow continued, “that the ideas which are now attached to several of these things must be done away with, if it be wished to understand the original meaning of these designations.”²⁵⁷ Rather than names based upon “rough resemblances in external appearance,” appellations should take account of “the more delicate peculiarities of structure, and particularly of the really histological composition.”²⁵⁸ The original meaning of tumors lay in reformed terminology. The chemistry and microscopy of tumors, not the names of men and places of discovery (eponyms), should determine designations in order to impute etiology and pathogenesis in the name and, thus, differentiate “*the mere form and the true nature.*”²⁵⁹

Virchow disavowed the term ‘epithelioma’—the name of the cancer diagnosed in General Grant and President Cleveland. He concluded that the term epithelioma was

²⁵³Virchow, *Cellular Pathology*, 464.

²⁵⁴*Genesis* 2: 19-20.

²⁵⁵Virchow, *Cellular Pathology*, 463.

²⁵⁶*Ibid.*

²⁵⁷*Ibid.*

²⁵⁸*Ibid.*, 464.

²⁵⁹*Ibid.*, 466. Italics in the original.

“completely inadmissible” because it “is by no means the only tumour whose elements bear the character of epithelial cells.”²⁶⁰ The new pathologist of Virchow’s generation emphasized differences, not similarities. Müller had named the tumor ‘cholesteatoma’; Cruveilhier, ‘tumeur perlée’ (translated by Virchow as ‘Perlgeschwulst’—pearly tumor). Dr. George R. Elliott’s pathological diagnosis of epithelioma on Ulysses S. Grant in the winter of 1885 highlighted his observational finding of pearly “cell nests.”²⁶¹ Virchow pointed out that the application of the same name to cancers that exhibited pearl-like globules but otherwise behaved differently was misleading and perilous to proper diagnosis and prognosis. Thus he heralded the micropathologic truism that seemingly conclusive diagnostic findings must be tempered by their surroundings; i.e., by the company they keep.²⁶²

Nevertheless, Virchow did pay homage to the problem of precedent. “Only it is not, I think, advisable...at once to proceed to create new names for every thing, and by means of these new names to render things which have long been known strange to the minds of people in general.”²⁶³ Tumor terms may even admit descriptions of mere form, against which he usually railed, but only when “conjoined with a real difference in the tissue.”²⁶⁴ That ‘real difference,’ discernible neither to the naked eye nor to the touch, derived from the pathological physiology of the tumor—the union of form and function based upon the ability of the observer to differentiate

²⁶⁰Ibid., 482.

²⁶¹Steckler and Shedd examined Elliott’s line drawings of Grant’s histopathology in 1976 and confirmed that the pearl-like tissue (now termed “keratin pearl formation”) was consistent with squamous cell carcinoma—the more histologically-oriented modern term for epithelioma. See Chapter 3, Footnote 161.

²⁶²Virchow was not the first to announce the importance of the elements surrounding suspicious cells. Carl Bruch had made the point in his 1847 monograph, *Die Diagnosis der bösartigen Geschwülste* (Mainz), as cited by Rather, *The Genesis of Cancer*, 111 and 207 Footnote 131.

²⁶³Virchow, *Cellular Pathology*, 464-5.

²⁶⁴Ibid., 466.

cells and tissues under the microscope. That distinction, to a growing extent, depended upon a clearer definition of the cell and its surroundings as visualized by more accurate microscopy.

And that, in turn, reflected advances in staining and improved microtechnique.

Virchow's *Die Krankhaften Geschwülste*

(*The Morbid Tumors*)

1863-1867

Rudolf Virchow poured the soul of his life's work into the lectures that constituted his ambitious and massive three-volume tome on tumors. The microscope, rarely mentioned explicitly, is implicit throughout. The preparation and staining of specimens, as in *Die Cellularpathologie*, is also tacitly omnipresent. Today, medical research publications typically include an explanation of methodology. Such was less commonly found in the pathology publications of the nineteenth century, so it is difficult to know Virchow's methodology exactly. Nevertheless, his application of advances in microtechnique years after the tumor publications of Müller in the 1830s is clear from the cell pathologist's lectures and writings from the late 1850s and early 1860s. The great contribution of Virchow and his microscope was to change the conception of cancer from pure morphology to a new focus on structure and function.

Die krankhaften Geschwülste is, in many ways, a strange work. Based upon a series of thirty lectures he presented from 1862-1863, Virchow never completed what was surely intended to be his definitive treatise on tumors. The three volumes written in German—sixteen chapters in the first, five in the second, and four in the unfinished third—were translated into French, but only one of the chapters has been set into English, and that in 1868.²⁶⁵ The last five lectures,

²⁶⁵My thanks to Elizabeth Taylor at the New York Academy of Medicine for her research into these translations. The sole lesson translated into English is Chapter XXII, Rudolf Virchow, "Struma Exophthalmica (Vascular Bronchocele and Exophthalmos), by Professor Virchow. Translated, with Notes and Observations, by J. Warburton Begbie, M.D.," *Edinburgh Medical Journal* (1868).

which were to include the only chapter on true malignancies, were never published.²⁶⁶ There is no evidence that they were ever set down on paper. Nevertheless, the necessity of the microscope to uncover the nature of tumors in Virchow's work is clear and consistent.

Some medical historians criticized the tumor tomes as uninspiring—or worse. Professor L. J. Rather, for example, wrote that Virchow's *krankhaften Geschwülste* offers “nothing new with respect to the histogenesis of tumors.”²⁶⁷ Nevertheless, Virchow's work is a stealth attack on the misunderstandings and misinterpretations of the cancer researchers and practitioners of his day. In the space of twenty-five published lectures he sought to disabuse his select but influential audience on notions he felt ran counter to his own perception of the histoanatomy and cellular pathophysiology of tumors. He did so by answering a series of implied questions.

Is the microscopic diagnosis of tumors credible?

Cognizant of the history of medicine, Virchow aimed to stanch the European exodus from diagnostic microscopy he had witnessed since the heyday of his mentor. Like many new technologies, the post-Listerian microscope initially engendered a burst of youthful enthusiasm in the 1830s and 1840s.²⁶⁸ Müller's *Finer Structure* furthered that excitement, but the initial promise of microscopy for medical diagnosis was tempered by poor microtechnique and limited clinical-micropathological correlation. Not surprisingly, physicians soured on the use of the microscope for cancer diagnosis. Virchow, high on cell theory and its applications to the

²⁶⁶Much of the rest of Virchow's enormous *oeuvre* has been translated into English. Speculation abounds as to why *Die krankhaften Geschwülste* was never translated—perhaps because potential translators waited for the last five chapters to be published (they never were); perhaps because Virchow's theory of connective-tissue carcinogenesis was stillborn upon publication (primarily as a result of the contradictory work of his own students); perhaps because the uncompleted project was deemed unworthy of the master. For further thoughts on this conundrum, see Ackerknecht, *Rudolf Virchow*, 98, Rather, *The Genesis of Cancer*, 135.

²⁶⁷Rather, *The Genesis of Cancer*, 135. Professor Rather's interest centered on the causes of cancer, but, despite this orientation, he composed a brief but honest analysis of *Die Krankhaften Geschwülste* from an etiologic perspective. See pages 135-137 and ff.

²⁶⁸*Ibid.*, 101.

pathology of new-formations, knew that this disenchantment was misplaced. The microscope, Virchow asserted, was undoubtedly the proper tool for the scientific study of tumors. Clinical utility would follow. His treatise made this clear by integrating the microscopic with his macropathological findings.

Virchow also sensed the reluctance of seasoned practitioners to adopt microscopy as the preferred method of tumor diagnosis. After all, he reasoned, the clinical analysis of patient symptoms and signs had served physicians as cancer markers for millennia.²⁶⁹ Far-thinking surgeons like Samuel Gross in the United States quantified the failings of this “physiologic” method of cancer diagnosis in the early 1850s, but for the average mid-nineteenth-century doctor, cognitive inertia and experiential dissonance inhibited the use of this recently improved diagnostic instrument. Cautious practitioners required proof of efficacy. Only accurate microscopic cancer diagnoses would do. Further, the yield of microscopical diagnosis should ideally surpass traditional gross diagnosis.

What is a Tumor?

Virchow began his argument favoring the micropathological analysis of tumors with an attempt to define and, *eo ipso*, classify them. His famous quip, that no one—even under torture (“Blut pressen”)—could say what a tumor actually was, realistically revealed the haphazard state of tumor understanding, consensus, and nomenclature in Virchow’s day.²⁷⁰ The problem was not that physicians could not recognize tumors. The expression indicated nothing more than the presence of a swelling. Medical men from time immemorial had labeled all sorts of lumps and

²⁶⁹Ibid.

²⁷⁰Virchow’s full quotation is: “Wollte man auch Jemand auf das Blut pressen, das er sagen sollte, was Geschwülste eigentlich seien, so glaube ich nicht, dass man irgend einen lebenden Mensch finden würde, der in der Lage wäre, dies sagen zu können.” *Die Krankhafter Geschwülste*, 1:3. Quoted by Ibid., 215 Footnote 68. Loosely translated, Virchow said that he did not believe that anyone, even under torture, could find one person alive who could say what a tumor actually was.

bumps as tumors. Indeed, everything seemed to be called a tumor: wens, tubercles, gummas, goiters, invasive malignancies—many of the diagnoses preceded by eponymous attributions.²⁷¹

His historical interests added depth and context to what would otherwise have been a hodgepodge of tumor designations without obvious connection to their underlying pathology. Johannes Müller celebrated that the microscope could differentiate benign from malignant swellings. Thereby, he attempted to achieve the dual goals of a more accurate, restrictive definition of malignancy and, concomitantly, the elimination of unnecessary, potentially dangerous surgeries for benign lesions. Virchow revised his teacher's emphasis from the anthropocentric benign and malignant to the more 'objective' anatomic and generative. How do tumors differ, he asked, in terms of their macro- and microanatomy? He began by exploring the question of the centuries: What is their origin?

Where do tumors come from?

Virchow did not significantly alter his description of the macroscopic and microscopic anatomy of "pathological new-formations" from the last chapter of *Die Cellularpathologie* (1858) to the initial volume of his expansive *Die Krankhaften Geschwülste* (1863). In Lecture XX of the former work, for example, he followed the traditional classification of tumors as epitheliomas, colloids, papillary tumors, and tubercles.²⁷²

He did, however, innovate the addition of process—how does a tumor become a tumor—to microanatomy in the newer work. The first six chapters of *Geschwülste* constitute an introduction to tumors. Therein lies the crux of his microscope-enabled theory of tumor

²⁷¹The only chapter of Professor Virchow's tumor text translated from the original German into English describes "an exceedingly remarkable connexion of goitre with affection of the heart and large staring eyes." The malady is today known as Graves' Disease—or so it is entitled in the United States (Virchow attributed the first description of the disease to Von Basedow, whose name remains in European circles)—a form of hyperthyroidism considered to be over activity of the thyroid gland. It is not a malignant cancer. Virchow, "Struma Exophthalmica." Quotation from page 882.

²⁷²Virchow, *Cellular Pathology*, 462-67.

development—and his influence on subsequent generations of cancer investigators and practitioners. Although, as noted, the three volumes did not include a specific chapter on malignancies, the arguments on process can be applied to all tumors and can best be framed by a series of questions.

Do tumors originate in the tissue in which they are found? Müller had grappled with the concept of heterology and found it unsupportable. Others believed that tumor cells and tissues never occurred naturally,²⁷³ but this idea implied that all tumors, including malignancies, were heterologous. Such a classification rendered the contribution of tumor origin less helpful to diagnosis, for similar source sites would be unlikely to allow growths to be distinguished on that basis. Virchow followed a different line of reasoning. He strove to comprehend tumor development in four dimensions—over time as well as space. To him, tumors could appear in different places at the same time, or at the same place at different times. Thus, in Virchow’s less static conception, heterology did not contribute toward an understanding of the pathogenesis of tumors. The more important question was tissue-specific origin.

Do tumors originate in all tissues? Virchow believed that growths began only in connective tissue. Within those vast layers thought to connect the outside (ectoderm) and inside (endoderm) of the organism resided undifferentiated cells capable of transformation into tumors. He no longer accepted the cyblastemic explanation that a “structureless, jelly-like mass” germinated tumors.²⁷⁴ No, the substrate for tumor cells was the connective tissue itself. This conclusion was the source of great controversy with students and colleagues.

²⁷³Ackerknecht, *Rudolf Virchow*, 100. For the origins of the concepts of homology and heterology, see Jacob Wolff’s discussion of Laennec’s early nineteenth-century classification of tumors in Jacob Wolff, *The Science of Cancerous Disease from Earliest Times to the Present*, trans. Barbara Ayoub, Science History Publications ed., 3 vols., vol. 1 (New Delhi, India: Science History Publications, 1907; reprint, Science History Publications/U.S.A. a division of Watson Publishing International 1989), 76.

What causes susceptible connective tissue to transmogrify into tumors? As he had written in *Die Cellularpathologie*, Virchow asserted that cancer juice (*succus*) was the immediate cause of tumor formation.²⁷⁵ Connective tissue was the “soil” (as Müller termed it);²⁷⁶ cancer juice the fertilizer. The more juice, the worse the growth of the tumor. Succulent lesions forbode malignancy. Virchow’s cancer juice explained the initiation of the primary tumor and, in the case of malignancy, its metastases, but he did not specify the nature of this pernicious fluid. Nevertheless, the implications of the connective tissue-cancer juice hypothesis for the diagnosis and treatment of cancer were enormous. They fixed the site and instigator of tumorigenesis for others to confirm or refute—a cornerstone of scientific progress.

What caused the secretion of cancer juice and sensitized tissue to its transforming effects? In other words, to use the language of the time, what were the “exciting” and “predisposing” causes of tumor formation?²⁷⁷ Dyscrasia—an imbalance of humors that dominated the notion of cancer causation for centuries and formed the foundation of constitutionalism—did not appeal to Virchow. Tumor preparation, staining, and observation under the microscope led this medical reformer to profess that all tumors originated locally. Further, the cause was also local. Chronic, circumscribed irritation was the most prevalent exciting cause of tumors. Tissues became predisposed to the ominous effects of chronic irritation through a variety of factors. Following the eternal yin-yang of causation, some were

²⁷⁴The quotation is from Theodor Schwann, who advocated the blastema theory. See Theodor Schwann, “On the Analogy in Structure and Growth of Animals and Plants,” in *Johannes Müller and the Nineteenth-Century Origins of Tumor Cell Theory* (Canton, MA: Watson Publishing International (Science History Publications, U.S.A.), 1838), 155.

²⁷⁵Virchow, *Cellular Pathology*, 485.

²⁷⁶Müller, “Müller, Morbid Tumors,” 98.

²⁷⁷P. S. Conner, “Cancer: Has It a Constitutional or Local Origin?,” *The Cincinnati Lancet and Clinic* 2 (1879): 382.

internalist and others externalist.²⁷⁸ Clearly, certain tumors recurred in select families from one generation to another. Hereditarian predisposition, the hallmark of internalism in the nineteenth century, appeared in a variety of *Geschwülste* including consumption, goiters, skin and breast cancer.

On the other hand, tumor patients without a family history seemed exposed to external factors that predisposed them to the disease. Ramazzini's nuns with breast cancer and Pott's chimney sweeps with scrotal malignancies were just two early examples of a list of cancer-predisposed "occupations."²⁷⁹ The number of tumor-job correlations grew rapidly during the middle and late nineteenth century as interest in the compilation of medical statistics waxed. Trauma, however, was considered the most prevalent external predisposing factor. Cancer was statistically more prevalent in women, and many female patients related histories of recent injury to their breasts or "internal organs" (uterus) at the time of tumor diagnosis. Further, some parts of the body were more susceptible to trauma than others. If the cause of cancer was dyscrasia, Virchow believed, such geographical predisposition would be unlikely. He collected voluminous statistical evidence to support his externalist contention that trauma predisposed tissues to tumorigenesis.²⁸⁰

Localism Promoted

Rudolf Virchow concluded from his clinicopathological microscopic studies that tumor growth was a local phenomenon.²⁸¹ He was, as Dr. Ackerknecht concluded, "the first to

²⁷⁸In the cyclical battle between internalist and externalist explanations of cancer over the centuries, Virchow's internalist leanings were eventually overthrown by the rise of germ theory, one of the strongest forces to support externalism in the history of medicine.

²⁷⁹Ramazzini, *Diseases of Workers*, 191. and Pott, *The Chirurgical Works of Percivall Pott*, 403.

²⁸⁰Ackerknecht, *Rudolf Virchow*, 101.

emphasize local tumor causes in Germany,”²⁸² and Germany was at the center of the application of the microscope to diagnosis as well as the incubator of scientific cancer medicine. The fact that Virchow did not recognize *in situ* carcinoma as cancer²⁸³—rather, he insisted on the presence of tissue invasion and/or metastasis to affirm a diagnosis of malignancy—did not nullify his assertion that cancer originated locally rather than systemically. The localistic argument was simply the logical conclusion of researchers based upon their microscopical observations. As a result, cancer surgery, ridiculed and rejected in Virchow’s day and only a few years after its condemnation by Gross and others, received renewed enthusiasm under localism. Nevertheless, fears of operative morbidity and mortality stilled the hands of most would-be cancer-curing surgeons.

The microscopic diagnosis of cancer, for all its theoretical allure as a means of accurate, early tumor diagnosis, nevertheless, remained problematic in the clinic. Virchow’s salvo against constitutionalism bolstered localism on an investigational level, but its value in the clinic milieu remained unproven. This explained the persistence of constitutional cancer ideology amongst General Grant’s consultants twenty years later. As theory (localism) drove practice (surgical treatment of cancer), so new technologies served to bridge the gap between traditional and modern. Developments in microtechnique fostered those new technologies during the third

²⁸¹Virchow’s contributions to tumor pathology were innumerable, but, for the purposes of this discussion on the history of the microscope and cancer in the nineteenth century, his promulgation of localism is most important. His authoritativeness in other realms of medicine can be discerned by the fact that names he coined for various disease phenomena are still used today. Examples include leukemia (1845), thrombosis (1848), amyloid (1854), neuroglia (1854), embolism (1858), and leukocytosis (1858).

His immortalized neologisms went far beyond medical terms. Although generally opposed to Bismarck’s social policies, he supported the Iron Chancellor’s campaign against Catholicism’s Papal infallibility, labeling it *Kulturkampf* (culture clash)—a term that had enormous repercussions throughout the remainder of the nineteenth and twentieth centuries.

²⁸²Ackerknecht, *Rudolf Virchow*, 100.

²⁸³Rather, *The Genesis of Cancer*, 135.

quarter of the nineteenth century—some based upon the hardware of industrialization, others on the felicitous confluence of chemistry and microscopy.

Looking back, Virchow's primary investigations on the role of cell pathology in cancer were astounding in light of the relatively primitive microscopic instruments and techniques of his day. His achromatic, aspherical microscopes harbored deficiencies in focus and resolution that were not rectified until later in the century. Lack of uniformity hampered specimen preparation and comparison. Specimens were often poorly preserved and subject to autolysis. Biopsies were rare.²⁸⁴ A few natural dyes represented the totality of microscopical stains. However, by the time of President Cleveland's tumor biopsy thirty years after the publication of the first volume of Virchow's tumor treatise, microtechnique had advanced into the modern era.²⁸⁵ Progress in microtechnique in the intervening years involved staining, the microtome, and the microscope. It began with a happy accident.

A Most Fortunate Young Man

²⁸⁴The 'biopsy' was not unheard of during Virchow's productive years, but it was quite rare. Surgeons had removed specimens from living patients for centuries—if not millennia—but the first known attempt at the routinization and mechanization of specimen removal from the living organism came in 1847. In that year, Emile Kuess, Professor of Physiology at Strasbourg, developed an instrument that produced tissue pieces that today would be called 'punch biopsies.' Kuess was a microscopist who worked with the French surgeon Charles Sédillot, who only the year before remarked that "We ought not delay in imitating (the Germans) and in demanding from the microscope the last resources of its power in the diagnosis of cancer." (See his *Recherches sur le cancer*, reprinted in Sédillot, *Contributions à la chirurgie*, 1: 448-617; as quoted by Ibid., 455 and 206 Footnote 125.) Budding nationalism aside, Kuess's biopsy tool had limited value, because it necessitated a second operation—fraught with all the risks and dangers of the first—if the initial specimen was diagnosed as cancer.

Having written of biopsies in the abstract, please remember that the actual word 'biopsy' was not coined until the last years of the century. See James R. Wright, Jr., "Relationship of Surgical Oncology and Pathology in Early 20th Century America," in *History of Ideas in Surgery: Proceedings of the 17th International Symposium on the Comparative History of Medicine--East and West*, ed. Yosio Kawakita, Shizu Sakai, and Yasuo Otsuka (Susono-shi, Shizuoka, Japan: Ishiyaku EuroAmerica, Inc., 1997), 246, 64 Footnote 16, and 47.

²⁸⁵Although more and varied stains and precision instruments were to be invented in the twentieth century, among the major facets of modern light-microscopical microtechniques only frozen section biopsies remained the major undiscovered technique at the time of Cleveland's 1893 biopsy. For decades, microscopists had frozen tissue specimens as part of slide preparation, but surgical biopsies processed with the frozen section technique were unknown until 1895 and did not gain popularity until the early twentieth century. The interesting and controversial history of the frozen section is detailed in Wright, "Surgical Pathology."

The greatest advance in microscopy stains occurred in 1856 in England with the serendipitous discovery of synthetic aniline dyes. Aniline is a derivative of benzene, a compound of innumerable chemical interactions because of the alternating threesome of double bonds that enforce its hexagonal ring-like structure. Michael Faraday, the famed physicist of electromagnetism, discovered benzene in 1825.²⁸⁶ With the rise of chemistry in the first decades of the nineteenth century, many notables worked on the properties of this extraordinary compound. One was August W. von Hofmann, a German invited to London during the years of European rapprochement to build an educational center for English chemists.²⁸⁷ Von Hofmann's laboratory focused interest on the synthesis of various benzene-based compounds—like aniline, a colorless, poisonous benzene derivative used to manufacture rubber, varnishes, and other chemicals.

Beginning in 1855, William Perkin, then a seventeen-year-old British chemistry prodigy, assisted von Hofmann. Perkin's curiosity was unbounded. His parents helped him to establish a make-shift laboratory at home so that he could continue his research after hours. During the Easter of 1856, when most of his colleagues were frolicking on holiday, Perkin decided to experiment with the unappealing aniline rather than a more propitious substrate. Although this beginning seemed rather inauspicious, the long-term result of his vacation enterprise was nothing less than the birth of the synthetic organic chemical industry. As he remembered at a dinner-party extravaganza thrown in his honor at the ritzy Delmonico's Restaurant in New York City in 1906, he had at first synthesized "a black and more unpromising product (than aniline) we now

²⁸⁶Clark and Kasten, *History of Staining*, 203.

²⁸⁷*Ibid.*, 204.

know as the ‘*mauve dye*.’”²⁸⁸ Most chemists would have discarded the dark purple residue, but Perkin, through either youthful ignorance or impetuosity, decided to test it further.

Dyers evaluated the purplish pigment with encouraging results. As a result of Von Hofmann’s naysaying, Perkin decided to manufacture the synthetic dye on his own.²⁸⁹ The youth, however, had neither funds nor business experience. Nevertheless, with the collaboration (and contributions) of his father (who wanted him to be an architect, not a chemist likely destined for a life of poverty) and brother, the chemical manufacturing firm of Perkin and Sons was formed. The synthetic dye caught on like wildfire. Within a few years, Queen Victoria thrilled the world with her mauve-colored couture, postage stamps were dyed mauve, and William Perkin retired a rich man at the age of thirty-six.

1856

Beyond Perkin’s substantial contributions to fashion, chemistry, and esthetics, his synthesis of mauve dye (also known as aniline purple) ushered in a revolution in microscopical staining. Perhaps, if one were to look back for the origin of twenty-first-century cancer medicine, it would be 1856. In that year, Louis Pasteur noted that microorganisms caused fermentation, thus opening the field of microbiology and the concept that life and disease appeared in myriad but related forms; Gregor Mendel began his work with pea plants, inaugurating modern genetics and the idea that life and disease may be programmed and even, in some ways, predetermined; and, in that year, William Perkin took the residue from his aniline experiment and began the synthetic organic chemistry industry—including the production of

²⁸⁸Quoted by Ibid., 205. Italics in Clark & Kasten.

²⁸⁹Ibid.

synthetic dyes that would stain Pasteur's microorganisms, Mendel's units of heredity, and generations of cancer cells.

Virchow, whose 1855 pronouncement that all cells, including cancer cells, derived from previous cells, did not use Perkin's discovery to stain the specimens that laid the groundwork for either *The Cellular Pathology* or *The Morbid Tumors*. Although the mauve dye gave birth to a new and profitable industry (the real reason for Perkin's 1906 fest), the first recorded use of the synthetic aniline stain in microscopy was not until 1862.²⁹⁰ Nascent scientific medicine and microscopy in particular, benefited from societal and cultural changes fostered by industrialism and the growing popularity of the application of science to everyday life. Virchow's microtechnique may have been confined to the natural staining, that in itself represented a significant advance over Müller's lack of staining, but Virchow's students benefited from the new stains, novel methods of specimen preparation, and innovative lens systems abetted by William Perkin's mauve dye.

FROM SCIENCE TO PRACTICE:

The Birth of Medical Microscopy

Microscopy has had...two periods of brilliant achievement in the course of its history: the seventeenth century and the latter half of the nineteenth century.

-E. Nordenskjold²⁹¹

The great advances in microanatomy and cell biology which stem from the period 1870-1900 may thus be attributed on the one hand to the technical advances in the microscope and its lenses, but also on the other hand to the equally important developments in the preparative techniques.

-Saville Bradbury²⁹²

²⁹⁰Bracegirdle, *A History of Microtechnique*, 70, 102 Footnote 42, and 343. The first American to use aniline dyes for microscopic staining was probably Dr. Joseph Janvier Woodward in 1864. See Francelia Butler, *Cancer through the Ages: The Evolution of Hope* (Fairfax, VA: Virginia Press, 1955), 41.

²⁹¹Cited by Gray and Gray, "History of Microtechnique and Microtomy," 260, Peter Irons, *The History of the Supreme Court* (Chantilly, VA: The Teaching Company, 2003), DVDs. from E. Nordenskjold, *The History of Biology* (New York: Tudor, 1928).

Advances in Microscopy & Microtechnique

Part One: Staining

The personal wealth Perkin acquired from the industrial application of his colorful compound engendered a new rush to synthesize dyes that, when employed by microscopists, highlighted different types of cells (and their previously indistinct organelles). Proponents and espousers of cell theory had themselves projected these now-accepted units of life into the scientific consciousness. As a result, pathologists and, years later, practitioners, included the microscopic in their daily purview of cancer and other diseases. Over the last decades of the nineteenth century, medical microscopy—at first on the Continent and Britain and then in the United States—became practical, useful, and effective in the care of patients. Progress in staining was one of three major advances in microtechnique—along with microtomes and optical improvements—in the second half of the nineteenth century that fostered the acceptance of the microscope in medicine in the West.

As late as the 1860s, microscopists, even in Germany, rarely stained their specimens with anything other than natural carmine—if they stained at all.²⁹² Müller, Virchow, and their intellectual descendants made great strides in cell theory and histology despite these limited preparations. Practical application to patient care, however, was inhibited by poor education, microscopical inexperience, and non-standardization of techniques among the majority of practitioners. Nevertheless, experimental pathologists sought stains that highlighted tissues and cells of their own special interest. Many of these eventually became dyes used in routine patient care.

²⁹²Bradbury, *Evolution of the Microscope*, 249.

²⁹³Bracegirdle, *A History of Microtechnique*, 321, Clark and Kasten, *History of Staining*, 42.

Initial advances in microscope slide staining accrued from the discovery of new natural dyes and their chemical refinement. As the writings of Virchow scientized medicine for a new generation of pathologists, the benefits of well-delineated, stained slides became apparent to research-oriented investigators. At first, the number of natural dyes was limited. During the middle of the nineteenth century, however, increased global trade and improvements in transportation, fostered by industrial capitalism, coupled with heightened popular interest in the naturalist explorations of Humboldt, Darwin, and others, brought new plant specimens with novel natural chemicals to Europe and England.²⁹⁴

Natural Hæmatoxylon

Hematoxilin, one of the most enduring of the natural stains, is a purple-red dye that colors cell nuclei, chromosomes, muscle-fiber striations, and other sundry structures. It clearly differentiates nucleus and cytoplasm, a distinction that became more meaningful as the optical resolution of microscopes further improved in the last decades of the nineteenth century.²⁹⁵

Hematoxylon, the original name of the dye, is an extract from the heartwood of the logwood tree (*Hematoxylon campechianum*) that thrives in tropical climes.²⁹⁶ Wilhelm von Waldeyer, the famed nineteenth-century German histologist whose epithelial theory of carcinoma development remained dominant long into the next century,²⁹⁷ was the first to apply

²⁹⁴For a beautiful and elegantly illustrated exposition of the interplay of science, culture, religion, and art in pre-Darwinian America, see Barbara Novak, *Nature and Culture: American Landscape and Painting 1825-1875* (New York: Oxford University Press, 1980; reprint, 1981), especially Chapters IV, "The Geological Timetable: Rocks," and VI, "The Organic Foreground: Plants."

²⁹⁵Cytologists, whose history reveals another example of the important distinction between knowledge of structure and function, discerned salient features of the anatomy of the nucleus and cytoplasm decades before they knew what they did or the processes that those cell components governed.

²⁹⁶The most important source of hæmatoxylon was Campeche, a city on the northeast portion of the Yucatan peninsula with a history filled with swashbucklers and buccaneers. See Charles L. Mitchell, "Staining with Hæmatoxylon," *Proceedings of the Academy of Natural Sciences of Philadelphia* (1883): 297.

the natural dye in microscopy. In 1863, he used hæmatoxylon to stain the axons (long processes) of neurons (nerve cells).²⁹⁸ The initial product of his use of this natural stain was poor, but others soon discovered that a distinctive purple-red dye could be obtained from this arboreal derivative by different methods of chemical treatment. The end result was a stain that has been used to this day to highlight cell components of cancers and other pathological specimens.

Hematoxylon served as a representative of the advantages and disadvantages of natural microscopy stains. In the 1880s, Charles L. Mitchell, an American “PH. D., M. D.,” enumerated these points in Philadelphia not, as might be expected, to a group of pathologists or practitioners at the august College of Physicians, but rather to the city’s Academy of Natural Sciences. The non-medical venue emphasized that, in the United States at that time, practitioners were not a fitting or even interested audience for a discourse on microscopy stains.²⁹⁹

As Mitchell spoke to the naturalists, he noted that the advantages of staining with hæmatoxylon were significant. The dye took to the specimen rapidly, clearly differentiated various anatomical structures, and left a “beautiful tint” that was easy on the eyes and invariably inviting.³⁰⁰ Most important, it produced a “more perfect definition and clearness of outline” than carmine, the reigning natural dye. The vivid red stain is not selective, for it “colors the whole mass exclusive of fat.”³⁰¹ Indeed, the most critical known parts of the cell at that time—cell wall

²⁹⁷See Malkin, *Out of the Mist*, 338, Roderick E. McGrew and with the collaboration of Margaret P. McGrew, *Encyclopedia of Medical History* (New York: McGraw-Hill Book Company, 1985), 50.

²⁹⁸As with any claimed “first,” there is controversy. In 1883, Charles Mitchell gave the honor of the first to use hæmatoxylon to Boehmer (F. Böhmer, probably 1865). See Mitchell, “Staining with Haematoxylon,” 297. A century later, Clark and Kasten gave the nod to Waldeyer (1863). See Clark and Kasten, *History of Staining*, 43 and 62. In truth, both men used different preparations of the same chemical.

²⁹⁹Mitchell, “Staining with Haematoxylon.”

³⁰⁰*Ibid.*, 297.

³⁰¹L. Tait, “On the freezing process for section-cutting; and on various methods of staining and mounting sections,” *J. Anat. Physiol.* 9 (1875): 250-258; as quoted by Clark and Kasten, *History of Staining*, 64.

(or cell membrane), nucleus, and nucleolus—“all stand out clearly and with perfect distinctness and sharpness of outline—a result not to be attained by the use of any other coloring material.”³⁰²

Unfortunately, hematoxylin also had disadvantages. At a time when preservation techniques like refrigeration and dessication were either non-existent or in their infancy, the shelf-life of hematoxylin was brief. It quickly became “thick, cloudy and filled with a grumous sediment.”³⁰³ Beauteous violet transmogrified to dirty brown and then colorlessness. Horse and buggy—let alone overseas clipper ships or steamers—could hardly be used to transport slides stained with hematoxylin to faraway pathologists and practitioners for corroboration or educational purposes. The natural stain lacked two of the three optimal qualities of a specimen stain—ease of preparation, clearness of definition, and permanence. The hematoxylin of the 1860s to early 1880s was an improvement on what had been available earlier, but its shortcomings spurred others to better solutions.

The fact that Dr. Mitchell’s purpose in his presentation to the Academy was to publicize a process for the preparation of a new derivative of this stain, which he modestly entitled “Mitchell’s Hématin Staining Fluid,”³⁰⁴ is less relevant than the implication that staining had become an active and growing field in Europe and America in the years surrounding the death of General Grant. Indeed, not until the 1890s was hematoxylin for staining prepared by methods that approximate those used in the twentieth century.³⁰⁵ Mitchell’s work is one of many examples that reveal microscopic staining to be a dynamic field of applied chemistry in the

³⁰²Mitchell, "Staining with Haematoxylon," 297.

³⁰³Ibid.

³⁰⁴Hematin, the active staining principle, is the oxidized product of hematoxylin.

³⁰⁵Clark and Kasten, *History of Staining*, 66-67.

1880s. Nevertheless, his story also shows that medical microscopy, at least in the United States, was inchoate.

Synthetic Eosin

In 1871, at the start of the salad days of the development of synthetic dyes, Heinrich Caro discovered eosin, the “E” of the popular stain “H & E”—Hematoxylin and Eosin.³⁰⁶ The number of newly synthesized stains grew rapidly during the late 1870s and 1880s, inspired by the germ theories of Pasteur and then Koch. A dynamic interrelationship developed whereby germ theory propelled the creation of new stains and new stains buttressed germ theory. In Europe, medical microscopy flourished.

A German histologist first proposed use of the chemical duo hematoxylin and eosin in 1875.³⁰⁷ Today, the pair commonly vivify cancer cells and other biopsy specimens under the microscope. They work well together because, whereas hematoxylin stains the nucleus and its chromatin, eosin stains the cytoplasm.³⁰⁸ Together they provide the visual contrast necessary for reproducible, reliable microscopic interpretations.

The Importance of Being Stained

The rapidly growing field of synthetic dyes manufactured for profit by European industry combined with other developments in microtechnique to bring medical microscopy to the practitioner. Attention shifted from natural to synthetic dyes in the years following Perkin’s

³⁰⁶Eosin and methylene blue, two of the longest-lived synthetic dyes, were discovered by the same scientist, Heinrich Caro, in the 1870s. He developed eosin in 1871 and methylene blue in 1876. *Ibid.*, 77-78.

³⁰⁷A. Wissowzky, “Über das Eosin als reagenz auf Hämoglobin und die bildung von Blutgefäßen und Blutkörperchen bei Säugethierund Hühnerembryonen,” *Arch. mikr. Anat.* 13 (1876): 479-496. The paper was published the year following the proposal. Cited by Bracegirdle, *A History of Microtechnique*, 71 and 103 Footnote 69.

³⁰⁸The word ‘eosin’ is derived from the Greek *eos*, meaning ‘dawn’—reminiscent of the pink-red that colors the sky before the rising of the sun on a clear day.

fortuitous discovery. Aniline blue and fuchsin, two of the new synthetics, were first applied to specimens in 1863, but the real growth in synthetic staining did not occur until the late 1870s.³⁰⁹ The decades following the 1860s bore the stamp of the more readily produced artificial stains. Nevertheless, microscopists utilized these dyes only slowly at first. Brian Bracegirdle recorded the introduction of only five synthetic dyes during the 1860s.³¹⁰ During the 1870s and 1880s, however, a profusion of new stains appeared, many of which, including eosin, methylene blue, and Gram's stain, are still in use today.³¹¹

Although the chemistry of staining is beyond the scope of this dissertation, the drives and objectives of those who developed that chemistry are not. In the last third of the nineteenth century, microscopists quickly discovered that different stains highlighted different pathoanatomical structures and could thus be a great adjunct to diagnosis. The more stains, the better the ability to pinpoint cellular anomalies, for the first and perhaps most difficult duty of the student of microscopy (and medicine) was (and is) to distinguish abnormal from normal.

The thrill of new histopathological discoveries spurred researchers to innovative techniques. Advances came fast and furious. Schwarz inaugurated double staining, the application of two dyes to the same specimen, in 1867.³¹² Gibbes, in 1880, became the first

³⁰⁹The 1926 edition of the *Encyclopaedia Britannica* incorrectly noted that microscopical staining methods were first used in 1872. See The Encyclopedia Britannica, *The Encyclopedia Britannica: A Dictionary of Arts, Sciences, Literature & General Information*, 13th ed., vol. I (London: The Encyclopedia Britannica Company, Ltd., 1926), 512. As we have shown, stains were applied by Hooke and Leeuwenhoek centuries earlier. New to the 1870s was the veritable explosion in the number of synthetic stains.

³¹⁰Bracegirdle, *A History of Microtechnique*, 343.

³¹¹Of the 36 synthetic dyes that Bracegirdle lists as first used between 1862 and 1893—from the year of the first known use of a synthetic stain to the year of President Cleveland's secret cancer—fully twenty-eight (28), or slightly less than four out of five (78%), were launched in the 1870s and 1880s. Fifteen were first used in the 1870s and thirteen (13) in the 1880s. See *Ibid.*, 343-44.

C. Gram introduced the "Gram stain" in his seminal 1884 article, "Über die isolirte Färbung der Schizomyceten in Schnittund Troken-präparaten," *Fortsch. D. Med.* 2 (1884): 185-189.

histologist to publish on triple staining.³¹³ Microscopists stained specimens with increasing numbers of different dye combinations, but soon confusion trumped comprehension and clarity. By 1896, A. B. Lee, in the preface to his influential *The Microtometist's Vade Mecum*, wrote that the great age of experimentation with microscopic stains had passed. Adding more stains to the slide, he asserted, would no longer lead to further insights.³¹⁴

Cell biologists reaped a rich harvest from the exuberant growth in the number of synthetic dyes during the 1870s and 1880s. Microscopists reliably differentiated the major intracytoplasmic organelles—mitochondria and endoplasmic reticulum—for the first time, boosting interest in the workings of the cell unit as well as its subcellular components. In addition, chromatin dyes like hematoxylin focused attention upon the fundamental cellular processes—meiosis, fertilization, maturation, and mitosis—years before scientists were aware of their links to reproduction, genetics, and cancer biology.³¹⁵ Improvements in microtechnique enhanced cell analysis, and progress in cytological anatomy fostered developments in physiology. As a result, within the lifetimes of many who witnessed the dawn of cell theory, medical scientists began to forge the link between cellular form and function—a hallmark of modern medical science.

Cancer cells, lacking the regimental architecture of normal cells, stood out boldly under the revelations of stains like hematoxylin and eosin. Their nuclei often appeared bizarre—large, replete with multiple intra-nuclear organelles (nucleoli), and abnormal in position. The cells themselves characteristically disregarded the typical shape of cells in that tissue or organ.

³¹²Ibid., 68 and 101 Footnote 22.

³¹³Ibid., 72 and 103 Footnote 73.

³¹⁴London: Churchill, 4th ed., 1896. Cited by Ibid., 72, 57, and 96 Footnote 1.

³¹⁵Clark and Kasten, *History of Staining*, 108-09.

Normal, round cells became polygonal, thick, and elongated. Normal, elongated cells became heaped up and distorted. Cells adjoining other cells lost their respectful neighborliness and piled atop one another. More striking than even these conformational changes was the appearance of a multitude of dividing cells—rarely seen in normal specimens—on the same slide. The ability to stain the nucleus and cytoplasm differentially, as with H & E, contributed greatly to these new insights in cancer histopathology.

Nevertheless, the great European advances in staining and histopathology in the late nineteenth century did not immediately sway the cancer practitioner in the United States to the value of medical microscopy. This is not to deny that many American scientists were fascinated by the concept of histological diagnosis. Rather, the case for cancer microscopy lacked support among practitioners. Clinical diagnosis predominated. For the majority of physicians in the early 1880s, the relevance, accuracy, and necessity of scientific advances engendered by new stains and cell theories for cancer diagnosis remained remote and unproven.

The Road to Legitimacy and Acceptance

The growth of clinical confidence in the new cornucopia of artificial stains in the 1870s and 1880s was both gradual and punctuated—gradual, in that dependence on natural stains derived from precedent and experience; punctuated, in that the by-then established union of chemistry and microscopy found new life with the rise of biochemistry and the renaissance of germs as causative agents of disease. An extraordinary confluence of persons and events was necessary to overcome past prejudices against medical microscopy. The result was the practitioners' acceptance of the legitimacy of medical microscopy and, ultimately, its application to cancer diagnosis and treatment.

Above all, clinicians required that the microscopy of the scientist be useful for the everyday practitioner. Utility was not easy to prove, for much negative historical evidence in terms of inaccurate microscopical cancer diagnoses preceded late-century improvements in staining and microtechnique. The individual to convince the clinical world of the pragmatic value of microscopy would ideally combine deep knowledge of chemistry and expertise at microscopy with a fascination for human disease. In the 1870s, a young man appeared in the German scientific community with those qualifications. That man—the “master dyer”—was Paul Ehrlich.³¹⁶

The Man with the Rainbow Fingers

Paul Ehrlich (1854-1915) was an unlikely candidate to bring staining to the practitioner. An indifferent student, he cut many classes and showed little interest in academics. Even during medical school, his professors believed he would not pass the state examinations necessary to obtain his medical license. His iconoclastic personality led to personal difficulties with others on more than one occasion. During Robert Koch’s momentous visit to Breslau in 1876 to proclaim the disease-generative capability of the anthrax bacillus, Julius Cohnheim, Virchow’s “most distinguished pupil”³¹⁷ and Ehrlich’s instructor,³¹⁸ introduced the twenty-two-year old to Dr.

³¹⁶Quotation from Donald Fleming, *William H. Welch and the Rise of Modern Medicine* (Baltimore: The Johns Hopkins University Press, 1954; reprint, 1987), 45.

³¹⁷Esmond R. Long, *Selected Readings in Pathology*, Second ed. (Springfield, IL: Charles C. Thomas, 1961), 183.

³¹⁸Julius Cohnheim was well known in his own right for his embryonal rest theory of cancer formation. He postulated that select cells from the embryo remained latent during growth and maturity. A violent stimulus—harkening back to the nineteenth-century belief in the “irritation” theory of cancer causation—transformed them into cancer cells. A workable explanation of Cohnheim’s theory in an otherwise polemical text can be found in Mitchel D. Auerbach, *A New Concept of Cancer: With a Brief History of Changing Cancer through the Ages* (New York: Pageant Press, 1955).

Cohnheim’s theory, like the connective tissue theory of his mentor Virchow, stimulated heated debate in its time.

Koch.³¹⁹ Stated Cohnheim, “this is little Ehrlich. He is very good at staining, but he will *never* pass his examinations.”³²⁰ Cohnheim’s prediction of Ehrlich’s inevitable test failure was wrong, but the instructor’s recognition of his student’s proficiency at staining was more correct than he could have imagined.

Young Ehrlich grew up in a world of chemistry, dyes, and histology. Marsha Marquardt, Ehrlich’s personal secretary and biographer in later years, detailed his early obsession with the molecular interactions among different substances. “When at school in Breslau he liked to try chemical experiments, and during the holidays made all sorts of mixtures in the laundry at home.”³²¹ Indeed, his interest in stains was incorrigible. Interactions with some of the best medical chemists of his age further stimulated his inquisitive approach to staining. At Strasbourg, another of the several schools he attended during his medical education, he had the good fortune to fall under the tutelage of Wilhelm Waldeyer. He was a distinguished anatomist whose proclivity for medical chemistry was well known. As noted, he was the first to apply hematoxylin to biological specimens.³²² Paul Ehrlich extended the application of the

³¹⁹Robert Koch was himself a young man only a decade older than Ehrlich. Koch’s career in bacteriology had begun merely four years earlier when his wife presented him with a microscope for his birthday. C. D. Haagensen and Wyndham E. B. Lloyd. *A Hundred Years of Medicine* (New York: Sheridan House, 1943), photograph opposite 132.

³²⁰Sarah R. Riedman and Elton T. Gustafson, *Portraits of Nobel Laureates in Medicine and Physiology* (London: Abelard-Schuman LTD, 1963), 52. Italics in the original.

³²¹Martha Marquardt, *Paul Ehrlich* (New York: Henry Schuman, 1951), 6.

³²²Wilhelm von Waldeyer-Hartz (1836-1921) also propounded the epithelial origin of cancer. Although at odds with the theories of Virchow (connective tissue) and Cohnheim (embryonal cell rests), Waldeyer’s theory was accepted in American circles by the 1880s. See, for example, Carl Hempel Reed, “The Histogenesis of Carcinoma,” *Philadelphia Medical Times* 13 (1883): 253.; A. Ernest Maylard, “Carcinoma Considered Chiefly in Its Pathological Aspects,” *Glasgow Medical Journal* 25, no. 5 (1886): 342-43.; and John Lindsay Steven, “The Origin of Cancer,” *Glasgow Medical Journal* 25, no. 6 (1886): 427..

Waldeyer also coined the term ‘chromosome’ (“colored body”) for the dense dye coloration taken up by the nuclear strands during staining with chemicals like hematoxylin.

contributions of Cohnheim and Waldeyer (and their teachers Virchow and Müller) from the microscope slide to the medicine cabinet.

William Henry Welch, keen American observer of the scientific medicine scene during his post-graduate sojourn in Europe, witnessed medical-student Ehrlich working at the University of Breslau with Cohnheim and the new aniline dyes in 1877.³²³ So taken was Welch with Ehrlich and was Ehrlich taken with stains that Welch found Ehrlich “always running around among us with blue, yellow, red and green fingers.”³²⁴ Even his face revealed traces of the dyes he used in his experiments.³²⁵ His cousin on his mother’s side, Karl Weigert, was also preoccupied with staining. He was nine years older than Paul, and probably the first ever intentionally to stain bacteria.³²⁶ The two remained lifelong friends, constantly sharing their unending curiosity about stains and scopes.³²⁷ In the Johns Hopkins Medical Archive, there is an aged photograph of Julius Cohnheim’s pathology group taken during the summer of 1877, probably donated by William Welch.³²⁸ Cohnheim and the young Ehrlich stood in the center. The newly-minted American M.D. and Karl Weigert sit at the left.³²⁹ A look of intelligence and

³²³Dr. Welch graduated from Columbia’s College of Physicians and Surgeons in 1875 without training in microscopy. He pursued post-graduate studies in Europe from 1876-1878 and returned to America with a wealth of new ideas that led to the establishment of the first pathology laboratory in the United States (at Bellevue Hospital) in 1879. He went on to have an enormous influence on the development of the Johns Hopkins School of Medicine in the late nineteenth century, medical education in the twentieth century, and medical microscopy.

³²⁴Quotation from Fleming, *William H. Welch and the Rise of Modern Medicine*, 45.

³²⁵Marquardt, *Paul Ehrlich*, 14.

³²⁶Flexner and Flexner, *William Henry Welch*, 99.

³²⁷Marquardt, *Paul Ehrlich*, 7.

³²⁸Johns Hopkins Medical Archives, "Julius Cohnheim's Pathology Group, Breslau, in the Summer of 1877," in *Paul Ehrlich's Receptor Immunology: The Magnificent Obsession*, ed. Arthur M. Silverstein (San Diego: Academic Press, 1877; reprint, 2002), Plate 1.

³²⁹Welch’s study with Cohnheim in Breslau (now Wroclaw, Poland) reaped a great benefit. It began in 1879 when Welch, as noted, shipped the fruits of his European experience across the Atlantic to establish the first

determination—combined with vision—pervaded the cloistered atmosphere. Highlighted in the center of the photograph, propped up on a table, stood a microscope—silent but essential.

Ehrlich became obsessed with the staining of biological entities. He even carried his stains beyond the laundry and the laboratory to the boardinghouse where he ate his meals as a student. Years later, after he won the 1908 Nobel Prize for his work on the side-chain theory of immunity, the innkeepers' daughter reminded him of the great "despair" he caused with his fixation. All the towels of the inn, she remembered, betrayed "great spots of dye in every shade of red and blue which no amount of washing could remove. Even the billiard table itself, on which he had made his experiments because there was no other table, was covered with such spots."³³⁰

Ehrlich's monomaniacal preoccupation with staining was founded in his inherent genius for chemistry and a deep ambition to apply it to the study of living things. As he wrote to an American physician in his later years, "My real natural endowment lies in the domain of Chemistry; and mine is...a kind of visual, three-dimensional Chemistry. The benzene-rings and structural formulae really disport themselves in space before my mind's eye."³³¹ Ehrlich's great achievements—in the fields of bacteriology, immunology, cancer, and pharmacology—can be traced to this inner vision of multi-dimensional molecules.

pathology laboratory in the United States. In 1883, John Shaw Billings was asked to organize a new medical institution in Baltimore—sheltered from the entrenched interests of Boston, New York, and Philadelphia. Billings asked Cohnheim to recommend a pathologist for the new facility. Professor Cohnheim responded that "the person best suited for the chair of general pathology is Mr. Welch of New York." At that time, Welch was a relative unknown only a few years out of medical school. Hence Billings selected Welch to head pathology at Johns Hopkins and German scientific medicine gained a foothold in the United States. In 1910, Abraham Flexner cemented the German-American affiliation when he chose Hopkins as one of the model medical institutions in his extremely influential report on "Medical Education in the United States and Canada: A Report to the Carnegie Foundation for the Advancement of Teaching." For further details, see Malkin, "Comparison of the Use of the Microscope in Pathology in Germany and the United States During the Nineteenth Century," 87.

³³⁰Marquardt, *Paul Ehrlich*, 15.

³³¹Paul Ehrlich, "Letter: P. Ehrlich to C. A. Herter," in *The Collected Papers of Paul Ehrlich*, ed. F. Himmelweit, *The Collected Papers of Paul Ehrlich* (London: Pergamon Press, 1909), 9.

“Contributions to the Theory and Practice of Histological Staining”

In 1878, Ehrlich completed his thesis for the medical doctorate—a seminal treatise on the application of chemistry to biology. He acknowledged Cohnheim, Waldeyer, and Weigert in the introduction, but the thrust of his paper, translated from the German as “Contributions to the Theory and Practice of Histological Staining,” expressed a new biochemical synthesis that set forth an innovative understanding of life through “the chemical conception of dyeing.”³³² The ideas he developed in his doctoral paper recur repeatedly through his research on bacteria, the immune system, cancer, and drug therapy. In essence, the paper represented the novel perception of life as a manifestation of chemical interactions.

“In (the) modern histological literature,” he began, “the theoretical basis” of staining “has received but little consideration.”³³³ Ehrlich sought to rectify what he believed to be a grave omission and, in the process, elucidate the nature of cellular chemistry. He strove to discover not just the what and when of histological staining, but also the how and why. One of his major questions concerned “the way in which the stains are fixed by the tissues.”³³⁴ Was it a physical process whereby the pigment simply adhered to the cell and its constituents—leaving both chemical and biological conjoined but intact? Or was it a chemical process that involved a reaction that changed both? The answer became a question of fundamental importance to man’s quest to alter the natural history of disease.

³³²“Beiträge zur Theorie und Praxis der histologischen Färbung,” University of Leipzig, 1878. A complete translation into English, entitled “Contributions to the Theory and Practice of Histological Staining,” can be found in F. Himmelweit, ed., *The Collected Papers of Paul Ehrlich*, 4 vols., vol. 1 (London: Pergamon Press, 1956), 67-98.

³³³*Ibid.*, 67.

³³⁴Paul Ehrlich, “Contributions to the Theory and Practice of Histological Staining,” in *The Collected Papers of Paul Ehrlich*, ed. F. Himmelweit, *The Collected Papers of Paul Ehrlich* (London: Pergamon Press, 1878; reprint, 1956), 68.

After delving into the historical literature on the “mechanical” vs. “chemical” explanations of staining, Ehrlich demonstrated through reproducible physical and chemical means that stains combined with cellular constituents to transform both.³³⁵ The reaction of A with B yielded C, not A plus B. As one piece of evidence, he showed that the weight of the final product differed from the sum of its constituents. In addition, he proved that dyes combined with organic acids and bases to form salts. Deep knowledge of chemistry and stains allowed him to employ specific dyes and reactions to bolster his argument. In a footnote that referred to a specific reaction, Ehrlich explained, in a great understatement, that “I have dwelt at some length on these concepts—to my knowledge not previously advanced—because I think that they are of general medical interest.”³³⁶ The purpose of his medical thesis may have been the expostulation of a theoretical basis for the histological staining process, but the consequence was the beginning of the pharmaceutical industry. As Perkin began the synthetic organic dye industry, Ehrlich began the ethical drug industry. The two industries are closely related—chemically and historically—for Perkin’s synthetic aniline dyes were the precursors of Ehrlich’s modern drugs.³³⁷

From Consumption to Tuberculosis:

Ehrlich’s Staining Attracts the Practitioner

³³⁵Ibid., 73.

³³⁶Ibid., 72.

³³⁷Ehrlich entitled the second part of his 1878 thesis, wherein he more fully explored the relationship between specific aniline dyes and the study of tissues, “The Place of Aniline Dyes in Chemistry, Technology and Histology.” Ibid., 76-98.

The discovery of trypan red (1904), salvarsan (Ehrlich’s famous “Compound 606” for syphilis, 1907 and 1909), and neosalvarsan (“Compound 914,” 1912) occurred after the analytical period of this work, but they flowed directly from Ehrlich’s research on aniline dyes, as he noted himself. See Ehrlich, “Letter: P. Ehrlich to C. A. Herter,” 10.

Ehrlich's elucidation of the biochemistry of the staining process did not directly interest the American practitioner in medical microscopy. He had enhanced understanding and curiosity in microscopic staining from a research perspective, but demonstration of the direct usefulness of the import of these reactions for the practitioner was lacking. His liaison with Robert Koch changed all this.

Julius Cohnheim's offhand disparagement in 1876 of Ehrlich's poor study habits to the visiting Dr. Koch led to one of the greatest misstatements in the history of science. Cohnheim, a great experimental pathologist, was no fool. He immediately grasped the enormous implications of Koch's identification of disease-causing germs. In particular, Cohnheim was struck by the finding that bacilli were plant-like particles that changed from bacilli to spores and back again depending upon their microenvironment. The "climate" provided by the body's heat and ever-flowing nutrients created the perfect culture medium and thus breeding ground for bacillary reproduction. Koch realized that from the point of view of the host animal the consequence of such bacterial propagation was infection and, if it took place in the bloodstream (one of the parts of the animal most accessible to nineteenth-century pathologists), caused septicemia. Koch demonstrated his bacteriological findings during that 1876 visit to Breslau. Cohnheim was enthralled. Upon his return to the laboratory, he allegedly called out to his young researchers, including Ehrlich:

Let everything stand and go to Koch! This man has made a great discovery which, in its simplicity and exactitude of method, is the more remarkable as Koch is separated from all scientific associations, and everything which he has done is absolutely complete. Nothing remains to be done. I regard it as the greatest discovery yet made in bacteriology, and I believe Koch will astound and shame us all with discoveries yet to come.³³⁸

³³⁸Flexner and Flexner, *William Henry Welch*, 100.

Robert Koch, though a country practitioner at the time, had studied with Müller's student Henle, an intellectual brother to Virchow. Thus, despite his current clinical position, Koch had the background of a scientific medical researcher. His 1876 discovery of the pathogenicity of the anthrax bacillus and, more importantly in the long run, the Henle-Koch postulates, revolutionized the diagnosis and causes of infectious disease and thrust the microscope into clinical consciousness.³³⁹ Nevertheless, the bacteriological revolution did not occur overnight. Many practitioners in America, for example, initially disdained the notion that bacteria caused disease.³⁴⁰

The German Ehrlich, however, did not hesitate to accept Koch's precepts. Heeding Cohnheim's impulsive exhortation, he followed Koch to Berlin and was working with Koch when the latter announced to the Berlin Physiological Society on March 24, 1882 that the cause of tuberculosis was a bacillus.³⁴¹ Koch had succeeded in staining bacilli with aniline dyes,³⁴² but his methodology was too cumbersome and time-consuming to permit the routine microscopic

³³⁹Koch was not the first to discover the anthrax bacillus or its presence in infected animals. In 1849, Davaine and Pollender, French and German medical practitioners, respectively, independently noted bacteria in the blood of anthrax-infected cows. Pollender detailed the finding in a paper published in 1855. He called the organisms 'bacteria' or 'bacteridia.' See Foster, *A Short History of Clinical Pathology*, 53.

In 1865, William Budd published an article in the *Lancet* that took note of Davaine's previous findings on anthrax (*Lancet* 1865, i: 47; cited by Foster, *A Short History of Clinical Pathology*, 55). Thus Koch was not the first to identify the anthrax bacillus or its invasion of the animal host, but he was the first to identify, isolate, and obtain a pure culture of the bacillus for injection into another animal to prove the causative nature of the organism—thus fulfilling the four major tenets of the Henle-Koch postulates of disease causation.

³⁴⁰For a comprehensive review, see Phyllis Allen, "Americans and the Germ Theory of Disease" (Dissertation, University of Pennsylvania, 1949), 178. Many of Allen's arguments were questioned—if not disputed—by Tomes and Warner two generations later in 1997. See Nancy J. Tomes and John Harley Warner, "Introduction to Special Issue on Rethinking the Reception of the Germ Theory of Disease: Comparative Perspectives," *Journal of the History of Medicine* 52 (1997).

When it comes to the acceptance of bacteria-caused diseases, like so many other radical changes in thought, hindsight is always 20-20. Few could imagine, in the late nineteenth century, how theories of germs would come to grip minds of both popular and medical persuasion. But presentism—the notion that the value of the past is as prologue to the present—is a fallacy under which historians live through the influence of a public that enjoys valorization of the present as the vindication of the errors of the past.

³⁴¹Sigerist, *The Great Doctors*, 369.

³⁴²Rather, *The Genesis of Cancer*, 168.

analysis of infected tissue. Ehrlich, now at the height of his inventiveness with stains, found a way to circumvent Koch's difficulties and originated a quick and facile stain for the deadly bacillus that could be of use in a clinical setting.

Ehrlich's discovery of a practical stain for the TB bacillus *in vivo* was achieved in the great tradition of scientific discovery—serendipity, or, more accurately, as Ovid wrote, preparedness meeting opportunity. Ehrlich may have been “a more original genius than Koch,”³⁴³ but Ehrlich attributed his discovery of the stain for the tuberculous bacillus to “Glück” (luck)—one of his famous four “G’s.”³⁴⁴ One night, Ehrlich, always experimenting with new dye combinations, left some stained TB slides on the edge of a stove in order to dry and went home for a few hours rest. Early the next morning he discovered, to his shock, that the cleaning lady had already fired up the stove—with the slides still lying on its surface! He ran to the slides and inspected them. To his utter astonishment, he found that “[T]hey were wonderfully stained, and on examining them under the microscope he found the tubercle bacilli standing out in them in clumps.”³⁴⁵

His combination of phenylamine with methyl violet or fuchsin, heat-dried to perfection, created an intense stain. He then added acid and found that whereas the acrid solution eliminated the color from much of the slide, the TB bacillus resisted decolorization and held the stain fast.³⁴⁶ The acid-fast nature of the tuberculous bacillus was uncovered and with it a new means

³⁴³Flexner and Flexner, *William Henry Welch*, 394. Carl Salomonsen, a Danish pathologist and close friend of William Henry Welch who studied with Cohnheim, Ehrlich, and Welch at Breslau in the 1870s, delivered these words of praise to Welch in 1924.

³⁴⁴The investigator of today will appreciate the timeless role of Ehrlich's four G's in scientific discovery: Geld (money), Geduld (patience), Geschick (cunning), and Glück (luck). See Riedman and Gustafson, *Portraits of Nobel Laureates*, 55.

³⁴⁵Marquardt, *Paul Ehrlich*, 25-26.

of rapid identification of the cause of tuberculosis. The whole process took little more than fifteen minutes and showed that the “white plague”—one of the most feared diseases of the nineteenth century—could be reliably diagnosed with the microscope within the confines of the clinic.³⁴⁷

Word of Ehrlich’s new method of staining the TB bacillus spread rapidly by means of journals and correspondences through the scientific community. It was reported in the American literature in July, 1882—only months after Koch’s initial announcement of the discovery of the bacillus.³⁴⁸ Koch abandoned the staining method that had led him to the discovery of the bacillus and adopted the Ehrlich procedure. In the tenth issue of the 1883 *Deutsche Medizinische Wochenschrift* (*German Medical Weekly*), Koch publicly paid tribute to the young genius. As Koch wrote, “With Ehrlich’s method of staining, the recognition of tubercle bacilli could readily be made use of in diagnosis. We owe it to this circumstance alone that it has become a general custom to search for the bacillus in sputum, whereas, without it, it is likely that but few investigators would have concerned themselves with tubercle bacilli.”³⁴⁹ Koch discovered the bacillus. Ehrlich made its identification practicable.

Koch’s proof of the infectious nature of germs, combined with Ehrlich’s methodology for the quick, easy, and reliable visualization of bacteria, opened the floodgates to a universe of bacteriological causation. During the 1880s and 1890s, researchers discovered and named dozens of bacterial pathogens. Most were described by German investigators who had early

³⁴⁶The American Monthly Microscopical Journal, “Staining Bacteria,” *The American Monthly Microscopical Journal* 3 (1882).

³⁴⁷Ibid.

³⁴⁸Ibid.

³⁴⁹Cited by Marquardt, *Paul Ehrlich*, 27.

noted the diagnostic potential of the microscope.³⁵⁰ It was now recognized that diseases had real, learnable, reproducible causes. The idea, invoked by religion, that sin was the cause of disease, was thoroughly discredited by the science of visible, identifiable microbial agents and the new concept of medical proof laid down by the Henle-Koch postulates. With the aid of stains and the microscope, bacterial etiologies were sought for all manners of illness, including cancer.

In the long run, the practical value of Ehrlich's stains exceeded their investigational worth, for practitioners now had an acceptable method of disease diagnosis that had eluded them throughout history. Koch had found that consumption, long thought to be a form of cancer or at least indistinguishable from true lung cancer,³⁵¹ was infectious and, very importantly, easily diagnosable.³⁵² Here was the confluence of chemistry, microscopy, and real-world medicine that Müller, Virchow, Cohnheim, and others had only dreamed of decades before. Ehrlich succeeded in linking stains and the microscope with clinical medicine. Nevertheless, the transition of staining from pure chemistry to applied medicine had only just begun. Other advances in microtechnique added to the growing allure of the idea of microscopical medical diagnosis even

³⁵⁰Many of these discoveries—I would call them “sightings”—were later found to be spurious. Nevertheless, the enthusiasm for the identification and eponymization of these “micro-organisms” was—excuse me—infectious.

³⁵¹The differentiation of tubercle disease from lung cancer was so difficult that many nineteenth-century physicians believed them to be different forms of the same disease. Bayle, for example, named pulmonary tuberculosis “cancerous phthisis.” See Onuigbo, “Lung Cancer in the 19th Century,” 121. Two generations later, Cooke called the two “interchangeable creations.” Thomas Weeden Cooke, *On Cancer: Its Allies and Counterfeits*, 2 vols., vol. 1+2 (London: Longmans, Green, and Co., 1865), 13.

I must note that although sputum diagnosis of tuberculosis based upon Ehrlich's staining procedure permitted rapid diagnosis, the clinical differentiation of TB and lung cancer, to a large extent, awaited the application of Röntgen's X-rays to clinical medicine beginning in the last years of the nineteenth century.

³⁵²One of Koch's famous maxims dictated “one germ, one disease.” Today, the broader reductionist thesis that each disease has a unique cause is again under attack as the elucidation of the genome reminds us of the role of the host in the host-parasite equation. Nevertheless, Koch's postulate undergirded the triumphs (and evils) put forth in the name of public health in the late nineteenth and early twentieth centuries as anti-germ crusaders prophylactically struck out against perceived social and medical repositories of germs.

before the microscope became a ubiquitous instrument of cancer research and modern medicine. In the meantime, however, Paul Ehrlich continued to apply his cell-coloring gifts to a wide range of human diseases, including cancer.

The Staining of White Blood Cells and their Cancer:

Leukemia

Ehrlich also contributed directly to the study of cancerous diseases. As in his other endeavors, those achievements depended heavily upon his combined knowledge of chemistry, dyes, and histology. During the 1880s, Ehrlich applied his ingenious technique of differential staining with aniline dyes (*Farbenanalyse*), which he first discovered in 1877, to white blood cells. This marked the birth of modern hematology.³⁵³

The true nature of a seeming excess of white blood cells in the circulation lay cloaked in confusion for most of the nineteenth century. In 1827, Velpeau rendered the first clinically accurate description of a patient with leukemia (bone marrow cancer with proliferation of white blood cells) when he noted “pus” in the blood of a sick man.³⁵⁴ Physicians, limited by primitive microtechnique, were unable at that time to microscopically separate the different elements of the “white” portion of the blood. Thus Thomas Hodgkin, one of the most astute among them, inadvertently included in his classic 1832 study of seven patients with enlarged spleens and lymphadenopathy (“Hodgkin’s Disease”) cases of leukemia.³⁵⁵ In the 1840s, when the second great wave of enthusiasm for the microscope in the study of human disease swept Europe,³⁵⁶

³⁵³Paul Ehrlich, “Beitrag zur Kenntnis der Anilinfärbungen und ihrer Verwendung in der mikroskopischen Technik,” *Arch. Mikr. Anat.* **13** (1877): 263-277. See Hajdu, “Cytology,” 673.

³⁵⁴*Cancer Bulletin* 17 (Nov-Dec 1965): 105. Pus is a mixture of enzymes, cells, and tissue components. The most abundant cells are white blood cells, which fight infection and confer future immunity.

³⁵⁵Long, *Selected Readings in Pathology*, 112.

investigators found more baffling cases of large numbers of white cells in the bloodstream. They labeled it a distinct disease. In keeping with the nationalistic tendencies of the era, each of three major European nation-states claimed the discovery of this fatal condition as its own—Alfred François Donn  of France (1844),³⁵⁷ Rudolf Virchow of Germany (1845),³⁵⁸ and John Hughes Bennett of England (1845).³⁵⁹

Pathologists and clinicians questioned whether the excess of white blood cells was a secondary response to infection (pyemia) or the result of primary overproduction (leucocythemia). Virchow, in 1856, urged medical opinion toward the notion of excess synthesis rather than suppuration. Thus, he named the disease leukemia and it stuck.³⁶⁰ Virchow also supplied one of the last major pieces of the descriptive puzzle with his improved microscopy in 1870 when he noted the morphological differences between the two major types of white blood cells, myelocytes and lymphocytes. Both may be involved in cancer of the blood.

³⁵⁶The first wave was in the seventeenth century.

³⁵⁷A. Lennox Thorburn, "Alfred Francois Donne, 1801-1878, Discoverer of *Trichomonas Vaginalis* and of Leukaemia," *British Journal of Venereal Diseases* 50 (1974). Donn 's description of leukemia was published in *Cours de microscopie compl mentaire des  tudes m dicales*, the compendium of his lectures on microscopy and medicine.

³⁵⁸Rudolf Virchow, "Weisses Blut," *Neue Notizen aus dem Gebiete der Natur- und Heilkunde* 36 (Weimar, 1845): 151. Germany was not officially a nation-state in 1845. For the sake of accuracy, Germany at that time was a Confederation controlled by Austria. Otto von Bismarck—Virchow's political nemesis—engineered the German Empire engineered in 1871.

³⁵⁹John Hughes Bennett, "Case of Hypertrophy of the Spleen and Liver, in which Death took place from Suppuration of the Blood," *Edinburgh M. & S. J.* lxiv (1845): 413-423, reprinted by Ralph H. Major, *Classic Descriptions of Disease, with Biographical Sketches of the Authors, The Classics of Medicine Library* (Springfield, IL: Charles C. Thomas, 1932; reprint, 1994), 466-69.

Virchow addressed the question of priority r  the recognition of leukemia as a distinct disease entity. He claimed, in his inimitable fashion, that although *neither* he nor Bennett was the first to describe the disease, the German got it right and the Englishman wrong. "It is incorrect, as some recent authors state," wrote Virchow, "to divide the discovery between Bennett and me, as simultaneous. Neither Bennett nor I observed the first case of leukemia. We both, however, had the opportunity almost simultaneously to observe such a case. Bennett considered his case one of pus formation in the blood (pyemia—LK) and six years after I had immediately described mine as white blood (leukemia) and only after I had gradually developed this doctrine in a series of articles, did he accept this doctrine." See Major, *Classic Descriptions of Disease*, 471.

³⁶⁰Walter Seufert and Wolf D. Seufert, "The Recognition of Leukemia as a Systemic Disease," *Journal of the History of Medicine and Allied Sciences* 37, no. 1 (1982): 34.

With knowledge of leukemia at this morphological level, Ehrlich made two direct additions—and one critical, indirect contribution—toward a further understanding of the disease. As early as his University days he had evinced an interest in staining blood corpuscles. His 1878 doctoral thesis elaborated on “the affinity of eosin for haemoglobin,” a major constituent of red blood cells.³⁶¹ Almost a decade later, Ehrlich not only confirmed that leukemia represented excess production of white blood cells (thus affirming Virchow’s leucocythemia), but concluded that the disease was primary to the hematopoietic system—the parts of the body like the bone marrow that produce blood cells.³⁶² This finding was a giant step forward, because it went beyond the descriptive pathology of Donné, Virchow, and Bennett to the source and site of the problem. Not surprisingly, Ehrlich’s discovery was based upon new dyes and chemical procedures he introduced in 1880, at the height of his prowess.

In 1891, deep into his research on the side-chain theory of immunity and four years after his identification of the blood-forming organs as the key site in the pathogenesis of leukemia, Ehrlich made his second contribution when he succeeded in differentiating the disease into two predominant types—lymphocytic and myelogenous leukemia. This was his last great direct discovery in the field of cancer. In the first decade of the twentieth century,³⁶³ he made forays into the battleground of cancer pharmacotherapy without marked success. He considered those years some of the most unproductive of his very generative professional life. In some ways, this drive to cure cancer paralleled his later chemistry-based innovations, but his research in this field lacked the foundational insights of chemical structure and function that guided his successful work in immunology and the development of antimicrobial agents. In frustration and disgust, he

³⁶¹Ehrlich, "Contributions to the Theory and Practice of Histological Staining," 97.

³⁶²Eugene Stransky, "Contributions to the History of Leukemia," *Episteme* 4 (1970).

³⁶³The actual years were 1901-1909. These were also the years of his great discoveries of salvarsan and his methodology for synthesizing new drugs.

abandoned the cancer research that he could only hope would have been the crowning glory of an extraordinary career in the elucidation of human chemistry.³⁶⁴

In 1909, as Ehrlich frantically tested hundreds of compounds to find the “magic bullet” (targeted therapy that kills the cause of disease without injuring the host) against syphilis, others recognized his contributions to the study of cancer of blood corpuscles and expanded on them. L. Selling at Johns Hopkins, for example, noted that benzene, the forerunner of synthetic stains, killed white blood cells.³⁶⁵ The discovery of the leukotoxic attributes of benzene, a direct outgrowth of Ehrlich’s studies on benzene-based aniline dyes and their histologic and chemotherapeutic properties, led to its use in the treatment of leukemia and its introduction as the basis of countless chemotherapeutic agents.

The Nobel Prize Lecture

Stockholm, Sweden

December 11, 1908

Thus Ehrlich, a direct intellectual descendant of Müller, Virchow, Cohnheim, and Koch, joined together clinical medicine and the microscope by means of dyes and the staining process through his deep knowledge of chemistry and histology. In his 1908 Nobel Prize Lecture, he paid homage to the thoughts and techniques that had brought him to Stockholm. He lauded anatomy, “the *alpha* and *omega* of scientific knowledge,” and the microscope, which he claimed

³⁶⁴Paul Ehrlich was only one of many renowned medical researchers to fail to discover the secret of cancer therapy despite great success in other formidable endeavors. Henry Sigerist noted this ineffectuality in the light of genius in 1932, when he wrote: “I remember the great Berlin surgeon August Bier said to me one day, ‘If a great scientist at the end of a brilliant career wants to make a fool of himself, he takes up the problem of cancer.’” See Henry E. Sigerist, “The Historical Development of the Pathology and Therapy of Cancer,” *Bulletin of the New York Academy of Medicine* 8, no. 11 (1932): 653.

³⁶⁵Lee, ed., *Dates in Oncology*, 80. William Henry Welch was then the pathologist and administrator at this institution that was to have such a great influence on American medicine.

had opened new vistas for the study of disease.³⁶⁶ He detailed the immunological experiments that had fostered the side-chain theory of immunity for which he received the Prize and neared the close of his discussion with an analysis of the derivatives of benzene that had made his chemical research possible. Benzene, the molecule of Perkin's rich dyes, had become the backbone of both staining and chemotherapeutics. As he concluded his lecture, Ehrlich revealed that his interests now focused upon "the mode of the action of remedies," based upon *de sedibus et causis pharmacorum*.³⁶⁷ Even insights into pharmacodynamics (the process by which a drug acts upon the body) and pharmacokinetics (the process by which a drug is absorbed, distributed, metabolized, and eliminated from the body), however, were not his ultimate purpose. Instead, his goal in the treatment of all diseases, including cancer, had become nothing less than "a complete cure by a single injection"—*therapia sterilisans magna*.³⁶⁸

Ehrlich's genius realized that if staining was a chemical process that targeted some cell components but not others, then chemicals—drugs—could differentially affect cell processes and beneficially alter the course of disease. The German scientist applied his acumen during the late nineteenth and early twentieth centuries when germs dominated medical consciousness. Hence he focused on the treatment of parasitic and bacterial diseases. The fruits of his labors in cancer were minimal at best. Nevertheless, his fundamental insights into the chemistry of the cell through microscopy and his conception of the "magic bullet" continue to reap rewards today in

³⁶⁶Paul Ehrlich, "On Partial Functions of the Cell," in *The Collected Papers of Paul Ehrlich*, ed. F. Himmelweit, *The Collected Papers of Paul Ehrlich* (London: Pergamon Press, 1909), 183.

³⁶⁷That is, "the seats and causes of drugs." This is likely a play on the title of Giovanni Morgagni's famous treatise on the anatomy of organ systems, *De sedibus et causis morborum* (*The Seats and Causes of Disease*, 1761).

³⁶⁸Ehrlich, "On Partial Functions of the Cell," 194. Nonetheless, Ehrlich's main target remained the microbial diseases.

the study of cancer through its cause and treatment.³⁶⁹ For what, in the final analysis, is cancer chemotherapy but a stain without color?

Advances in Microscopy & Microtechnique

Part Two: Microtomy

As chemistry and the improved microscope formed the foundation of Paul Ehrlich's advances in cancer and medicine, so, too, his contributions helped to foster a relationship between the microscope and medicine. But the interdependence did not catch on at once. Ehrlich's 1882 practical stain for the tuberculous bacillus had less immediate impact on the clinical linkage of cancer medicine and microscopy in America than one might surmise. The reasons were many. First, the causative nature of the bacillus in human disease was not immediately accepted—like many (if not most) revolutionary thoughts in science and medicine.³⁷⁰ Dr. George Dock remembered that Koch's discovery of the tuberculous bacillus “was received by medical teachers and undergraduates with amazement, or disbelief, and even by ridicule.”³⁷¹ Second, flaws in the processing and viewing of microscope specimens persisted. Hence Dr. Elliott's microscopical analysis of General Grant's biopsy remained an ancillary and merely supportive diagnostic procedure in 1885. By the time of President Cleveland's biopsy in 1893, however, microscopy had become the primary mode of tumor diagnosis. What changed? Progress in microtechnique contributed mightily to this watershed event in the history of cancer,

³⁶⁹Paul Ehrlich's 1906 description of a “magic bullet” against pathogenic bacteria is as true of cancer chemotherapy today as it was of germs then. “It will...be easy to effect a cure,” he wrote, “if substances have been discovered which have a specific affinity for these bacteria and act...on these alone...while they possess no affinity for the normal constituents of the body...such substances would then be...magic bullets.” www.pei.de/English/infos/epaul.htm. Accessed 3 February 2003.

³⁷⁰Note the skeptical comments accompanying the initial announcement of Koch's discovery of the TB bacillus in the forerunner of today's *The New England Journal of Medicine*. See the Boston Medical and Surgical Journal, “The Bacillus of Tuberculosis,” *Boston Medical and Surgical Journal* 106, no. 16 (1882).

³⁷¹Dock, “Clinical Pathology in the Eighties and Nineties,” 675.

for improved specimen preparation reduced the vagaries of the ancient art to a more mechanized and dependable process. As a result, inconsistencies in microtechnique became much less of a factor in microscopical interpretation.

The revolution wrought by staining was only one of the major contributions to advances in microtechnique in the late nineteenth century. Another was the mechanical microtome. Well into the nineteenth century, microscopists cut most specimens by hand. Mechanical microtomes—marvels of engineering—sprouted and flourished with the industrial revolution like so many of the technologies that helped modernize medicine. The number of different microtomes grew slowly but steadily from the 1830s of Müller to the 1870s of Ehrlich. Thereafter, as technological, biological, institutional, and cultural events combined to give new meaning and impetus to the need for and acceptance of scientific medicine and medical microscopy, the number of microtomes swelled to flood tide.

Bracegirdle found that only three new microtomes were invented in the 1830s.³⁷² During the 1840s, five more became available.³⁷³ By 1870, however, microscopists had constructed at least twenty-five new and different microtomes since the days of Müller, Schleiden, and Schwann.³⁷⁴ Most of these instruments were made of metal hard enough to slice wood and other natural substances. Nevertheless, human tissue sectioned by mechanical microtomes remained rare in Europe and nearly non-existent in America during these years. Naturalists and early devotees of medical microscopy on both sides of the Atlantic showed little predilection for anything more than the hand-held knife until at least the 1860s in Germany and the 1880s in the

³⁷²Bracegirdle, *A History of Microtechnique*, 117.

³⁷³*Ibid.*, 118.

³⁷⁴*Ibid.*, 122, 17.

States.³⁷⁵ Until those years, the quality of specimens prepared by early microtomes was often poor. In particular, hand-cut tumors created uneven specimens with thick and thin sections. Thickened portions on the prepared slide required variable depths of focus, thus adding an additional layer of complexity to microscopical analysis. Errant diagnoses resulted, a significant cause of scant practitioner interest in medical microscopy until microscopists corrected these problems.

The evolution of the microtome during the second half of the nineteenth century is a study in mechanics that transformed the device from an extension of the hand to an extension of the mind. Thought superseded skill. The first mechanical microtomes performed like superior hands—steadier and more evenly measured than the average appendage. Wood, the basic material of scientific tools during the early years of the century, gave way to metal—the foundation of the manufacturing revolution. The knife blade had been metal for some time, but its cutting edge became finer and more honed to the task of exact sectioning. Coarse and fine screws on the microtome added consistency to the slice, just as these variable adjustors improved the resolution capabilities of the microscope. It was not unusual for the same scientist to tinker with both the microtome and the microscope. Specialization, then called “specialism,” was rare.³⁷⁶ The microscope craftsman was often an artisan who processed the specimen from beginning to end. Microscopists applied ideas synergistically from technique to interpretation and strengthened both. Their goal was nothing less than the most true-to-nature visualization

³⁷⁵Ibid., 126 and 321.

³⁷⁶Rosemary Stevens, *American Medicine and the Public Interest: A History of Specialization*, Updated with a New Introduction ed. (Berkeley: University of California Press, 1998), 47-48. Although pathology was one of the earliest specialties, medical microscopy in America, a subset of what Stevens’ terms “laboratory specialism,” had become an integral part of the clinicians’ training rather than the exclusive bailiwick of the pathologist by the final years of the century. William Henry Welch and other German-trained physicians in the United States played no small role in the drive toward specialization.

possible. Reproducibility of specimen preparation was a major contributor toward this objective, and microtomal sectioning was an early step in the process.³⁷⁷

Cancerous tissue was especially amenable to the mechanical microtome, for the curled-up, flimsy, decomposed nature of the excised tumor could be more precisely cut, preserved, and prepared with the new machine. In consequence, the histopathologist, cancer investigator, and their patients benefitted mightily from the mechanical microtome. Improvements in each step of the processing of the specimen from organism to slide increased the probability of an accurate diagnosis.

By the last quarter of the nineteenth century, the utility of the mechanical microtome surpassed the mere cutting of predictable, thin sections. Mechanized reproducibility created serial sections of uniform thickness that allowed different investigators to compare similar slices from the same specimen, thereby obviating the ambiguities posed by unequal, improvised sections cut with a hand-held knife. The mechanical microtome also quickened the pace of sectioning. One investigator invented a microscope-based microtome that cut the astounding total of five thousand sections in the five year period from 1866 and 1870. By 1885, the same number could be sliced in one day.³⁷⁸ In addition, microscopists discovered that the simple act of raising the specimen on an inclined plane allowed the production of thinner and therefore even more numerous slices from each specimen—up to 120 per centimeter.³⁷⁹ These finer sections that followed the invention of new techniques synergized with advances in microscope optics to augment the resolution and sharpness of the refracted image during the 1870s and 1880s.

³⁷⁷Beautiful hand drawings in Bracegirdle's *Microtechnique* illustrate the evolution of the microtome. See especially Bracegirdle, *A History of Microtechnique*, 117-267.

³⁷⁸*Ibid.*, 129-30.

³⁷⁹*Ibid.*, 134.

Microscopical interpretation came to depend less on artifactual whimsy and more on reproducible standards.

The American pathologist George Dock may have used his old-fashioned hand-held knife microtome in Rudolf Virchow's microanatomy class as late as the mid-1880s,³⁸⁰ but a few years hence mechanical microtomes became standard in research laboratories and then early clinical pathology laboratories on both sides of the Atlantic.³⁸¹ True to the industrial revolution that begat them, the mechanical parts of the fine-sharpened instruments became interchangeable and less expensive. Carl Zeiss, for example, introduced machine-drilled components to his remarkably modern bench microtome in 1877.³⁸² Microscopists first employed motor-driven microtomes in the 1880s.³⁸³ It is no wonder that the number of articles on the subject in the *Surgeon-General's Index Catalogue* increased enormously from 1885 to 1893.³⁸⁴

The freezing microtome, which constituted a powerful addition to the armamentarium of the surgeon in the late nineteenth and early twentieth century through its use in the preparation of the frozen section,³⁸⁵ did not generate significant interest among microscopists until the 1870s.³⁸⁶ Even then, the freezing tubs that cooled the specimen to make it harder and thereby more

³⁸⁰Dock, "Clinical Pathology in the Eighties and Nineties," 672.

³⁸¹Ibid., 680.

³⁸²Bracegirdle, *A History of Microtechnique*, Plate 36.

³⁸³Clark and Kasten, *History of Staining*, 203.

³⁸⁴Microscopy, the larger category that includes microtomes, did not attain its own section in the *Catalogue* until years after the initial volume of 1879. Billings originally lumped international papers on microscopy in a catchall anatomy section.

³⁸⁵Wright, "Surgical Pathology," 296-97.

³⁸⁶Bracegirdle, *A History of Microtechnique*, 135. Raspail, who surmised decades before Virchow that all cells derive from prior cells, designed a freezing apparatus in 1825. It was probably the first of its kind. Ibid. Scientists utilized the freezing microtome sparingly until later in the century for reasons related to the history of the surgical biopsy. Much more on the biopsy later in this chapter.

amenable to sectioning, were cumbersome and unwieldy. In 1876, as the young Ehrlich explored human chemistry with his multi-colored stains, R. Hughes first utilized the cooling power wrought by the evaporation of ether to originate “an entirely new principle of freezing”—one essentially independent of laboratory temperature.³⁸⁷ By the mid-1880s microscopists had a wide range of microtomes at their disposal. The mechanical microtome became so indispensable to microscopy that the American firm Bausch & Lomb added it to their increasingly popular and affordable microscope sets in 1885.³⁸⁸

Of the various physicians who cared for patients with tumors, those who performed surgery pressed hardest for the development of rapid sectioning and other microscopical techniques for the diagnosis of cancer. As cancer surgery became less painful and dangerous toward the end of the century, the ability to prove the diagnosis while the patient was still under anesthesia became a goal for the patient, surgeon, and histopathologist alike. Immediate pathological diagnosis also reduced the risk to the patient engendered by the need for a second operation to remove a tumor confirmed only after the usual two-to-three week post-operative microscopical process.

In 1889, the Boston surgeon John Collins Warren, scion of the “First Family of Surgery,”³⁸⁹ offered a new technique for “the early diagnosis of malignant growths” that involved taking a punch biopsy and examining the specimen on the spot “with the freezing

³⁸⁷Ibid., 138 and citation at 283 Footnote 51.

³⁸⁸Purtle, "History of the Microscope," 259.

³⁸⁹Rhoda Truax, *The Doctors Warren of Boston: First Family of Surgery*, First Printing ed. (Boston: Houghton Mifflin Company, 1968). Truax’s section on J. Collins Warren (1842-1927), Book V, is entitled “The Birth of Modern Surgery.” Thus, Truax situated J. C. squarely in the midst of this late-nineteenth-century revolution in medicine.

microtome.”³⁹⁰ Little ballyhoo attended the publication of the article, leading to the possibility that use of the freezing microtome to aid the development of frozen sections was already more widespread than represented in the literature of the early 1890s.³⁹¹ By 1893, the year of Cleveland’s tumor surgery, W. Thelwall Thomas was already using the freezing microtome to mount microscope slides whereby “many sections are easily diagnosed in ten minutes.”³⁹² Two years later, Nicholas Senn, chairman of surgery at Rush Medical College in Chicago, urged all surgeons to avail themselves of the freezing microtome for immediate pathological diagnosis. At the same time that hospitals were rapidly becoming the site of choice for cancer surgery, he wrote in his textbook that “The freezing microtome should have a place in the operating room of every hospital.”³⁹³ Thus, by the end of the nineteenth century, the now-ubiquitous mechanical microtome routinely generated multiple, uniform, thin specimen sections that aided rapid surgical diagnosis.

³⁹⁰John Collins Warren, “The early diagnosis of malignant growths,” *Trans. Am. Surg. Assoc.* 7 (1889): 9-24.

³⁹¹James R. Wright, Jr., in his celebrated article on “The Development of the Frozen Section Technique,” did not agree. He believed the technique was not invented until 1895. Regardless, Wright and I agree that the procedure did not become widespread until the early twentieth century. Also see Footnote 283 in this Chapter.

³⁹²W. Thelwall Thomas, “A Note on Rapid Methods of Preparing Sections for the Microscope,” *The Liverpool Medico-Chirurgical Journal* 13 (1893): 491. Thomas also suggested that the concept of the frozen section was hardly new to the year of his journal article, for he wrote that “the above processes are not put forward as anything new, being simple adaptations of well-known methods.” *Ibid.*, 492. It is not unusual for clinicians to discover and utilize innovative practice techniques without immediately publishing them. The credit, however, usually goes to the first published popularizer.

³⁹³Nicholas Senn, *The Pathology and Surgical Treatment of Tumors* (Philadelphia: W. B. Saunders, 1895): 107. Cited by Wright, “Surgical Pathology,” 299 Footnote 16.

Advances in Microscopy & Microtechnique

Part Three: Lenses & Designs

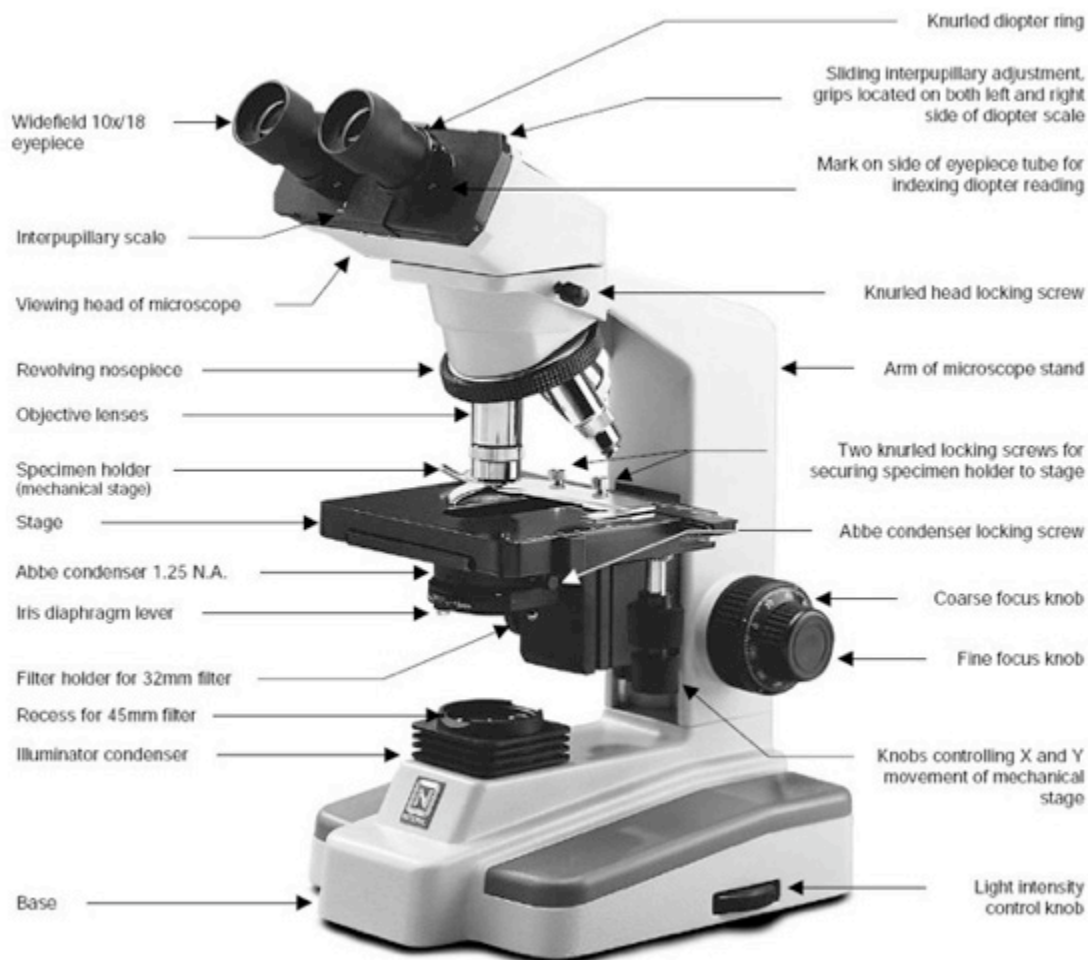


Figure 1. A Modern Light Microscope³⁹⁴

Progress in mechanical microtomy and tumor staining improved the preparation and interpretation, respectively, of the microscope slide—but they did not improve the microscope. That transformation, unfinished despite the second-wave revolution in lens optics in the 1820s, also occurred during the critical period in the making of modern cancer of the late nineteenth

³⁹⁴<http://www.adafruit.com/blog/2009/08/01/choosing-a-microscope/> accessed November 14, 2012.

century.³⁹⁵ The “improved” microscopes of the Mayo Brothers, for example, incorporated lens systems that were advanced far beyond the aberration-reduced microscopes of Joseph Jackson Lister. As in the history of microtomes and staining, progress in the development of new and better lenses for microscopes occurred in bursts, propelled by scientific insights and cultural-biological synergies.

The microscope lenses fashioned by Selligue, Chevalier, and J. J. Lister in the early years of the nineteenth century mitigated the spherical and chromatic aberrations of more primitive lenses. Johannes Müller, Rudolf Virchow, and the young Paul Ehrlich opened a new world of cancer at the microscopic level with lenses ground to fit the theories of Lister and his contemporaries. Nevertheless, the urge to exceed established limits—to visualize the smallest of the small and then some—gave impetus to a new generation of manufacturers (née lens grinders) who, standing firmly on the newly-developed principles of chemistry and optics, sought to further enhance both the magnification and resolution of the microscopic image.

The work of Ernst Abbe of the Zeiss firm...essentially changed the basis for the manufacture of microscope optics from trial and error techniques, and put it on a sound mathematical footing.

—Donald L. Padgitt³⁹⁶

Dr. Carl Zeiss opened a small optical shop in Jena, Germany in 1846 and began producing microscopes the next year. Twenty years later, Zeiss had the good foresight to invite Ernst Abbe, a young physicist and mathematician at the local University, to become his research director. Professor Abbe, a theoretician who developed a penchant for optics, has been called, in the words of an eminent historian of microscopy, “the foremost figure in the development of the

³⁹⁵The first-wave revolution of lens optics included the late sixteenth- and seventeenth-century developments led by Galileo, Hooke, Leeuwenhoek, and others.

³⁹⁶Padgitt, *Early American Microscopes*, 142.

microscope in the latter part of the 19th century.”³⁹⁷ Abbe was hardly the only scientist to contribute to the creation of the modern microscope in the last decades of the nineteenth century, but his ability to shift seamlessly from academia to industry contributed greatly to his success in both. He was a polymath who revolutionized the microscope and launched it into the industrial age.

During his career at the University of Jena and at Zeiss, Ernst Abbe conceived notable additional theoretical underpinnings for the physics of optics. Nevertheless, it was his pragmatic application of his theoretical work that advanced the microscope from an object-magnifier of limited resolution to a modern instrument of scientific precision. He accomplished this in a series of small but discrete steps. Over time, he incorporated the new manufacturing concepts of standardization and interchangeability of parts into the construction of the microscope.

Between 1866, when he began his association with Zeiss, and 1888, when he became sole owner of Zeiss works upon the death of its founder, Abbe achieved prodigious advances in microscope optics. He fabricated the best optical lenses of the nineteenth century, constructed a much-improved substage condenser to better illuminate the specimen, perfected the oil immersion system to a degree hardly surpassed to this day, and developed the numerical aperture system that allowed the standardization of lenses (including camera *f*-stops) and the creation of a modern industry. As Ehrlich melded chemistry and biology, Abbe brought together seemingly disparate elements of chemistry, lens physics, immersion systems, and optical theory to manufacture the best light microscopes ever. Although difficult to choose the best gem from among his many precious accomplishments, the creation of the apochromatic lens was probably his greatest achievement.

³⁹⁷Saville Bradbury, "Microscopes (Measurement and Observation)," in *The New Encyclopaedia Britannica*, ed. Philip W. Goetz (Chicago: Encyclopaedia Britannica, Inc., 1987), 742:1b.

The Apochromatic Lens

As new ideas in physics led to a better understanding of the geometry that governed lens function, so new insights in chemistry enhanced the construction of improved microscope lenses. Objectives, the lenses closest to the specimen or object, had always been composed of the finest glass—free of bubbles and impurities—but different crystals in their make-up further enhanced the quality and sharpness of the images they projected. In 1838, Sir David Brewster, a Scottish clergyman, optical experimentalist, and physicist, found that the addition of calcium fluoride augmented the quality of lens glass. Fluorspar or fluorite, its alternate names, is a colorless, translucent crystalline mineral in its pure state that “internally dispersed” transmitted light.³⁹⁸ When Zeiss opened his optical shop in the 1840s, he did not initially use Brewster’s superior lens glass.³⁹⁹ Abbe, however, did.

In 1868, the twenty-eight-year-old Abbe, now active in both the theory and practice of the microscope, discovered that the addition of pure, crystalline fluorite to lens glass, when oriented in a certain direction, essentially eliminated coma, chromatic, and spherical aberrations once and for all.⁴⁰⁰ He called it Jena glass and the lens ‘apochromatic’—from the Greek ‘without color.’ Nevertheless, Abbe’s research finding did not immediately translate into the production of a new microscope lens system, for objectives with apochromatic lenses required a dozen or more elements for their construction. Such a manufacturing tour de force was difficult

³⁹⁸Clark and Kasten, *History of Staining*, 152. George Stokes later renamed Brewster’s concept of “internal dispersion” of light ‘fluorescence.’ In 1852, aware of the presence of luminescence in nature and dissatisfied with the idea of internally dispersed light, Stokes gave birth to the modern term. Ibid. This property of certain minerals to disperse light internally formed the basis for the invention of the twentieth-century fluorescent microscope.

³⁹⁹Purtle, "History of the Microscope," 258.

⁴⁰⁰<http://www.history.mcs.st-andrews.ac.uk/history/References/Abbe.html>: 2. Accessed March 30, 2003.

to achieve at the time, because the increased complexity magnified the difficulty of manufacturing considerably.

A decade passed before Zeiss manufactured the first prototype lenses with Jena glass. In 1884, when General Grant first suffered the foreboding peach pain, Abbe and Zeiss collaborated with Friedrich Otto Schott, a glass chemist, to found the Jena glassworks.⁴⁰¹ Within two years, Zeiss began manufacturing microscopes with the Jena glass apochromatic lens systems. Word of the new, high-quality lenses disseminated rapidly. In 1889, an American, Christopher Johnston, singled out “the renowned apochromatic objectives of Germany, with all their recognized excellence and improvements.”⁴⁰²



Figure 2. Zeiss markets the first lot of an entirely new type of microscope objectives: Apochromats (1886)⁴⁰³

Even microscopists of the time noted that the apochromatic lens system was a milestone in the chronology of the microscope. In 1891, J. H. Wilson celebrated just such a history when he pronounced that in the past “three or four years” the apochromatic objective of Abbe, Schott, and the Carl Zeiss company had “a fresh start given to microscopy.”⁴⁰⁴ Never before had the

⁴⁰¹Jena glass, which incorporated fluorspar, was particularly resistant to shock and heat. The Jena glassworks produced excellent quality glass that was used in the manufacture of many precision tools and instruments for scientific research of all kinds.

⁴⁰²Christopher Johnston, “The American Objective as Compared with German,” *Maryland Medical Journal* 21 (1889): 131. The ulterior motive for Johnston’s presentation, however, was to vaunt the American lens objectives of Tolles and Spencer over the German. Johnston claimed the American lenses were cheaper and more versatile. Nevertheless, Dr. Johnston did concede that Abbe’s apochromatic lenses were advantageous for taking photographs through the microscope—the process known as photomicroscopy.

⁴⁰³ http://microscopy.zeiss.com/microscopy/en_de/about-us/history.html accessed November 14, 2012.

microscopic image been so clear, sharp, and free from the centuries-old artifacts of shifting shapes and colors. Ernst Abbe and his contemporaries, combining basic science with industrial know-how, created lenses that projected images of such rich detail that cancer cells could be visualized with *wissenschaftliche Objektivität*.⁴⁰⁵ They combined their collective knowledge of mineralogy, chemistry, physics, and optics long before the interdisciplinary emphasis of today to create a technologically advanced fluorspar-containing lens system that, in the field of visible light microscopy, has not been improved upon to the present time.⁴⁰⁶

Coming of Age in Microscopy:

LIGHT, AIR, and OIL

The apochromatic lens system furthered the accurate projection of the microscopic image, but, along with staining and microtomy, failed to address some of the increasingly important shortcomings of microscopy in the latter half of the nineteenth century. These included the magnification and illumination of the specimen, as well as the standardization of the instrument through the manufacture of its parts. One by one, Ernst Abbe attacked these problems. At the end, he succeeded in the construction of the finest light microscopes ever known.

A Better Light

The system began with the light source. All microscopes require a source of energy to project an image of the specimen into the viewer's eye. In a light microscope, that energy is

⁴⁰⁴Wilson, "The History of the Microscope," 213.

⁴⁰⁵The phrase may be translated as "scientific objectivity." Nevertheless, as Peter Novick points out in his discussion of historical "objectivity enthroned," the notion of scientific objectivity contains within it many hierarchies of meaning. I have used the phrase to capture the richness of that semantic depth. Leopold von Ranke's famous goal, to capture the past "wie es eigentlich war," was also the quest of Abbé and his scientific confreres with respect to nature at the microscopic level. See Peter Novick, *That Noble Dream: The "Objectivity Question" And the American Historical Profession* (New York: Cambridge University Press, 1988; reprint, 1994), 24-31.

⁴⁰⁶Clark and Kasten, *History of Staining*, 203.

supplied by the particles (photons) and waves that constitute the visible spectrum. Light may be transmitted directly from a source or reflected indirectly by a mirror. Over the centuries, the engine of light energy changed. Descartes, Hooke, and Leeuwenhoek utilized candle flame to illuminate their objects.⁴⁰⁷ They also took the sun as their source, for its energy spectrum is the broadest. Nevertheless, the obvious limitations on the use of the sun (nighttime, clouds) and the danger attendant upon the use of candles (risk of fire) limited their value for microscopical illumination.

At the beginning of the last quarter of the nineteenth century, gas was the most common source of light energy. The advent of Thomas Alva Edison's incandescent lamp in 1879 replaced gaslight with the new light of electricity. Within two years after his invention, Edison began construction of the world's first central electric power plant.⁴⁰⁸ The electrified light bulb of the last years of the nineteenth century provided a source of light energy that eliminated the problems with natural light. In early 1883, C. H. Stearn predicted to the Royal Microscopical Society that "ere many months are over, there seems a probability that in many places gas will be entirely superseded by electrical illumination."⁴⁰⁹ He even had the audacity to suggest that someday an electric light could become "a permanent attachment to the Microscope itself."⁴¹⁰ No one in his right mind would have suggested attaching a flaming candle to a microscope! Thus, it is no surprise that light microscopes began using electricity-generated light sources as

⁴⁰⁷Hooke, *Micrographia*, Figure 5 opposite page 2.

⁴⁰⁸On September 4, 1881, the Edison Electrical Illuminating Company first supplied electricity to its major customers—the monied men of the financial district in lower Manhattan known as "Wall Street." J. P. Morgan, whose offices were down the block from the New York Stock Exchange, was a major investor in Edison's venture.

⁴⁰⁹C. H. Stearn, "On the Use of Incandescence Lamps as Accessories to the Microscope," *Journal of the Royal Microscopical Society* 3 (1883): 29.

⁴¹⁰*Ibid.*, 30.

soon as they became available. When institutionalized and corporatized, electricity generated a new world industry and a reliable source of microscopical illumination.

During the decade of the 1880s, the introduction of electricity to microscopy ushered in a small revolution. General Grant's brush with electricity was little more than an "electric cap" worn to assuage his pain.⁴¹¹ In contrast, multiple aspects of President Cleveland's medical management eight years later—from the microscope light that illuminated his biopsy specimen to the cautery that stanching bleeding at surgery—depended upon electrical devices.⁴¹² As electricity lit up the industrial world in the late nineteenth century, turning night into day and inside into outside, so it changed the crucial element of the light microscope—the source of illumination.

Between Light and Stage: The Substage Condenser

Despite the radical change electricity wrought in the nature and dependability of the light source, it was only the beginning of the modernization of the microscope. The present-day microscope of cancer diagnosis and research evolved from a series of improvements to each of its components. During the nineteenth century, from bottom to top, each element underwent changes in construction and constitution in form and/or substance. Electrical light was a change in substance; its transmission to the eye through numerous lenses, a transformation of form more than substance. Advances in optical theory led to progress in the engineering of components. A

⁴¹¹The New-York Times, "Gen. Grant's Suffering. Dr. Douglas Summoned to Him Early This Morning.," *The New York Times*, 29 March 1885. I do not mean to suggest that the first use of electricity in medicine was as a microscope light source. Far from it. For centuries, physicians had used electricity to treat many ailments, especially neuropathies (broadly, diseases of the nervous system). For an example in the use of electricity to treat cancer, see George M. Beard, "A New Method of Treating Malignant Tumors by Electrolyzing the Base," (Albany: Charles van Benthuysen & Sons, Printers, Stereotypers and Binders, 1874).

⁴¹²W. W. Keen, "The Surgical Operations on President Cleveland in 1893," *The Saturday Evening Post*, 22 September 1917, 53.

good example was the development of the substage condenser, which gathers light from the source and directs it to its object.

How best could one transmit or reflect light through the specimen to create the bright, glareless, evenly-lit optimal viewing field? Microscopists determined that a sort of “relay” was best to gather, bundle, focus, and transmit the light from source to slide. Early in the history of the microscope, as depicted in the illustrations of Descartes, Hooke, and others, a concave mirror reflected light onto the specimen. By the nineteenth century, a substage (light) condenser filled that function.⁴¹³ Although Charles Chevalier included a condenser as part of his “Microscope Universal Achromatique” in 1834,⁴¹⁴ Ernst Abbe deserved credit for its modern design.

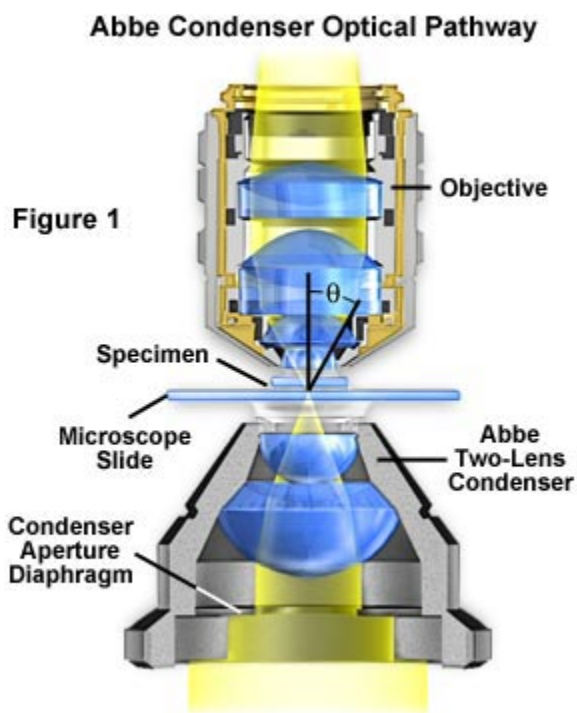


Figure 3. Abbe Condenser Optical Pathway⁴¹⁵

⁴¹³The first light condenser may have been constructed by P. Bonnani in 1698, but the substage condenser was not a common feature of the microscope until the nineteenth century. See Nelson, "Historic Microscopy," 223.

⁴¹⁴Purtle, "History of the Microscope," 256.

⁴¹⁵ <http://micro.magnet.fsu.edu/primer/anatomy/condensers.html> accessed November 14, 2012.

In 1870, Abbe, by then a university physicist and director of Zeiss research, noted that, just as the objective lens gathered light transmitted through the specimen and transmitted it toward the eyepiece lens, so a combination of lenses below the slide could “condense” (etymologically, ‘thicken’) the source light and project it in a more concentrated form onto the slide. Enhanced slide illumination resulted. Thus, Abbe’s intricate yet purposed construction of two or three planoconvex lenses in tandem collected light from its source, concentrated it, and transmitted it in parallel bundles through the specimen on the slide. The substage lenses of the condenser created an optical pathway that minimized scatter and maximized light conservation for both the objective and ocular lenses. When combined with his apochromatic and immersion lenses, Abbe’s substage condenser yielded a microscopic image of the most perfect clarity of detail and brightness of illumination ever known.

The great theoretical leap in practical microscopy may have occurred with the development of aspherical, achromatic lenses in the 1820s, but the better mousetrap—in the form of the Abbe-devised Zeiss microscope with substage condenser and apochromatic objectives—did not appear until the late 1880s. It, not the Listerian scope of an earlier generation, revolutionized the microscope for medicine just as bacteriology and the growth of cancer medicine necessitated the ability to visualize individual microbes and cells at higher magnifications. Light transmission through the condenser, slide, and majority of lenses rarely resolved and illuminated the image sufficiently at a magnification of more than 400X.

Air vs. Oil

The apochromatic lens added detail to the magnified image at 400X. This degree of enlargement was adequate to discern the basic structure of tissues and cells, but not their intricate components or bacteria. The study of bacteria and cancer cells required a magnification closer to

1000X—two and a half times the usual light-microscope magnification. With the growth of bacteriology in Europe in the 1870s and 1880s, microbiologists and medical researchers investigating cancer and other diseases found the power of the microscope insufficient for their needs. They strove to visualize microorganisms and intracellular organelles at greater magnification.

Just as the apochromatic lens represented a step beyond the achromatic lens, so the immersion lens system, wherein the air of the slide-air-objective lens interface is replaced by a non-opaque substance of higher refractive index, permitted image resolution at higher levels of magnification and gave the bacteriologist what he wanted. The immersion lens system was comprised of the condenser, intermediary fluid, glass slide, specimen (in an appropriate mounting medium), cover slip (or cover glass), second intermediary fluid (between slip and lens), and the immersion lens.⁴¹⁶ Altogether, the system successfully resolved images at the high magnifications required by microbiologists and histopathologists by reducing the loss of refracted light. The old “dry” lens systems, where air served the role of the intermediary fluid, refracted considerable amounts of light outside the capture zone of the objective. The higher refractive index of the immersion system minimized light loss.

The theoretical solution to the loss of refracted light lay in the aperture question. How large should the opening be that receives light into the lens? Should maximum light be admitted to the objective lens, thus increasing the ability to illuminate the specimen at higher magnifications at the cost of increased aberrancies, or should the light cone be tight and focused so as to highlight detail at the expense of illumination? Dry lenses were fine at lower magnifications, but Abbe sought a fluid other than air to optimize the microscopical triad of

⁴¹⁶This is the complete “homogenous immersion system.” Microscopists have used many “immersion fluids” over the years, but the most prevalent substitutes for air between condenser and slide and cover slip and objective included oil, water, and glycerin.

illumination, magnification, and detail at higher powers. The problem with air was its refractivity.

The Refraction Corruption

Air limited the resolution of the Listerian microscope at higher magnifications. Specifically, the air interface between object and objective restricted well-defined image enlargement due to light refraction. The physics of the laws of refraction were formulated during the seventeenth century by Willebrord Snell (who first described the laws of refraction), Christiaan Huygens (who developed the wave theory of light), and Isaac Newton (who declared that light consisted of particles and, coincidentally, that the problem of chromatic aberrancies could never be solved⁴¹⁷) and later augmented by a host of Western scientists in the nineteenth century. These natural laws explained the problem. As light passed on its journey from its source through the slide, specimen, objective, tube, and eye-piece onto the retina of the viewer, it encountered media with different refractive properties. Each interface, true to the etymology of refract ('to break up'), altered the character and direction of light projected onto the next element. Chromatic and spherical aberration were two products of refraction, but reduced resolution at increased magnification was a third. Physicists of geometrical optics reasoned that they could obtain a more magnified and sharper image by minimizing light loss through refraction. Substances with similar refractive indices that transmitted light seemed an ideal solution because loss of light due to interfacial bending could theoretically be eliminated. In essence, the light would remain uncorrupted.

Oil Immersion

⁴¹⁷Booth, "The Aperture Question," 119.

In late 1885, John Mayall, Jr., a member of the Royal Microscopical Society, presented a series of five lectures in London entitled the “Cantor Lectures on the Microscope.”⁴¹⁸ Mayall delivered an excellent history of microscopes that reached to the first half of the nineteenth century and contributed several tidbits to the history of refraction in microscopy. He noted that Robert Hooke, in the seventeenth century, was the first to find that immersion of the objective lens in oil could improve the magnification and resolution of the microscopic image.⁴¹⁹ David Brewster, who made numerous contributions to the theory and practice of optics,⁴²⁰ discovered around 1812 that immersion of the objective lens in oil significantly reduced light refraction.⁴²¹ Brewster ascertained the theory that explained Hooke’s empirical finding. Diminished light dispersion occurred in the immersion system because the refractive indices of oil and glass or water are much closer to each other than to those of air and glass or water.⁴²² In consequence, less light “bounced” off the oil-glass or water-glass interface than that of air and glass. Light lost at the air-glass interface through refractive scattering did not pass through the objective lens, thus diminishing the level of illumination.⁴²³ On the other hand, the light transmitted through the oil-

⁴¹⁸Mayall, "Cantor Lectures on the Microscope".

Mayall also played a significant role in the history of the microscope in the United States. Over the years, he chose and distributed one hundred and forty-one historic microscopes to (what would become) the core of the Billings Microscope Collection of the Medical Museum of the American Armed Forces Institute of Pathology. See Blumberg, Smith, and Leeper, *Billings Microscope Collection*, v.

⁴¹⁹Mayall, "Cantor Lectures on the Microscope", 15.

⁴²⁰Sir David Brewster (1781-1868) also played a seminal role in the physics of polarized light (1811), which formed the theoretical basis for the polarizing microscope (William Nicol, 1827). Brewster also invented the kaleidoscope (1816) as a result of his investigations of the reflection of light off angled mirrors.

⁴²¹Nelson, "Historic Microscopy," 226.

⁴²²Water is the most prevalent compound in most microscopical specimens, so its refractive properties must be taken into account when computing the angle of light transmission through specimens on slides. Microscopists also used water as the intermediary fluid between slide and objective.

⁴²³The Refractive Index of (synthetic) oil is 1.515. This is about the same as glass, the main component of the slide and cover slip. In contrast, the Refractive Index of air is 1.0003. Water/saline has a Refractive Index of

glass system flowed unscattered into the objective lens. A more magnified yet intact image resulted, although still limited in Brewster's era by the major aberrations of the pre-Listerian microscope. Nevertheless, the oil-immersion lens system was born.

Early nineteenth-century microscopists attempted to produce lenses of diverse materials to overcome large refractive differences that diminished magnification. Unfortunately, they met with little success. In 1824, for example, Andrew Pritchard produced a diamond objective, but the lens of the "jewel microscope," as it was called, was laborious to grind and impossible to maintain.⁴²⁴ The purpose, however, was identical to that of oil immersion—maximization of illumination at higher levels of magnification. Throughout the nineteenth century, no system proved more suited to this goal than oil immersion.

In the early 1840s, Amici of Italy, now working with the new aspherical, achromatic lenses, constructed several oil-immersion and water-immersion lens systems.⁴²⁵ Like so many other innovative technologies and practices in science, adoption took time. Oliver Wendell Holmes, dean of early American microscopists, remembered it was not until 1853 that he witnessed "the first immersion objective I had ever seen, very possibly the first that was ever in the country."⁴²⁶ Its manufacturer was Amici. Five years later, Robert B. Tolles, an American who had apprenticed with native pioneer American microscope manufacturer Charles A. Spencer, constructed the first immersion lenses in the United States.⁴²⁷ Universal adoption of the

1.333; glycerin 1.4695. The average refractive index of living cells is 1.35—very close to that of salt water, as might be expected of life that evolved from the blue of the "Blue Planet."

⁴²⁴Turner, *Great Age of the Microscope*, 8, Endnote 1.

⁴²⁵Jacker, *History of the Microscope*, 115.

⁴²⁶Holmes, "An Address Delivered at the Annual Meeting of the Boston Microscopical Society," 606.

⁴²⁷Booth, "The Aperture Question," 120.

immersion systems, however, did not occur until the critical period of the last years of the century,⁴²⁸ catalyzed by bacteriology and the cultural valorization of science. Ernst Abbe was again a major contributor.

Ernst Abbe brought the nineteenth-century oil immersion lens system to its pinnacle. In 1870, four years into his affiliation with Zeiss, he developed an oil immersion lens system that permitted resolution of the fine detail of an object to one quarter of a micron in size.⁴²⁹ This was four times greater than that achieved by the best Listerian microscope and allowed detailed visualization at the cellular and microbial level.⁴³⁰ When combined with his oil immersion objective of the same year,⁴³¹ Abbe perfected a system many decades in the making. Perhaps microscopist ‘athletes,’ each seeking to compete in their visualization of smaller and smaller objects, thrilled at the power of Abbe’s new oil immersion lens. Nevertheless, full acceptance of the immersion system by the microscopical community awaited the germ theories that added purpose to capability.

In 1879, Abbe, Zeiss, and Schott manufactured an entire oil immersion system that transmitted light from the source to eye with minimal refracted light loss. It was an amazing accomplishment that melded theory and practice through precise engineering. The similar refractive properties of the various media minimized peripheral loss of bent light waves. The Zeiss apochromatic oil immersion system projected the most detailed image at the highest magnifications ever achieved by means of the maximum capture of transmitted light. Abbe was not the first to attack the problem of the invisible role of intermediary fluid, but his use of oil as

⁴²⁸Ibid., 121.

⁴²⁹A micron is one millionth of a meter, or one ten-thousandth of a centimeter.

⁴³⁰Malkin, *Out of the Mist*, 133.

⁴³¹Ibid.

the immersion fluid, in conjunction with his other optical advances, brought the microscope into the modern era.

Microscopists universally adopted oil immersion systems during the 1880s,⁴³² at about the same time that synthetic aniline dyes and mechanical microtomes revolutionized microtechnique. All three developments served as impetuses for the practitioner's acceptance of the microscope in medicine. Many believe they have not been improved upon in over a century.⁴³³ The multifold increase in magnification permitted by oil immersion lens system allowed microbiologists to visualize in greater detail the newly-accepted scourges of mankind—pathogenic bacteria. In addition, these improvements gave the cancer researcher and then the clinical pathologist the ability to visualize anomalous intracellular components, like the nuclei of cancer cells. Nevertheless, the microscopic diagnosis of cancer was still in its early stages. As one contemporary textbook author opined, clinical cancer microscopy had advanced merely to the point where a definitive diagnosis of cancer could be made in cases of “*immediate danger*”—i.e., in patients with far-advanced carcinoma.⁴³⁴

New theories and technologies made possible advances in the knowledge of cancer for microscopist-researchers. Nevertheless, most clinicians had only begun to consider the microscope a tool of value to their daily practice. Investigational curiosity drove technologic developments, but additional changes, often derived from the processes and methodologies of the industrial revolution, expanded the use of the microscope to include both research and clinical practice. Only then did the microscope become a ubiquitous symbol of medicine.

⁴³²Carl Friedlaender, *The Use of the Microscope in Clinical and Pathological Examination*, trans. Henry C. Coe, 2nd ed. (New York: D. Appleton and Company, 1885), vii.

⁴³³Clark and Kasten, *History of Staining*, 203.

⁴³⁴Friedlaender, *The Use of the Microscope*, 173. Italics in the original.

SUPPLY: Microscopes for All

Standardization

One of the great triumphs of science and medicine at the end of the nineteenth century was the embrace of the concept of standardization. Uniformity of production, which encompassed diverse entities from drugs and their dosages to the apertures of lenses, constituted part of the Progressive drive toward efficiency.⁴³⁵ Prior to the last decades of the nineteenth century, skilled artisans manufactured microscopes by hand. Each component was conceived, produced, and inserted into the instrument—one piece at a time. One can only imagine the care, precision, and time that went into the production and assemblage of the hand-made microscope. Hence the quality of early microscopes strongly depended strongly upon the craftsmanship of the individual. The industrial revolution transformed ‘manufacturing’ (the original meaning of which was ‘working by hand’) into a process that constructed template-driven, machine-made copies. These reproductions were themselves grounded in tools making tools, mass production, and mass marketing. The American microscope of the late nineteenth century was part and parcel of this development.

The design of the template for each component of the microscope was the result of a decades-long, tedious process of trial and error mixed with flashes of genius. The light source, substage condenser, slide, cover glass, objective lens, and eyepiece all underwent a process of punctuated evolution over the course of the century.⁴³⁶ Standardization of these parts was the

⁴³⁵By the “triumph” of standardization, I do not mean to imply that standardization did not and does not have drawbacks. One need only witness the reduction of patient individuality in many spheres of medicine, the one-size-fits-all stance of the government and other institutions toward the medical profession (e.g., “practice guidelines”), and the medico-legal concept of “the standard of the community,” to get a sense of its disadvantages. Nevertheless, standardization did foster tremendous progress in medicine at a time when individuality dominated and often balkanized approaches to diagnosis and therapy.

key to the increased availability of microscopes in the late 1800s. Greater numbers of microscopes helped to hasten their adoption by medical practitioners, for rare produce, no matter how desirable, can be embraced by only a few.

Standardization, like politics, results from a dynamic interrelationship among major players with vested interests. In the case of the nineteenth-century microscope, those parties included microscopists, microscopical societies, and microscope manufacturers. Microscopists supported their societies through fees and specialty articles for publication. Microscopical societies, which originated in the middle of the nineteenth century but did not make significant inroads into medicine until the 1880s,⁴³⁷ expressed the interests of their members to manufacturers. Through journals and meetings, societies conveyed information from manufacturer to member. Manufacturers responded to the pleas and demands of the collective societies to give microscopists what they wanted. Microscopists, in turn, bought the microscopes of the manufacturer and thus supplied the manufacturer with the resources necessary to keep the triangle operational. In this schema, all benefited.⁴³⁸ Many developments in late nineteenth-century microscopy resulted from the growing feedback and synergies between these three interest groups.

GLASS

The Glass Slide

Perhaps the earliest example of intermutual technological dynamism that led to standardization was that of the glass slide. Early sliders, the forerunners of glass slides, were of

⁴³⁶My apologies to paleontologists Stephen Jay Gould (deceased) and Nils Eldridge, who in 1972 proposed the idea that uniform periods in evolution are disturbed by times of rapid change. They named this fluctuation ‘punctuated equilibrium.’

⁴³⁷Warner, "Popular Microscopy," 16 and 30.

⁴³⁸Just as in the metaphor of the political “iron triangle,” many interactions were contentious. Usually, however, action followed interrelational inputs.

rectangular shape, probably to conform to the geometrical limitations of the microscope stage on which microscopists placed them.⁴³⁹ They were of multiple lengths and widths, well into the nineteenth century.⁴⁴⁰ Further, although wooden sliders were initially the most common, their composition varied over time. Microscopists found that glass, the production and forms of which underwent technological revolutions of its own in the first half of the century,⁴⁴¹ was a more desirable platform upon which to preserve and display the specimen. Glass obviated the need to punch specimen holes in wooden sliders and transmitted source light through the specimen without significant obfuscation.

Standardization of the glass slide production process increased its availability and, eventually, its ubiquity. In essence, it transformed the slider into the slide. But why standardize glass slides? Standardization makes specimen comparison and storage easier. One of the first actions of the Microscopical Society of London, founded in 1839 for the “improvement of the Microscope as a Scientific Instrument,” was the standardization of the dimensions of the glass slide to 3 x 1 inches.⁴⁴² Initially the prescription applied only to slides for its own cabinet.⁴⁴³ The change did not immediately replace sliders outside the Society, for scientific intercourse was geographically limited, different countries had their own designs, and no direct or indirect enforcement power existed. Nevertheless, over the ensuing decades, the Society cabinet slide

⁴³⁹For an illustration of the first known slider, see Bracegirdle, *A History of Microtechnique*, 19, Figure 4.

⁴⁴⁰*Ibid.*, Colour Plate I.

⁴⁴¹Mechanical glass pressing, invented in the mid-nineteenth century, allowed the rapid production of cheap yet good-quality glass. This process made glass available to the average private home. Other advances in glass technology during the century, through both the revival of old techniques and the advent of new ones, eventuated in the varieties of colored and clear glass available today.

⁴⁴²Bracegirdle, *A History of Microtechnique*, 111.

⁴⁴³The initial mandate also allowed a size of 3 x 1½ inches, but the 3 x 1 inch dimensions quickly prevailed. See Bracegirdle, “The Development of Biological Preparative Techniques for Light Microscopy, 1839-1989,” *Journal of Microscopy* 155, no. 3 (1989): 307, 309.

became the norm for commercial, cultural, and practical reasons. The 3 x 1 inch glass slides were easy to manufacture, aesthetically appealing, and microscopically pragmatic for viewing and stacking. By the late 1880s, mountmakers found it expedient to adopt the dimensions prescribed by the Society. In consequence of the Society's clout, few bought slides of different width and length. Manufacturers ceased production of slides of other sizes. To this day, the dimensions of the glass slide initiated by the Microscopical Society in the second quarter of the nineteenth century remain universal.⁴⁴⁴

The Cover Glass

The cover glass, a thin slip of translucent material placed on top of the slide and specimen for preservation and refractivity, has a history of its own that adds another chapter to the story of standardization. It was rarely used prior to the early nineteenth century, perhaps in part because rapid specimen deterioration was the norm. The first wave of microscope innovation during the 1820s and 1830s led to the popularity of the cover glass as a method of specimen preservation. It decreased evaporation of water, the major molecular constituent of most specimens. In addition, it solved the problem of the unequal thickness of most specimens—thinner here, thicker there. Depth irregularity made uniform focus impossible. The lumpy-bumpy character of specimens forced microscopists to adjust the depth of focus constantly as they moved ever so slightly across the field of vision—a very tedious and often frustrating chore. The cover glass, through pressure applied manually or mechanically between cover and slide, flattened the specimen surface and permitted more even transmission of light.⁴⁴⁵

⁴⁴⁴Bracegirdle, *A History of Microtechnique*, 112.

⁴⁴⁵Jan Ingen-Housz offered these insights as early as 1785, but few followed his direction at the time. See Hoff, "Jan Ingen-Housz and the Cover-Slip," 366-67.

By the 1840s, the utility of the cover glass was well known. Its availability and uniformity, however, were limited, because microscopists in those years cut their own cover glasses from large sheets of glass.⁴⁴⁶ This made the process time-consuming and potentially dangerous, for hand-cut glass surfaces were hazardous to all who worked with them. The mid-century industrial revolution in glass swept away dissimilarities in the manufacture and dimensions of the cover glass. Adoption of the 3 x 1 inch glass slide also dictated, to a large extent, the dimensions of the cover glass. Thus, advances in glass technology that made window glass and the glass slide ubiquitous in the nineteenth century also produced a more universal and uniform cover glass.⁴⁴⁷

Cover Glass Optics

As the magnification power of lenses without the distortions of aberrations increased, microscopists discovered that the lowly cover glass also influenced the optics of the microscope. They found it to be an integral part of the serial optical pathway with a refractive index of its own. Dry systems refracted light from cover glass to air to objective lens, lending light loss at each interface. At low magnifications, such as those used to discern tissues and groups of cells, the quantity of light lost was inconsequential. When viewing through high-powered lenses, however, the loss of light at the cover glass-air interface was a notable detriment. Thus, increased magnification in a dry system with a cover glass required greater illumination. The redoubtable Ernst Abbe, as research director for Zeiss, discovered that the refractive index of the cover glass was similar to that of the oil he used in his oil-based immersion system. Thus, the cover glass, when used in conjunction with an oil intermediary and his oil immersion lenses,

⁴⁴⁶Bracegirdle, *A History of Microtechnique*, 114.

⁴⁴⁷Gray and Gray, "History of Microtechnique and Microtomy," 260.

allowed maximum conservation of light and the greatest resolution at the highest magnifications. The optics of the cover glass became an integral component of the optics of the oil immersion system.

In addition to the role of the cover glass in the preservation of the specimen and the optics of the microscope, at least three specific events led to the standard adoption of the cover glass. These milestones, as with so many other advances in microscopy, occurred during the third wave of microscope development in the last quarter of the nineteenth century.⁴⁴⁸ First, in 1877, Robert Koch, then famous among the German medical researchers for his foray into the causes of disease through microbiology, discovered that the application of heat to the cover glass improved the fixation of bacterial preparations. This permitted easier and more consistent identification of pathogens as well as clearer photomicrographs.⁴⁴⁹ Not long thereafter, Paul Ehrlich found that the same method could be used successfully to fix blood smears.⁴⁵⁰ The methodology of cover-glass heat fixation endures today.

Second, the Abbe oil-immersion system, with the essential contribution of the cover glass, became the predominant standard for scientific research. The Abbe system, developed in collaboration with Zeiss and Schott in 1878-1879, required the refractive index of the cover glass to minimize light loss.⁴⁵¹ Progress in manufacturing techniques led to the production of

⁴⁴⁸As noted, the first wave encompassed the initial development of the microscope in the late sixteenth through seventeenth centuries. The second wave included the conceptualization and production of aspherical, achromatic microscopes in the early nineteenth century.

⁴⁴⁹Robert Koch, "Untersuchungen über Bacterien, VI. Verfahren zur Untersuchung, zum Conserviren und Photographiren der Bacterien," *Cohn, Beiträge Biol. Pflanz.*, 2 (1877): 399-434. See Bracegirdle, *A History of Microtechnique*, 62 and 98 footnote 60.

⁴⁵⁰Paul Ehrlich, "Beiträge zur Kenntnis der granulären Bindegewebszellen und der eosinophilen Leukocythen," *Arch. Anat. Physiol.* (1879): 166-169. Note Bracegirdle, *A History of Microtechnique*, *ibid.*, 63 and 99 footnote 61.

⁴⁵¹Clark and Kasten, *History of Staining*, 203, Jacker, *History of the Microscope*, 116.

machine-cut slides and cover glasses, obviating the dangers and inconsistencies of hand-cut glasses. As Zeiss microscopes that incorporated the system became widespread in the 1880s and 1890s, so did the cover glass. The success of the Zeiss company in marketing its high-quality microscopes throughout the world augmented the standardization of microscope components, including the cover glass.

Nevertheless, the third and single most important factor leading to the ubiquitous adoption and standardization of the cover glass was probably the acceptance of the uniform dimensions of the glass slide by the late 1880s. Once microscopists accepted a standardized slide, the requisite dimensions of the cover glass followed, for the specimen could be sliced to fill the center of the slide as covered by the glass. In return, the length and width of the cover glass need not exceed the specimen area. The thickness of the cover glass, the third dimension, was of less concern, for Abbe and others found immersion lens resolution to be independent of thickness.⁴⁵² By the time of President Cleveland's cancer in the early 1890s, the glass portions of the microscope—lenses, slides, and cover glasses—were, for all practical purposes, of standard composition, size, and shape.

Focus on

F*O*C*U*S

Rack and Pinion Steering

A microscope is more than its lenses. It encompasses an entire support structure, the parts of which, like a fine-tuned watch, work in unison to keep the image transmitted on a wave of light in focus. Whereas specimen illumination depends upon the light accumulated by a series of lenses (measured by Abbe's standard-setting numerical aperture), the clarity of the image is

⁴⁵²Clark and Kasten, *History of Staining*, 203.

highly dependent upon the focal length—the distance from the lens to the focal point at which the refracted light waves converge. Movement, even by a fraction of a centimeter, of the barrel of the microscope that supports the lenses can convert a finely-delineated image into a blurry mess. At the beginning of the nineteenth century, several mechanisms achieved focus. By the end of the century, nearly all light microscopes utilized coarse and fine adjustments similar to those used on today's instruments. As in the evolution of glasses in the nineteenth century, so, too, both industrial and microscopical inputs led to the adoption of standardized mechanisms to attain and maintain focus.

The problem of focus was older than the microscope, for the Ancients discovered that movement of a single convex lens toward or away from the source of light moved the beams in and out of focus. Refracted light focused at only one point. The addition of lenses in *seriatim*, as in the microscope, created multiple focal points, the end product of which must focus on the viewer's retina to achieve clarity of composition. How could this be done? Natural philosophers dreamed and improvised many solutions. Some moved the specimen; some the stage; some the lens. Leeuwenhoek moved the specimen on a pin that moved up and down. The only moving part on his simple microscope was the spit that skewered the specimen. He designed and built his microscopes so that the resolution of the specimen was specific to a particular lens and specimen. Thus the object was always in focus, but only for that sample. One microscope, one specimen. His solution was masterful but impractical.⁴⁵³



Leeuwenhoek
Microscope
(circa late 1600s)

Figure 4. Leeuwenhoek Microscope

⁴⁵³<http://micro.magnet.fsu.edu/primer/museum/images/leeuwenhoek.jpg> accessed December 9, 2012.

In the early years of microscopy, many microscopes, including those of Leeuwenhoek, were held or placed on a horizontal axis, like binoculars scouring a flat plain. The stage holding the slide could be moved back and forth on such a surface, like the slide of a trombone. The vertical orientation of microscopes, which usually prevented specimens from sliding off the stage, necessitated up and down movement of the barrel. At first, microscopists moved the barrel manually. In 1665, Robert Hooke, the originator of many microscope technologies during the initial age of invention, introduced a system of coarse and fine adjustments that utilized a tube that slid over a rod.⁴⁵⁴ The coarse adjustor brought the image into general view; the fine adjustor honed in on its detail.

In the late seventeenth century, P. Bonnani became the first to use a rack and pinion mechanism for coarse and fine adjustments.⁴⁵⁵ As in the automobile, the gears in the microscope translate circular into linear motion. The driver turns a steering wheel; the microscopist rotates small wheels between thumb and forefinger that change the length of the microscope barrel. Cars use rack and pinion steering, whereby a pinion, or small cogwheel, engages a larger, mated rack. The two mesh together to transform small movements of the steering wheel into larger motions of the vehicle. Similarly, the movement of the barrel of the microscope uses the same mechanism, translating the circular motion induced by the fingers into a vertical movement of the barrel. In consequence, the distance between the objective and the eyepiece is made greater or less so as to adjust it to the focal length of the refracted image. The coarse adjustment translates a turn of the wheel into a large movement. The fine adjustment uses a different set of

⁴⁵⁴Purtle, "History of the Microscope," 253.

⁴⁵⁵Nelson, "Historic Microscopy," 223.

wheels to cause relatively large motions of the wheel to lead to only slight movements of the barrel. The result is sharp focus of the magnified image on the retina.

Gears on gears became the preferred mechanism to achieve coarse and fine focus in the eighteenth century. In 1746, Martin-Adams attached the adjustments to the stage, thus coordinating the means of focus.⁴⁵⁶ Selligues and Chevalier of Paris, whose lenses in the 1820s ushered in the first wave of nineteenth-century microscopy, improved the fine focus to take advantage of reduced spherical and chromatic aberration. William Tulley of London, whose early achromatic lenses served as a model for American microscope lens manufacturers,⁴⁵⁷ also devised a mechanism for a finer focus at about the same time.⁴⁵⁸ Nevertheless, perfection of the rack and pinion adjustment system for both coarse and fine focus awaited the work of Swift in England in the early 1880s.⁴⁵⁹ By then, machine-made parts had greatly altered the landscape of microscope manufacturing.

Interchangeability

As the standardization of different parts of the microscope contributed to the increasing availability of the instrument through the nineteenth century, so also did other legacies of the industrial revolution. In the mid-nineteenth century, microscopes of the best quality already featured rack and pinion adjustments, but they were painstakingly made by hand. Note that handcrafting did not preclude standardization. In 1858, the Microscopical Society of London required that objective lens threads, which allowed the microscopist to screw the lens into position above the stage, be of the same dimensions so that they could be interchanged between

⁴⁵⁶Ibid., 225.

⁴⁵⁷Padgitt, *Early American Microscopes*, 5.

⁴⁵⁸Wilson, "The History of the Microscope," 172.

⁴⁵⁹Bracegirdle, "Modern Optical Microscope," in Bud and Warner, eds., *Instruments of Science*, 392.

microscopes. This “political” mandate, as it was called,⁴⁶⁰ augured well, for standardization was the mother of interchangeability long before the technologic revolution. Standardization made interchangeability possible; machine-made parts made it practical.

The industrial revolution led to the replacement of handcrafted microscope pieces with machine-made equivalents beginning in Europe in the 1870s.⁴⁶¹ By 1885, Zeiss in Germany and Bausch & Lomb in the United States manufactured machined lenses and focus adjustments that became integral elements of their increasingly popular microscopes.⁴⁶² Thus, interchangeability of parts followed standardization of design. The ability to substitute a new lens or adjustment for one that was poorly made, broken, or outmoded achieved what handcrafted pieces never could—longer shelf-life, mass production, and lower overall cost. The age of medical microscopy was at hand, but increased supply did not generate an industry in a vacuum. The other element was the increased desire for the product by potential consumers.

DEMAND: All for Microscopes

The economic relationship between supply and demand is deceptively complex. It is often difficult to assign priority between the two, although economists have done so for centuries.⁴⁶³ The growth of the microscopy economy in the nineteenth century was no exception. There had always been demand for microscopes, particularly among natural philosophers. Nevertheless, not all who would consume, could consume. The manufacturing revolution of the second half of the century increased supply, which increased demand, which further increased supply. An equilibrium eventually developed between supply and demand

⁴⁶⁰Ibid.

⁴⁶¹Ibid.

⁴⁶²Mayall, "Cantor Lectures on the Microscope", 68-69 and 89.

⁴⁶³In the last century, for example, Keynesian economics promoted demand over supply. Reaganomics later stressed supply-side economics.

driven by price, quality, and technology—at least until something new came along. The result of this ratcheting up of the pervasiveness of microscopes in medical and scientific communities led to new visions of old phenomena. One disease that received increased scrutiny from this perspective was cancer.

What generated increased demand for microscopes and the microscopical point of view? The “take-off” period for medical and cancer microscopy occurred in the last two decades of the nineteenth century.⁴⁶⁴ Many factors contributed to this watershed era for cancer and the microscope. Among the most salient were the confluence of lower price with better quality, changes in the needs and professional desires of physicians, increased utility, and motivations of necessity. All stimulated demand for microscopes.⁴⁶⁵

Price

Markets for tangible goods, including microscopes, generally follow a supply-demand formula where demand is inversely related to price.⁴⁶⁶ The higher the price, the lower the demand. The lower the price, the higher the demand. Economists gauge the relationship between price and demand in terms of ‘elasticity’—the more demand increases or decreases with a change in price, the more elastic the demand is said to be.⁴⁶⁷ In these terms, the demand for microscopes was very elastic in the late nineteenth century.⁴⁶⁸

⁴⁶⁴The phrase “take-off” is often attributed to W. W. Rostow, an American economist whose several books, including *The Stages of Economic Growth* (1960) and *How It All Began: Origins of the Modern Economy* (1975), tout the role of technology in the improvement of the human condition.

⁴⁶⁵Advertising, a major stimulant of demand, aims at each of these four pillars. I will not discuss microscope advertising, except to say (1) that print advertisements for microscopes can be found in the earliest nineteenth-century American scientific journals, but that (2) to gauge its exact contribution to demand is impossible.

⁴⁶⁶The price of a good is related to a host of factors—especially supply. Nevertheless, *ceteris paribus*, price is usually inversely proportional to supply.

⁴⁶⁷Elasticity is defined as the “percentage change in some dependent variable (e.g., the demand for microscopes) resulting from a one percent change in some independent variable (e.g., price of microscopes).” See

Prior to the end of the nineteenth century, a quality microscope was a costly instrument. Ownership was limited to rich individuals and well-endowed institutions. Technical advances in the design of lenses and microscope attachments added to an already-hefty total price that was already beyond the means of many researchers and most medical students.⁴⁶⁹ The substage condenser, for example, useful as it was to augment the illumination of medical specimens, increased the price as well as the weight and complexity of the instrument. Cost was a recurring theme in microscopy discussions from the time of the purchase of the first microscope in the British-American colonies, probably by Cotton Mather in 1685.⁴⁷⁰ As late as 1884, the year of General Grant's painful peach episode, R. Hitchcock complained that the value of the microscope was hindered by its high cost.⁴⁷¹ Ernst Abbe, whose extraordinary career took him from the pristine vaults of academic optical research to the worldly concerns of the manufacturer, was not insensitive to the accretive costs of his improvements to the microscope.⁴⁷² His "Abbé illuminator," for example, provided higher quality at lower cost than

Sherman Folland, Allen C. Goodman, and Miron Stano, *The Economics of Health and Health Care*, Second ed. (Upper Saddle River, NJ: Prentice Hall, 1997), 599.

Health care and its offshoots were not very elastic in the last half of the twentieth century, but elasticity may increase if governments and third-party payers successfully alter supply and demand for health care as well as patients' out-of-pocket expenses.

⁴⁶⁸Demand for microscopes increased as the cost of each instrument decreased in the last two decades of the century. Nonetheless, the reader should not impute a direct causal relationship between the two. This chapter section will suggest other reasons for the increased demand for microscopes at that time, but lower prices for scopes with improved optics remained the most important.

⁴⁶⁹Although 'price' and 'cost' are often used interchangeably, there is a strict difference between them that I have attempted to follow. Price is the amount asked for an item; cost is the amount paid.

⁴⁷⁰Warner, "Popular Microscopy," 9.

⁴⁷¹R. Hitchcock, "Recent Studies on the Theory of the Microscope, and Their Practical Results as Regards the Use of the Microscope in Scientific Investigations," *The New York Medical Journal* 40 (1884): 339.

⁴⁷²Ernst Abbé's biography reads like a European Realist-Age triumphalist novel. In 1876, Carl Zeiss made Abbé a partner in Zeiss works as a reward for his outstanding contributions to the optics of the microscope. Upon Zeiss's death in 1888, Abbé became sole owner of the firm. Abbé's subsequent expansion of Zeiss into international markets proved extremely successful. In 1891, a now-wealthy Abbé founded the Carl Zeiss Foundation for scientific research *and* social improvement to honor his deceased forebear. Decades before welfare

its predecessors. Although not as elaborate as other achromatic condensers, it was an improvement priced significantly less than the competition.⁴⁷³

Whereas progress in technology tends to increase the cost of patient care today, it decreased the cost of microscopes in the nineteenth century. It was just as difficult to price “add-ons” such as apochromatic lenses, substage condensers, and immersion systems in the late nineteenth century as it is to value advances in internal body imaging and endoscopic surgery today. Diachronic comparison of the price of a microscope made in 1850 with that of a more modern scope manufactured in the 1890s is, to a large extent, to compare a Ford Model-T with a 2004 Toyota Camry. Yes, they are both wildly popular automobiles, but how do you assign a 1920s value to air bags, anti-lock brakes, and three-point safety belts that did not exist then? Technologic advances over time add value that is impossible to measure in current-value U. S. dollars or Deutsche marks.

The contemporaneous quantification of quality is also difficult. How is one to compare an 1853 compound microscope, sold in Philadelphia for US\$2.50,⁴⁷⁴ with one made the same year with a price tag of US\$360?⁴⁷⁵ The disparity in price explains only part of the difference in quality. Nevertheless, it is possible to compute a general valuation of the effect of technical advances and quality differences on demand. From the 1850s to the 1890s, the quality of lower-priced microscopes improved and many more came to market. In addition, expensive, high-

capitalism gained a foothold in the United States, Abbé, in 1896, introduced revolutionary employee-friendly workplace reforms to Zeiss works. These included a cooperative corporate structure with profit-sharing among employees and the University of Jena, an eight-hour work day, paid holidays, sick pay, and retirement pensions. He died in 1905.

⁴⁷³Hitchcock, "Recent Studies on the Theory of the Microscope," 339.

⁴⁷⁴Cassedy, "The Microscope in American Medical Science," 88.

⁴⁷⁵Padgitt, *Early American Microscopes*, 17.

quality light microscopes persisted—even thrived—to reach their modern state of perfection in the 1890s.⁴⁷⁶

Advertisements and textbooks of microscopy of the era noted the wide variation of the cost of microscopes and correlated price with intended use. In 1876, the year of the United States Centennial Exposition in Philadelphia, McAllister sold a functional “Household” microscope for US\$5.⁴⁷⁷ This was a price within the reach of the burgeoning middle class interested in fostering the education of its children at a time when advanced schooling was becoming a ticket to a lucrative career. In addition to affordability, the rise of Darwinism played a not insignificant role in fostering demand for this instrument of the natural sciences. Darwinism, if not Charles Darwin himself, gave an enthralled public the impetus to look more closely at the natural world around them, including its microscopical aspects.

John Jacob Bausch was a German-born immigrant who came to America in 1849 at the age of nineteen steeped in the traditions of his homeland in lens-making and eyeglass manufacturing. Four years later, he and Henry Lomb, another native-born German, established a small optical firm in Rochester, New York. The power-driven machinery Bausch witnessed at the Centennial Exposition inspired him to apply the new technology to the mass production of microscopes.⁴⁷⁸ In 1883, seven years after the Centennial, Bausch & Lomb charged US\$45 for a very utilitarian “Universal” microscope. Thereby, they met the need to create a better-quality microscope at an affordable price.

⁴⁷⁶Clark and Kasten, *History of Staining*, 203.

⁴⁷⁷Padgitt, *Early American Microscopes*, 123.

⁴⁷⁸*Ibid.*, 95.

At the same time, Bausch & Lomb priced their more advanced “Professional” scopes at US\$125-175, possibly in an attempt to compete with the standard-setting Zeiss microscopes.⁴⁷⁹ Other manufacturers on both sides of the Atlantic also offered instruments of different quality and cost. Although high-priced and low-priced microscopes had existed throughout the century, a truly bifurcated market with much higher minimal standards of resolution and magnification had developed by the early 1890s. There were scopes for interested laymen and scopes for occupation-driven experts, both of which fulfilled the aims of their buyers well.

By 1894, James E. Reeves noted in his popular microscopy text—now aimed at physicians rather than natural scientists—that “a very good microscope fitted with all needful accessories for medical and ordinary bacteriologic work may be had for the very low price of \$50.00 or \$60.00, and a very complete outfit, such as will answer the physician for a lifetime—can be purchased for \$100.00, or less.”⁴⁸⁰ Only a generation before, a scope of the same resolution and magnification, if it could be found and even without the modern appurtenances, would have cost a king’s ransom. Improved microscope manufacturing, engendered by theoretical and industrial advances, actualized the would-be microscopist’s dream of high quality at low cost. Demand followed.

Desire – The Aura of Science

Economics was not the only driver of increased demand for microscopes in the late nineteenth century. The burgeoning public appreciation for science and its applications led to its privileged position in society—another characteristic of modern times in the West—and contributed to the desire for microscopes and microscopy.

⁴⁷⁹Ibid., 97.

⁴⁸⁰Reeves, *A Hand-Book of Medical Microscopy*, 36.

Science acquired a new, enhanced cachet in the last decades of the century. No longer the province of Goethean Faustus cogitating in self-enclosed, darkened cloisters,⁴⁸¹ the post-bellum industrial revolutions in Europe and America sparked profound interest in science at all levels. Evolution, theorized by a naturalist on observations filtered through the hypotheses of men such as Thomas Malthus with his dismal exponential philosophy and Charles Lyell of geological uniformitarianism, taught the unsettling idea of change to a society formerly fixated on the immutability of nature and the cyclical propensity of time. Inventors such as Edison captivated the public with technological wizardry that expanded the human senses by capturing ephemeral voices forever on slowly-moving disks (phonograph, 1878) and expanded day into night by creating a new light (incandescent lamp, 1879) that was safer, cheaper (eventually), and brighter than previous nightlights.

In medicine, Louis Pasteur excited public interest with the notion that the microscopic world, invisible to the naked eye, included powerful and dangerous enemies—an idea that even many scientists would have dismissed as magic not long before. In a move of pure genius and persistence such as characterize the birth of many revolutionary movements, he stubbornly clung to the concept that just as bacteria altered the chemistry of organic materials during fermentation, so they could modify the internal composition and milieu of the human body to create disease. Later, the French chemist showed that related forces could be mustered in the friendly form of inoculations to protect the individual against diseases like anthrax (1881) and rabies (1885).

Darwin and Pasteur, two scientists deeply rooted in the Victorian ethos with their foibles, failures, and astonishing successes, represented only the exposed tip of a very deep iceberg. An increasingly powerful press, now living in a space-and-time-shortened universe, catered these

⁴⁸¹Goethe's *Faust* begins at night "in a high-vaulted, narrow Gothic chamber." Johann Wolfgang von Goethe, *Faust*, ed. Robert Maynard and Mortimer J. Adler, trans. George Madison Priest, *The Great Books of the Western World* (Franklin Center, PA: The Franklin Library, 1832; reprint, 1978), 15.

miracles to an eager public. Newspapers and magazines captivated ordinary men and women daily with previously unimaginable scientific marvels. As part and parcel of this valorization, laboratory science and its practitioners, including medical microscopists, rose in public esteem.

One consequence of this new-found (yet historically recurrent) praise for applied science was the rise of specialism. Laboratory science converted the spectrum of microscopists from the pleasure-seeking rich and the curious of mind to a more corporate scientist—less individual, more likely part of a group; less independent, more reliant on the rising University; and more reliant on business or (at least on the Continent) government for support and sustenance. On a more ideological plane, Faust, the polymath, dramatic symbol of Romantic intellectualism in the early nineteenth century, became unthinkable—a relic of a foregone era—as science evolved into compartmentalized professionalism later in the century. Goethe had dabbled in botany and politics in addition to his literary interests. Virchow, who did not accept Pasteur’s germ theory of disease until late in his life (for was not the cell—that most “social” of biological entities—supreme?), used his brand of socialism to link humanitarianism and the German government as he connected cell theory to disease. On the other hand, Abbe, a model of scientists to come, was a University professor and a company man. Unlike Virchow, his position in the scientific community of the late nineteenth century was more consonant with that of new-generation men like Koch and Ehrlich, whose great discoveries germinated under institutional auspices.

Each generation may have its coterie of Renaissance men, who, in science and medicine, expand the discipline in ways undreamed by those who came before. Nonetheless, by the end of the nineteenth century the breadth of the interests of the members of the microscopical societies narrowed. The majority of microscopists, formerly men of many fields, now came from medical

science.⁴⁸² The old amateurs and connoisseurs of microscopy—who pursued many different callings for their livelihoods—faded into the background, unable (or unwilling) to meet the training demands of the new breed of microscopists. Men of science, such as pathologists and practitioners, who used the microscope as an instrument of discovery and diagnosis, began to dominate forums dedicated to the former after-dinner bauble. Further, as the cultures of science and religion grew closer toward the end of the century,⁴⁸³ scientist-microscopists awed and dazzled quondam connoisseurs of microscopical Nature with the elucidation of the structure and sometimes function of God’s creations in their utilitarian pursuit of health and wellness over sickness and disease. In short, the pleasures of the microscope of bygone ages was transformed into the intellectual and pragmatic pursuits of a new generation of microscope professionals—laboratory scientists, from technicians to theorists. The dilettante’s toy became the pathologist’s tool. It was, as the American Francis Donaldson wrote in his 1853 appeal for “The Practical Application of the Microscope to the Diagnosis of Cancer,” a “peculiar pleasure”⁴⁸⁴—grounded in productivity, efficiency, and professionalism rather than diversion and dabbling.

By the end of the nineteenth century, science had become, *de facto*, a public religion. The microscope, now an instrument of science and medicine, held a privileged place at its altar. Physicians and other practitioners, long fearful of errant microscopical diagnoses, now viewed microscopy in a new light. Demand for microscopes grew apace. No longer could a respectable

⁴⁸²Warner, "Popular Microscopy," 31-32.

⁴⁸³How microscopy reflected the transformation of the cultures of religion and science over the previous two centuries! In the seventeenth century, for example, Thomas Sydenham and John Locke averred that the microscope was unethical and immoral in that it carried human experience "beyond the domain of common sense, the realm accessible to the naked eye and the unassisted hand." Wolfe, "Sydenham and Locke on Anatomy," 209.

⁴⁸⁴Francis Donaldson, "The Practical Application of the Microscope to the Diagnosis of Cancer," *The American Journal of the Medical Sciences* 25, no. 1 (1853): 47 Footnote.

clinician question its role in medicine. The microscope and microscopy had become medical desiderata.

Increased Utility

Want and need added new reasons to the demand for the microscope in medicine. Desire without utility, however, is doomed to ephemerality. Proof of the value of the instrument in the care of the everyday patient by the practicing physician required reinforcement, especially given the negative aura that dogged diagnostic microscopy from earlier years.

Further, improved utility alone was necessary but not sufficient to fan the demand for microscopes. Mass manufacturing, driven by advances in optical research and economies of scale, propelled the construction of affordable modern light microscopes. Mass marketing heightened interest. The growing presence of microscopes in medical schools and clinics served to familiarize and accustom new generations of students and practitioners to this not-so-new-as-newly-improved-and-pervasive method of investigating clinical cancer. Interest led to more discoveries, which further stimulated excitement in medical microscopy borne by desire and utility. Nevertheless, the rise of cancer microscopy did not occur in a medical vacuum.

Culture & Economy:

Utility from Systemic Efficiencies

In addition to the invigorating intellectual environment occasioned by the growing frenzy for medical microscopy, broader developments in society aided the demand for microscopes in the late 1880s and early 1890s. Synergies abounded between the community of medical microscopists, the industrialists of mass production, and the society that sanctioned both. As a modern skyscraper cannot stand without its supportive skeleton, so the economic and cultural

foundations of the age—the basis of any significant historical development—undergirded the demand for and utility of the microscope.

The Standard of Living

The United States as a whole experienced a marked increase in the standard of living after the Civil War. The Gross National Product, a broad measure of the economy, almost doubled from the end of the Civil War to the early 1890s.⁴⁸⁵ The index of average daily wages increased forty-four percent across all industries from 1860 to 1880—and another eighteen percent in the next decade despite an overall deflationary environment.⁴⁸⁶ In some industries, such as the building trades, the rise was even more spectacular.⁴⁸⁷ In addition to the increase in wages, average daily hours worked actually decreased from 10.3 to 10.0.⁴⁸⁸ Laborers received more pay for less time worked. Productivity increased as manufacturers took advantage of new machines, markets, and men.

Although for every John D. Rockefeller or Andrew Carnegie there were millions of hardscrabble workers eking out a living, laborers (especially the skilled) and owner-manufacturers grew in number and wealth as the century progressed. More could afford to seek the professional help of regular physicians for their ills, and many did. The rise of the urban middle class, which included many medical practitioners, contributed mightily to this trend. For those fortunate enough to benefit from these economic changes, opportunities formerly available

⁴⁸⁵U. S. Bureau of the Census, *The Statistical History of the United States from Colonial Times to the Present*, ed. Committee on Historical Statistics of the Social Science Research Council, Revised ed. (Stamford, CT: Fairfield Publishers, Inc., 1965), Series F 1-5 on page 139. In the period 1869-1873, The GNP was approximately \$6.71B in modern-day prices. By 1889-1893, it rose to \$13.1B. In constant 1929 dollars—a popular yardstick for nineteenth-century monetary comparisons—the rise was almost 300%, from \$9.11B to \$26.1B.

⁴⁸⁶*Ibid.*, Series D578-88 and D73-77 on page 90.

⁴⁸⁷*Ibid.*

⁴⁸⁸*Ibid.*, Series D573-77 on page 90.

only to the privileged few became realities for growing numbers of Americans.⁴⁸⁹ For example, philanthropy made professional education more attainable for many previously excluded from such rarefied pursuits. These developments had a major effect on the advent of scientific medicine in general and cancer microscopy specifically, and thus warrant a closer analysis.

Philanthropy

In the United States, science and microscopy, heretofore the province of the dabbler of independent wealth, benefited from the rise of the new affluence.⁴⁹⁰ In particular, donations to institutions of “higher learning” for the investigation of cancer by men (and women) of means increased. Often, as previously noted, these were people personally touched by cancer—a disease thought by many to have a peculiar predilection for the upper classes. This dedicated largesse found its way to pathologists for purchases that invariably included microscopes.

In 1899, Caroline Brewer Croft gave the enormous sum of \$100,000 to Harvard University to establish a Cancer Commission to study the disease.⁴⁹¹ Three years later, Mrs. Collis P. Huntington, widow of the Western railroad magnate, donated a similar amount to the General Memorial Hospital for the Treatment of Cancer and Allied Diseases, the then-current name of the New York Cancer Hospital, to establish the Collis P. Huntington Fund for Cancer

⁴⁸⁹See, for example, Roy Rosenzweig, *Eight Hours for What We Will: Workers and Leisure in an Industrial City, 1870-1920* (Cambridge: Cambridge University Press, 1983). This is not to imply that the final decades of the nineteenth century were free of economic rollercoasters—even for those who benefited from the new economy. Witness the economic recession/depressions of the 1870s, 1880s, and mid-1890s. Even during flush times, wages provided bare subsistence for most laborers, although the opportunity for immigrant employment in the United States often outstripped that of the “mother” country. Actual prosperity visited only a select few. The urban-immigrant denizens of Jacob Riis’s “other half” and the Populists of the South and West illustrate how uninclusive and misleading a universal expression like “the gay ‘90s” can be. Nevertheless, historical comparison must be made with workers’ historical measures of “wealth,” not with those of the twenty-first century safety-net state.

⁴⁹⁰Thorstein Veblen, *The Theory of the Leisure Class: An Economic Study of Institutions*, 100 vols., *The 100 Greatest Masterpieces of American Literature* (Franklin Center, PA: The Franklin Library, 1899; reprint, 1979), 282.

⁴⁹¹The Chairman of the Commission was the eminent Dr. J. Collins Warren.

Research.⁴⁹² This Fund brought the young pathologist and microscopist Dr. James Ewing—who would dominate scientific cancer thinking for much of the first half of the twentieth century—to Memorial Hospital. It also established the Loomis Laboratory for Research in Experimental Pathology at the new Cornell University Medical College as a major cancer research center.⁴⁹³

As was the case earlier in the nineteenth century, pathology, microscopy, and cancer formed a potent triad in the investigation of the neoplastic diseases. The increased flow of philanthropic funds into cancer research late in the century added new fuel to the nascent flame that was scientific medicine. In the process, the fruits of laboratory discoveries, more often than not supported by microscopical findings, fostered further utility for microscopy in the diagnosis and prognosis of the cancer patient.

Medical Education

The greater availability of wealth in post-bellum America also stoked the growth of institutions devoted to medical education—part and parcel of the general trend toward higher education and the growth of the University at the time. Abraham Flexner noted in his highly influential “Bulletin Number Four” in the *Medical Education in the United States and Canada* for the Carnegie Foundation that the quantity of new medical schools doubled between 1876 and the beginning of the twentieth century.⁴⁹⁴ To be sure, not all were affiliated with institutions of higher education and many subsequently failed. Nevertheless, the increased number was a response to heightened demand for medical education fostered by the new scientific medicine,

⁴⁹²General Memorial Hospital, "Seventeenth Annual Report for the Year 1901," (New York: General Memorial Hospital for the Treatment of Cancer and Allied Diseases, 1902), 15.

⁴⁹³Harold Rusch, "The Beginnings of Cancer Research in the United States," *Journal of the National Cancer Institute* 74, no. 2 (1985): 392.

⁴⁹⁴Flexner recorded that in 1876 there were about seventy-three (twenty-six plus forty-seven) medical schools, a number that, in his words, "has been since then much more than doubled." Flexner, *Medical Education in the United States and Canada*, 6.

the growing cachet of the medical and scientific professions, and the increased availability of means to pursue education beyond adolescence.

Curricula also underwent a revolution. Compare the bookish medical education received by J. Marion Sims in the form of donnish lectures at Charleston Medical College in the 1830s with the increasingly hands-on laboratory experience of medical students at Columbia and Michigan in the 1880s.⁴⁹⁵ The days when Sims's father could quip to his medical-student son that medicine was a "profession for which I have the utmost contempt" because "there is no science in it" had passed.⁴⁹⁶ The development and acceptance of medical microscopy were integral parts of this scientific revolution in medicine as they had been in Europe for decades.

Increased demand for formal medical education in scientific medicine in the United States at the end of the nineteenth century increased the number of physicians adept at microscopy. Again, American practitioners lagged behind their European confreres—especially Germans—in this regard. From a practical perspective, medical microscopy began on the Continent in the 1830s under the tutelage of researchers using the new, improved achromatic, aspherical microscopes. Alfred Donné in France and Johannes Müller in Germany were trail blazers in cancer studies.⁴⁹⁷

⁴⁹⁵For example, compare J. Marion Sims's description of his own medical education in his autobiography with some of the student reports of medical lectures from the late 1880s. See Francis R. Baker, compiler, "Dr. Francis Delafield's 'Lectures on the Practice of Medicine,'" Reported and Arranged by E.A. Tucker in *Archives & Special Collections of the Health Sciences Library of Columbia University* (New York: 1888), Joseph Didier Montmarquet, "The Practice of Medicine: Notes Taken at Prof. Delafield's Lectures," in *Archives & Special Collections of the Health Sciences Library of Columbia University* (New York: 1889), J. Marion Sims, *The Story of My Life*, ed. H. Marion-Sims (New York: Da Capo Press, 1884; reprint, 1968), 138ff.

For the history of microscopy at the University of Michigan during the last decades of the nineteenth century, see Stowell, "Microscopy in the University of Michigan," 63-64.

⁴⁹⁶Sims, *Story of My Life*, 116.

⁴⁹⁷*British Medical Journal* 1875, ii, 473 as cited by Foster, *A Short History of Clinical Pathology*, 26.

One of Donné's students, John Hughes Bennett, brought his new-found passion for microscopic diagnosis, initially via cytology, across the Channel to introduce medical microscopy to England and Scotland in the early 1840s.⁴⁹⁸ Pathologic anatomy, including the study of cancer, was the spur. In 1841, Bennett became perhaps the first physician to advocate to his colleagues and students the use of the microscope in the daily practice of medicine.⁴⁹⁹ By 1849, he urged routine differentiation of cancerous and non-cancerous tissues by microscopy.⁵⁰⁰ For, as he himself explained it that year, "The only physical proof we can arrive at of the existence of cancer, is by means of the microscope."⁵⁰¹ Thus, the first official European instruction in medical microscopy occurred in the 1840s and 1850s.

The Boston Brahmin Oliver Wendell Holmes, whose Parisian medical training in the early 1830s was conspicuously *sans* microscopy,⁵⁰² nevertheless transported a "simple Raspail microscope" back to Boston.⁵⁰³ Not until the early 1850s, however, did he initiate one of the first American courses in medical microscopy. This was at the Tremont Street Medical School,

⁴⁹⁸Hajdu, "Cytology," 672.

⁴⁹⁹John Hughes Bennett, *The Employment of the Microscope in Medical Studies* (Edinburgh: Stewart, 1841).

⁵⁰⁰John Hughes Bennett, *On Cancerous and Cancroid Growths* (Edinburgh: Sutherland and Know, 1849), 221. Bennett, an Enlightenment rationalist soul in the body of a physician, noted that the microscope was an essential, albeit insufficient, instrument for confirming a diagnosis of cancer. "The only physical proof we can arrive at of the existence of cancer, is by means of the microscope," he wrote. Nevertheless, "it is from a union of all these circumstances (symptoms, signs, etc.—LK), combined with a minute examination of the growth, under such magnifying powers as will clearly display its cells and other primary elements, that we ought to found a diagnosis, and not from one or the other separately." Bennett, *On Cancerous and Cancroid Growths*, 222.

⁵⁰¹Bennett, *On Cancerous and Cancroid Growths*, 221.

⁵⁰²Holmes wrote that while a student in Paris, he could "not remember ever hearing one word about the microscope or the results obtained from its employment." Quoted by Cassedy, "The Microscope in American Medical Science," 81.

⁵⁰³Catherine Drinker Bowen, *Yankee from Olympus: Justice Holmes and His Family* (Norwalk, CT: The Easton Press, 1943; reprint, 1990), 67. This simple microscope remained on display at the Harvard Medical School for more than a century. Holmes did not purchase his first compound microscope until 1847, shortly before he began instructing others in microscopy. See Hunt and Hunt, "Dr. Oliver Wendell Holmes," 79.

which later merged with Harvard Medical School.⁵⁰⁴ Instruction in microscopy remained an option at only a small number of select schools for many years thereafter. William Henry Welch, who corroborated the diagnosis of President Cleveland's cancer in 1893, confessed shortly after graduation from Columbia's medical school in 1875 that he knew "nothing about the microscopical appearances."⁵⁰⁵ His educational sojourn in Germany was meant, at least in part, to remedy this self-perceived deficiency. In the late 1870s, he brought his new skills in laboratory science home to lead a generation of rising medical microscopists. Nevertheless, these early efforts at the teaching of medical microscopy did not imply that it had become a regular part of the medical school curriculum. Not until 1885 in England (on the occasion of the introduction of an expanded curriculum), and several years later in the United States, did microscopy become a requirement in most medical schools.⁵⁰⁶ Britain lagged behind Germany, and the United States lagged behind both. Greater focus on histology, embryology, and cancer in Europe in the middle of the nineteenth century contributed decades later to increased demand for training in microscopy in American medical schools and, subsequently, by their practitioner graduates.⁵⁰⁷

In the late nineteenth century, medical research and education, with fits and starts, moved under the auspices of the university. Philanthropists dotted the academic landscape with eponymous institutions from Stanford in California (1885) to Rockefeller in New York (1901).

⁵⁰⁴Hunt and Hunt, "Dr. Oliver Wendell Holmes," 82.

⁵⁰⁵Quoted by Flexner and Flexner, *William Henry Welch*, 70-71.

⁵⁰⁶Bracegirdle, *A History of Microtechnique*, 329.

⁵⁰⁷In the *Index Medicus*, Series I., of the early 1880s, John Shaw Billings listed microscopy under the general heading of "Anatomy, Histology, and Embryology." Articles on cancer microscopy, rare and almost always case reports, could also be found in this section. Investigations of macroscopic or clinical cancer received their own heading under "Cancer" or the organ involved.

Universities and medical colleges strengthened ties between microscopy and the natural sciences while developing microscopical perspectives on human biology, pathology, and cancer medicine. Microscopes became institutional equipment rather than personal instruments, increasing their visibility and utility as tools for the practitioner. Thus, by the end of the nineteenth century, the growth of medical research and education on both sides of the Atlantic, fostered by economic growth and individual philanthropy, ignited an urge for microscopy by the American practitioner.

CULTURAL SYNERGIES TOWARD CANCER MICROSCOPY

The Modern Urban Landscape

More general themes, commonly identified as the turn toward “modernity,” added to the desire for microscopy. Urban growth was one. The move to the city increased demand through the creation of synergies in transportation and communication that freed health care and its growing technologies from the tethers of time and distance.⁵⁰⁸ As a result, the cost to transport microscopes from manufacturer to purchaser declined over the last decades of the nineteenth century.⁵⁰⁹

The growing popularity of Alexander Graham Bell’s telephone in cities, especially after Thomas Edison’s enhancements in the late 1870s, increased manufacturing efficiency and gave producers the ability to better gauge real-time demand for their products. The ingredients of

⁵⁰⁸Similar developments in rural communities, in general, occurred decades later. Although the mail-order king Richard Warren Sears, who brought big-city consumer products by mail to town and country alike, published his first catalogue in 1887, my review of his Catalogue offerings as late as the Fall of 1900 failed to reveal any microscopes or associated scientific equipment for sale. See Roebuck and Co. Incorporated Sears, *Consumers Guide: Cheapest Supply House on Earth; Our Trade Reaches around the World* (Northfield, IL: DBI Books, Inc., 1900; reprint, 1970).

⁵⁰⁹For a general discussion of industrial synergies in the late nineteenth century, see Jeremy Atack and Peter Passell, *A New Economic View of American History from Colonial Times to 1940*, 2nd ed. ed., 1 vols. (New York: W. W. Norton & Company, 1994; reprint, 1994), Chapter 17, “The changing structure of american industry,” and especially 468.

modern marketing were born. Inventions like Linotype typesetting (1884) decreased the cost of print communication. In turn, lowered costs helped speed the word of microscopical findings through dedicated microscopical societies' publications and further stimulated demand through widespread advertising.⁵¹⁰

Advances in the state of the free market system—from production to consumption—in the late nineteenth century are well known and hardly unique to microscopy or even medicine, but they emphasize the extraordinary effect of the industrial revolution on the augmentation of the supply-demand equation for microscopes and microscopy in medical practice.

Competition

Manufacturing competition increased demand through greater choice. Capitalist economies have always been characterized by competition and, as Karl Marx wrote, the impulse to squash it.⁵¹¹ Consolidation came later to microscope manufacturing than other industries, perhaps because of its strong international flavor, so that competition for market share reached its height in the early 1880s. Improved quality at lower cost resulted.

The 1880s were boom times for microscope makers. Between 1880 and 1882, more microscope manufacturers were in business than at any other time before or since in the history of the United States. This was a consequence of the success of American producers like the Bausch & Lomb and the H. R. Spencer Optical Company (later the American Optical Company), as well as the popularity of microscopes at the 1876 Exposition and the founding of the

⁵¹⁰Warner, "Antebellum Medical Microscopy," 368.

⁵¹¹The drive to monopoly is only one spur of competition. Other factors, too numerous to detail, tilted accumulators of capital—the bourgeoisie of Karl Marx's world—toward competition. See "The Accumulation of Capitals and the Competition Among the Capitalists" in Karl Marx, *Economic and Philosophic Manuscripts of 1844*, ed. Dirk J. Struik, trans. Martin Milligan (New York: International Publishers, 1964; reprint, 1973), 82-91.

American Microscopical Society in 1878. During those years an estimated twenty manufacturers sold into the market.⁵¹²

Demand expanded rapidly and optical manufacturers rose to meet it, but few survived. By 1900, only two American microscope manufacturers remained.⁵¹³ Consolidation wrought by corporate behemoths during the years of Machiavellian industrial capitalism at the end of the century swallowed the smaller producers, but their ideas, techniques, and advances—as well as their factories—lived on in the cultures of capitalism.

Nationalism

Nationalistic tendencies encouraged the growth of the American microscope manufacturing sector in the 1880s and thereafter. Cross-Atlantic microscopists touted their own German and English microscopes as the best, but Americans began to question these conclusions after the Bicentennial. In short, the American exceptionalism trumpeted by historians in arenas such as politics and geography also applied to microscope production. “American” became synonymous with quality.

The beginnings of microscope manufacturing in the United States were hardly auspicious. In the mid-nineteenth century, demand for American microscopes was small. Pioneer American microscope manufacturers included Charles A. Spencer (1813-1881), who made his first microscope objectives at the age of twelve⁵¹⁴; Robert B. Tolles (1821-1883), Spencer’s one-time apprentice; and John Bausch and his partner, Henry Lomb, who began the

⁵¹²See graph at Turner, *Great Age of the Microscope*, 14. Also note Padgitt, *Early American Microscopes*, 142.

⁵¹³Turner, *Great Age of the Microscope*, 14.

⁵¹⁴Oscar W. Richards, "American Microscope Makers and Introduction to the Collection," *Journal of the Royal Microscopical Society* 83 (1964): 123. Spencer did not manufacture his first complete (achromatic) microscope until 1847. Cassidy, "The Microscope in American Medical Science," 83.

production of microscopes in 1872,⁵¹⁵ nineteen years after they opened their first optical shop in Rochester, New York.⁵¹⁶ All took advantage of the high cost of European lenses and scopes (including shipping costs) in the United States to fulfill what little home-soil demand existed.

By the 1880s, however, the expanding market for microscopes, an increasingly exclusive tariff policy,⁵¹⁷ and growing feelings of nationalism,⁵¹⁸ encouraged home-grown manufacturers. American microscopists began to express the belief that objective lenses manufactured in the United States were every bit the match of their German counterparts. In 1889, Christopher Johnston proclaimed that “the renowned apochromatic objectives of Germany, with all their recognized excellence and improvements, in *no way surpass* in their performance the best objectives of our best American makers.”⁵¹⁹ American-made lenses were better than their European counterparts, he continued, because they “are adapted to a larger range of work”⁵²⁰—a versatility quite useful to pathologists and practitioners viewing cancer specimens. And, by the

⁵¹⁵Jacker, *History of the Microscope*, 121, 75.

⁵¹⁶Richards, "American Microscope Makers," 125.

⁵¹⁷The McKinley Tariff of 1890 was “probably the most thoroughgoing protective measure ever passed up to that time,” wrote the historian Clarence Carson. Most “protected” items were staple manufactured goods rather than specialty items like microscopes. See Clarence B. Carson, *The Growth of America 1878-1928*, ed. Beth A. Hoffman, vol. IV, *A Basic History of the United States* (Wadley, AL: American Textbook Committee, 1985; reprint, 1995), 86-89. Democrat Grover Cleveland argued vociferously against the high tariffs in 1887 and 1894, but the 1890 Tariff was passed during the administration of Republican Benjamin Harrison. Cleveland’s contention was that the Federal government did not need tariff revenue because the country was running a surplus! See J. Rogers Hollingsworth and Bell I. Wiley, eds., *American Democracy: A Documentary Record*, 2 vols., vol. II: 1865-1961 (New York: Thomas Y. Crowell Company, 1961; reprint, 1963), 76-80. Cleveland achieved minimal success after the Democrats returned to dominance in 1892, resulting in the passage of the Wilson-Gorman Tariff Act of 1894. Still, although the Act lowered the levy on many items, it raised the tariff on others. President Cleveland could not bring himself to either sign nor veto the bill.

⁵¹⁸General Grant noted that pride in the United States increased, to no small degree, from the healing of sectional Civil War rifts. He worked assiduously toward this goal and believed, by the time of his death, that he had succeeded. Many other factors, both national and international, spurred the growth of nationalistic feelings in the late nineteenth century.

⁵¹⁹Johnston, "The American Objective as Compared with German," 131. Italics in the original.

⁵²⁰*Ibid.*

way, he added, they cost “40 to 80 per cent. less.”⁵²¹ By the 1880s, several American manufactures rivaled their European counterparts in quality and cost as never before. Makers of microscopes and objective lenses were part of this powerful trend toward industrial and political nationalism.

Market Strata

As in earlier years, the quality of microscopes on both sides of the Atlantic at the end of the nineteenth century varied considerably. In the United States, the higher-quality, lower-cost microscopes experienced the greatest growth in market share. To a large extent, the institutions and individuals that purchased these instruments constituted only a small portion of the total marketplace years earlier. Many medical students and practitioners, for example, acquired their first microscopes during the last two decades of the century.⁵²² Increased numbers of public health facilities and the new in-hospital laboratories added to the institutional stampede for new instruments of better quality.⁵²³ In medical student classrooms, doctors’ offices, public health units, and research laboratories, the microscope became an intrinsic component of the medical landscape. So overwhelming had its importance to medicine become that it now became identified as an iconic symbol for medicine.

Entrepreneurs recognized the increased craving for medical microscopes and seized the opportunity to profit from the growing demand, especially for the more affordable microscopes. In 1878, the Indianapolis Lyceum of Natural History sponsored the National Microscopical Congress for the purpose of creating a national organization dedicated to the “progress of

⁵²¹Ibid.

⁵²²Warner, "Popular Microscopy," 30.

⁵²³George Dock, who trained in medicine during these years, noted that until the 1880s, “hospitals had no laboratories and there were few facilities for the use of microscopes.” See Dock, "Clinical Pathology in the Eighties and Nineties," 671.

microscopy.”⁵²⁴ In attendance was Professor J. E. Smith, who voiced his bitter complaint about the “high cost of student microscopes” and the dearth of instruments available for purchase on a student’s budget.⁵²⁵ Manufacturers had sold so-called “student models” since the 1840s, but, although their price was reasonable, their quality was poor.⁵²⁶ John W. Sidle of the Philadelphia manufacturing firm of Sidle and Poalk responded to Smith and decided to take bold action. He suggested to the Professor—perhaps invoking the spirit of the Zeiss-Abbe collaboration—that they should design, manufacture, and market a microscope of improved quality and lower cost targeted at medical students. The famous “Acme” microscope was born. After 1884, it was produced by the newly-named Acme Optical Works. The Acme became one of the most successful student microscopes in history.⁵²⁷ Others copied their success. By the 1890s, a plethora of microscopes filled every niche of the market. At the close of the century, a microscope of superior optical quality could be purchased for twenty dollars. Only a generation earlier, an instrument of similar quality—if obtainable—would have cost hundreds.⁵²⁸

Quality, Cost, and the Cachet of Science

Confounding the usual effect of lower cost on quality, technological developments fostered higher quality at lower cost. Competition followed. The prodigious scientific and commercial efforts of Ehrlich, Abbe, Zeiss, Smith, Sidle, and others in the late nineteenth century led to a fracturing of the microscope marketplace from high-end to low-quality and the

⁵²⁴Simon Henry Gage, "Microscopy in America (1830-1945)--Selections," *Transactions American Microscopical Society* 83, no. 4 (Supplement) (1964): 83. The American Society of Microscopists, later the American Microscopical Society, was born at this convocation.

⁵²⁵Richards, "American Microscope Makers," 125.

⁵²⁶Padgitt, *Early American Microscopes*, 17.

⁵²⁷Purtle, "History of the Microscope," 259.

⁵²⁸Padgitt, *Early American Microscopes*, 128.

entry of new manufacturers into the field—many catering to specific clientele.⁵²⁹ The contributions of these newcomers furthered the production of good-quality microscopes at affordable prices, thus opening the world of the microscope beyond well-endowed institutions and researchers to students, practitioners, and others who a generation earlier had not the means to purchase their own scopes.

In the greater scheme, the advent of scientific medicine in general and its attendant instrumentation in particular lent credibility, authority, and visibility to the previously benighted vocation of medicine and attracted a following eager for the application of science to the treatment and cure of disease.

MICROBIOLOGY:

THE NEW FRONTIER – MICROSCOPY RISING

The Power of Necessity

In retrospect, the search for pathogenic bacteria, other microbes, and the means of their destruction served to propel the consolidation of the hitherto-splintered medical profession and converted the microscope from the limited research tool of the early and mid-nineteenth-century to an instrument of necessity for the medical student, practitioner, and public health official in the late nineteenth century. Bacteriology and the re-professionalization of medicine that followed in its wake impelled microscopy toward widespread acceptance by physicians. Microscopy became the basis for the diagnosis, treatment, and prognosis of many diseases—including cancer.

Germ Theories, Bacteriology, and Microscopical Mistakes

⁵²⁹Turner, *Great Age of the Microscope*. See especially the line graph on page 14.

Germ theory was the idea; scientific medicine the foundation; bacteriology the call to action. Together they were, in nineteenth-century terms, the “exciting cause” of medical microscopy. They served as base and framework for the use of the microscope in daily practice. Early cancer researchers had utilized the microscope to good effect long before the development in the 1820s of optically satisfactory aspherical, achromatic scopes. The generations of Müller, Virchow, and Ehrlich employed the microscope to discover many of the pathoanatomical features of cancer and derived elemental principles of its natural history. Nevertheless, the average practitioner was not part of this conversation and the findings of the giants rarely figured into the everyday diagnosis and treatment of the disease.

Surprising as it may seem through the backward-gazing, presentist eyes of laypersons today, the acceptance of theories of germs and the discipline of bacteriology, in the main, resulted from a slow and hard-fought battle rather than the sensational “Eureka!” portrayals in popular works.⁵³⁰

The average physician and surgeon in the United States remained skeptical of the value of germ theory and microscopy for patient care well into the 1880s.⁵³¹ The counter-intuitive nature of disease-causing germs and a history of erroneous microscopical diagnoses hampered their acceptance at the practitioner level. Physicians avoided unpleasant, anxiety-provoking confrontations between patient and doctor that resulted from microscope-derived false results; diagnostic errors followed inexperience, authoritarianism, and poor technique. Overcoming the prejudice against the microscope was a laborious task, but improved education reduced errors

⁵³⁰For many of the historical facts, see Allen, "Americans and the Germ Theory of Disease", Phyllis Allen Richmond, "Some Variant Theories in Opposition to the Germ Theory of Disease," *Journal of the History of Medicine and Allied Sciences* 9 (1954).. For a more recent analysis—and a critique of Phyllis Allen Richmond’s work—see Tomes and Warner, "Rethinking Germ Theory."

⁵³¹For a case study of one particularly bacillo-conscious community—viz., Buffalo, New York, see George E. Haddad, "Germ Theories, Scientific Medicine, and the Buffalo Medical Community," in *Medical History in Buffalo 1846-1996*, ed. Lilli Sentz (Buffalo: State University of New York at Buffalo, 1996), 119, 42.

and augmented accuracy. Acceptance of the tenets of bacteriology by Europeans from the late 1860s on and by many American physicians beginning in the 1880s played a significant role in turning practitioners toward the idea of microscopical diagnoses.

The perceived necessity to apply germ theory to common clinical situations compelled the practitioner to learn microscopy. Increased training in medical colleges and at hands-on social gatherings improved microscopical competence and the accuracy of pathological diagnoses. Consequently, the microscope became an essential weapon in the growing arsenal of instruments against disease. Further, at a time when many believed that any and perhaps all disease could be caused by germs, other pathological conditions like cancer became the focus of the microscope.⁵³² In sum, the concept of the infectious germ fostered new acceptance, knowledge, and utility of an instrument that had been extant for 300 years. Medical microscopy came of age as bacteriologists overcame the prejudices of a tradition of disdain that followed upon frequent misinterpretation—itsself based upon inexperience, authoritarianism, and poor technique.

Inexperience

Dr. Oliver Wendell Holmes, who taught microscopy at Harvard from the 1850s until the 1880s, was in a unique position to judge the errors of students. Poetically summing up his many years as an instructor, he quipped that “if a mistake in looking through a microscope is within the bounds of possibility, the young student will be certain to make it. If there is an air-bubble, or a crack in the glass or a speck of dust, or anything of the sort which has no business in the field of vision, his eye seems instinctively to fasten upon it, as the needle leaps to the magnet, as lover’s

⁵³²Ludmerer, *Learning to Heal*, 76.

hands fly to each other the moment the train enters the railway tunnel.”⁵³³ Visual flights of fancy, however, were not restricted to students, as we will see in our study of cancer germs.

Indeed, Holmes’s students were more fortunate than most, for they benefitted from the interactive tutelage of an articulate, interested, and experienced teacher. As late as the early 1890s, the lament of William Henry Welch—who received no microscopical training at Columbia in the 1870s and decried the fact that in medical schools “of laboratory training there was none”—to incorporate such education at the university level went unheeded.⁵³⁴ In 1893, Jacob D. Cox, in his Presidential Address to the American Microscopical Society, suggested that “systematic and thorough training in the use of the microscope is highly desirable, and that the university is the school to which we naturally look for the means to meet the want.”⁵³⁵ Cox appealed for microscopical training as part of perhaps every “liberal education,” a plea that did not come to pass.⁵³⁶ Nevertheless, his reason is enlightening, for he endeavored to remove “the doubt, the error, and the cost through which we ourselves (microscopists—LK) have had to make our way.”⁵³⁷

Before the 1880s, therefore, microscopical training facilities were negligible. Few practitioners could claim formal educational experience. Some medical schools made microscopic pathology a required course in the 1880s.⁵³⁸ More programs, following the example

⁵³³The quotation is from 1877, as cited by Hunt and Hunt, "Dr. Oliver Wendell Holmes," 86.

⁵³⁴Quotation from Flexner, *Medical Education in the United States and Canada*, 10. The original source was William H. Welch, "Development of American Medicine," *Columbia University Quarterly Supplement*, December 1907.

⁵³⁵Cox, "A Plea for Systematic Instruction in the Technique of the Microscope at the University," 15.

⁵³⁶*Ibid.*, 16.

⁵³⁷*Ibid.*

⁵³⁸Esmond R. Long, *A History of American Pathology* (Springfield, IL: Charles C. Thomas, 1962), 142.

of Johns Hopkins Medical School (which opened in 1893), added the course in the 1890s. Not coincidentally, *The Microscope, a monthly journal for naturalists, physicians, and druggists*, was first published in 1893.⁵³⁹ By the time of Abraham Flexner's 1910 report on *Medical Education*—which condemned didacticism in favor of the “hands-on” clinical and laboratory approach of German-modeled Johns Hopkins—knowledge of microscopy, beginning at the pre-medical school level, was *de rigueur*.⁵⁴⁰

Microscopical experience for most would-be physicians today begins in the undergraduate study of biology and other life and physical sciences. From the perspective of the older clinicians of the late nineteenth century, however, there existed a generational learning gap between investigators who used the scope as part of their research and medical students of the 1880s and 1890s who learned technique and interpretation firsthand.⁵⁴¹ Thus, as knowledge of medical microscopy became a necessity during the renaissance of germ theory, a full transitional generation perused textbooks of non-medical and specialized medical microscopists to learn microscopy at a mature age. These were the practitioners who, when young, had denounced the validity and practicality of microscopic findings to the clinic at a younger age, and now, after many years of medical practice, sought instruction from microscopists with all levels of experience to apply the tenets of those germ theories to their daily work. The learning curve was steep and highly dependent upon the quality of their microscopical education—and that, like experience, was variable.

⁵³⁹Vol. 1, no. 1 was published in January 1893.

⁵⁴⁰Flexner, *Medical Education in the United States and Canada*, 25-26. Dr. Kenneth M. Ludmerer detailed some of these developments in his medical-education case study of Washington University in St. Louis and then expanded his findings to include other medical schools. See Ludmerer, *Learning to Heal*, 79-81.

⁵⁴¹The generational gap among physicians introduced by the rise of routine microscopical education in the late nineteenth century was not unlike that associated with differences in computer skills between younger and older generations at the present time.

Microscopy, even in the hands of the most skilled, is not an exact science.⁵⁴² The microscopist, like the historian, gathers evidence—visual inspection for the former, documentary inspection for the latter—and formulates an interpretation. The accuracy of that interpretation depends upon a number of intangibles—the precision of technique, experience, memory, and personal interests. Even generalists have their pet subjects. The growing experience of medical microscopists in the late 1880s and early 1890s, the rise of specialism, and the rapid and widespread dissemination of new findings via publications supplanted the ignorance of inexperience into the knowledge of experience.

Authoritarianism

Experience frequently lessens error, but the authoritarianism of ill-conceived dominant voices may compound it.⁵⁴³ How is one to overcome the addiction of tradition if its message is broadcast in the guise of precedent and superiority? How could the microscope, a plaything of the rich, become an instrument of scientific medicine when generations of clinicians were educated in the belief that its use led to inaccurate diagnoses? In the microscopical study of cancer, where universal truths in the nineteenth century were based upon single, exceptional cases, traditional attitudes and beliefs were especially difficult to overcome.

More than a century before the 1962 publication of Thomas Kuhn's analysis of scientific revolutions, the Baltimorean Francis Donaldson felt the drag of tradition.⁵⁴⁴ Donaldson, an

⁵⁴²The requirement for greater precision was a driving force of science, technology, and medicine in the nineteenth century. To no small extent, this necessity opened new windows into the nature of things. Microscopy—with its finer lenses and more exact focal points—was a prominent example of this larger desideratum.

⁵⁴³Eric J. Cassell, "Medical Ethics: Consent or Obedience? Power and Authority in Medicine," *The New England Journal of Medicine* 352, no. 4 (2005).

⁵⁴⁴See Thomas S. Kuhn, *The Structure of Scientific Revolutions*, ed. Otto Neurath, Second Edition, Enlarged ed., *International Encyclopedia of Unified Science* (Chicago: The University of Chicago Press, 1970). In particular, note Kuhn's Chapter VII, "Crisis and the Emergence of Scientific Theories." Therein he portrays the revolution from old to new with the metaphor of conceptual tools: "So long as the tools a paradigm supplies

American pioneer in cancer microscopy, knew well whereof he spoke. *The New-York Times* praised him in the 1880s when it noted that his early 1850s writings were “the first...to give a full and careful description of the cells of cancer.”⁵⁴⁵ “The facts,” Donaldson proclaimed in his prescient 1853 article that pleaded for the routine use of the microscope in cancer diagnosis, were the vanguard of progress, for they “reveal, overturn, or more or less modify existing theories, upon which are based all their (clinicians’—LK) practical deductions.”⁵⁴⁶ In essence, he wrote, it is “not to be wondered at, that there should have been then, as there ever will be, a violent contest between routine and tradition on the one side, and the progress of science on the other.”⁵⁴⁷ Thus, in the same year that Samuel David Gross proclaimed the futility of surgery for the treatment of cancer, Donaldson appealed to traditionalists to open their eyes and minds to new truths about the disease revealed by the microscope. In the main, his message was incomprehensible to the majority of his practicing contemporaries. It fell stillborn from his pen, farsighted but unappreciated.

Authoritarian pronouncements fill all ages, fortified by the power of the proven past. In 1889, one of the four reasons given by Edward Schaeffer for the distrust of microscopy by clinicians was the microscopical diagnoses of “men of high reputation,” right or wrong, which

continue to prove capable of solving the problems it defines, science moves fastest and penetrates most deeply through confident employment of those tools. The reason is clear. As in manufacture so in science—retooling is an extravagance to be reserved for the occasion that demands it.” From Kuhn, *The Structure of Scientific Revolutions*, 76. For our purposes, the hands of the clinician are the “old,” the microscope the “new,” and the acceptance of germ theory “the occasion that demands it.”

⁵⁴⁵New York Times, “Cancers—Microscopic Diagnosis: Donaldson's and Smith's Papers on (Editorial),” *The New York Times*, 27 June 1881, 4:7.

⁵⁴⁶Donaldson, “Microscope and Cancer,” 45.

⁵⁴⁷Ibid., 46. As I have sought to contrast cancer traditionalists and modernists in the late nineteenth century, Donaldson looked back to William Harvey for a time of special conflict. “But here, as in the time of Harvey,” wrote Donaldson, “when the same contest was carried on with no little ardour, the innovations of science must finally prevail, although at each step it must fight its way.” Ibid.

were held beyond reproof.⁵⁴⁸ Even when clinical findings clearly contradicted the “Master’s” analysis, the inevitable result, as Schaeffer noted, was “a sort of composite opinion, from which all true original judgment has been eliminated.”⁵⁴⁹

The belief of the old guard that the use of the word “medical” in the term medical microscopy was oxymoronic died, killed by broad-minded professors and their adventurous, younger, medical students. These were the pioneers of the late nineteenth century who became comfortable with the idea and value of the microscopic image as they learned bacteriology, mycology, and parasitology through the lens. Nineteenth-century student notebooks in Columbia’s *Archives and Special Collections* on the Health Sciences Campus reveal the evolution of the perceived cause of contagion from miasmatic vapors to bacterial microorganisms. Concomitantly, they describe their associated investigative disciplines from sanitation to microscopical examinations. During the 1887-1888 academic year, for example, Francis R. Baker compiled Dr. Francis Delafield’s “Lectures on the Practice of Medicine.”⁵⁵⁰ Lecture 18 noted the recently-accepted notion that infectious diseases are caused by “pathogenic, micro-organisms which are taken in by one channel or another and then grow and multiply in the appropriate part of the body.”⁵⁵¹ Further, “It is probable that for each separate infectious disease

⁵⁴⁸Schaeffer, “On the Microscopical Diagnosis of Cancer,” 404. The other three reasons all involved the experience of the microscopist with respect to preparation and observation.

⁵⁴⁹*Ibid.* It is interesting to note that authoritarianism, which relates to the more modern expression of “expert opinion,” no longer ranks high in the contemporary era of evidence-based medicine. Strata of evidence today include Level A, where conclusions are founded on high-quality randomized controlled trials and meta-analyses; Level B, based upon non-randomized clinical trials, cohort studies, and other more limited forms of investigations; and Level C, to which consensus and “expert opinion” have been relegated. The lowest grade, Level D, includes anecdotal evidence—the predominant form of evidence in nineteenth-century medicine and, especially, pharmacotherapy. See J. Siweck and et. al., “How to Write an Evidence-Based Clinical Review Article,” *American Family Physician* 65 (2002).

⁵⁵⁰Baker, “Lectures on the Practice of Medicine,” n.p.

⁵⁵¹*Ibid.*, 97.

there is a separate and peculiar micro-organism.”⁵⁵² The belief system of the German Koch had by then permeated the teaching of this American medical school professor, as had the bacteriologist’s microscopical techniques, overturned the dogmas of legions of authoritarian microscopy naysayers.

Revolutions may occur in bursts, but long-held erroneous ideas fall slowly. A measure of the old tempered the new, for Professor Delafield of Columbia, even in his teachings of avant-garde bacteriology, divided the infectious diseases of the late 1880s into three subclasses—miasmatic, contagious, and unnamed—as though his groupings were more historical than pathological.⁵⁵³ Nonetheless, his classifications depended upon microscopic investigations of the bacteria and their host tissues. Thus, just as anti-contagionists like Frederick Campbell of Buffalo and Dr. Peter of Paris were denouncing germ theory and the use of the microscope for microbiological diagnosis in the mid-1880s, others promoted its use for bacteriology, cancer, and other diseases of the modern era.⁵⁵⁴

Medical microscopy in the 1880s—born in microscopical optics, colored by stains, and enriched by manufacturers and bacteriologists—destroyed the entrenched authoritarian position based upon the tradition of anti-microscopical clinical didacticism and replaced it with the universal acceptance achieved by microscopy in modern diagnosis. In consequence, the convergence transformed the idea of cancer from a malicious, unpredictable, incurable

⁵⁵²Ibid.

⁵⁵³Professor Delafield’s categorization depended upon the natural habitat of the organism—outside the body, inside, or both, respectively. This classification represents a brilliant transition from the internalist paradigm of Virchow to the externalist models of the bacteriological generation led by Pasteur, Koch, Ehrlich, et. al.

⁵⁵⁴For a cogent discussion of the push-and-pull history of germ theory during the last two decades of the nineteenth century in a case study of Buffalo, later a hotbed of cancer research, see Haddad, "Germ Theories." Haddad cited the original sources for the denial and refutation of germ theory by Campbell and Peter as Frederick R. Campbell, "Chemical versus germ theories of disease," *Buffalo M&S J* 24 (Jun 1885): 483 and Peter, "The Inconsistencies of Germ Theories," *Journal de Med. de Paris*, translated in the *Buffalo M&S J* 26 (25) (Jan 1886): 265-8.

macroscopic evil to a disease of potential manageability and curability through early microscopic diagnosis.

Poor Technique

Unrepresentative specimens, inadequate tissue, poorly prepared slides, and errant use of the microscope contributed to poor microscopical technique. Microtechnique advanced with the effort to achieve a detailed, undistorted microscopical image at high magnification. Many improvements followed innovations in sectioning, fixation, embedding, mounting, and staining. Nevertheless, the advances of masters of microscopy required a special impetus to sway students and practitioners toward the routine medical use of the instrument.

That stimulus was the fascination with microbes. Microtechnique improved as the necessity of microscopy swept over medicine. Upon closer analysis, the drive toward improved microtechnique required better specimens, more uniform and improved slide preparation, finely-honed use of the optical microscope, and, perhaps most important in the long run, a sea change in the interactions between practitioners and pathologists. As in other fields of science, each built upon the advances of the other.

Specimens: The Autopsy of the Living

The procurement of surgical specimens characteristic of the true underlying pathology of a tumor or other solid lesion was a major concern of microscopists in the late nineteenth century. Many pathologists at the time believed that a common cause of erroneous microscopical diagnoses was the poor quality of tissue submitted for analysis.⁵⁵⁵ Part of the problem was sampling error, part was inadequate knowledge and/or experience as to how to obtain such specimens, and part was the almost childish competition between clinicians and pathologists.

⁵⁵⁵Henry C. Coe, "The Clinical *Versus* the Microscopical Evidences of Malignant Disease," *The New York Medical Journal* 45 (1887): 681, Schaeffer, "On the Microscopical Diagnosis of Cancer," 405.

Sampling error, the chance return of a false negative (or positive) result from a sample, has been the bane of all physicians who obtain specimens from unseen locations inside the body for centuries. Consider the example of liver cancer. Primary liver cancer, known as hepatocellular carcinoma, arises from foci in the liver. Unlike leukemia, which is evident in essentially all blood samples, liver cancer is localized. Today, the liver can be imaged without surgery by fluoroscopy, ultrasound, computerized axial tomography (CAT scanning), and magnetic resonance imaging (MRI), among other modalities. The “spot” on the liver thought to represent cancer is imaged. The operator passes the fine needle used to obtain the biopsy under visualization directly into the lesion in question. Suction is applied and a thin sliver of tissue is sucked into the gathering tube. Chances of obtaining a sample of the pathology are high. Imagine the time before physicians could visualize the inside of the living body from the outside. What was the probability that the biopsy needle, passed “blindly” through the skin in the upper right quadrant of the abdomen, would yield a piece of the circumscribed lesion? Although imaging techniques lay in the future, the growing ability to explore the interior of the diseased body in the late nineteenth century allowed surgeons to sample pathologic lesions under direct visualization. More accurate diagnoses followed, but who would make them?

Turf Wars

At least until the end of the nineteenth century, it was not clear whether the diagnosis of cancer should be made by practitioners, including surgeons and clinicians, or pathologists. Practitioners, long vexed by incorrect microscopical diagnoses, taunted microscopist-pathologists for much of the century. “Nothing gives the [clinician] more solid satisfaction,” wrote the cancer surgeon Henry C. Coe in 1887, “than to catch a pathologist in a slip.”⁵⁵⁶ Coe knew whereof he spoke, for he had witnessed both sides of the acrimonious debate over the

⁵⁵⁶Coe, “The Clinical *Versus* the Microscopical Evidences of Malignant Disease,” 679.

value and control of medical microscopy as it became the standard for cancer diagnosis late in the nineteenth century. He was a surgeon who operated at the Woman's Hospital in New York and assisted at the first cancer operation at the just-opened New York Cancer Hospital on December 9, 1887.⁵⁵⁷ He was also skilled at pathology, for he translated Carl Friedlaender's popular microscopy text into English and modestly wrote that he was "a dabbler in pathology myself."⁵⁵⁸

Such was the antagonism between them that the surgeon-practitioner would play the pathologist-microscopist for a fool—purposefully goading the microscopist into a flawed diagnosis on the basis of a poor specimen or inadequate (and sometimes intentionally misleading) clinical information. "There seems to be an instinctive feeling of jealousy or distrust between the two," explained Coe.⁵⁵⁹ "How often," he writes, "are portions of the same tumor sent to different pathologists, whose reports seem to be contradictory because their specimens are essentially different in structure!"⁵⁶⁰ Consistency and accuracy demanded better biopsies and more respect between contending professionals.

Microbiology, a unifying force for the medical profession, necessitated good specimens, made the pathologist the reigning microscopy expert, and helped foster cooperation between practitioner and pathologist. Representative surgical specimens brought clinician and microscopist closer together in a common cause: the scientific diagnosis and implied prognosis

⁵⁵⁷Memorial Hospital Archives, "New York Cancer Hospital (Old Memorial)," in *Hayes Martin Collection* (New York: n.d.).

⁵⁵⁸Quotation from Coe, "The Clinical *Versus* the Microscopical Evidences of Malignant Disease," 679. The microscopy text was the already-cited Friedlaender, *The Use of the Microscope*. On September 25, 1885, Dr. Coe donated his personal copy of Friedlaender's text, inscribed "Harry C. Coe, M.D. of New York" to the New York Academy of Medicine, where it resides today.

⁵⁵⁹Coe, "The Clinical *Versus* the Microscopical Evidences of Malignant Disease," 679.

⁵⁶⁰*Ibid.*, 681.

for the benefit of patient and physician alike. Collaboration replaced rancor. Germs became the common enemy, thereby eliminating internecine quarrels. The road to good biopsy specimens and professional amity had been long and rocky.

The Root of Human Disease: Can the Microscope Find It?

Although the idea of a biopsy—removing living tissue for examination (or even cure)—is primarily a twentieth-century phenomenon, its roots lie in the critical period of the late nineteenth century but its origins may be as old as man. The earliest known surgical treatise, *The Edwin Smith Surgical Papyrus*, includes the equivalent of forty-eight case reports reaching back to the third millennium BCE. Case thirty-nine contains clear instructions for “breaking open the swellings and drawing off the pus” of breast lesions that fit the description of cancer.⁵⁶¹ Though not a biopsy in the sense of the removal of tissue for examination, this glimpse into Ancient Egyptian medicine represents the not-so-intuitive idea that human suffering could be relieved by direct human intervention. The extraction of living tissue for examination is an extension of that abstract principle. A corollary is that specimen analysis, via microscopy for example, may aid treatment and suggest prognosis. Such is the goal of the microscope in medicine.

Early Medical Microscopy:

From Cytology to Cytopathology

The quality of the results of microscopical analysis is highly dependent upon the nature of the specimen obtained for investigation and the preparation of that specimen for viewing under the microscope. Poor specimens and poor techniques, *ceteris paribus*, lead to poor results.

⁵⁶¹James Henry Breasted, ed., *The Edwin Smith Surgical Papyrus*, Two vols., vol. One & Two, *The University of Chicago Oriental Institute Publications* (Chicago: The University of Chicago Press, 1930; reprint, 1984), 364.

Thus the acceptance of the microscope into clinical medicine in the late nineteenth century was related to improvements in biopsy and cytological techniques—as well as the ideas behind them.

Cytology is the study of the cell.⁵⁶² In medical circles today, however, “cytology” is often used as a synonym for cytopathology, the proper term for the study of disease changes within cells. Cellular and tissue specimens from diseased organs constitute the raw materials for the two different categories of modern microscopical diagnosis; viz. cytopathology and histopathology. The former, grounded in the examination of individual cells or cell types, qualifies as cytopathology. The latter, histopathology, is the study of disease based upon tissue biopsy proper. Both disciplines matured during the nineteenth century. For most of the century, cytopathology was the study of choice for the diagnosis of cancer and other anatomical disorders. It was most popular among researchers and pathologists in the middle decades of the century. Histopathology began to dominate in the later years.

The Cell

Cancer is a cellular disease, but it was not recognized as such until centuries after the “discovery” of the cell. Indeed, long before cell-based theories of the early 1800s pointed toward the cell as the anatomical and physiological unit of life, microscopists fancied cells as structural rather than functional components of the organism.⁵⁶³ Robert Hooke, in 1665, christened the polygonal structures he discerned in cork as ‘cells’ from their resemblance to small chambers, but their diagnostic potential lay unrecognized and unexplored for some time. In 1767, Felix Fontana, an Italian herpetologist, described individual cells from the slough of an eel. He characterized them as a “mass of globules,” undoubtedly a consequence of the optical

⁵⁶²Cytology is properly defined as the study of the anatomy, physiology, pathology, and chemistry of the cell. As the knowledge base of cell science advances, so do its sub-disciplines.

⁵⁶³I am indebted to the work of Dr. Steven Hajdu for this section. See Hajdu, "Cytology."

distortions produced by the microscopical aberrations of the era.⁵⁶⁴ These are among the first-known explorations into the architecture and science of the cell—decades before the work of Schleiden and Schwann.

The revolution in microscope optics of the early nineteenth century produced the fertile soil for the technical and cognitive advancement of the scientific study of the cell. In the early 1820s, R. J. H. Dutrochet, a French biologist, concluded from his scrutiny of cells that the structure and function of all living beings “with no exceptions” were dependent on the cell.⁵⁶⁵ He is often credited as the originator of cell biology.⁵⁶⁶

Importantly, cell-gathering methods in the nineteenth century were not uniform. Thus these fragile structures were subject to gross artifactualization and interobserver variability. The most common technique may have been to scrape or shave skin from an animal. As noted above, the advent of the aspherical, achromatic microscope in the early decades of the nineteenth century fostered an enthusiasm and penchant for biological and human research unsurpassed until the 1870s and 1880s. Indeed, of the fourteen “pioneers of cytology” listed by Dr. Steven I.

⁵⁶⁴Microscopists, probably as a consequence of spherical aberration, commonly described cells as ‘globules’ and ‘globular’ until the advent of aspherical microscopes. Alfred Donné, a pioneer cytopathologist, studied medicine on the temporal cusp between uncorrected and corrected microscopes. He was awarded his doctorate in 1831 for his study of ‘globules,’ but by the 1840s, consistent use of aspherical, achromatic, non-coma microscopes led to his abandonment of the term ‘globule’ and his adoption of ‘the cell’ and its attendant expansive nomenclature. See L. J. Rather, Patricia Rather, and John B. Frerichs, “Biographical Notes,” in *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory* (Canton, MA: Watson Publishing International (Science History Publications, U.S.A.), 1986), 163.

Also of note is that Fontana, in addition to his claim as one of the first cytologists, was probably the first to describe the nucleus and nucleolus of the cell. In the eighteenth century, he recorded that “the globules contained in the middle part a small body likewise spotted in the middle.” Although Robert Brown is generally credited with the first description of the nucleus in 1831, and Gabriel Valentin, another Johannes Müller student, with the first report of the nucleolus in 1836, it appears that the Fontana preceded them both. For more, see Hajdu, “Cytology,” 669.

⁵⁶⁵A. R. Rich, “The Place of R. J. H. Dutrochet in the Development of Cell Theory,” *Bulletin of the Johns Hopkins Hospital* 39 (1926): 330-365.

⁵⁶⁶Schleiden and Schwann added to the insights of Dutrochet when they grouped cells into “communities” to describe the critical contributions of cells to organ function. See Jacker, *History of the Microscope*, 137.

Hajdu in his table listing “first report(s)” of the microscopical analysis of various body specimens, nine are from the watershed period of the 1830s and 1840s.⁵⁶⁷

The revolutionary idea that cells could be obtained by suctioning them from the inside of an organism (similar to today’s needle aspiration) was first used successfully by E. Stanley in 1833, not long after the publication of Lister’s seminal writings on corrective lens combinations.⁵⁶⁸ The notion that the body could be legitimately “invaded”—especially to aid in the diagnosis and treatment of disease—was born with the decline in the theoretical inviolability of the human body that grew with the increased secularization of society in the nineteenth century. Four years after Stanley’s cellular aspiration, the Frenchman Alfred Donné examined cells from diverse body fluids to initiate the discipline of exfoliative cytology—the examination of cells stripped from their site of origin for microscopical diagnosis. Exfoliative cells, whether derived from secretions, sediments, or washings, remain the mainstay of cytopathology.⁵⁶⁹

The Cancer Cell and Cancer

The investigation of abnormal cells as a window into disease followed naturally and swiftly upon the rise of cellular physiology in the late 1830s and 1840s. Pioneers like Stanley, Donné, and Müller spawned a generation of devotees who advanced the study of cellular pathology at the microscopic level. Müller was one of the first in the study of cancer. His 1838

⁵⁶⁷Hajdu, "Cytology," 674, Table 1.

⁵⁶⁸E. Stanley, "Abscess of the Liver, with Hydatids," *Lancet* 1 (1833). Cited by Hajdu, "Cytology," 674.

⁵⁶⁹The procurement of cells for cytological examination from the internal organs of living persons was primarily a twentieth-century development. Despite ever-improving imaging techniques, it is still a work in progress. Nevertheless, in 1882, Rosenbach reported the discovery of stomach cancer in cells from gastric washings. This was only a year after Billroth performed the first “successful” partial gastrectomy on a 43-year-old woman with the disease. See O. Rosenbach, “Über die Anwesenheit von Geschwulstpartikeln in dem durch die Magenpumpe entleerten Mageninhalt bei Carcinoma ventriculi,” *Deut. Med. Wschr.* 8: 452, 1882, as cited by Bernard Naylor, "The History of Exfoliative Cancer Cytology," *Michigan University Medical Bulletin* 26 (1960): 291 and 95 Footnote 16.

treatise, *On the Finer Structure and the Forms of Morbid Tumors*, is essentially a description and analysis of growths of all kinds at the cellular level, as his illustrations attest.⁵⁷⁰

Research in cytopathology on the Continent inspired the application of the microscope to medicine in England. In 1841, John Hughes Bennett, deeply influenced by his postgraduate studies with Alfred Donné at the University of Paris in the mid-1830s,⁵⁷¹ became one of the first to envision the microscope as an instrument useful in the daily practice of medicine.⁵⁷² Through his teachings and writings, Bennett expanded the work of Hodgkin and Lister to sow the seeds of medical microscopy in England.⁵⁷³

As Müller intuitively and cognitively gravitated toward the importance of the microscopical analysis of tumors, so the potential for the application of the microscope to the investigation of cancer caught the attention of Bennett. Inflammatory and neoplastic growths were often difficult to distinguish on clinical grounds. The microscope, by virtue of the very different types of cells that constituted each growth, allowed such differentiation—although this distinction was far from clear at first.⁵⁷⁴ Like his German contemporary, Bennett also used the

⁵⁷⁰See Müller, "Müller, Morbid Tumors." and Hajdu, "Cytology," 679 Figure 2.

⁵⁷¹Donné received his doctorate in Paris in 1831 for his research into the microscopy and chemistry of the "globules" of blood, pus, and mucus. Rather, Rather, and Frerichs, "Rather, Biographical Notes," 163. In current vernacular, chemistry and microscopy were then *the* "hot" topics.

⁵⁷²*British Medical Journal* 1875, ii, 473. Cited by Foster, *A Short History of Clinical Pathology*, 26.

Note that Bennett, whose life interest was kindled by the microscope, and Oliver Wendell Holmes, who could "not remember ever hearing one word about the microscope" while a student in France, both studied in Paris in the mid-1830s. As is true of the birth of many new ideas, where and with whom one learns can make all the difference. (Footnote quotation from Cassedy, "The Microscope in American Medical Science," 81.)

⁵⁷³Hajdu, "Cytology," 672. Dr. Hadju concluded that Bennett "introduced microscopy in England." Given the rich history of English microscopy from Hooke, long before Bennett, forward, this should be restated that Bennett introduced *medical* microscopy into England.

⁵⁷⁴Inflammatory lesions contain "inflammatory cells" such as polymorphonuclear leukocytes, lymphocytes, and macrophages. Tumors are comprised of neoplastic cells, whether benign or malignant, that have a more irregular and often bizarre (in the case of malignancies) appearance. The distinction is much clearer today than it was in the first half of the nineteenth century.

microscope to discriminate between benign and malignant tumors. Unlike Müller, however, Bennett sought to apply his findings to clinical rather than research situations. Indeed, one of Bennett's earliest studies examined ulcer exudates microscopically to attempt to distinguish the gross appearance of a benign inflammation from cancer.⁵⁷⁵ The macroscopic differentiation between benign and malignant lesions continues to baffle practitioners to this day. Bennett recognized the ability of microscopy to aid in this critical distinction long before other practitioners.

The first wave of the application of the corrected microscope to early scientific medicine included Müller, Bennett, and Donné of Paris. In 1844, Donné published his popular lectures on the microscope and medicine in his seminal *Cours de microscopie complémentaire des études médicales*. This was the first atlas of cytology and, only a few years after the invention of photography,⁵⁷⁶ contained the first photomicrographs—photographs taken through the microscope.⁵⁷⁷ Donné's idea created a small revolution. Soon thereafter others, including Hermann Lebert (1845), F. A. Pouchet (1847), and Gottlieb Gluge (1850), contributed to the pictorial classification of cells that Donné had initiated.⁵⁷⁸

⁵⁷⁵Foster, *A Short History of Clinical Pathology*, 14.

⁵⁷⁶If photography is defined as the use of light to create an image on chemically-treated paper (a photochemical effect), rather than drawings based upon the *camera obscura*, then Joseph Nicéphore Niépce produced the first photograph in 1826. (The photograph captured his hardscrabble barnyard and required an eight-hour exposure.) William Henry Fox Talbot invented the first photographic “negative” with silver chloride—the basis of photography until the digital age—in the early 1830s. Louis-Jacques-Mandé Daguerre produced the first “daguerreotype” on a silvered copper plate in 1837. Donné thus worked and lived in the early age of photography and combined two innovations, medical microscopy and photography, to create a third—photomicrography.

⁵⁷⁷Hajdu, “Cytology,” 670. Deborah Jean Warner noted that the first American photomicrographer was “the Boston Daguerreotypist John A. Whipple” in 1851. See Warner, “Antebellum Medical Microscopy,” 376 Footnote 45.

⁵⁷⁸On Lebert, more below.

F. A. Pouchet was one of the first to study cell changes over time. In his 1847 atlas, *Théorie Positive de L'Ovulation Spontanée et de La Fecondation des Mammifères et de L'Espèce Humaine* (Paris: J. B. Bailliere, 1847), he pioneered the cytology of vaginal cells throughout different stages of the menstrual cycle. This was a direct

Hermann Lebert, a disciple of one of the founders of quantitative (and therefore scientific) medicine, Pierre-Charles-Alexandre Louis,⁵⁷⁹ travelled easily between France and Germany. Like other physicians in this era, Lebert learned and practiced in both countries.⁵⁸⁰ Early in his career, he developed a particular interest in cancer and especially in the microanatomy of cancer cells.

One of the interesting questions raised by Lebert and his contemporaries in the formative phase of cancer microscopy went to the heart of the disease and broached a discussion that reverberated through the century. Conceptually akin to the late twentieth-century dispute as to whether cancer was an environmental (external) or genetic (internal) disease, Lebert became part of an 1840s coterie of investigators who believed that the cancer cell was unique. Again, the new microscope instigated the rise of the perennial question: Was cancer one disease or many? For example, was breast cancer identical to stomach cancer except for its location? Were the cells of breast and stomach cancer intrinsically the same? Lebert and others on both sides of the debate contended that perhaps the microscope could answer this question of crucial importance to cancer diagnosis, treatment, and prognosis. More accurate specimen interpretation, dependent upon improved technique, laid the cornerstone of its resolution, but even before the development of superior microtechnique, the achromatic, aspherical microscope led to first fruits.

Is the Cancer Cell Unique?

forerunner of the work of Charles Rupert Stockard, Aurel A. Babes, and George Papanicolau that led to the introduction of the cervical smear for the early diagnosis of cervical cancer—the “Pap smear”—in the late 1920s.

Gottlieb Gluge, in his 1850 atlas, expanded the work of Schleiden, Schwann, and Müller to further characterize cancer cells microscopically. See Hajdu, “Cytology,” 670-74.

⁵⁷⁹In the mid-nineteenth century, Francis Donaldson called Pierre-Charles-Alexandre Louis a “Baconian” physician—an intellectual descendant of Francis Bacon—because of his emphasis on the application of the scientific method to the study and practice of medicine. Donaldson, “Microscope and Cancer,” 51.

⁵⁸⁰Lebert studied medicine in Berlin, obtained his M. D. from Zurich, and practiced in Paris (where he published his 1845 cytology atlas), Zurich, and Breslau. See Rather, Rather, and Frerichs, “Rather, Biographical Notes,” 167. Lebert’s influence on the young Ehrlich (who studied in Breslau contemporaneously), if any, is not known to me.

The Debate Begins

Cancer had always been a disease apart. Even Galen, who in the second century branded it *praeter naturam* (contrary to nature), clearly understood that there was something uniquely different about cancer. Physicians described the characteristics of cancer consistent with Galen's description, but the underlying explanation for the disease eluded them. The microscope opened a new chapter in the quest for the cause and treatment of cancer, because researchers like Müller quickly discovered that there was something remarkable about cancer cells that might be used to formulate a general explanation of the disease from the inspection of specific, individual cells.⁵⁸¹

The advent of the Listerian microscope allowed researchers to question the nature of cancer cells that penetrated to the core of then-current theory. By the 1840s, constitutionalism, dominant in the United States through the nineteenth century at least until the years of General Grant's cancer, was fully entrenched.⁵⁸² Belief in a characteristic cancer cell was consistent with constitutionalism because the cancer cell (which could "hide" anywhere within the organism), rather than the anchored tissue or organ involved, was the locus of disease. Therefore, the site of origin of the cell was less important than the cell itself. Experience supported cancer constitutionalism, for the excision of cancer in one location often led to its reappearance elsewhere. Further, the constitutional theory of the cancer cell dictated systemic therapy, for local removal of cancer failed. The result was the treatment of disease with patented potions transported by avenues of vessels to all cells of the body. The sad conclusion was well known—the incurability of cancer.

⁵⁸¹This identification and interpretation of anomalous single cells is the essence of cytopathology.

⁵⁸²Lawrence Koblenz, "Medicine, God, and Belief Schisms: The Evolution of Fever Causation and Treatment in the Antebellum United States." Unpublished paper, Columbia University, 1996: 6.

Years before improved microtechnique and cellular staining enhanced the accuracy of microscopical studies, Lebert's consummate 1845 cytology atlas, *Physiologie Pathologique*, challenged unbelievers like Müller who refused to accept the singularity of the cancer cell.⁵⁸³ Lebert's "corps fusiformes fibroplastiques" drew particular contention, for he held that the intracellular cigar-shaped bodies could be found only in cancer cells.⁵⁸⁴ These microscopic elements represented an early example of the power of the microscope to polarize opinions on just *what* the viewer thought he saw through the eyepiece. Lebert's later work on cancer, published in 1851 as *Traité Pratique des Maladies Cancéreuses, &c*, continued his focus on the unique nature of the cancer cell and became a milestone for the pathoanatomical studies of tumors in Europe and America for many years to come. Indeed, the discord over the question of the uniqueness of the cancer cell created adumbrations of future controversies. Thus, although the improved microscope projected a reproducible, real image on the mind's eye, the interpretation of that image could vary greatly. The battle for the interpretation of microscopical cancer had been joined. It soon involved America.

The Controversy Moves West

Francis Donaldson

Hermeneutical arguments on the nature of cancer and the cancer cell also stimulated debate in the United States. It was not a widespread controversy, for well into the nineteenth century American physicians questioned the value of medical microscopy and microscopists in the States lagged behind those of Europe (especially France and then Germany) in both number

⁵⁸³The full citation is *Physiologie Pathologique ou Recherches Cliniques, Experimentales Et Microscopiques Sur L'Inflammation, La Tuberculisation, Les Tumeurs, La Formation Du Cal, Etc.* (Paris: J. B. Bailliere, 1845). Hajdu includes a copy of the title page and representative drawings in Hajdu, "Cytology," 671.

Edward J. Parker elucidated many of the elements of the unique-cancer-cell debate in an 1855 article. See Edward H. Parker, ed., "Use of the Microscope in the Diagnosis of Cancer," *The American Medical Monthly* 3, no. 2 (1855).

⁵⁸⁴Rather, *The Genesis of Cancer*, 110.

and expertise. Nonetheless, by the middle of the century, a handful of American mavericks advocated the value of the microscope in medical research.⁵⁸⁵ A still smaller subset investigated tumors microscopically, although most microscopists in general agreed on its application to the investigation of cancer.

Francis Donaldson, whose prophetic (although unheeded) writing on cancer microscopy in 1853 urged homegrown physicians to consider the utility of the microscope in patient care, was one of these early American pioneers. An intellectual disciple of Lebert, he set out “to test...the accuracy of (Lebert’s) statements” in his plea for the “Practical Application of the Microscope to the Diagnosis of Cancer.”⁵⁸⁶

Donaldson’s micropathoanatomical study of cancer cells is more an encomium on the work of Lebert than a critical analysis of the European’s interpretations and conclusions. Rather than start without prejudice and systematically attempt to verify Lebert’s findings, Donaldson adopted Lebert’s assumptions on the anatomical classification and uniqueness of cancer cells and from there extended the Parisian’s classification. Lebert, for example, divided “morbid growths” into three varieties—cancerous tumors, fibroplastic tumors, and epithelial tumors.⁵⁸⁷ Donaldson further subdivided cancer-cell types into caudated cells, fusiform cancer-cells, concentric cancer-cells, and “the Compound or Mother-Cell of Cancer.”⁵⁸⁸ Donaldson drew his own pictures of these representative cells, but when his personal experience with a cancer-cell type was limited, he proved his intellectual indebtedness to Lebert by borrowing one of the Frenchman’s

⁵⁸⁵James Cassedy and Deborah Jean Warner identify many of these early American microscopical researchers in Cassedy, "The Microscope in American Medical Science.", Warner, "Antebellum Medical Microscopy."

⁵⁸⁶Donaldson, "Microscope and Cancer," 51.

⁵⁸⁷Ibid., 54.

⁵⁸⁸Ibid., 61-62.

drawings.⁵⁸⁹ In this vanguard American journal article, Donaldson showed that he had grasped the essence of mid-century European cancer microscopy and its literature—the starting-point for much American cancer research in the nineteenth century.

As Donaldson manifested his affinity for Lebert, so he criticized Müller’s disparagement of the existence of a unique cancer cell. Donaldson did not attack Müller directly. Instead, he faulted the German’s source material. Donaldson proclaimed that Müller, whom he deferentially referred to as “the distinguished physiologist,” saw only part of the whole because he trusted the wisdom of others rather than his own investigations.⁵⁹⁰ “He did not find a constant element in cancer,” wrote Donaldson, “because he considered as unquestionably cancer, what the surgeons had extirpated as such. He observed the tumours, but not the patients.”⁵⁹¹ Thus, concluded Donaldson, Müller erred in a fallacy of circular reasoning—his microscopical specimens revealed cancer because the surgeons who had extirpated them had already diagnosed them as malignant. Müller’s conclusions, implied Donaldson, supported the then-current misguided terminology of cancer rather than its biologic nature. Donaldson argued that this was misleading and prejudiced Müller’s microscopical interpretations and classifications. Further, it clouded Müller’s judgment on the uniqueness of the cancer cell—in part, thought Donaldson, because many of Müller’s surgical specimens were not cancer at all. Solely researching cells on a slide was insufficient and potentially fraught with error.⁵⁹² Instead, argued Donaldson, Müller and his

⁵⁸⁹Ibid., 62 and Plate II. Fig. 2. The plate reproduced Lebert and Donaldson’s interpretation of the concentric cancer cell—a cell with a prominent nucleus and nucleolus.

⁵⁹⁰Ibid., 50.

⁵⁹¹Ibid.

⁵⁹²There is more than a bit of irony here, for Müller had advised the public in a commemorative 1836 lecture that medical students “should learn (by example, not by precept) how to combine clinical findings and pathologic anatomical findings at the bedside”—especially with respect to cancer. See Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 11.

fellow cancer investigators must extend their sphere of observation to both the removed tissue and the bedside examination of the patient—the tumor *in situ*. Only then can the micropathologist validly conclude whether the specimen is or is not cancer. And then he can he decide whether the cancer cell is or is not unique.

Müller’s “great merit,” Donaldson acknowledged, “was in leading the way.”⁵⁹³

Nevertheless, the Baltimorean alleged, micropathologists had moved past the pioneer work of Müller. The Berlin anatomy professor had struggled to differentiate cancer from growths of all types on the basis of the appearance of the cancer cell. The young progressives who succeeded Müller undertook the finer task of describing the geometrical and other characteristics of different cancer cells as well as their nuclear and nucleolar inclusions. In addition, Donaldson sought to unify the nature and language of cancer based upon microscopy and the unique cancer cell. “It is improper to attempt to divide cancer into so many species [such as the scirrhus, encephaloid, colloid, and fungus hæmatodes tissue-based varieties of his day—LK] as they all have the same common pathology.”⁵⁹⁴

Samuel David Gross

Francis Donaldson was not the only American enamored of Lebert’s theory of the uniqueness of the cancer cell. The versatile Samuel Gross, who portrayed the gloomy prognosis in his *On the Results of Surgical Operations in Malignant Diseases* to the American Medical Association in the Spring of 1853, shared the Baltimorean’s admiration for Lebert. In part, Gross’s belief derived from his expansive vision of the surgeon in medicine. More than a generation before the acceptance of medical microscopy in the everyday life of the practitioner,

⁵⁹³Donaldson, “Microscope and Cancer,” 51.

⁵⁹⁴Ibid., 55.

Gross wrote that “surgeons must be pathological anatomists, and pathological anatomists must be microscopists.”⁵⁹⁵ Despite his pessimism on the ability of surgery to cure cancer, Gross recognized that the diagnosis of cancer without the microscope was laden with inaccuracy and danger. Whereas Donaldson worried about cancer micropathologists’ lack of clinical correlation, Gross worried about surgeons’ microscopical inexperience. “The cancer-cell,” he wrote, “must be found, recognized, and unraveled; mere external appearances must pass for nothing.”⁵⁹⁶ Once found, the diagnosis of cancer would follow, because “All carcinomatous growths have a peculiar structure, of which a particular cell, now usually known as the cancer-cell, is the distinctive feature.”⁵⁹⁷ From whom did Gross learn this? “We are indebted to Lebert,” he openly acknowledged.⁵⁹⁸

Gross went one step further. He differentiated malignant from benign cancer cells, for the difference between tumors of these two natures, he held, was a difference of degree, not kind. Declared Gross: “The malignity of the morbid growth is generally in proportion to their number and the perfection of their development.”⁵⁹⁹

Donaldson & Gross

Donaldson and Gross exhibited the hallmark of the medical scientist—asking the right questions. Although their questions would be debated and argued for generations to come, their efforts to bring European ideas to America—and to ask the right questions—started researchers

⁵⁹⁵S. D. Gross, M. D., “On the Results of Surgical Operations in Malignant Diseases,” *Transactions of the American Medical Association* 6 (1853): 9-10.

⁵⁹⁶*Ibid.*, 10.

⁵⁹⁷*Ibid.*, 11.

⁵⁹⁸*Ibid.*

⁵⁹⁹*Ibid.*

on the path toward the discernment of the uniqueness of the cancer cell and its relationship to the “normal” cell.

Twentieth-century physicists sought to develop a unified theory of the universe based upon the known nuclear, electromagnetic, and gravitational forces of their day. Similarly, Donaldson believed in a unified theory of the cancer cell. He also knew that the microscope was the key to understanding its nature. Likewise, Gross found the use of the microscope in cancer medicine interesting and intriguing,⁶⁰⁰ but Donaldson championed its use unreservedly. The Baltimore micropathologist entreated medical men of all persuasions in the United States (where, he admitted, “the practical use of the instrument is not generally understood in its application to medical science”⁶⁰¹) to use the microscope for clinical as well as investigational purposes. He urged the adoption of the microscope in medicine based upon its potential ability to reveal the unknown—the very foundation and singularity of cancer.

Over the course of the nineteenth century, use of the microscope advanced the study of cancer from the descriptive to the analytic. Prescient thinkers like Donaldson even applied his interpretation of microscopic cancer to attempt to reconstruct the disease *de novo* from its elements, something that Robert A. Weinberg and colleagues would achieve in the laboratory a century and a half later.⁶⁰² Despite the reluctance of clinicians to adopt the medical microscope in mid-century, Donaldson’s efforts and brilliance did not languish unappreciated for long. In 1881, almost thirty years after the publication of “The Practical Application of the Microscope to the Diagnosis of Cancer,” *The New-York Times* editorialist (despite misspelling the

⁶⁰⁰Dr. Gross concluded that “what the microscope and animal chemistry, guided by the hand of modern science, may do for the subject, it would perhaps, be premature to predict.” *Ibid.*, 160-61.

⁶⁰¹Donaldson, “Microscope and Cancer,” 44.

⁶⁰²William C. Hahn and Robert A. Weinberg, “Review Article: Mechanisms of Disease: Rules for Making Human Tumor Cells,” *The New England Journal of Medicine* 347, no. 20 (2002).

microscopist's name⁶⁰³) could not imagine his degree of understatement when he maintained that Donaldson's paper "never received due credit for his researches."⁶⁰⁴ Nevertheless, the early American proponent of cancer microscopy lived until 1891—long enough to witness the routine use of the microscope for the diagnosis of cancer.

Early Medical Microscopy:

The Biopsy

One of the reasons for the slow adoption of the microscope by the medical community in the nineteenth century involved the nature of microscopy itself. Microscopy is a process of many steps. Although the cell is the ultimate unit of histological as well as cytological analysis, the landscape in the two microscopic examinations is different. In cytology, the cell is the primary focus. Cells may be harvested by many means, including aspiration and biopsy. In histology, the cell *and* the company it keeps are essential to diagnosis. The biopsy is crucial.

The modern-era biopsy, the use of which Donaldson defended as early as 1853 as essential to cancer medicine, probably began in 1847 in Strasbourg, France. Emile Kuess, a professor of physiology there, took the equivalent of "punch biopsies"—small, round pieces of tissue excised by a sharp instrument from beneath the skin—for microscopical examination for cancer. The description of his surgical procedure⁶⁰⁵ from an 1847 issue of the *Monthly Journal of Medical Science* could have been written for a textbook of today: "On plunging this instrument into a tumor to any depth, we can extract a minute portion of the tissue of which its various layers are composed. In this manner a microscopic examination of the tumour can be

⁶⁰³The *Times* article cited him as Dr. Donalson. New York Times, "Cancers—Microscopic Diagnosis: Donalson's and Smith's Papers on (Editorial)," 4:6.

⁶⁰⁴*Ibid.*, 4:7.

⁶⁰⁵By definition, biopsy is a surgical procedure because it removes tissue from the body.

practiced on the living subject, and its nature ascertained before having recourse to an operation."⁶⁰⁶

Nevertheless, few practitioners at the time were so sanguine. Clinicians considered biopsies unhelpful (at the very least) for most of the nineteenth century. Early acceptance of the diagnostic biopsy was limited to cancer researchers, pathologists, and those rare physicians who served as all three. Several reasons, many of which coalesce in the main ideas of the above discussion, explain its poor reception. The fundamental reason was the widespread rejection of the microscope by practitioners who believed that microscopical diagnoses were more likely to be wrong or misleading than right.

Much of the skepticism surrounding the value of the biopsy followed problems with the procurement and handling of the tissue specimen itself. First, tumorous tissue from a living patient was difficult to obtain without pain and risk. Even in Europe, few advocated antisepsis until the 1870s.⁶⁰⁷ Anesthetics and analgesics abated pain, but they relied on potentially injurious chemicals like ether and chloroform and alcohol and opium, respectively. Their side

⁶⁰⁶Editor, *Monthly J. Med. Sci.*, 1847, 7: 853-855, as cited by Wright, "Relationship of Surgical Oncology and Pathology in Early 20th Century America," 247. Unfortunately, such biopsies for micropathological diagnosis often took weeks to prepare for viewing. Thus, they could not aid the surgeon at the time of operation unless a second procedure took place weeks hence. Thus, a "positive" biopsy—which confirmed the serious nature of the disease—required a second, potentially deadly, operation. Rapid microscopical diagnosis with the frozen section, which allowed definitive surgery based upon a microscopical diagnosis at the time of the initial surgical biopsy, lay decades in the future.

⁶⁰⁷Examine the career of Ignaz Philipp Semmelweis (1818-1865), who reported the contagious nature of puerperal ("childbed") fever around 1846-1847 (several years after Oliver Wendell Holmes presented his 1842 paper "On the Contagiousness of Puerperal fever" to the Boston Medical Society). Semmelweis went mad in his unsuccessful attempt to convince his obstetrical colleagues that *they* transmitted disease from one pregnant woman to another. In his frustration, Semmelweis' brain, according to Henry Sigerist, "failed" and he was admitted to a lunatic asylum. (Holmes faced similar opposition in America, but reiterated his views in an 1855 paper entitled "Puerperal Fever as a Private Pestilence.") In a scenario that only Dante could conjure up, the immediate cause of Semmelweis' death was an infection acquired by contact during a medical procedure. For a highly readable account of the tragedy of Ignaz Semmelweis and the futility of his early advocacy of antisepsis, see Sigerist, *The Great Doctors*, Chapter 41, especially pp. 356-58. In another coincidence, Joseph Lister applied his first antiseptic wound dressing in 1865—the year of Semmelweis' death. See Owen H. Wangensteen, "Preludes to Lister and the Interdependence of the Sciences," *Surgery* 58 (1965): 931, 33. Holmes lived until 1894, long enough to enjoy the vindication of his contagion theory—unlike Semmelweis.

effects were usually unmanageable and sometimes deadly. Second, preparative microtechniques, especially before the widespread adoption of mechanical microtomes in the second half of the century, were cumbersome, time-consuming, and limited in their ability to reproduce anomalies for reliable comparison with other specimens.⁶⁰⁸ Inconsistencies abounded. Third, successful tissue procurement and preparation did not assure easy analysis. Prior to knowledge of the chemistry and cell-organelle targeting of stains, “reading” a biopsy was difficult. Inaccuracies were common.

Early biopsies often led to erroneous microscopical interpretations and diagnoses. This diminished their acceptability and thus their utility to practitioners. Improvements in the procurement and processing of biopsies awaited the flowering of microbiology later in the century, which spurred advances in many of the facets of microtechnique. Given the difficulties with the histological biopsy, it is therefore not surprising that cytopathology dominated histopathology among cancer micropathologists for much of the nineteenth century. Cytological specimens were easier to obtain than tissue biopsies, required little preparation, rendered less confusion in interpretation, and were less complicated to learn and teach.

Nevertheless, the concept of tissue diagnosis had always been intellectually compelling. As biopsies became safer, microtechniques improved, and new theories and practices of surgery buttressed the value of the tissue biopsy, ideas became realities. Theory and technology drove practice.⁶⁰⁹ The next chapter will explore the three great “A”s of late nineteenth-century

⁶⁰⁸As late as 1893, W. Thelwall Thomas complained that even though advances in microtechnique (including fixation and staining) had sped up slide preparation considerably, it still took too long. Two to three weeks were still often required. Instead, he suggested the use of a freezing microtome to produce a specimen akin to a frozen section in hours rather than weeks. See Thomas, "A Note on Rapid Methods of Preparing Sections for the Microscope," 491, 493.

⁶⁰⁹Economic considerations played a role in nineteenth-century practice as in contemporary medicine. Nevertheless, economics was a less important factor in cancer medicine during the nineteenth century than today and is not the focus of this argument.

surgery—Anesthesia, Analgesia, and Antisepsis—that vaulted surgery from the last-ditch effort to salvage Fanny Burney to the curative operation on Grover Cleveland. In the process, surgery became a first-line consideration in the algorithm of cancer medicine. Firmly founded on the cognitive transformation from the theory of whole-body constitutionalism to focused localism, the biopsy came of age with the realization of possibility (safer surgery) and probability (the local nature of disease).

**American Biopsy Pioneer:
The Rise and Fall
of
Dr. Joseph Janvier Woodward
(1833-1884)**

By the third quarter of the nineteenth century, researchers in Europe supported the tissue biopsy and its microscopical analysis as the most accurate method for the diagnosis of cancer.⁶¹⁰ In the United States, advocacy and acceptance came more slowly. Nevertheless, one American physician in particular championed tumor biopsy and furthered Donaldson’s plea for the value of the microscope in cancer medicine. In the process, that physician carried the medical analysis of tumorous diseases to the dawn of the modern era. His name—U. S. Army Lieutenant Colonel Joseph Janvier Woodward.

Woodward was born into the Philadelphia of the early 1830s that Alexis de Tocqueville analyzed on his sojourn in the United States. The Frenchman attempted to capture the American spirit for a European readership. Woodward returned a portion of the favor a generation later

⁶¹⁰In this regard, I include total tumor excision as a form of biopsy. Total excision remains the best “specimen” for accurate diagnosis for most pathologies.

when he transplanted European ideals of medical microscopy to the practice of medicine in the United States.⁶¹¹

J. J. Woodward is most famous for his authorship of the medical sections of the Civil War classic, *Medical and Surgical History of the War of the Rebellion*.⁶¹² Nevertheless, his interest in cancer micropathology long preceded the Second American Revolution.⁶¹³

Woodward never explained the basis of this interest, but two of his professors at the University of Pennsylvania appear to have deeply inspired his proclivity for microscopy generally and cancer microscopy specifically.⁶¹⁴ William Edmonds Horner (1793-1853), dean of the medical faculty at Penn, wrote the first American text on pathological anatomy and has been credited by at least one medical historian with introducing medical microscopy to America.⁶¹⁵ Woodward's interaction with Horner was limited, but in 1843-1844 Dean Horner published a treatise on histological anatomy accompanied by an anatomical atlas. Included were microscopical illustrations drawn by Henry Hollingworth Smith (1815-1890).⁶¹⁶ Professor Smith was a great influence on young Woodward, with whom he seems to have worked closely.⁶¹⁷

⁶¹¹I find de Tocqueville particularly compelling with regard to the ideas of information transmission and cognitive inertia. Among his many notable quotations, he wrote that "I cannot help fearing that men may reach a point where they look on every new theory as a danger, every innovation as a toilsome trouble, every social advance as a first step toward revolution, and that they may absolutely refuse to move at all for fear of being carried off their feet." Alexis de Tocqueville, *Democracy in America*, vol. 2, pt. 3, ch. 21 (1840). This insight is an apt description of the relationship of the microscope to cancer medicine in America prior to the last years of the nineteenth century.

⁶¹²John Shaw Billings, "Memoir of Joseph Janvier Woodward," *Biographical Memoirs* 2 (1886): 298.

⁶¹³Among others, Charles A. Beard and James P. McPherson subtitled the Civil War the "Second American Revolution." See Charles A. Beard and Mary R. Beard, *The Rise of American Civilization*, First ed., 2 vols., vol. 2 (New York: The Macmillan Company, 1927), Chapter XVIII, James M. McPherson, *Abraham Lincoln and the Second American Revolution* (New York: Oxford University Press, 1991).

⁶¹⁴Henry W. Edmonds, "Woodward and the Changing Concept of Cancer, 1858-1873," *Military Surgeon* 109 (1951): 314.

⁶¹⁵William Edmonds Horner, *A Treatise on Pathological Anatomy* (Philadelphia: Carey, Lea & Carey, 1829). The historian is Deborah Jean Warner and the incident was Horner's microscopic examination of the gastrointestinal tracts of cholera victims in 1835. See Warner, "Antebellum Medical Microscopy," 368.

In 1853, fresh out of medical school, Woodward's aptitude for microscopy afforded him an early opportunity to make a living. Like Oliver Wendell Holmes before him, Woodward gave private lessons in both microscopy and histopathology.⁶¹⁸ Microscopy was becoming wildly popular among the public, with one contemporary writing about a "microscope mania."⁶¹⁹ In the medical sphere, microscopic pathology was a rising discipline in a select group of American medical schools as in Europe, the medical mecca for postgraduate studies at the time.⁶²⁰ Within a few years, Woodward became a noted member of the Pathological Society of Philadelphia, rubbing shoulders with Samuel D. Gross, one of its founders.⁶²¹ Dr. Henry Smith, however, remained his chief mentor. Throughout his career, Woodward's fastidiousness in the laboratory and in his writings mimicked that of his mentor Henry Smith—as did his interest in cancer.⁶²² Almost all of Woodward's initial cancer and "pathological histology" published reports drew on Smith's surgical pathology specimens.⁶²³

⁶¹⁶William Edmonds Horner, *Special Anatomy and Histology* (Philadelphia: Lea & Blanchard, 1843), Henry Hollingworth Smith, *Anatomical Atlas, Illustrative of the Structure of the Human Body* (Philadelphia: Lea & Blanchard, 1844).

⁶¹⁷Edmonds, "Woodward and the Changing Concept of Cancer, 1858-1873," 314, 15.

⁶¹⁸Billings, "Joseph Janvier Woodward," 297.

⁶¹⁹Warner, "Popular Microscopy," 7.

⁶²⁰Dr. Horner played no small role in the development of "minute anatomy" in the United States. See Warner, "Antebellum Medical Microscopy," 371. Joseph Leidy, also an anatomist at the University of Pennsylvania, added to the interest in microscopic anatomy with the publication of his *The Flora and Fauna within Animals*, a study of animal parasites, in 1853. See Foster, *A Short History of Clinical Pathology*, 31. Nevertheless, as late as 1870, microscopy (including histopathology) was only taught in optional demonstration courses at the University of Pennsylvania. See Edward T. Morman, "Clinical Pathology in America, 1865-1915: Philadelphia as a Test Case," *Bulletin of the History of Medicine* 48 (1984): 203.

⁶²¹Edmonds, "Woodward and the Changing Concept of Cancer, 1858-1873," 315.

⁶²²*Ibid.*

⁶²³*Ibid.*

During the 1850s, the necessary underpinnings for the use of the biopsy in America lay undeveloped and overseas. Basic microtechnique and staining in the States were, at best, primitive. Woodward, through his interest in tumor micropathology, improved the foundations of microscopy and became perhaps the first to establish the scientific study of the cause and microscopic anatomy of cancer in the United States.⁶²⁴ Between 1858 and 1860, the twenty-something Philadelphian published ten medical papers, eight of which included biopsied cancer specimens and their microscopic appearance.⁶²⁵

The Civil War diverted Woodward from the study of cancer, but his enthusiasm for microscopy remained unabated. He joined the Union Army in 1861 and was appointed to the Surgeon-General's office in Washington, D.C. in 1862 where, with minor digressions, he spent the rest of his life. Shortly after his appointment in the Capitol City, he was assigned to assist Dr. John H. Brinton, who served Surgeon General William Hammond, in the collection of battle-related medical specimens for a proposed military museum. That humble beginning evolved into the esteemed National Museum of Health and Medicine of the Armed Forces Institute of Pathology.⁶²⁶ The years 1864 and 1865 at the newly-instituted Army Medical Museum were most productive for Woodward and initiated his greatest contributions to the science of medical microscopy and cancer medicine—viz., photomicrography and aniline staining.

⁶²⁴Schoenberg wrote that Woodward's 1873 cancer lecture "represents the beginning, in the United States, of objective research into the nature of neoplastic disease." See Bruce S. Schoenberg, "Joseph Janvier Woodward and an Early American View of Cancer," *Surgery, Gynecology, and Obstetrics* 136, no. 3 (1973): 456. I believe, however, that the work of Oliver Wendell Holmes, Waldo Irving Burnett, and Samuel David Gross, all of which began in the early 1850s, years before Woodward's, represented "objective research" in the neoplastic diseases. Had Dr. Schoenberg limited his statement to the scientific microscopical documentation of cancer, I would agree with him.

⁶²⁵The other two papers were on tuberculosis and a "heart clot." Billings provided a list of Woodward's publications in chronological order. See Billings, "Joseph Janvier Woodward," 300-07. Billings's list of Woodward's 1858-1860 publications is on page 300.

⁶²⁶Butler, *Butler, Cancer*, 44.

The Heliostat and the Beginnings of American Photomicrography

The frequent erroneous diagnoses of cancer under the microscope distressed Woodward.⁶²⁷ He sought to devise an advanced technological system that would minimize such errors, even if he could not directly rectify the cognitive problem of wrongful interpretation. In 1864, his staunchly-held belief in the value of the microscope in the diagnosis of cancer led him to devise a photomicrographic system that was the best of its day.⁶²⁸

Although Lebert had pioneered photography through the microscope two decades earlier, Woodward—unlike Lebert—used reproducible machine-made parts, stimulated by the demands of the Civil War, to construct a “heliostat.” This jumble of metal and mirror (akin to the light reflector on a modern microscope) captured the rays of the sun and relayed them through the lenses of a horizontally-oriented microscope. As Woodward described it, the lenses then projected the magnified image onto a photographic plate that could be positioned at the precise focal point of the multiple lenses so as to record an undistorted likeness of the specimen.⁶²⁹

The final product was a photograph of the magnified image that provided a static objectivity missing from the usual slide examination. Gone was the in-and-out-of-focus projection common during viewer-adjusted microscopy. Woodward froze his best-focused images in time on durable photographic plates. As he justifiably demonstrated in later cancer lectures, several observers could interpret one of his high-quality microphotographs at the same

⁶²⁷Billings, "Joseph Janvier Woodward," 298.

⁶²⁸Woodward was assisted by Dr. Edward Curtis, with whom he also collaborated on Abraham Lincoln's autopsy. Interestingly, Lincoln's postmortem was limited to the President's head. Schoenberg, "Joseph Janvier Woodward and Cancer," 456.

⁶²⁹See Joseph Janvier Woodward, "On Microphotography with High Powers," *Quarterly Journal of Microscopical Science, London* vi (1866): 165 and Joseph Janvier Woodward, "On Photo-Micrography with the Highest Powers, as Practiced in the Army Medical Museum," *American Journal of Science and Arts, N. Haven* xlii (1866): 189.

time, thereby eliminating one contribution to inter-observer variability.⁶³⁰ Years later, microscopists continued to admire the results of the compulsiveness and attention to detail that went into the creation of Woodward's photomicrographs. In 1883, *The American Monthly Microscopical Journal* crowed that Woodward's apparatus created "the finest photographic work with the microscope that has yet been seen."⁶³¹

America Takes Up Aniline Dyes

Colonel Woodward was also a pioneer in the use of microscopy dyes. Around 1864, he became the first to apply aniline dyes to microscopical staining in America.⁶³² Although F. W. Beneke in 1862 in Germany may have been the first to employ such dyes to stain microscopical specimens in Europe,⁶³³ Woodward initiated their use on the western side of the Atlantic. His paper "On the use of aniline in histological researches, with a method of investigating the histology of the human intestine," reveals his desire to integrate chemistry and histopathology a decade before the early exploits of the multi-color-fingered Ehrlich.⁶³⁴

⁶³⁰Image preselection for photography had and has its downside. What if the chosen biopsy section was not representative of the underlying pathology? Other microscopists scanning the prepared specimen might have discovered better areas for photographic display. Here the skill and experience of the photomicrographer were (and are) of paramount importance.

⁶³¹The American Monthly Microscopical Journal, "The Army Medical Museum," *The American Monthly Microscopical Journal* 4 (1883): 237.

⁶³²Edmonds, "Woodward and the Changing Concept of Cancer, 1858-1873," 318.

⁶³³Clark and Kasten, *History of Staining*, 42.

⁶³⁴The complete citation is J. J. Woodward, "On the Use of Aniline in Histological Researches, with a Method of Investigating the Histology of the Human Intestine, and Remarks on Some of the Points to Be Observed in the Study of the Diseased Intestine in Camp Fevers and Diarrhoeas," *American Journal of Medical Science* n.s. 49 (1865). Note that Woodward's investigation of camp fever on the microscopic level took place at the same time that Lister worried about contagion in another part of the world. Camp fever and contagion were not definitively linked in the mid-1860s. Camp fever, now known to be a variant of epidemic typhus caused by *Rickettsia prowazeki* and transmitted by body and head lice, was particularly virulent during the inhuman conditions of war.

The closeness in time of Woodward's adventures in photomicrography and aniline dye staining was not coincidental. Stains highlighted selected elements of photomicrographs, making them easier for an observer or audience to see and, hopefully, correctly interpret. Woodward's exploits in microscopical photography and chemistry moderated the evils of misdiagnoses caused by poor microtechnique. In addition, they persuaded some physicians in the United States to use the biopsy in the diagnosis of cancer. The visible results of his labors, delivered in a landmark lecture in the early 1870s, underscored the importance of his earlier successes.

The First Toner Lecture:

The Adolescence of Cancer Microscopy in the United States

Colonel Woodward's research in the fields of cancer, photomicrography, and staining culminated in his epochal March 28, 1873 lecture "On the Structure of Cancerous Tumors and the Manner in Which Adjacent Parts are Invaded."⁶³⁵ This was the first Toner Lecture, presented in the red-brick Gothic building that then constituted the Smithsonian Institution. Dr. Joseph M. Toner—philanthropist, lecture sponsor, and later President of the American Medical Association—was a prominent Washington physician who included among his friends and colleagues Woodward and J. Marion Sims.⁶³⁶

⁶³⁵Joseph Janvier Woodward, *On the Structure of Cancerous Tumors and the Mode in Which Adjacent Parts Are Invaded* (Washington: Smithsonian Institution, 1873).

⁶³⁶The prodigious Toner Collection at the Library of Congress contains numerous books and manuscripts, including many of the papers of J. Marion Sims. The final document in the Sims file in the Toner Manuscript Collection, dated December 5, 1874, is his resignation letter to the Board of Governors of the Woman's Hospital precipitated by the refusal of the Governors, at the behest of the Ladies' Board, to allow Sims to admit cancer patients. A copy of the letter and other comments on Sims' relationship with Toner may be found in *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 7 folder 113 "Sims, J. Marion; Toner Collection, 1873-1881," and *Memorial Hospital Archives*, Record Group 500 Hayes Martin Collection, Box 7 folder 109, "Sims, J. Marion: Biographical 1847-1962."

Dr. J. M. Toner later wrote Woodward's "Necrology" for the *Journal of the American Medical Association*. See J. M. Toner, "Necrology: Joseph Janvier Woodward," *Journal of the American Medical Association* 3 (1884).

The cancer histopathologist delivered the lecture soon after President Grant's second inaugural and during one of the first days of Spring.⁶³⁷ In a sense, his remarks and slides represented the beginning of a new era in the micropathology of cancer. His achievement lay not in joining others in proposing yet another cancer cure—for such were numberless and uniformly without merit⁶³⁸—but in his mastery of the European cancer literature and the application of the scientific method to the study of cancer in America.

True to the ideal of the natural scientist that he was, Woodward began his lecture by disclaiming knowledge of the cause or cure of cancer that seemed the major preoccupation of researchers and charlatans of the age. "The time has not yet come," he noted at the beginning of his lecture, "for any one to tell why cancers originate or how they can be prevented or cured."⁶³⁹ Nevertheless, he remained deeply interested in causation because he believed it held the key to cure. His lecture, derived like much American research pathology of the day from the leading lights of Europe, recapitulated the pathogeneses of cancer proposed by Müller, Rokitansky (blastema beginnings), Virchow (connective-tissue corpuscles), Thiersch (epithelial origins), Waldeyer (who generalized Thiersch's concept), and Classen (leukocyte migration). Woodward expressed qualifications about Classen's theory, but it was the most recent postulate on the cause of cancer and so had special importance for an American physician who, like so many others at

⁶³⁷President Grant was inaugurated for his second term on March 4, 1873, little more than three weeks prior to Woodward's lecture.

⁶³⁸For an example of an old-fashioned, well-publicized cancer cure in the early 1870s—firmly intertwined with money and politics—see the various writings on Cundurango, a cancer-cure wonder drug touted by many including President Grant's first-term Vice President, Schuyler Colfax. See, for example, Flores & Wing, Copies of letters, 1871. A fascinating story about the drug and its origins may be found in New York Times, "Cundurango, as a Remedy for Internal Cancer-----," *The New York Times*, 10 June 1871. Dr. W. S. W. Ruschenberger provided an excellent, if primitive, scientific analysis of this miracle medicine that mesmerized the print media for a good decade. See W. S. W. Ruschenberger, M.D., "A Report on the Origin and Therapeutic Properties of Cundurango," (Washington: Government Printing Office, 1873).

⁶³⁹Woodward, *On the Structure of Cancerous Tumors*, 1.

the time, stood in awe of European (and especially German) medicine. It was also appealing because it linked cancer to the latest knowledge on the avidly investigated and very fashionable topic of inflammation.⁶⁴⁰ Woodward syncretized the essence of cancer as the “transformations and degenerations” of cells—an idea firmly grounded in the works of Müller, Lebert, Virchow, and their students.⁶⁴¹ He concluded his opening section on the cause of cancer with an explanation more prescient than he could have imagined. Cancer, he concluded, could be explained “by the ordinary normal laws of development and growth.”⁶⁴²

Woodward strongly believed that ignorance of cancer causation or cure should not thwart investigative efforts into the nature of the disease, for the problem of cancer was real and growing. He warned that the recently completed 1870 United States Census reported in excess of six thousand cancer deaths, more than ever before.⁶⁴³ This was an enormous number at the time and, in a world of developing quantitative epidemiology, he had no explanation for it. Nevertheless, Woodward’s early realization of the growing incidence of cancer made him one of the first in America to acknowledge the problem and discuss it in an open forum. A generation

⁶⁴⁰A. Classen, “Über ein Cancroid der Cornea und Sclera, ein Beitrag zur Entwicklungsgeschichte der Carcinome,” *Virchows Arch. Pathol. Anat.*, 1870, 50: 56, as cited by Schoenberg, “Joseph Janvier Woodward and Cancer,” 460, 62.

⁶⁴¹Woodward, *On the Structure of Cancerous Tumors*.

⁶⁴²*Ibid.*, 35. Recent work into the molecular biology of the neoplastic cell implicates normal processes of cellular growth and development (run amuck through “transformations and degenerations”) in cancer causation. For a very readable but rapidly aging account of modern-day investigations into the cause of cancer, see Robert A. Weinberg’s scientific *One Renegade Cell* and the autobiographical *Racing to the Beginning of the Road*. Robert A. Weinberg, *One Renegade Cell: How Cancer Begins*, First Edition ed., *The Science Masters Series* (New York: Basic Books, 1998), Robert A. Weinberg, *Racing to the Beginning of the Road: The Search for the Origin of Cancer* (New York: W. H. Freeman and Company, 1998).

⁶⁴³Conforming to the gendered conception of cancer in Victorian America, Woodward tabulated 2,301 male deaths from cancer and 3,923, almost twice as many, among women. See Woodward, *On the Structure of Cancerous Tumors*, 1.

later, the problem of cancer would bewitch the minds and hearts of laymen and researchers alike with wonder and excitement, as well as fear and dread.⁶⁴⁴

Woodward, dissatisfied but unbowed by the poor state of current knowledge of the cause, cure, or statistics of cancer, continued on to his forte—the micropathology of cancer. Indeed, the real strength of Woodward's remarkable presentation lay in his exhibition of cancer biopsy photomicrographs. The heliostat, horizontal microscope apparatus, and aniline dyes served him well, for his seventy-four plates created a veritable nineteenth-century atlas of breast cancer when such compilations were rare.

Not surprisingly, given his meticulousness, Woodward emphasized the criticality of microtechnique. Adequate specimen preparation—from sectioning to staining—required an attention to detail that could be developed only with care and practice. Nothing less than the future of cancer research depended upon painstaking microtechnique, he believed, for the micropathological misdiagnosis of non-malignant lesions as cancer—one of the *bête noires* of medical microscopy in the eyes of many practitioners—enabled quacks to claim cures where there was nothing that needed to be cured. Caustics, poultices, and plasters held out easy, but false, hope to those truly suffering from cancer. Patients misdiagnosed with cancer on the basis of faulty microtechnique or microscopic misinterpretation received unnecessary treatment and inflated the charlatan's boastful claims. Further, Woodward averred, poor microtechnique caused scientific investigations into the nature of the disease to suffer. Should microtechnique fail or confound medical practitioners, the work of his life—technical and meticulous to the verge of compulsion—would count for naught. Careful microtechnique and the faithful capture

⁶⁴⁴An excellent example is the epidemiologic and scientific account of W(illiam) Roger Williams, *The Natural History of Cancer with Special Reference to Its Causation and Prevention* (London: William Heinemann, 1908), 51-59.

of the microscopic image onto the photographic plate for all to see and from which all could learn were essential to the acceptance of the biopsy in the diagnosis of cancer in America.

Woodward's Toner Lecture of 1873 captured the young but vigorous spirit of cancer research in America. He drew heavily upon European investigations into the disease, but added something new and different through the visual clarity of his photomicrographs and the dawning approach to research and teaching that they represented. His honesty in disclaiming knowledge where there was none was a fresh breeze in a stale atmosphere often saturated with false claims and hyped hopes. Above all, his meticulous process, technological savvy, and honest interpretive temperament augured well for the study of cancer through biopsy and microscopy in the United States—if not for Woodward personally.

An American Tragedy

The acclaim Woodward received for his heliostat, stained cancer preparations and fastidiously captured images on micrographs contributed to his ultimate downfall, depression, and demise.⁶⁴⁵ Indeed, his fame tragically caused him to be involved in a world-altering event that began on a hot Washington morning in the early summer of 1881. That incident, on July 2, 1881, was the assassination attempt by “madman” Charles Guiteau on the life of James A. Garfield, President of the United States. As a major figure in the Surgeon-General's office, President of the American Medical Association, and a physician famous for his literary and technological skills, the White House immediately involved Dr. Woodward in the care of the wounded President.

⁶⁴⁵During the late nineteenth century, professional achievement and respect were often measured by the societies to which one had been elected. At the time of his death at a relatively young age of fifty, Woodward had been elected President of the American Medical Association (1881), President of the Washington Philosophical Society, member of the National Academy of Sciences, the Association for the Advancement of Science, the College of Physicians of Philadelphia, and the Academy of Natural Sciences of Philadelphia—among others. See Billings, "Joseph Janvier Woodward," 299.

Woodward was forty-seven years old and at the height of his career when the delusional office-seeker's bullets⁶⁴⁶ cut down the President at the Washington train depot on that fateful Saturday at the start of the Independence Day weekend.⁶⁴⁷ The noted surgeon-micropathologist J. J. Woodward was one of several doctors who attended the President.⁶⁴⁸ They were led by Dr. D. W. Bliss, the doomed Garfield's personal physician.⁶⁴⁹

Nationwide controversy erupted almost immediately in the press and in medical circles over the diagnosis and treatment of the President. Should the physicians locate the bullet? Should they remove the bullet? Was surgical exploration indicated? How should it be

⁶⁴⁶Guiteau fired two shots. One grazed the President's arm, but the other penetrated his back between the tenth and eleventh ribs on the right side. See D. W. Bliss et al., "Record of the Post-Mortem Examination of the Body of President J. A. Garfield, Made September 20, 1881, Commencing at 4.30 P. M., Eighteen Hours after Death, at Francklyn Cottage, Elberon, New Jersey," *The American Journal of the Medical Sciences* 82 (1881): 401, Stanley A. Fish, "The Death of President Garfield," *Bulletin of the History of Medicine* 24 (1950): 380.

⁶⁴⁷A little-known irony is that James A. Garfield received the Republican nomination for President only after the failure of none other than Ulysses S. Grant to attain his Party's nomination for a third term. Charles E. Rosenberg, *The Trial of the Assassin Guiteau: Psychiatry and Law in the Gilded Age* (Chicago: University of Chicago Press, 1968), 1. Had the Republican Stalwarts been more successful in promoting their two-term President to a third consecutive term, Woodward's demise—as well as Garfield's—might have been very different.

⁶⁴⁸Stewart Fish reported that there were six "original" attending surgeons, including J. J. Woodward. Nevertheless, consultants from Philadelphia (including Dr. David Hayes Agnew of Thomas Eakins' famous "Agnew Clinic" painting) and New York (Dr. Frank H. Hamilton) and elsewhere, swelled the numbers to the theatrical "circus" noted by General Grant less than four years later. Fish, "The Death of President Garfield," 381, 386. Also in regard to Presidential attendants, see the next footnote. In addition, it must be emphasized that General Grant's months-long cancer agony lacked a major element that contributed an important epilogue to Garfield's medical ordeal—the carnival-like trial of Charles Julius Guiteau. For further trial details, see Rosenberg, *The Trial of the Assassin Guiteau*.

⁶⁴⁹Many well-wishers and self-aggrandizers—including physicians, inventors, sanitary engineers, Congressmen, and others—made Garfield's two-and-a-half month terminal ordeal into the media frenzy that General Grant desperately sought to avoid in 1885. Among those attending President Garfield were Dr. Fordyce Barker, who had a role in the care of many Presidents, including Grant; Dr. George Shrady (later another of Grant's consultants), who wrote "Surgical and Pathological Reflections on President Garfield's Wound"; Alexander Graham Bell, the recent inventor of the telephone (1876), whose efforts to find a non-invasive instrument to locate the bullet led to the development of the modern metal detector; and George Waring, the sanitary engineer whose report on the (un)sanitary features of the President's "home hospital" in the Executive Mansion set off the White House sanitation scandal, a condemnation—partly political and partly a genuine concern about the miasmatic conditions—of the antiquated plumbing. On Shrady's interaction with Garfield, see Richard Goldhurst, *Many Are the Hearts: The Agony and Triumph of Ulysses S. Grant* (New York: Thomas Y. Crowell Company, 1975), 146. On Bell, see "Unsolved History," *Discovery Channel*, broadcast August 26, 2003, 20:00-21:00 ET. On George Waring and the White House sanitary scandal, see Nancy Tomes, *The Gospel of Germs: Men, Women, and the Microbe in American Life* (Cambridge, MA: Harvard University Press, 1998), 68-74.

performed? Who should perform it? Was the President otherwise sufficiently healthy to undergo such an operation? As time passed they added: What was the source of his recurrent fevers? The unsolicited wisdom of second guessers and arm-chair quarterbacks flooded the pages of the popular and medical press. Everyone had an opinion, but Woodward and his medical colleagues had to make the tough decisions and take the real actions that made them fully accountable in the event of a poor outcome.

Soon after the shooting, the President began to develop fevers. The question of possible infection from the “ball” (as the bullet was called) arose.⁶⁵⁰ Theories of germs were beginning to influence American medical thought, but they were by no means prevalent.⁶⁵¹ As the President commenced recurrent high fevers, physicians both within and without the treating group urged immediate extraction of the bullet. Others believed exploration would only reduce Garfield’s possibility of survival. Initially, Woodward sided with those who argued in favor of exploration and bullet removal. This faction hoped that withdrawal of the bullet would eliminate the cause of the febrile episodes, although the exact reason why it should do so remained a matter of dispute.⁶⁵² Antiseptic—let alone aseptic—technique was not observed.⁶⁵³ While the debate

⁶⁵⁰The attending physicians also considered the possibility that the President, like his wife, was suffering from malaria, which was still prevalent in the swampland that was Washington, D. C. at the time. Accordingly, Garfield received quinine sulfate (along with copious quantities of morphine) as part of his therapy. Fish, “The Death of President Garfield,” 382. The accepted effect of climate on illness, a common concern in the nineteenth century, encouraged the President’s removal to “escape the malarious influence of the Washington climate at this season.” On September 6, 1881, a special train transported the President to his summer home near Long Branch, New Jersey—also the warm-weather retreat of General Grant. See Fish, “The Death of President Garfield,” 385.

⁶⁵¹Fish, “The Death of President Garfield,” 379. Dr. Fish dealt specifically with the case of President Garfield. For more general attitudes toward germ theory in America, see, for example, Phyllis Allen Richmond, “American Attitudes toward the Germ Theory of Disease (1860-1880),” *Journal of the History of Medicine and Allied Sciences* 9 (1954). and Nancy Tomes’ answer/rebuttal to Richmond in Nancy J. Tomes, “American Attitudes toward the Germ Theory of Disease: Phyllis Allen Richmond Revisited,” *Journal of the History of Medicine* 52 (1997).

⁶⁵²Dr. Barnes opposed efforts to remove the bullet. He argued that many Civil War veterans lived long, healthy lives with bullets in them. Barnes may well have been correct, for Garfield’s autopsy revealed that the bullet had become “encysted”—safely sequestered within a walled-off cyst. The cause of death was determined to be a

raged, Surgeon-General Joseph K. Barnes devised a clever, make-shift air conditioning system that blew air over the surface of ice blocks to cool the febrile patient.⁶⁵⁴

Woodward and many of his colleagues did not believe in the principles of Listerism.⁶⁵⁵ He and the other physicians in the treatment group repeatedly explored the wound with dirty, uncovered fingers and poor sanitary technique. The first probing occurred only minutes after the shooting at the railroad station.⁶⁵⁶ One homeopathic physician, possibly a relative or friend of the President, ran to the White House after hearing of the shooting, turned Garfield on his side, and stuck his filthy finger into the wound. He proclaimed, remarkably, "My God, General! You ought to have surgical advice."⁶⁵⁷ Surely, Major General Garfield had no lack of surgical advice, but unclean fingers planted the seeds of infection into his back early and frequently.

The press and many in the medical establishment castigated Woodward in particular for his dirty probing, for he was one of the best known members of the group. They thought he should know better, but Woodward was not convinced that germs on his fingers could cause

ruptured aneurysm of the splenic artery, which may have been set in motion by the initial, bullet-induced trauma to the large artery. See Fish, "The Death of President Garfield," 388, Leo Rosenhouse, "White House Doctor," *Private Practice* (1972): 62.

⁶⁵³Dr. D. W. Bliss, the physician in charge of the President's medical care, concluded that "most approved antiseptic dressings were used during the entire progress of the case," but the evidence recited in the next paragraph supports my contention that antiseptic conditions were not followed. See D. W. Bliss, "Report of the Case of President Garfield, Accompanied with a Detailed Account of the Autopsy," *The Medical Record* 20, no. 15 (1881): 399.

⁶⁵⁴Rosenhouse, "White House Doctor," 62. U. S. Navy engineers implemented the plan on July 10. In all, half a million pounds of ice were used to lower the President's temperature over the course of his illness. Rosenberg, *The Trial of the Assassin Guiteau*, 9.

⁶⁵⁵Mary C. Gillett, "Woodward, Joseph Janvier," in *American National Biography Online* (Oxford University Press, 2000), 2.

⁶⁵⁶Rosenberg, *The Trial of the Assassin Guiteau*, 3.

⁶⁵⁷J. Collins Warren, "Case of President Garfield: Statement of Dr. J. Collins Warren," *Boston Medical and Surgical Journal* 105, no. 20 (1881): 464.

Garfield was the commanding Colonel of the 42nd Ohio Volunteer Infantry during the Civil War. His bravery during the Battles of Shiloh and Chickamauga led to his promotion to Major General of the Volunteers. As Civil War heroes like Grant were often referred to by their military rank rather than their political station, so many called Garfield 'General' rather than 'President.'

disease. He responded by compulsively detailing a record of the President's condition. He posted updates to his journal on a daily and sometimes hourly basis. Lacking a clear path of action, the record-keeping may have served as an outlet for frustrated inaction. Others conjured up more nefarious reasons.⁶⁵⁸

Eventually, Dr. Bliss, the group leader, argued against surgical exploration and Woodward reluctantly agreed. The medical attendants probed the main wound, but they concurred that surgical exploration to extract the ball was too dangerous.⁶⁵⁹ Garfield rallied, then failed. Again he rallied and again he failed. Fever continued to recur intermittently. The press had a seemingly never-ending story—the likes of which General Grant and others later sought desperately to avoid—that filled each day's newspapers. After a long and tortuous illness, filled with rancor and even cries of malpractice, the President died on September 19th.

Woodward co-signed the "Official Bulletin of the Autopsy on the Body of President Garfield"⁶⁶⁰ and published "The Official Record" of Garfield's autopsy.⁶⁶¹ His report concluded that the immediate cause of death was a ruptured splenic artery. Perhaps the pistol ball caused the initial damage that led to the fatal hemorrhage. Perhaps the abdominal infections weakened the arterial wall. Those familiar with the medical controversies of the case knew, however, that the major problems for most of the President's course were the pus, draining sinuses, and

⁶⁵⁸An anonymous editorialist at the time wrote in Woodward's obituary that the micropathologist created the detailed record "to publish as a defense, if such were needed, at some future time." Anonymous, "Obituary of Surgeon Joseph Janvier Woodward, U. S. A.," *Medical News* 45 (1884).

⁶⁵⁹Bliss, "Report of the Case of President Garfield," 398-99.

⁶⁶⁰J. J. Woodward, et. al., "Official Bulletin of the Autopsy on the Body of President Garfield," *The Medical Record* 20 (1881). As noted in Footnote 621, Woodward also took part in the limited postmortem on President Abraham Lincoln. Thus the Colonel was the only pathologist ever to have participated in the autopsies of two presidents. Edmonds, "Woodward and the Changing Concept of Cancer, 1858-1873," 329.

⁶⁶¹J. J. Woodward, "Official Record of the Post-Mortem Examination of the Body of President James A. Garfield," *American Journal of Medical Science, Philadelphia* 82 (1881).

recurrent fevers that weakened and emaciated the formerly robust Chief Executive. At post-mortem, the bullet track—poked and prodded by so many different fingers and unsterile probes—was filled with pus. Infection raged throughout the abdomen.⁶⁶²

Woodward felt guilty. What if he had stuck to his initial conviction and individually demanded extraction of the assassin's ball? What if his fingers had caused or even contributed to the President's pus-filled cavities? Woodward never recovered from the malpractice charges and emotional anguish he suffered from his possible contribution to the President's death.⁶⁶³ Exoneration by the majority of the medical community that affirmed the "conservative" treatment of the President after his death failed to ease his conscience.⁶⁶⁴

The formerly-prolific physician wrote only one article after his Garfield reports, an unrepresentative valedictory on "Modern philosophical conceptions of life."⁶⁶⁵ The Surgeon General characterized Woodward as "of a sensitive, highly strung, nervous organization," adding, "The confinement, anxiety, and labor to which he was subjected in his attendance upon the late President Garfield during his long illness proved too much for a mind and body already overstrained by incessant [sic] labor and precipitated the illness which finally terminated his life."⁶⁶⁶ Beset by the demons of obsessive-compulsiveness and depression, Woodward traveled

⁶⁶²Bliss et al., "Record of the Post-Mortem Examination of the Body of President J. A. Garfield," 399-400.

⁶⁶³Dr. George F. Shrady, editor of *The Medical Record* (New York) and physician-attendant to President Garfield, General Grant, and Emperor Frederick III, summarized the legal and medical aspects of malpractice. See George F. Shrady, "The Question of Malpractice in the Case of the Late President Garfield," *The Medical Record* 20 (1881). J. Collins Warren, who apparently was not invited to participate in the President's care, penned his own trenchant critique of Garfield's medical management. See Warren, "President Garfield."

⁶⁶⁴According to Shrady, a majority of physicians believed that exploratory surgery on the President was too risky and might hasten the patient's death. See Shrady, "The Question of Malpractice in the Case of the Late President Garfield." Certainly, Shrady agreed that exploratory surgery was dangerous. Nevertheless, criticism of Garfield's medical care was vocal and made good press.

⁶⁶⁵J. J. Woodward, "Modern Philosophical Conceptions of Life," *Bulletin of the Philosophical Society, Washington* 5 (1883). Cited by Billings, "Joseph Janvier Woodward," 307.

abroad—the panacea of the time for ills of all natures—but the attempt failed to cure him.⁶⁶⁷

Depression deepened into melancholia. In 1884, Woodward died in a Pennsylvania sanatorium at the age of fifty-one⁶⁶⁸—possibly a suicide.⁶⁶⁹ His was a spirit broken.

The Legacy of J. J. Woodward

The tragic demise of Dr. Joseph Janvier Woodward did not diminish his indispensable contributions to the micropathology of cancer. His early papers on cancer helped shaped the surgical and pathological debates of mid-century America on the dreaded disease. His use of the heliostat and aniline dyes advanced the technology and applicability of microscopy to cancer. His photomicrographs lent uniformity to the inconstant results and teachings of early American microtechnique. After a war-time hiatus, his return to the micropathology of cancer in 1872 led to the first publication on cancer in the history of the Medical Department of the United States Army.⁶⁷⁰ His 1873 Toner Lecture established a bridge between European theory (especially on cancer causation) and American pragmatism, leading to a better understanding of the disease. His micropathology slide collection began a storehouse of visual texts for generations of students and professors to come. His meticulous attention to detail and dogged pursuit of the scientific method in pathology (though perhaps propelled by his own neuropathology) advanced cancer medicine in America from the cognitive empiricism of his forebears to the scientific rationalism of modern times.

⁶⁶⁶Billings, "Joseph Janvier Woodward," 299.

⁶⁶⁷Gillett, "Joseph Janvier Woodward," 2.

⁶⁶⁸Butler, *Butler, Cancer*, 43.

⁶⁶⁹Gillett, "Joseph Janvier Woodward," 2.

⁶⁷⁰J. J. Woodward, "Report on the Minute Anatomy of Two Cases of Cancer," *Surgeon General's Office* (1872). Cited by Edmonds, "Woodward and the Changing Concept of Cancer, 1858-1873," 318-19.

Woodward's contributions to the micropathology of cancer were not forgotten either by his contemporaries or his successors. In 1881, George F. Shrady concluded that "[Woodward's] testimony concerning microscopical appearances cannot be questioned."⁶⁷¹ Two generations later, James Ewing, the famed pathologist of neoplastic diseases at Memorial Hospital and Cornell University Medical College in New York City, determined upon reviewing Woodward's oeuvre that "one cannot help expressing admiration for a man who collected pathological material under such difficulties and then submitted it to an analysis and study which in scientific scope and detail has hardly been surpassed in American literature."⁶⁷² The collection of cancer microscope slides he began with the Army Medical Museum grew into the renowned repository at the Armed Forces Institute of Pathology.⁶⁷³ Thus it was befitting of the accomplishments of the man that when ground was broken for the construction of part of the Walter Reed Medical Center in the mid-twentieth century—long after the acceptance of the biopsy, microtechnique, and photomicrography he propounded and defended as tools in the fight against cancer—imbedded within the shaft of the spade used to break that ground was one of Lieutenant Colonel Joseph Janvier Woodward's microscope slides.⁶⁷⁴

“Clinical Biopsy”—An Oxymoron?

Dr. Woodward was a man ahead of his time. Nevertheless, his forward-thinking advocacy of the biopsy for cancer diagnosis, in contradistinction to his overly conservative medical treatment of President Garfield, gained only slow acceptance in America. By the time

⁶⁷¹George F. Shrady, "Surgical and Pathological Reflections on President Garfield's Wound," *The Medical Record* 20, no. 15 (1881): 405.

⁶⁷²Butler, *Butler, Cancer*, 43.

⁶⁷³*Ibid.*, 43-44

⁶⁷⁴*Ibid.*, 44.

of Woodward's death in 1884, as shown in the case study of General Grant, clinical assessment—governed by inspection, palpation, and the long-term course of the disease—still dominated cancer diagnosis. Microscopical examination for cancer played at most an ancillary diagnostic role. The accurate diagnostic interpretation of the tissue biopsy remained in doubt. On the other side of the Atlantic, however, surgical and political developments were brewing that would erode practitioner resistance to acceptance of medical microscopy and the clinical/surgical (as opposed to pathological) biopsy and make the microscope the center of cancer diagnosis.

That turning point in microscopical cancer diagnosis, based upon developments in the 1870s, played out in dramatic fashion in Europe in the late 1880s. Indeed, by the early 1890s, advances in surgery changed the venue of many cancer operations from residential kitchens and bedrooms to specialized hospital suites.⁶⁷⁵ Specimen removal from surgical patients became safer and more tolerable. Further, the biopsy evolved into a routine part of the operation rather than an infrequent venture fraught with additional risk. Microtechnique improved cancer biopsy-slide preparation to a level of detail and uniformity unknown a generation before. In the United States, these developments caused medical practitioners to give microscopical biopsy diagnosis a fresh look. As distinct from past generations, clinicians now based microscopically-determined diagnoses upon the (living) biopsy rather than the (dead) postmortem specimen. Nevertheless, as in so many developments in medicine in the nineteenth century, Europe, not America, was the epicenter and catalyst of change.

From ridicule to *de rigueur*:

The Development of the Surgical Biopsy

⁶⁷⁵I do not know how many non-emergency cancer operations were performed on boats in the 1890s, but I suspect very few. For obvious reasons, the venue of President Cleveland's operation was exceptional.

The clinical biopsy for cancer obtained at the time of surgery had achieved prominence in Europe only a few years earlier. In the 1870s, Carl Ruge, a gynecologist at the Women's Hospital in Berlin, began to use the biopsy for all his neoplastic diagnoses.⁶⁷⁶ He dubbed it "Stuckendiagnose," thus encompassing both process and goal in one word. His justification for the clinical biopsy, which placed him at odds with the standard *modus operandi* of the medical community at the time, evolved from his insightful observation that more than fifty percent of the clinically-assessed cancer diagnoses of a prominent colleague were microscopically unconfirmable.⁶⁷⁷ Ruge's perception was that microscopical diagnosis, theretofore rooted in the pathological rather than the surgical, more accurately and consistently differentiated benign from malignant tumors than clinical observation alone. Rather than accept the authoritarianism of the elder gynecologists, Ruge argued that microscopic diagnosis based upon biopsy at surgery should become the gold standard of cancer diagnosis. For his advocacy and routine use of the diagnostic biopsy (and steadfastness in the face of prodigious opposition), historians rewarded Ruge with the appellation "Father of the Biopsy."⁶⁷⁸

In the early 1880s, Ruge and his associate Johann Veit brought into doubt the custom of the country when they suggested that curetted tissue—more akin to swabs than swaths—could also be used to diagnose cancer microscopically.⁶⁷⁹ This idea further rankled the establishment, in part because the dominant concept of cancer pathology at the time held that cancer could only

⁶⁷⁶Wright, "Surgical Pathology," 317.

⁶⁷⁷The physician in question—the "leading Berlin gynecologist," as George Rosen called him—was Carl Schroder. Ruge found that Schroder misdiagnosed ten of twenty-three (43.5%) cervicouterine tumors as malignancies. George Rosen, "History of Pathology: Beginnings of Surgical Biopsy," *American Journal of Surgical Pathology* 1 (1977): 362.

⁶⁷⁸Wright, "Relationship of Surgical Oncology and Pathology in Early 20th Century America," 247. Wright's sources for this appellation are Voker Becker, "100 Jahre stucken-diagnose," *Arch. Gynecol.*, 1979, 227: 193-204; Robert Meyer, "Carl Ruge," *Zbl. Gynak.*, 1926, 25: 1618-1625; and George Rosen, "Beginnings of surgical biopsy," *Am J. Surg. Pathol.*, 1977, 1: 361-364.

⁶⁷⁹Wright, "Surgical Pathology," 317. Also see Rosen, "Beginnings of Surgical Biopsy," 362.

be considered in the presence of tissue invasion or metastasis.⁶⁸⁰ Scooped tissue was less likely to reveal invasion or metastasis than regular specimens that tended to be larger and contain more tissue. Ruge and Veit argued that cancer could be diagnosed from the appearance of a cell or small group of cells rather than requiring the later-stage tissue invasion or proof of distant spread. Hidden within this argument was the ghost of the earlier nineteenth-century concept of the unique cancer cell.

Ruge and Veit offered a compelling argument for biopsy-based cancer diagnosis, but it might not have won over the majority of practicing physicians—especially in America—had it not been for the tragedy of the heir apparent to the throne of the powerful German Empire. The watershed event in the development of the clinical biopsy followed a prince of a man with a most sanguine future—perhaps, as some have written, a savior of peace in a Europe ravaged by intermittent wars who could be destined to alter the course of world history.⁶⁸¹ This man of concord and conciliation became the reluctant vessel in which the battle was fought over the utility of the microscope in the diagnosis of cancer. The outcome reverberated throughout international political and medical circles and greatly influenced the course of cancer history. The trials and tribulations of that heir, Crown Prince Friedrich—macroscopic and microscopic, nationalistic and individualistic—solidified the modern microscopical diagnosis of cancer.⁶⁸²

⁶⁸⁰Perhaps the most famous application of this concept was Rudolf Virchow's erroneous diagnosis of 'no cancer' on the biopsy specimens of Crown Prince Friedrich of Germany in 1887. See below.

⁶⁸¹R. Scott Stevenson, *Morrell Mackenzie: The Story of a Victorian Tragedy* (London: William Heinemann, Ltd., 1946), 1 and W. David McInnis, William Egan, and J. Bradley Aust, "The Management of Carcinoma of the Larynx in a Prominent Patient, or Did Morell Mackenzie Really Cause World War I?," *The American Journal of Surgery* 132 (1976): 515, R. Scott Stevenson, *Morell Mackenzie: The Story of a Victorian Tragedy* (London: William Heinemann, Ltd., 1946), 1. McInnis, et. al. derived much of their paper from Stevenson, *Morell Mackenzie*.

⁶⁸²Crown Prince Friedrich, Crown Prince Frederick, Crown Prince Friedrich Wilhelm, Emperor Friedrich III, Kaiser Frederick III, and Frederick the Noble were all one and the same. German 'Friedrich' is English 'Frederick' or 'Frederic.' I have opted to use the name by which his countrymen knew him best.

A Prince's Tragedy: Cancer Unhinges Europe and the Biopsy

In January, 1887, less than two years after General Grant died of throat cancer, Crown Prince Friedrich, a fifty-five-year-old liberal, fish-out-of-water democrat in the politically-charged, conservative climate of Chancellor Bismarck's Germany, began to suffer hoarseness, which affected the lustrous singing voice of which he was so proud.⁶⁸³ The gravelly voice, as an isolated symptom, was no surprise, for, like many Victorians, he indulged in pipe smoking, which was a cultural phenomenon.⁶⁸⁴ (If any physicians connected pipe smoking with throat cancer at the time, that association was unconvincing to the majority.) In time, however, his medical history became an impetus to the destruction of the already-weakened foundations of traditional cancer.

The events that followed the onset of Friedrich's "cold" illustrate many of the transitional elements that affected the nature of cancer diagnosis and treatment on both sides of the Atlantic in the late nineteenth century. The new trend toward microscopical cancer diagnosis based upon surgically-obtained biopsy tissue, of which President Cleveland's case study was an example, nevertheless at the same time retained some of the old diagnostic and treatment model that was dominated by clinical assessment, as in General Grant's medical history. Indeed, the case of the Crown Prince led to new viewpoints on the microscopical definition of cancer, that at the same time damaged the exalted reputation of the grand master of Western pathology—Rudolf Virchow—and shattered the fragile ego of the celebrated "father of British laryngology"—Morell Mackenzie. Indeed, the tragedy of Prince Friedrich was as much a study in medical personalities as it was a milestone in the history of cancer.

⁶⁸³Much of the story of the last two years of Friedrich's life is drawn from the works of Sir Morell Mackenzie, *The Fatal Illness of Frederick the Noble* (London: Sampson Low, Marston, Searle & Rivington, 1888), McInnis, Egan, and Aust, "Frederick William's Cancer.", Stevenson, *Morell Mackenzie*.

⁶⁸⁴TIME The Weekly Newsmagazine, "Cancer Man Ewing: He Wants Six \$10,000,000 Weapons.," *TIME*, 12 January 1931, 24.

Prince Friedrich, a pawn among kings and queens in the chess game of nineteenth-century European politics, was a complicated man. He was a devoted dove in a nest of hawks; a neo-socialist in post-Metternich autocratic Europe; and a kind, generous, and almost reticent soul embedded within a milieu of militarism. He was not inexperienced at war, for, despite his pacific proclivities, he fought many battles as the scion of a belligerent father.⁶⁸⁵ Nevertheless, like Grant and Cleveland, he found himself bewildered and dependent upon others in the face of personal, life-threatening disease.

Hoarseness Persistent

For two long months after the onset of hoarseness the Crown Prince procrastinated in seeking medical advice, despite worsening symptoms. Like General Grant before him, Friedrich's postponement emphasizes the time lag between symptom onset and medical examination that was common in the nineteenth century. In March, 1887, Dr. Wegner, the Prince's personal physician, sensed from Friedrich's behavior that something more than a common cold afflicted this patient and intervened.

Wegner consulted Dr. E. Gerhardt, a renowned laryngologist at the Royal University in Berlin. Professor Gerhardt performed the Prince's first of many direct vocal cord examinations on March 16. The German laryngologist was dismayed to find a growth on the left vocal cord. It was relatively small, measuring about 2mm by 4mm.⁶⁸⁶ The Professor, who used the only recently-available but by then-standard cocaine as topical anesthesia, attempted to obtain a biopsy. This was the first of many unsuccessful snare biopsy attempts on the vocal cord

⁶⁸⁵The belligerent was Friedrich's father, Emperor Wilhelm I of Germany. Probably Friedrich's greatest military victory came at the beginning of the Franco-Prussian War. On August 4, 1870, Prussian forces under his command defeated the French at Weissenberg, Bavaria. Chancellor Bismarck had provoked the War only weeks before with his re-working of the conciliatory "Ems telegram" from then-King-of-Prussia Wilhelm I to the French.

⁶⁸⁶Ten millimeters equal one centimeter. One cm is less than 4/10ths of an inch. Thus the growth was about 1/10th of an inch in size—surely a difficult lesion to discern without excellent exposure, lighting, and magnification.

lesion.⁶⁸⁷ Despite his inability to garner biopsy tissue, Gerhardt concluded that the growth was “polypoid thickening”—a poorly-defined description of a tumor that owed more to clinical tradition than scientific diagnosis.⁶⁸⁸

As Friedrich failed to improve, frustration mounted and many more German physicians were called upon to attend upon the Prince. On April 7, 1887, they decided to apply the new electro-galvanic cautery (used on President Cleveland six years later by his surgeons) to fulgurate (destroy by electric current) the suspicious lesion. Gerhardt noted that the tumor “looked benign” (although he was already thinking “cancer”) but the onset of odynophagia (painful swallowing) and poor healing of the cautery site worried him.⁶⁸⁹

To Cut, To Cure: Surgery Recommended

Another month passed and the patient continued his downward spiral. Alarmed by increasing voicelessness and the enlarging, recurrent-after-fulguration vocal cord lesion, the Prince’s physicians sought yet another opinion. On May 15, Dr. Ernst von Bergmann, a highly-regarded Professor of Surgery in Berlin, advised complete operative extirpation of the growth. He neither visualized the lesion with indirect laryngoscopy nor sought biopsy material. Instead, he based his recommendation solely upon descriptive information provided to him by Gerhardt. The German physicians, finally relieved by von Bergmann’s suggestion for definitive treatment, scheduled surgery for the very next day.⁶⁹⁰

⁶⁸⁷A ‘snare biopsy’ utilizes a wire loop to lasso an abnormal-appearing growth. The tumor is cut off by pulling the loop tight around the lesion and is then submitted for pathological processing and microscopical interpretation. Biopsy types are often described by how they are obtained. These include needle biopsy, excisional biopsy, incisional biopsy, and punch biopsy. (Note: “Punch biopsies” are not obtained with fists. The biopsy in this last case is obtained by piercing or “punching” the lesion directly with a special instrument (e.g., punch biopsy forceps) that extracts a small, cylindrical specimen.)

⁶⁸⁸McInnis, Egan, and Aust, "Frederick William's Cancer," 516.

⁶⁸⁹Ibid.

⁶⁹⁰Ibid., 517.

Prince Otto von Bismarck, long-term Chancellor of the German Empire he worked so hard to create, heard of the planned operation and, concerned with the rush toward potentially life-threatening surgery, immediately informed the patient's father. Emperor Wilhelm I intervened, cancelled the planned tumor extirpation, and sought three additional opinions from his own medical advisors. On May 18, Dr. Von Lauer, Wilhelm's personal physician and medical director of the German army; Dr. Schrader, Surgeon-in-Ordinary to the Crown Prince; and Professor Tobald, an experienced and well-respected laryngologist based in Berlin, examined Friedrich. Tobald was so certain of his clinical interpretation that he concluded the lesion "could be considered cancer without any other diagnosis."⁶⁹¹ Surgery, he warned, should proceed forthwith.⁶⁹² The three consultants then unanimously agreed to recommend to the Crown Prince and his father that the larynx should be opened and the growth removed.⁶⁹³

True to the tradition of the time, the three new consultants made the diagnosis solely on clinical grounds. In this case, though, enough time had passed from the initial examination of the tumor so that the patient's medical course supported the clinical diagnosis of cancer. Time, as with many clinical entities, narrowed the diagnostic possibilities. Indeed, several factors, as valid today as they were then, contributed to the diagnosis: the growth recurred rapidly after what Gerhardt believed was his galvano-cautery-induced "destruction" of the lesion; the cautery site healed poorly—if at all; the tumor manifested an uneven, hard ("scirrhous") surface; the inner surface of the growth exhibited a persistently raw (irritated, unhealthy) appearance; the vocal cords became immobile; and, very importantly, there was no evidence that the problem

⁶⁹¹Stevenson, *Morell Mackenzie*, 68.

⁶⁹²Chloroform was the proposed anesthetic.

⁶⁹³Stevenson, *Morell Mackenzie*, 68.

could be explained by confounding diseases (especially tuberculosis and syphilis).⁶⁹⁴ None of this evidence, however, involved microscopical examination of biopsies from the lesion, an omission of little import to the Prince's German physicians as long as their diagnosis was unanimous, so no single advocate of surgery could be held accountable.

On the surface, the German consultants had little to lose with their prescription for surgery. If the laryngeal lesion was malignant and the Prince survived the surgery and its aftermath, they were heroes. If the tumor was benign (which they could not know without an accurate micropathological interpretation) and the patient lived, none would be the worse for it. What would occur, however, if the Prince did not survive the surgery or, if he did, his quality of life was compromised? What, for example, if he permanently lost his euphonious voice? This last was the Germans' concern, for the interweaving of medicine and politics complicated the situation dramatically.

Laryngeal Cancer: Nineteenth-Century Diagnosis and Treatment

The prescription for surgery was not to be taken lightly in 1887. Surgical removal of a growth on the vocal cord did not become routine until the twentieth century.⁶⁹⁵ The German

⁶⁹⁴McInnis, Egan, and Aust, "Frederick William's Cancer," 517, Stevenson, *Morell Mackenzie*, 68-69.

It is quite likely that Friedrich contracted syphilis during the Prussian military campaign of the late 1860s, but the role played by (what would be tertiary) syphilis in the Emperor's demise is unclear. Stevenson went so far as to suggest that "on careful examination of the available evidence there is more than a suspicion that the cancer supervened upon syphilis." See Stevenson, *Morell Mackenzie*, 164.

Medical historian-physician Dr. Robert J. Ruben of the Albert Einstein College of Medicine and New York City recalled, in a private conversation I had with him on April 4, 2005, that sources in his possession pointed toward syphilis as the primary cause of Emperor Friedrich's death. Thus far, I have not seen conclusive evidence to that effect. Findings at Friedrich's postmortem, noted by Stevenson, appear to refute this possibility but nevertheless leave room for doubt. See Stevenson, *Morell Mackenzie*, 134-35, 65. It is most likely that the Emperor died with syphilis but from cancer.

Nonetheless, the reader should recall that cancer microscopy was still in its formative years when Friedrich died. Furthermore, the diagnosis of syphilis was itself subject to the inconsistencies of clinical diagnosis until the advent of more objective tests in the twentieth century.

More pertinent to the matter at hand, however, is that those around Emperor Friedrich III *believed* he had died from cancer, not syphilis. In the study of history, what *was* is often less important than what was *thought to be*.

⁶⁹⁵During the last decade of the twentieth century, surgical excision for bulk removal of a cancerous larynx was itself replaced to a large extent by chemotherapy and radiotherapy. At present, laryngectomy is often reserved

physicians, in their operative recommendation, demonstrated an aggressiveness uncommon at the time. In the late 1880s, the larynx could be surgically approached externally (through the neck) or, less frequently, internally (through the mouth). The latter was relatively new, as Manuel Garcia had become the first to visualize the living vocal cords with a laryngeal mirror—a six-franc modified dentist's reflector—only in 1854.⁶⁹⁶ Although by the 1880s, physicians commonly used the laryngoscope, as it had become known by then, for clinical diagnosis, few operators were skilled in the use of the laryngoscope as an adjunct to the internal approach. On the other hand, the external approach found favor for ease of access and ready exposure of the pathological site.

The first reported excision of a laryngeal tumor was achieved externally by Koderik in 1750.⁶⁹⁷ In 1844, the Parisian physician Charles Henry Ehrmann surgically removed a laryngeal polyp—a protuberant mass with a broad base that appeared to grow up from the surface.⁶⁹⁸ Gurdon Buck, an American surgeon operating in New York City, reported the first definite laryngeal cancer operation in 1853,⁶⁹⁹ but the first successful cancer resection of the larynx did not occur until 1863. The surgeon who performed that Civil War-era resection was Henry B.

for "salvage." Everett E. Vokes and Kerstin M. Stenson, "Perspective: Therapeutic Options for Laryngeal Cancer," *The New England Journal of Medicine* 349, no. 22 (2003).

⁶⁹⁶Stevenson, *Morell Mackenzie*, 30-33. Garcia (1805-1906) was a Spanish singing teacher who lived and worked in London for most of his career. In September, 1854, he devised the reflecting mirror later called the laryngoscope after noting the true image of the sun reflected off the windows of the Palais Royal while he was strolling through its gardens and thinking how useful visualization of the vocal cords would be for a singing teacher. King Edward VII invested Garcia, later known as the "father of laryngology," with the honorific title of C. V. O.—Commander of the Royal Victorian Order—on his hundredth birthday.

Garcia's description of his invention can be found in his Manuel Garcia, "Physiological Observations on the Human Voice," *Proceedings of the Royal Society of London* 7 (1856).

See also David Charles Schechter and H. Mason Morfit, "The Evolution of Surgical Treatment of Tumors of the Larynx," *Surgery* 57, no. 3 (1965): 462.

⁶⁹⁷Schechter and Morfit, "The Evolution of Surgical Treatment of Tumors of the Larynx," 461.

⁶⁹⁸Lee, ed., *Dates in Oncology*, 31.

⁶⁹⁹Gurdon Buck, "On the Surgical Treatment of Morbid Growths within the Larynx," *Transactions of the American Medical Association* 6 (1853).

Sands, later one of General Grant's consultants.⁷⁰⁰ The real trailblazer, however, who benefited from the new tools of anesthesia and antiseptics, was another student of Johannes Müller—the Prussian-born Viennese surgeon Theodor Billroth.⁷⁰¹ He performed a successful laryngectomy on the last day of 1873, and pioneered surgical procedures for cancer in many different organ systems.⁷⁰² His daring, avant-garde techniques⁷⁰³ are followed to this day.⁷⁰³ Nevertheless, neither the German physicians nor the royal family consulted Billroth.

Laryngectomy, the proposed treatment for the Crown Prince's clinical diagnosis, remained a relatively new and dangerous procedure in the 1880s. The early use and utility of surgery derived from the fear that large laryngeal tumors could block the upper airway, leading to suffocation, hemorrhage, and a horrible death. On the other hand, the aphonia (voicelessness) that followed many "successful" laryngectomies devastated patients. In addition, survival rates—even in an era when, for some, "cure" was defined as post-operative discharge (rather than five-year survival)—were dismal. The first laryngectomy cancer cure (defined as multi-year survival without recurrence) did not occur until 1875.⁷⁰⁴ Even then, the operation probably would not have been successful without Trendelenberg's invention in 1871 of the inflatable

⁷⁰⁰John A. Kirchner, "A Historical and Histological View of Partial Laryngectomy," *Bulletin of the New York Academy of Medicine* 62, no. 8 (1986): 808.

⁷⁰¹Billroth, *The Medical Sciences in the German Universities*, v-vi. Introduction and biography by William Henry Welch.

⁷⁰²Schechter and Morfit, "The Evolution of Surgical Treatment of Tumors of the Larynx," 463-66.

⁷⁰³The "Billroth II" operation for persistent or life-threatening peptic ulcer disease (a common "treatment" until the advent of histamine-2 blockers in the late 1970s and proton pump inhibitors in the 1980s), creates a Roux-en-Y anastomosis and bypasses part of the stomach. Today, the Billroth II is sometimes performed for bariatric (weight-loss) surgery.

The English laryngologist, R. Scott Stevenson believed, however, that Billroth's 1873 triumph was performed on a patient with tuberculosis, not cancer. This may be another example of a mistaken microscopical cancer diagnosis. See Stevenson, *Morell Mackenzie*, 39.

⁷⁰⁴Schechter and Morfit, "The Evolution of Surgical Treatment of Tumors of the Larynx," 465, 69, and 76 Footnote 9.

tracheostomy cuff to prevent intra-operative aspiration. Indeed, death from surgery was the rule rather than the exception in the operative treatment of laryngeal tumors.⁷⁰⁵ As late as the early 1880s, the intra-operative mortality alone exceeded fifty percent.⁷⁰⁶ Thus, the planned surgical extirpation of the Crown Prince's tumor was not without controversy.

The English Consultant

Not surprisingly, the German physicians' proposed course of treatment went unheeded. The Royal family, frightened by the perils of laryngeal (or any other) surgery, demurred.⁷⁰⁷ Emperor Wilhelm, Bismarck, and Crown Princess Victoria, wife of Friedrich and eldest daughter of Queen Victoria of England, sought not a second, but a *seventh* medical opinion. This time, the opinion would not be German. The Crown Princess asked "Who is the leading English specialist for diseases of the throat?"⁷⁰⁸ Dr. Wegner suggested Morell Mackenzie of London.⁷⁰⁹ The other German consultants agreed. Vicky, as she was known to her friends and family, dispatched an urgent telegram to her mother to have Mackenzie dispatched to Berlin immediately.⁷¹⁰

On the night of May 18, 1887, Dr. James Reid, resident physician to the Queen of England, personally "invited" Dr. Morell Mackenzie, well-known nineteenth-century British laryngologist and author of the most widely-used textbook in the field, to come to Berlin "at

⁷⁰⁵Ibid., 465.

⁷⁰⁶Ibid., 467.

⁷⁰⁷Among known possible adverse consequences of laryngeal surgery at the time were total loss of voice, hemorrhage, infection, and death.

⁷⁰⁸Stevenson, *Morell Mackenzie*, 74.

⁷⁰⁹Ibid., 73.

⁷¹⁰The exact details of who said what to whom and who suggested Mackenzie to whom are uncertain. Stevenson spells out the variations in detail in *ibid.*, 72-76. The importance of precisely who called whom, and when, will become obvious as the political consequences of the Crown Prince's subsequent medical history becomes clear.

once.”⁷¹¹ On the assumption that Dr. Mackenzie would readily concur with their consensus diagnosis, the German physicians scheduled surgery to remove the Crown Prince’s presumed laryngeal cancer for 7 A.M. on Saturday, May 21, 1887 in the New Palace at Potsdam, just outside Berlin.⁷¹²

Medical Politics, Medical Nationalism

The German consultants misjudged Mackenzie. They believed he would simply endorse their diagnosis and treatment plan. They also underestimated the Royal family’s aversion to surgery, for reluctance characterized their inclination from the beginning. The dilemma to operate or not was classic and timeless—the German physicians recommended surgery; the family hesitated and sought additional (and, hopefully, different) advice. In this case, however, the exalted rank of the family compromised the often physician-dominated doctor(s)-patient relationship of the late nineteenth century. The “family,” of course, included the Emperor of Germany and the Queen of England—arguably the two most powerful monarchs in the world at the time. The patient was the Crown Prince, heir to the throne of the aged Emperor.⁷¹³ Could the family have known Mackenzie would only advise surgery with great reluctance? Perhaps—for in his acclaimed *Manual of Diseases of the Throat and Nose Including the Pharynx, Larynx,*

⁷¹¹Of all the notable laryngologists throughout England and the Continent, the choice of Mackenzie to treat the noble Friedrich may seem bewildering. Mackenzie was respected in his circle of physicians, but he was not the caretaker of royalty. Nevertheless, my further investigation revealed that Mackenzie’s 1880 textbook was highly regarded in Germany, that he spoke fluent German (unlike most English physicians), and that Queen Victoria insisted upon an English physician for her daughter’s husband. It should be noted that Dr. Mackenzie did not become Sir Morell until after his consultation in Germany—and before Emperor Friedrich’s death! See *Ibid.*, 12.

In the United States today, Mackenzie is widely known as the “father of British laryngology.” Telephone conversation with Dr. Moses Nussbaum, Chief, Division of Head and Neck Surgery, Beth Israel Medical Center, New York, New York, October 26, 2001. Mackenzie’s major textbooks—Morell Mackenzie, *A Manual of Diseases of the Throat and Nose Including the Pharynx, Larynx, Trachea, Oesophagus, Nasal Cavities, and Neck*, vol. 1 (London: J. & A. Churchill, 1880), Sir Morrel Mackenzie, *Diseases of the Pharynx, Larynx, and Trachea* (New York: William Wood & Company, 1880)., went through several printings.

Quotations from Stevenson, *Morell Mackenzie*, 69.

⁷¹²Stevenson, *Morell Mackenzie*, 69.

⁷¹³Emperor Wilhelm I, Wilhelm Friedrich Ludwig (1797-1888), was 90 years old in 1887.

Trachea, Oesophagus, Nasal Cavities, and Neck, he warned that for surgical cancer treatment in this area “palliative measures alone can be adopted.”⁷¹⁴ Attempts at curative surgery, he suggested, doomed the patient to an earlier demise.⁷¹⁵

The German press was chauvinistically indignant at the thought of an English consultant for the German Prince.⁷¹⁶ They denounced the British laryngologist upon his arrival. The Crown Prince’s six German medical consultants, however, apparently unaware of the Englishman’s anti-surgery proclivity, initially welcomed Mackenzie. Despite the fact that all six German consultants advised extirpative laryngeal surgery, both family and physicians agreed to allow Mackenzie to decide the Crown Prince’s diagnosis and treatment. The Englishman’s opinion would be final.⁷¹⁷ Under the circumstances, it was the politically correct decision, for the forces of international politics far outweighed the patient-physician relationship in this case.

Much rested on the outcome of this great medical drama, for the dovish Crown Prince sought to avoid warfare and the further militarization of Germany while his son and successor, later known to the world (during the First World War) as Kaiser Wilhelm (II), promoted militarism and nationalism, like his namesake and grandfather.⁷¹⁸ In addition, if Mackenzie failed at least to lessen the Prince’s symptoms, charges of medical sabotage could arise that would sunder the fragile international amity Queen Victoria sought to promote with the marriages of her children into the great reigning families of Europe and Russia. The incendiary background and high stakes, coming at the peak of European and, in particular, German-British

⁷¹⁴Mackenzie, *Diseases of the Throat and Nose*, 82.

⁷¹⁵*Ibid.*, 82-83.

⁷¹⁶McInnis, Egan, and Aust, "Frederick William's Cancer," 517.

⁷¹⁷*Ibid.*

⁷¹⁸*Ibid.*, 515.

competition for overseas colonies, natural resources, and new markets, transformed the case of Crown Prince Friedrich Wilhelm from a provincial exercise in nineteenth-century cancer medicine to a turning point in world history.⁷¹⁹

Morell Mackenzie

And

The Mandatory Method of Microscopic Cancer Diagnosis

Mackenzie arrived in Berlin on the afternoon of May 20, 1887 and proceeded immediately to the New Palace at Potsdam.⁷²⁰ It was the day before the scheduled surgery. In addition to his technical skill and talent for writing, he was a physician who kept abreast of the most recent international medical literature—much of it German. Bridging the transition from traditional to modern cancer, he believed that tumor biopsy trumped clinical examination in the diagnosis of laryngeal cancer. His was a minority opinion at the time.⁷²¹ Indeed, Mackenzie believed that surgery without histologic confirmation of cancer was unwarranted and hazardous. In this conviction, the self-righteous Mackenzie had no doubt and would brook no opposition.

Mackenzie made his insistence on the necessity of biopsy tissue for microscopical examination known shortly after arrival. The German physicians did not agree with his diagnostic mandate for histologic proof and, unfortunately, Mackenzie was not a politician deft at compromise. With more haughty confidence than savvy, Mackenzie instructed his colleagues that they had reached their conclusion on “insufficient grounds,” for they had, he later wrote, “omitted...the most obvious means of arriving at a correct diagnosis. The first thing to be done

⁷¹⁹Great Britain and Germany competed directly and indirectly for colonies during the middle 1880s. In 1885, for example, Britain proclaimed a protectorate in Southern New Guinea after Germany annexed the northern part of the island. Tensions between the two powers and their respective allies grew rapidly over the next two decades.

⁷²⁰Stevenson, *Morell Mackenzie*, 76.

⁷²¹*Ibid.*, 79.

was to pick off a piece of the growth through the natural passage and have it examined microscopically by an expert.”⁷²²

Mackenzie, in his *Fatal Illness*, further criticized the German consultants with one of the worst possible indictments of the day—viz., that they practiced unscientific medicine. “My colleagues,” he noted, “had not taken a very first step toward establishing their diagnosis on a scientific basis, nor apparently had they even thought of doing so.”⁷²³ In Mackenzie’s unwavering view of the diagnosis of tumors, the scientific basis of cancer diagnosis—the “positive proof of malignancy”⁷²⁴—was biopsy of the pathological growth followed by microscopical examination—clear and simple. Surgery was postponed.

Personalities

On May 21, the day after his arrival, Dr. Mackenzie graciously offered the honor of performing the biopsy to Gerhardt and Tobold. Both declined. They claimed inexperience with operative forceps. Adding fuel to a smoldering fire further heightened by his outsider status, Mackenzie tactlessly faulted them again. He gibed that a throat doctor who could not use forceps was like “a carpenter who cannot handle a saw.”⁷²⁵

Mackenzie did not know that Gerhardt had tried already to obtain biopsy tissue and failed. He believed that he had no choice but to obtain the biopsy specimen himself from the Crown Prince. He would show the Germans how it was done. Using the then-popular cocaine as a local anesthetic, the English laryngologist succeeded in procuring tissue where the German

⁷²²Mackenzie, *The Fatal Illness of Frederick the Noble*, 14.

⁷²³*Ibid.*, 15.

⁷²⁴McInnis, Egan, and Aust, “Frederick William's Cancer,” 518.

⁷²⁵Stevenson, *Morell Mackenzie*, 79.

specialist had failed. Mackenzie's specimen was tiny, but it was on the mark and obtained without the Prince suffering a complication.

The Greatest Living Pathologist

Mackenzie did not propose to interpret the biopsy under the microscope himself. Given the extraordinary circumstances, the highest level of expertise was necessary and expected. Further, Mackenzie, after his initial examination of the Prince's larynx, was not convinced the nodule was cancer. He concluded that "there was nothing characteristic in the appearance of the growth; and that it was quite impossible to give a definite opinion as to its nature."⁷²⁶ An independent, third-party pathologist could adjudicate the divergent clinical opinions of Mackenzie and the German consultants. Thus, growing contentiousness over the nature of the tumor required the most eminent pathologist—someone whose experience and prestige could resolve the dispute between the warring physician factions and impose a definitive diagnosis.⁷²⁷

To whom could the royal family and its august consultants entrust the interpretation of the biopsy? The Prince's life—indeed, the future of the royal family and perhaps Germany itself—depended upon an accurate diagnosis, for the diagnosis would determine treatment. Because of the weighty burden that would be placed on the shoulders of this pathologist, no one doubted who he would be. Rudolf Virchow, aging but still shrewd and full of fire, was the micropathologist of choice. Virchow was a histopathologist of world renown. Indeed, by the late 1880s he was almost a legend. In addition, though, it is likely that there was also a political

⁷²⁶Mackenzie, *The Fatal Illness of Frederick the Noble*, 14.

⁷²⁷Notice how quickly it was decided that Mackenzie's recommendations would *not* be final; viz., that the pathologist would act as arbiter.

twist to the choice of famous pathologist. Dr. Virchow, like the liberal Crown Prince, was no friend of Chancellor Bismarck.⁷²⁸

In Virchow it (the relations of pathological anatomy to clinical medicine) reached a perfection and maturity which in its fruitfulness is reminiscent of the most important and brilliant epochs in the history of science.

-Theodor Billroth, *The Medical Sciences in the German Universities*⁷²⁹

Professor Virchow accepted the challenge, but missed the diagnosis. The Crown Prince did have cancer, but Virchow did not make the diagnosis. In his defense, he serves as a reminder that the medical thinking tends to change slowly, and that a man—regardless of his field of endeavor—must be judged within the context of his own space and time. The surgeon Billroth, a contemporary of Virchow, surely omitted the Prince Friedrich calamity from his judgment when he wrote the statement quoted above. As one swallow does not a Summer make, however, so one blemish on an otherwise extraordinary career should not erase one's name from the wall of notables. Virchow's erroneous diagnosis of the Crown Prince's biopsy specimens did not diminish his decades of innovative thought in the eyes of his contemporary countrymen—but only because the blame of scandal was shifted successfully to another party, he became a more vulnerable scapegoat.

There are many explanations for Virchow's incorrect microscopical diagnosis. The biopsy material could have been of poor or even misleading quality. The pathologist may have interpreted good tissue incorrectly. On the other hand, he may even have committed what would today be termed malpractice. Few to ennoble Virchow as the paragon of "perfection and

⁷²⁸The conservative Bismarck and the liberal Virchow were political opponents for decades. On this, see Malkin, *Out of the Mist*, 144. Samuel David Gross, who visited Virchow in the 1870s, wrote in his autobiography that "In his political feelings [Virchow] is thoroughly republican, and it is said that Bismarck is more afraid of him than of any man in the German empire." Samuel D. Gross, *Autobiography of Samuel D. Gross, M.D., with Sketches of His Contemporaries*, ed. Samuel W. Gross and A. Haller Gross, 2 vols., vol. 1 (Philadelphia: George Barrie, 1887; reprint, The Heirs of Hippocrates Library, 1994), 233.

⁷²⁹Billroth, *The Medical Sciences in the German Universities*, 37.

maturity” after his involvement in the case of the Crown Prince. In essence, Virchow hindered the Prince’s cause and reduced the probability of a successful outcome.

A Profound Problem of Perception

Although the quality of the biopsy material that failed to make obvious the true nature of the tumor may have contributed to the erroneous diagnosis, something deeper—an ideational problem—contributed to the pathologist’s mistaken microscopic diagnosis.

Virchow’s mid-nineteenth-century conception of cancer was the key ingredient in his inability to reach the correct conclusion. The prominent pathologist required tissue invasion or metastasis to diagnose cancer. The Prince’s tumor met neither criterion at this early and potentially curable stage in its biological history. The interactive process between clinician and pathologist to achieve an accurate microscopic diagnosis illustrates the advantages and disadvantages offered by technological contributions to patient care. When they work well together, the combination can be life-saving. Unfortunately, as Mackenzie, Virchow, and the citizens of Germany and England were soon to learn, cancers do not come tagged with pre-printed diagnostic labels. Indeed, as even a first-year medical student soon discovers, diagnosis is not (and has never been) a straightforward process. Interpretation is key.

First Biopsy—Two Months after Clinical Diagnosis

On May 21, 1887, as noted, Dr. Mackenzie successfully obtained biopsy tissue from the now-controversial laryngeal growth. It was not an easy tumor to biopsy, for it lay behind a soft, easily-moveable fold. Such specimens are difficult to procure because they require the operator to retract the fold at the same time that he performs the biopsy—all with the same forceps. As a

result, the specimen was “small and superficial.”⁷³⁰ Nevertheless, the physicians immediately delivered the specimen with great anticipation to Professor Virchow.

The famed histopathologist reported his findings in this special case only two days later—much sooner than the two weeks accorded similar specimens for processing and reading only a few years earlier. In the carefully crafted language, Virchow circumscribed his gross description of the specimen as “a very superficial piece of mucous membrane.”⁷³¹ He found only one questionable area on microscopy—“nests of epithelial cells.” This phrase that could mean anything from irritation to cancer. Nevertheless, he concluded, “nothing was found that contradicted a simple irritative process.”⁷³²

Beyond his histological requirement for invasion or metastasis to support a diagnosis of cancer, Virchow also held to a popular cancer causation theory that colored his microscopical interpretations. He believed that cancer—laryngeal or otherwise—was the result of an ‘irritative process.’⁷³³ His interpretation of Mackenzie’s biopsy specimen under the microscope did not rise to a level sufficient for him to diagnose cancer. Virchow’s preliminary diagnosis was “pachydermia laryngis” (literally ‘thick-skinned larynx’), an inflammatory condition named years before by the Professor himself.⁷³⁴ Indeed, Wegner had informed Mackenzie even before the official report became available that “The great pathologist had failed to find any evidence of

⁷³⁰Stevenson, *Morell Mackenzie*, 80.

⁷³¹*Ibid.*, 81. Virchow published the biopsy reports in the *Berliner Klinische Wochenschrift* 24 (1887): 445, 585, 876. The reports were later translated into English and published in the *British Medical Journal* I (18 Feb 1888): 370.

⁷³²*Ibid.*

⁷³³Virchow, *Cellular Pathology*, 487. The notion that cancer was the direct result of irritation persisted well into the twentieth century. In 1915, the Japanese chemists Katsusaboro Yamagiwa and Koichi Ichikawa rubbed coal tar on the ears of rabbits to induce cancer. Had the Nobel committee awarded the Prize for Medicine during the First World War (1915-1918), it is quite possible that Yamagiwa and Ichikawa would have won the Prize because coal tar, the first proven carcinogen, hastened the movement away from irritation as the cause of cancer.

⁷³⁴Mackenzie, *The Fatal Illness of Frederick the Noble*, 22.

malignancy.”⁷³⁵ Nevertheless, he also informed the Englishman that the specimen was insufficient to definitively exclude the dread disease.⁷³⁶ Requests by pathologists for more and better biopsy specimens were not and are not unusual. Mackenzie planned to obtain more biopsy tissue the next day, May 24th.

On that day, however, three days after the initial biopsy, the Crown Prince exhibited signs of laryngeal congestion. Mackenzie postponed the second biopsy until the twenty-fifth, but was unable to obtain any tissue. Gerhardt examined the Prince shortly after the attempted second biopsy and recoiled in horror.⁷³⁷ He cordially but insistently demanded that Mackenzie revisualize the laryngeal folds. The Englishman found nothing more than congestion. Gerhardt totally disregarded Mackenzie’s findings and maintained that the Englishman’s failed biopsy attempt had injured the Prince’s vocal cord—perhaps irreparably. Pent-up frustration at Mackenzie’s refusal to sanction the German’s plan for surgery may have played a role in the growing antagonism between the rival laryngologists. Regardless, the situation only grew worse. The Virchow mediation failed. The diagnosis was inconclusive. Surgery was deferred. The whole biopsy process and microscopical interpretation required repetition.

Mackenzie’s Second Biopsy—Virchow’s Second Report

On June 8, 1887, almost three weeks after the first biopsy, tempers cooled and the Prince’s throat congestion abated. Mackenzie successfully biopsied the laryngeal lesion *per orum* with the aid of his mirrored laryngoscope. Indeed, reduced laryngeal swelling improved definition of the lesion and aided visualization so that the Englishman obtained much better biopsy tissue than at his first procedure. The two second-biopsy specimens were larger and

⁷³⁵Ibid.

⁷³⁶Ibid.

⁷³⁷Stevenson, *Morell Mackenzie*, 81-82.

thicker than that of May 21st. Mackenzie measured the June 8 specimens at 2mm by 3mm each, almost as large as the size of the tumor estimated at first examination and more than half the lesion seen at the time of the second biopsy. These fresh specimens were much more to Virchow's liking, for micro-pathology is a specialty, ironically, that often thrives on 'bigger is better.'⁷³⁸ Nevertheless, the eminent pathologist's findings on the second biopsy specimens were still equivocal.

Virchow reported that the second biopsy was indeed "deeper" and therefore more likely to be representative of the true nature of the tumor than the first. Still, the specimens revealed no evidence that fulfilled Virchow's hallmarks of cancer—tissue invasion or metastasis. "In no part," wrote Virchow, "could an ingrowth of this epithelial formation into the mucous membrane be detected."⁷³⁹ No invasion, no malignancy. Virchow, the acclaimed father of the concept of the cell as the unit of pathology, rejected the concept that a cancer cell or cells—a microscopical finding that could justify a diagnosis of cancer without invasion or metastasis—was sufficient for diagnosis.

Nonetheless, the pathologist noted in his official report that abnormal tissue was present. The pathology, however, was of a type insufficient to reach a diagnosis of cancer. Further, he believed that the absence of tissue invasion tended to exclude the possibility of cancer. "Although [this more central portion of the growth] is very much diseased," he wrote in his report, "the healthy condition of the tissue on the periphery allows a very favorable opinion to be formed as to prognosis."⁷⁴⁰ Still, Virchow hedged his conclusion with another cry for more tissue: "Whether such an opinion would be justified in respect to the whole disease cannot be

⁷³⁸Or, at least, the larger the specimen the more likely the pathologist has the tissue in hand to reach an accurate diagnosis—and avoid a misdiagnosis.

⁷³⁹Mackenzie, *The Fatal Illness of Frederick the Noble*, 33.

⁷⁴⁰*Ibid.*, 34.

ascertained with certainty from the two portions removed. However, there is nothing present in them which would be likely to excite the suspicion of wider and graver disease.”⁷⁴¹ Virchow’s conclusion was simple—no evidence of cancer *in the submitted biopsy specimens*.

The decision tree had always been simple: if cancer is detected, then operate. The problem lay in the “if cancer.” The clinicians simply wanted to know if the Prince’s laryngeal lesion was malignant. Rudolf Virchow, preeminent pathologist of the nineteenth century, could not tell them. In what was probably the single most important pathological diagnosis of his extraordinary career, he hedged. His final diagnosis on the second biopsy specimens was “a coarsely granular papillated tumor”—pachydermia verrucosa—akin to his first pathological diagnosis.⁷⁴² Nevertheless, Mackenzie thought better of the laryngeal tumor specimens he had sent to Virchow. If cancer was present, Mackenzie believed, the pathologist would have seen it on microscopical examination. Thus, to Mackenzie the verdict was clear: Virchow diagnosed no cancer, so there was no cancer, and surgical excision was not justified.

From Concept to Interpretation to Conclusion

Virchow’s traditional conception of cancer, as a malignant process that mandated contiguous tissue invasion or metastasis for diagnosis, was becoming outmoded at the time he interpreted Prince Friedrich’s biopsies. Because of his definition of cancer, the cell pathologist was unable to imagine carcinoma *in situ*⁷⁴³—i.e., cancer at its earliest stages before the nature of the neoplastic process carried cancer cells (in most cases) beyond the bounds of surgical cure.

⁷⁴¹Ibid.

⁷⁴²Ibid., 32.

⁷⁴³*In situ* means, literally, ‘in its original place.’ Carcinoma *in situ* generally refers to neoplastic cells that have not spread beyond their presumed site of origin. Thus, the cells of an *in situ* carcinoma have neither invaded surrounding tissues nor seeded distant organs.

The earlier nineteenth-century argument concerning the existence of a unique cancer cell—a neoplastic cell identifiable in and of itself prior to tissue invasion or metastasis—remained unsettled at the time of the German succession crisis. Virchow’s invasion/metastasis prerequisite upheld the older view of cancer based upon the gross pathological features of malignancies. Other micropathologists, whose views reflected the more modern nature of cancer in the waning years of the nineteenth century, may have reached a different conclusion on Mackenzie’s biopsy specimens. It is not far-fetched to speculate that, if Friedrich had developed his hoarse throat some years earlier, the consensus microscopical diagnosis would have been non-malignant. This non-cancerous diagnosis would have become just another example, albeit of high profile, of yet another errant microscopic diagnosis. On the other hand, had the Crown Prince developed that same hoarseness just a few years later, it is likely the biopsy interpretation would have been early-stage cancer and surgery would have commenced forthwith. As in so many aspects of medicine and life, timing is everything, for the seeds of modern cancer diagnosis planted decades before in the 1840s fast took root in the more hospitable environment of rapidly-changing late-nineteenth-century medicine.

The advent of the corrected microscope and the consequent insights of early cell pathologists formed the nucleus of modern cancer-cell biology. Hermann Lebert’s work in the 1840s and Karl Thiersch’s investigations of the 1860s originated a new idea that the cell was the nidus of cancer.⁷⁴⁴ In their experiential construction of cancer, malignancy was the offspring of a deranged cell—a cell that no longer appeared nor acted normal under the microscope.

⁷⁴⁴See H. Lebert, *Physiologie pathologique, ou recherches cliniques, expérimentales et microscopiques sur l’inflammation, la tuberculisation, les tumeurs, la formation du cal, etc.* (Paris: Baillière, 1845) and his somewhat later cancer monograph, *Traité Pratique des Maladies Cancéreuses, &c.* (Paris, 1851). Francis Donaldson, the American pathologist who greatly respected Lebert, ascribed the latter’s insights and success to his “finer and more powerful” microscope lenses. See Donaldson, “Microscope and Cancer,” 51.

In addition, whereas Virchow conceived that cancer was the result of an external irritative process that derived its physicochemical stimulus from connective tissue (itself an idea descended from his teacher Johannes Müller's blastema theory⁷⁴⁵), Thiersch and his adherents believed that cancer arose in the cells of the tissue in which it was found—without the need to postulate external instigators. Thiersch's conception was more simple and elegant than that of Müller or Virchow, but, coming later, bore a heavier burden of proof than did the earlier theory. Thiersch provided the necessary evidence in the 1860s and influenced a new generation of cancer practitioners who rose to prominence in the last years of the century. Included among them were American physicians such as William Keen and Joseph Bryant, who played crucial roles in President Cleveland's cancer surgery. Thiersch even drew the notice of the slightly older and more "conservative" Joseph Janvier Woodward, who noted the German's theory in his 1873 Toner Lecture.⁷⁴⁶ Thus, to the younger generation of physicians and surgeons, cancer, which had been thought to be extrinsic and constitutional by many in the older generation, was, instead, held to be intrinsic and local. Practitioners like Keen and Bryant argued that epithelial cancer,

Karl Thiersch's most influential work on the cause of cancer was *Der Epithelialkrebs, namentlich der Haut: eine anatomisch-klinische Untersuchung/mit einem Atlas mikroskopischer Abbildungen* (Leipzig: W. Engelmann, 1865).

Parenthetically, Thiersch's contemporaries lauded him for his work on wound infections. Grover Cleveland's surgeons used "Thiersch's solution" for antiseptics throughout the President's nautical surgery. Thiersch was believed to be the first scientist-physician on the Continent to apply surgeon Joseph Lister's antiseptic practices to surgery. See <http://whonamedit.com>, "Karl Thiersch," (New York: <http://whonamedit.com/doctor.cfm/476.html>, 2001). Accessed October 29, 2001.

⁷⁴⁵Blastema theory held that all cells originated from a cytoblastema (*omnis cellula e cytoblastema*)—an amorphous extracellular matrix that generated new cells. Theodor Schwann was one of its earliest proponents. See Rafter, Rafter, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 21. Rudolf Virchow disproved blastema theory when he showed that new cells came from old cells—*omnis cellula e cellula*—not an acellular matrix. Nevertheless, the cytoblastema remained a potent concept in the United States as late as the 1870s. On this last point, see Schoenberg, "Joseph Janvier Woodward and Cancer," 458.

⁷⁴⁶Edmonds, "Woodward and the Changing Concept of Cancer, 1858-1873," 319. "Conservative" was Edmonds' term for Woodward's transitional conceptual state between the old blastema-like theories and the new tissue-with-cells-specific theories of cancer causation. *Ibid.*

like that of President Cleveland, originated in epithelial tissue—not from, or under the influence of, mesodermal components like connective tissue and its “juices.”

In short, Professor Virchow’s concept of cancer as a disease whose diagnosis required much more than neoplastic cells, led inevitably to his conclusion that Mackenzie’s biopsies reveal “no cancer.” In turn, Mackenzie, whose knowledge of and first-hand experience with the risks of laryngeal surgery required microscopic proof of cancer prior to excision, concluded that extirpation of Prince Friedrich’s tumor could not be supported on the basis of Virchow’s conclusion.

Cancer pays no mind: The Nature of the Beast

The Crown Prince’s symptoms improved after the second biopsy. Because Mackenzie did not attain the German physicians’ plan for extirpative surgery, Friedrich instead received treatment designed to relieve his symptoms. Fulguration and topical agents led to only short-lived amelioration. As with the clinical course of many cancers (and other “chronic” diseases in general), symptoms waxed and waned. At times, the Prince would feel better and the whole family agreed that whatever caused the symptoms had surely disappeared. At other times, symptom recurrence cast a pall of gloom over the patient and those in his public and private spheres. One feels, one thinks, one acts, one hopes. Eventually, however, the nature of the disease will out.

Virchow’s no-cancer reading of the biopsies may have eased the diagnosis-related anxieties of Mackenzie and the German consultants. Meanwhile, however, the positive psychological effect of the interpretation on the patient, his family, and physicians had no (known⁷⁴⁷) influence on the physical tumor that continued to grow in the Crown Prince’s voice

box. Nevertheless, despite the best hopes and earnest wishes of the patient and family, symptoms did not improve over time. In difficult cases, sometimes only the passage of time reveals the true diagnosis. Continued observation and symptomatic therapy characterized the Prince's medical care. The lack of a micropathological diagnosis of cancer on the first two biopsies forestalled early definitive treatment and any realistic chance for a cure.

Ups, Downs, and Maybes

The inconclusive June 8 biopsy led to the end of treatment by committee. All concurred that the care of the Crown Prince should henceforth be solely under the direction of Dr. Mackenzie. Thus, it would be the Englishman's case to win or lose. After all, Mackenzie was the only one of the physicians who did not conclude that the tumor was cancer based on his visual examination, and the great Virchow's interpretation appeared to support a benign rather than malignant diagnosis. Perhaps the German physicians conceded that their diagnosis of cancer had been wrong. Perhaps they too were swayed by Virchow's non-malignant pathological interpretations of several biopsies over space and time. On the other hand, perhaps they still maintained their cancer diagnosis and found the palliative approach to treatment appalling. Perhaps the frustration of trying to put out the fire of cancer with a thimbleful of water was too much for them. Perhaps Princess Vicky and her regal English mother convinced the German royal family that Mackenzie was the man for the job. The historical record is unclear, but the result was not.

Dr. Mackenzie became the chief decision maker.⁷⁴⁸ Despite the lack of pathological confirmation of a malignant process, the growth of the lesion over time concerned the

⁷⁴⁷ Such is the nature of a beast whose reality is conceived and interpreted through the human mind. Perhaps the entire project called science is to find reality through the filter of human apprehension.

experienced laryngologist. He knew that even benign tumors could bleed or obstruct the airways, leading to death by asphyxiation. Thus, his plan was to attempt to remove the tumor—regardless of its true nature—completely through the mouth with his laryngeal forceps over several sessions. Failing this, he would entertain the possibility of external surgery—laryngo-fissure—as had been recommended by the German consultants for another diagnosis some time previously.⁷⁴⁹ Gerhardt was already preparing his legal defense against possible accusations of medical mismanagement, for he informed the Crown Princess in mid-June that surgery “would have to be performed under far less favourable conditions than would have been the case fourteen days ago.”⁷⁵⁰ Mackenzie knew that the passage of a fortnight was unlikely to have a material adverse affect on the patient’s prognosis, but he worried about the Gerhardt’s persistent posturing against him.

Tensions between Mackenzie and the local consultants grew more heated as Friedrich’s condition deteriorated. Those who had been honored to serve the Prince now wished they had never been called. Each sought to protect himself and his reputation. The Germans blamed the Englishman for the Prince’s worsening; Mackenzie pointed to Virchow’s benign diagnoses. Gerhardt retorted that Morell’s electrocautery treatments damaged the Crown Prince’s vocal cords beyond repair. Mackenzie rejoinder was that Gerhardt’s sloppy initial “burnings” were the culprit. Indeed, claimed the British laryngologist, Gerhardt’s treatments may have initiated

⁷⁴⁸Dr. Mackenzie may have become the sole medical decision maker, but he still had to win the approval of the Prince, Friedrich’s wife and family, and other non-medical interested parties like Bismarck.

⁷⁴⁹Laryngo-fissure is an older term for opening the larynx through an external excision. It is commonly performed for excision of a local cancer, but in the nineteenth century the procedure could be utilized to treat a variety of laryngeal pathologies. Synonyms for laryngo-fissure include thyrotomy and laryngotomy. For a brief history of the procedure, see Kirchner, "A Historical and Histological View of Partial Laryngectomy," 808-09.

⁷⁵⁰Stevenson, *Morell Mackenzie*, 83.

cancer, if cancer was present.⁷⁵¹ Gerhardt, claimed the Englishman, had “brutalized... a delicate organ like the larynx.”⁷⁵² The newspapers on both sides of the English Channel got wind of the flaring controversy and had a field day. As with Garfield and Grant, media frenzy followed. The hoped-for agreement among the physicians, the finality of an accurate diagnosis, and, above all, the cure of the Prince’s condition, all predicated upon a micropathological interpretation of tiny specimens, became less likely as time passed. Accusations replaced due diligence, to no small measure because the mindset on the basis of which the pathologist interpreted the biopsies was outmoded and flawed.

Friedrich the Noble

Crown Prince Friedrich remained above the fray. Diversion would be salutary. His deteriorating condition and squabbling doctors could not forestall his attendance at what would today be memorialized as “The Event of the Century”—Queen Victoria’s Golden Jubilee. On June 21, 1887, Queen Victoria—Queen of Great Britain and Ireland; Empress of India—was to be feted on the occasion of the fiftieth anniversary of her ascension to the throne. It was to be a procession and ceremony like no other. With characteristic cautiousness, Mackenzie urged the Crown Prince not to attend. Friedrich would not hear of it.

The Crown Prince, Princess Victoria, and their twenty-eight-year-old son, Wilhelm, traveled to England. Mackenzie went also, for the Queen—who took a shine to him for his resolute care of her son-in-law—invited him to represent the scientific community in the parade of professionals. Friedrich, in an attempt to adhere to his physician’s warning not to catch cold,

⁷⁵¹Mackenzie, *The Fatal Illness of Frederick the Noble*, 44. The Crown Prince tended to agree with Mackenzie.

It was not unusual at the time to believe that trauma, a form of “irritation,” could initiate cancer. Heat trauma was Mackenzie’s claim against Gerhardt. More commonly, many surgeons admitted that breast cancer was caused by physical injury to the breast, because breast cancer was often diagnosed after such an injury. *Post hoc ergo propter hoc*. The connection was temporally alluring but rationally illogical.

⁷⁵²McInnis, Egan, and Aust, “Frederick William's Cancer,” 519.

arrived a week early with his entourage and resided at the out-of-the-way Queen's Hotel. There he avoided potentially contagious crowds of well-wishers and the press, both of whom had the capability to make a bad situation worse.⁷⁵³

On the day of the grand Jubilee, the Crown Prince of Germany rose to the occasion. He handled his steed with the aplomb of a skilled equestrian despite the weighty burden of his full Teutonic military regalia in the summer sun. Nevertheless, onlookers reported that it was clear Friedrich's health was failing. Common sense adds much to even the most technologically-driven medical diagnosis, for while his physicians may have failed to reach a definitive clinicopathological diagnosis, the crowd noted how gaunt and haggard the Prince appeared. To the common man he appeared quite ill. Optimistic newspaper reports of his unending physical improvement to the contrary, Friedrich drew more sympathy than huzzahs from the exuberant crowds.⁷⁵⁴

Dissociation of Sight and Thought: The Quest for More Tissue

Dr. Mackenzie, ever the astute clinician, also noted the Prince's deteriorating appearance. After his return from England, the Englishman continued to chip away at Friedrich's laryngeal growth in his squat, stiff-backed Victorian operating chair, with the aid of his trusty mirror and forceps. On June 28, 1887, one week after the Queen's Jubilee, Mackenzie reported that he had succeeded in removing all visible evidence of the tumor. He immediately sent these final fragments to Virchow. The eminent pathologist-microscopist returned a detailed report, but the conclusion remained unchanged.⁷⁵⁵ The submitted tissue was once again quite superficial, he

⁷⁵³Stevenson, *Morell Mackenzie*, 83-87.

⁷⁵⁴*Ibid.*, 85.

⁷⁵⁵Professor Virchow's gross and micropathological findings were translated and published in the *British Medical Journal* for all interested parties to read. See Chapter 6, footnote 724.

noted. Indeed, Virchow discerned little more than mucous membrane (the outermost covering of the laryngeal tissues). He was unable to diagnose cancer, for “no alveolar structure, or deposition, or penetration of epithelial masses could anywhere be perceived in this tissue.”

Nevertheless, Virchow did note some “proliferating” elements but, revealingly, his conclusion did not find “the least support for the idea of a new formation penetrating inwards.”⁷⁵⁶ No tissue invasion, no cancer. Virchow was unmoved by the rapidly reproducing cells, clinical decline notwithstanding. The cognitive dissociation between the common-sense import of continued clinical worsening and the non-malignant pathology reports also failed to sway the stalwart Mackenzie. No microscopic proof of cancer, no extirpative laryngo-fissure. Other pathologists at the time held that such proliferation was a hallmark of cancer.⁷⁵⁷

Sir Morell

During the next four months there were periods of hope, but for the most part, fear dominated. On July 11, 1887, Dr. Norris Wolfenden, Mackenzie’s former assistant and the Prince’s resident physician during the mentor’s absence, noted that a “slight swelling” had reappeared on the larynx.⁷⁵⁸ Mackenzie reasoned that either his removal of the tumor had been incomplete and/or the lesion had regrown. He knew that some non-malignant tumors recurred, but he still could not be certain of the nature of this particular growth. He informed the Crown Princess (but not the Crown Prince) of this potentially ominous relapse. By early August the tumor grew to the extent that Mackenzie was forced to utilize a new galvano-cautery for excision. Again, the Prince rallied and his voice waxed stronger. For more than a month,

⁷⁵⁶These quotations are from the *British Medical Journal* report, as quoted by Stevenson, *Morell Mackenzie*, 88.

⁷⁵⁷See the Wilhelm von Waldeyer consultation below.

⁷⁵⁸Wolfenden was also Physician to the Throat Hospital in London. See Stevenson, *Morell Mackenzie*, 84.

frequent examinations failed to reveal evidence of another recurrence. The Princess and the royal families of Germany and England were delighted by Friedrich's symptomatic improvement. Perhaps Virchow's hedged but ultimately non-malignant microscopical diagnoses were correct after all. Dr. Mackenzie was the hero.

On the afternoon of September 7, 1887, Queen Victoria knighted Morell Mackenzie at Balmoral Castle. She noted in her journal that day that the honor was conferred at the express wish of the Crown Prince. She asked the newly dubbed Sir Morell what had caused "Fritz's" illness. The Queen's journal recorded that "he could not say much, but he thought it had been long coming on, and been entirely neglected. The little growth, which he removed, had come from the inflammation of the throat."⁷⁵⁹ Inflammation vs. neoplasia—again confusion reigned. In the absence of a biopsy-proven diagnosis of cancer, however, an inflammatory lesion seemed most likely.

Too Late

The date of Mackenzie's knighthood was the high-water mark for both Sir Morell and Prince Fritz. Thereafter the Heir Apparent deteriorated more steadily. Within weeks, the Prince's voice again became enveloped in hoarseness and Mackenzie discovered another recurrence. No longer buoyed by the benign pathology reports, Sir Morell finally confided to the Princess—now his confidant—that "the lesion had a distinctly malignant look."⁷⁶⁰ Vast clinical experience taught him that recurrence was one of the signposts on the road to the grave. What he could not predict was how long it would take.

The clinical finding that led to Sir Morell's newfound conclusion was a most ominous pathological formation. It was a distinct lesion similar to but spatially removed from the first.

⁷⁵⁹Ibid., 89.

⁷⁶⁰Ibid., 89, 91.

The first growth had been on the left vocal cord. This second tumor was below the right vocal cord. The previous micropathology was no longer directly relevant, for whatever had or had not been present on Virchow's biopsy slides was of no consequence now that this new tumor, separated from the first in space and time, had appeared. Mackenzie did not believe that he was in a position to question the accuracy of Virchow's previous interpretations. Indeed, criticism at this juncture could only bring invectives down on his own head, for it was none other than he himself—against the entire German enclave—who insisted on a microscopic diagnosis of malignancy to validate extirpative surgery. Sir Morell hoped to keep mum about the new finding. Nevertheless, he felt obliged to explain to the Crown Prince, who was beginning to show evidence of alarm symptoms,⁷⁶¹ that he had found a change in his throat.

“Is it cancer?”

On November 6, 1887, almost exactly three years after General Grant's anxious question to Dr. Douglas, the Crown Prince asked Sir Morell the same question—“Is it cancer?” In an answer quite similar to Douglas's reply to Grant, Mackenzie calmly informed Friedrich that “I am sorry to say, sir, it looks very much like it, but it is impossible to be certain.”⁷⁶² Without microscopical confirmation, he said time and again, the diagnosis of cancer remained uncertain.

Despite Dr. Mackenzie's equivocation, his great fear—that the Prince's atypical laryngeal growths were malignant—had come to pass. The Crown Prince had dreaded as much for quite some time, for he was aware of the dickering over the pathological interpretations and knew his condition was worsening. After a momentary pause to digest the frightful verdict, he grasped Sir Morell's hand. A cloud of chronic care appeared to lift from his countenance and he managed a

⁷⁶¹Alarm symptoms caused by laryngeal tumors include difficulty breathing, swallowing, and coughing blood. If progressive, they often mandate tracheostomy to avoid choking to death on one's own body fluids.

⁷⁶²Stevenson, *Morell Mackenzie*, 91.

weak smile. “I have been lately fearing something of the sort,” he whispered to avoid the gruff voice. “I thank you, Sir Morell, for being so frank with me.”⁷⁶³

Many patients exhibit a sense of relief upon learning that the diagnostic dilemma of their uncategorized disease is solved—even if turns out to be cancer. Prince Friedrich was one. That evening, all who saw him noted how gay and cheerful he had suddenly become. Despite the damnable hoarseness, he even talked more freely than in past months. In response to a polite question about his health, he replied that “Under the circumstances, I really must apologize for feeling so well.”⁷⁶⁴

Reality set in with a vengeance. As Elisabeth Kübler-Ross wrote in the late 1960s, (non-sudden) dying is a process that can often be dissected into stages of varying durations. The first stage, denial, precedes anger—the second.⁷⁶⁵ In public, the Prince assumed a cheery demeanor. His private life, however, revealed rapid progression to the second psychological stage. Crown Princess Victoria witnessed this darker side personally. In a letter to her mother she quoted an outcry from her husband that could represent all the anguish, meaning, and history of nineteenth-century cancer. “To think that I should have such a horrid, disgusting illness!” howled Friedrich. “I had so hoped to be of use to my country. Why is Heaven so cruel to me? What have I done to be thus stricken down and condemned?”⁷⁶⁶

Decisions

Diagnosis is prelude to treatment, for in the process of medicine effect must have cause. Whether treatment is thought to be efficacious for a given diagnosis, however, is a separate

⁷⁶³Dr. Mackenzie recorded this dialogue and Stevenson published it verbatim. See *Ibid.*

⁷⁶⁴*Ibid.*, 91-92.

⁷⁶⁵M.D. Kübler-Ross, Elisabeth, *On Death and Dying: What the Dying Have to Teach Doctors, Nurses, Clergy and Their Own Families* (New York: Macmillan Publishing Co., Inc., 1969).

⁷⁶⁶Quoted by Stevenson, *Morell Mackenzie*, 97.

consideration whose nature has evolved over centuries. In the nineteenth century, the measure of the value of therapeutics took a radical turn with the secularization and scientization of medicine.⁷⁶⁷ Statistics and the reproducibility of results began to guide judgments on efficacy even as diagnostic confirmation of cancer by microscopy became more widely accepted.

What was to be done now that Sir Morell, still the primary physician, all but conceded that Friedrich's laryngeal tumor was malignant? Because a syphilitic lesion could not be excluded with certainty, Mackenzie first applied potassium iodide to the laryngeal lesion. Predictably, the white crystals had no effect.⁷⁶⁸ On November 9, 1887, two new consultants, Professor von Schrötter of Vienna and Dr. Kruse of Berlin, examined the Crown Prince and immediately concluded that the tumor was malignant. Their diagnosis came without hesitation or doubt. Microscopic confirmation of their conclusion was unnecessary. They had an advantage of diagnosis not available to Mackenzie months before—a much longer period of observation. Von Schrötter and Kruse advised immediate extirpative surgery—as had the German consultants almost six months earlier.

Dr. Mackenzie's role in his patient's care shifted from diagnostician to personal consultant. He explained to the core family—Friedrich, wife Victoria, and son Wilhelm (with Bismarck in the shadows)—the advantages and disadvantages of surgery. Sir Morell and the Germans physicians dismissed the use of oral or topical medicinal cancer cures. Indeed, they

⁷⁶⁷Both secularization and scientization embrace the notion of 'change' as transformation, and particularly the belief that change is good. Those who dominated the self-conceived, static, pre-modern world had little desire for innovation and discovery.

⁷⁶⁸Clear differentiation of syphilis—"the great imposter"—from other diseases was not possible until the early twentieth century and, practically speaking, until after the First World War. See Morman, "Clinical Pathology in America, 1865-1915," 205. and Allan M. Brandt, *No Magic Bullet: A Social History of Venereal Disease in the United States since 1880 with a New Chapter on Aids*, Expanded ed. (New York: Oxford University Press, 1987), 40. Prior to the era of the laboratory diagnosis of syphilis, physicians treated many possible syphilitic lesions with anti-syphilitic agents like potassium iodide as a matter of course. Parallel paradigms persist today in the treatment of diseases that are difficult to diagnose or distinguish, but are at least partially amenable to treatment.

avoided them from the beginning, for they knew no scientific evidence that any were beneficial.⁷⁶⁹ Surgery was the sole serious treatment consideration. Nevertheless, the decision for surgery was not made without trepidation, for if cure routinely followed excision there would have been no hesitation months earlier. In May, 1887, Mackenzie and the German consultants could have suggested immediate surgery instead of delay. In truth, the decision in favor vs. against operative extirpation carried with it much uncertainty. Although an excellent result from laryngo-fissure offered the probability of cure, longer life, and the removal of that “horrid, disgusting” disease, such an outcome occurred rarely.

Mackenzie was quite cognizant of the risks of laryngo-fissure. He had been one of the first—perhaps *the* first—to publicize the woeful consequences of laryngeal surgery. In his internationally renowned 1880 text, *A Manual of Diseases of the Throat and Nose*, Mackenzie concluded that for cancers in this region “the disease must necessarily end in death, and the only doubt which can exist in the prognosis relates to the question as to how soon the malady may be expected to prove fatal.”⁷⁷⁰ Since surgical outcomes so often ended in disaster, “palliative measures alone can be adopted.”⁷⁷¹

In Sir Morell’s opinion, the prognosis for laryngeal cancer surgery had not appreciably improved during the few years since he penned those lines. No wonder he demanded a positive cancer biopsy prior to proposing surgery. Statistically, what was the prognosis circa 1887 if patient and physician chose extirpative surgery? More than one out of three patients died on the

⁷⁶⁹That said, the public suggested myriad home and proprietary medicinal remedies once knowledge of Friedrich’s cancer was leaked to the press on November 13, 1887—only days after all participants swore an oath of secrecy with respect to the Crown Prince’s now-universally-accepted cancer diagnosis. See McInnis, Egan, and Aust, “Frederick William’s Cancer,” 519, Stevenson, *Morell Mackenzie*, 97.

⁷⁷⁰Mackenzie, *Diseases of the Throat and Nose*, 82.

⁷⁷¹*Ibid.*, 82-83.

operating table.⁷⁷² Even partial extirpation—as oxymoronic as it was non-curative—could cause immediate death, by Mackenzie’s own reckoning, of about one in four.⁷⁷³ On the other hand, operative mortality had to be balanced against the average life expectancy of a patient with laryngeal cancer who did not elect surgery—two years.⁷⁷⁴

And what if the royal patient and his physician, in the best of all possible worlds, decided in favor of surgery *and* the patient survived the operation? What would life be like? Mackenzie was very sensitive to this possibility and explained it carefully to the Prince and the royal family. The first consideration was recurrence, for who could believe that cancer, like an unwelcome guest, would never return? In the 1880s, the public and most physicians agreed that “Once a cancer, always a cancer.”⁷⁷⁵ In addition, the risk of aphonia was high. The Prince and future Emperor might well have no voice—literally and probably figuratively. Could authority survive voicelessness? What influence, what power, would emanate from the silence of voicelessness? Even commoners who became aphonic as a consequence of laryngeal surgery claimed that a hellish life with cancer had become a life worse than death without it.⁷⁷⁶ What would be the Prince’s fate? Dr. Mackenzie presented all this and more to the Crown Prince and the royal family as the nineteenth-century equivalent of informed consent.

The German consultants did not agree with the Englishman’s dismal assessment of surgery. They dismissed Mackenzie’s claim that laryngo-fissure was such a high-risk procedure.

⁷⁷²McInnis, Egan, and Aust, "Frederick William's Cancer," 520.

⁷⁷³Mackenzie, *The Fatal Illness of Frederick the Noble*, 238.

⁷⁷⁴*Ibid.*, 205.

⁷⁷⁵Schechter and Morfit, "The Evolution of Surgical Treatment of Tumors of the Larynx," 470. quoting Felix Semon, "A discussion on the operative treatment of malignant diseases of the larynx," *British Medical Journal* 2 (1903): 113.

⁷⁷⁶Mackenzie, *The Fatal Illness of Frederick the Noble*, 239. Dr. Semon, another eminent British laryngologist in the 1880s, noted that those few who survived laryngectomy developed a "deplorable, even suicidal, mental state." Quoted by Stevenson, *Morell Mackenzie*, 97.

Instead, they argued that it was “not dangerous” and that it was the only way to ensure cure.⁷⁷⁷ Unlike Sir Morell, however, they did not present statistics to bolster their assertions.⁷⁷⁸ Neither did they repudiate his data, which included many evaluations and case reports from German physicians and patients.

Friedrich weighed the evidence and quickly decided for himself. He decided against laryngeal extirpation on the same day during the second week of November 1887 that the Mackenzie and the German consultants presented the options to him. He did, however, agree to tracheostomy if obstruction or bleeding into the airways necessitated a life-extending, palliative procedure. Then he made peace with those around him and resigned himself to his ultimate fate. In his diary for November 9, 1887, he wrote: “And so I suppose I must set my house in order.”⁷⁷⁹ In consequence, cancer had once again torn at the soul of the nineteenth-century psyche. No matter how long the body might live, the spirit languished.

To Cure—To Operate

To Prolong—To Palliate

Mackenzie made no secret of his aversion to extirpative laryngeal surgery. In his 1888 apology (in the sense of a Socratic ‘defense’) entitled *The Fatal Illness of Frederick the Noble*, Sir Morell made clear that the surgical conditions of the 1880s—despite significant advances over previous decades—required limitation of laryngo-fissure to carefully selected patients.⁷⁸⁰ As shown, the statistics on operative mortality were horrendous, and overall results were worse.

⁷⁷⁷Stevenson, *Morell Mackenzie*, 98-99.

⁷⁷⁸Mackenzie’s 1880 *Manual* included statistics on the operative results of “extirpation of the larynx.” His main outcomes table is reproduced in Schechter and Morfit, “The Evolution of Surgical Treatment of Tumors of the Larynx,” 469.

⁷⁷⁹Stevenson, *Morell Mackenzie*, 96.

⁷⁸⁰Mackenzie, *The Fatal Illness of Frederick the Noble*, Section II.—Controversial.

This concern for the poor outcomes of patients who underwent laryngectomy colored his requirement for pre-operative microscopical confirmation of neoplastic disease.

Generations of physicians and medical historians after the demise of the English laryngologist have written that Mackenzie's demand for a positive cancer biopsy prior to surgery was prescient. Dr. R. Scott Stevenson concluded in the 1940s that, "[I]n his insistence on biopsy he was well in advance of his time."⁷⁸¹ In the 1970s, Dr. W. David McInnis and colleagues agreed that his use of cancer microscopy for clinical confirmation "was well in advance of general medical opinion of the day."⁷⁸² There is little doubt that, from the sharp-eyed perspective of hindsight, Mackenzie's requirement for microscopical confirmation foreshadowed what would become routine procedure for practitioners not many years thereafter. His motive, however, may have been negative as well as positive. That is, in addition to having the foresight to define cancer at the microscopic level, he may have demanded a positive biopsy to restrict patient selection to those for whom the vicissitudes of surgery would not materially alter their predictable doom. It seems clear that, in general, he would rather not perform laryngectomy on a patient with vocal cord cancer unless the micropathological diagnosis was clear, the lesion amenable to extractions, and the patient highly motivated. Crown Prince Friedrich satisfied none of these criteria, let alone all of them.

Mackenzie predicted that the Crown Prince might live an additional eighteen months without surgery. This was an expectation based upon extensive clinical experience. It was also the period of analysis he used to define surgical cure.⁷⁸³ The medical statistics in Sir Morell's

⁷⁸¹Stevenson, *Morell Mackenzie*, 169.

⁷⁸²McInnis, Egan, and Aust, "Frederick William's Cancer," 518.

⁷⁸³"Cure" is an elusive concept associated with a cancer-free survival state. It is often defined in terms of time; e.g., a five-year survival after many cancer treatments (surgery, chemotherapy, radiation, etc.) may be defined as a cure—dependent upon cancer type.

day strongly supported his reluctance. Indeed, laryngo-fissure results were shocking. Only 8 of 138 (5.8%) laryngectomy patients followed through 1887 survived eighteen months.⁷⁸⁴ Since it is likely that many failed surgeries were never published, the post-operative survival rate was probably even less. Mackenzie's main argument to support his refusal to operate in May 1887, was that, even if Virchow had diagnosed cancer on the first biopsy, the Crown Prince's longevity and quality of life would be better without extirpative surgery. Indeed, Mackenzie concluded "that through the mild and painless operations performed by myself the dangerous methods recommended by Gerhardt and von Bergmann were prevented, and that I thereby not only prolonged the life of the Emperor, but also saved him much suffering."⁷⁸⁵

To Palliate: Tracheostomy

How much suffering did Sir Morell spare the Crown Prince? In December, 1887, as the New York Cancer Hospital, built at the insistence and with the funds of Charlotte Astor and Elizabeth Hamilton Cullum, first opened its doors,⁷⁸⁶ the Crown Prince appeared to improve clinically.⁷⁸⁷ Within a month, however, he began to feel increased difficulty breathing. As

In the last two centuries, surgeons and other cancer physicians have lengthened the time to the definition of 'cure.' In the mid-nineteenth century, a cure could be considered upon the immediate disappearance of a tumor after the application of heat, cold, or another appliance—even if the lesion rapidly reappeared. Surgeons at the New York Cancer Hospital in the late nineteenth century most commonly defined cure as no evidence of neoplastic disease at the time of discharge. More recently, five-year survival without recurrent cancer has been a typical definition of cure. In reality, I should think that cure is the total absence of an accurately diagnosed cancer from the end of the cancer treatment to the time of death. This requires a high level of scrutiny to which few individuals are subjected.

⁷⁸⁴McInnis, Egan, and Aust, "Frederick William's Cancer," 520.

⁷⁸⁵Mackenzie, *The Fatal Illness of Frederick the Noble*, 186. By "operations," Mackenzie meant the application of topical analgesics and anti-syphilitics. Surgery has long since come to the point where "operation" often meant complete or substantial (debulking, for example) excision of a tumor. Mackenzie's 'operations' were out-patient topical applications performed through the mouth, not the invasive surgery of surgery. Thus, in the parlance of the time, General Grant's consultants also treated him with 'operations.'

⁷⁸⁶By early December, 1887, Mrs. Cullum had already died of cancer and Mrs. Astor lay on her deathbed, probably with the same gynecologic neoplasm.

January, 1888 progressed, Friedrich lost more weight, coughed up increasing quantities of “tissue,” and became more and more uncomfortable. On the morning of February 9th, Friedrich’s routine larynx examination agitated Mackenzie considerably. Both left and right vocal cords appeared more inflamed and swollen than ever, thereby choking off the Prince’s airway. Sir Morell urged immediate tracheostomy. He feared that postponement would lead to death by asphyxiation. The German consultants in attendance agreed with the necessity of tracheostomy, but urged postponement until Professor von Bergmann could arrive. Mackenzie objected. If the Prince died waiting for von Bergmann, Mackenzie declared, he would take no responsibility for the avoidable death. Given his threat, the consultants would not wait, for none would risk blame should a catastrophe occur. At three o’clock that afternoon, Mackenzie and his assistants performed a prophylactic tracheostomy on the Crown Prince.⁷⁸⁸

The tracheostomy by-passed the obstructing cancer and reduced the patient’s dyspnea (difficulty breathing). The laryngeal redness and swelling that mandated the tracheostomy abated over the next few days. Friedrich felt much better. Mackenzie’s advocacy of palliation over extirpation appeared vindicated, for the Prince regained his gravelly voice thereafter by occluding the tracheostomy opening with his finger.⁷⁸⁹ Still, all recognized that cancer at this late stage consisted of watchful waiting with ever-fading hope.

New Pathologist, New Results: Microscopy Vindicated

⁷⁸⁷Friedrich’s temporary improvement was reminiscent of General Grant’s “honeymoon period” three years earlier. Waxing and waning of cancer symptoms is common, although growth of the underlying malignant pathology may be inexorable.

⁷⁸⁸Stevenson, *Morell Mackenzie*, 103-04.

⁷⁸⁹By occluding the tracheostomy opening the patient once again forces air past the vocal cords, thereby initiating sound. With a patent tracheostomy, air flows in and out of the opening below the vocal cords, so that little air causes cord vibration—the genesis of vocal communication. When breathing through a tracheostomy, a patient’s voice is minimal to non-existent.

News of the tracheostomy spread rapidly. The tracheostomy made clear to even the most inattentive citizen that something was terribly wrong with the Prince's health. Information about Friedrich's clinical course over the 1887-1888 year was leaked to the press. Pointed questions ensued. Why wasn't the cancer removed in May, 1887? Why did the doctors wait so long before they reached consensus on the diagnosis of cancer? And, particularly for the physicians, why did the biopsies fail to reveal cancer despite multiple specimens over several months? Mackenzie and Virchow received the brunt of the criticism. In the final analysis, did Mackenzie submit unrepresentative biopsy tissue that failed to contain the already-present cancer, or did Virchow misinterpret malignant biopsies as benign? And, if the eminent Virchow missed the diagnosis, why? Some pathologists wondered if it could be due to his outmoded and somewhat controversial requirement that a diagnosis of cancer mandated the presence of invasion or metastasis.

Within a short period of time answers to the above questions became more political than medical. Nevertheless, two tissue-related events occurred in early 1888 that may shed light on the answers to those critical questions. Perhaps the best determinant seems not to have occurred; viz., that subsequent generations of micropathologists reviewed and reinterpreted the biopsy slides, à la President Cleveland's biopsies.⁷⁹⁰

On January 26, 1888, about two weeks before the tracheostomy, Mackenzie presented yet another specimen to Professor Virchow for micropathological examination. This particular tissue was expectorated, for the Crown Prince sloughed and coughed up increasing amounts of tumor as the months went by. Virchow was aware that all the surgeons now agreed on the presence of cancer, but still he could not confirm their clinical diagnosis microscopically. On

⁷⁹⁰John J. Brooks, Horatio T. Enterline, and Gonzalo E. Aponte, "The Final Diagnosis of President Cleveland's Lesion," *Transactions & Studies of the College of Physicians of Philadelphia* 2, no. 1 (1980).

this pathology report, his fourth, he concluded that “distinctly isolated alveoli,” which would have at the very least suggested malignancy, “were nowhere to be discovered, in spite of assiduous researches.”⁷⁹¹

The subsequent tracheostomy led to an outpouring of blame and finger-pointing. A press statement set off partisan attacks that pitted the German consultants, the German newspapers, and German public officials against Mackenzie. The Germans castigated the Englishman for not excising the cancer when the possibility of cure arose months earlier. The Englishman blamed Virchow for misinterpreting the biopsy tissue. The pathologist criticized Mackenzie for submitting non-representative, cancer-poor material. In public as well as medical circles, Virchow exclaimed that Mackenzie “had missed the malignant lesion below the [vocal] cords.”⁷⁹² Who would dare accuse the most eminent pathologist of the century as having committed malpractice? Even the majority of English practitioners sided with the Germans. Were it not for the immediate support of Friedrich and Victoria (who revealed years later that Sir Morell had indeed considered the possibility of cancer all along but did not wish to undertake the requisite life-threatening surgery without proof), Mackenzie might have been totally overwhelmed by the charges against him.

Nevertheless, charges and countercharges flew in the media, and between Virchow, the German consultants, and Mackenzie. Finally, in March, 1888, the English laryngologist received a report that called into question the growing public verdict against him.

Wilhelm von Waldeyer Reappears

⁷⁹¹Mackenzie, *The Fatal Illness of Frederick the Noble*, 84.

⁷⁹²McInnis, Egan, and Aust, "Frederick William's Cancer," 520.

Professor Virchow went on vacation. Best known for his trailblazing in cellular pathology, the multi-talented scientist was also famed for his forays into German politics and archeological explorations. In early March, he set out to a dig in Egypt.⁷⁹³ Normally, there would have been little need to seek a substitute pathologist for the Crown Prince, because his condition appeared stable, but when Friedrich's cough became blood-tinged another clinical consultant—the famous pulmonologist Professor Kussmaul of Strassburg—was brought into the fray to determine whether the blood had originated from the throat or lungs.⁷⁹⁴ Kussmaul's awkward examination of Friedrich and unsupported conclusions—termed “comical” and “fantastic” by the Crown Princess⁷⁹⁵—irked Mackenzie and drove the Englishman to seek yet another pathological opinion on the blood-tinged expectoration without delay. The consultants considered the eminent Professor von Recklinghausen (“Virchow's most brilliant pupil”⁷⁹⁶), also of Strassburg, but finally settled upon the much closer Professor Waldeyer, then of Berlin.⁷⁹⁷

Wilhelm von Waldeyer had been Paul Ehrlich's and William Henry Welch's instructor at Strassburg over a decade before. Waldeyer was one of the great nineteenth-century German polymaths whose interests encompassed several aspects of human biology including anatomy, neurophysiology, biochemistry, embryology, and staining. He was the individual most

⁷⁹³Erwin Ackerknecht rendered an expansive picture of Virchow in Ackerknecht, *Rudolf Virchow*.

⁷⁹⁴Extension of the laryngeal cancer to the lungs would have been a most ominous sign that would have deemed Mackenzie's eighteen-month survival estimate wildly optimistic. Expected survival was critical to the Crown Prince, for his aged father's health was failing fast in the winter of 1887-1888 and Friedrich had many projects he wished to accomplish as Emperor before his own death.

⁷⁹⁵Stevenson, *Morell Mackenzie*, 108.

⁷⁹⁶Flexner and Flexner, *William Henry Welch*, 78.

⁷⁹⁷In addition to Waldeyer's proximity to the Prince, there may have been a character issue that led to the selection of Waldeyer over von Recklinghausen. As personality is so important to human intercourse—and yet so difficult to gauge through the veil of time—von Recklinghausen was widely known for his impatience, temper, and capriciousness. William Welch commented negatively upon von Recklinghausen's personality during his sojourn with both Waldeyer and von Recklinghausen at Strassburg. See *Ibid.*, 78-79.

responsible for the identification of the neuron (nerve cell) as the fundamental unit of the nervous system. Waldeyer's productivity in the investigation of cancer was legendary. Not surprisingly, his chief mentor, Karl Reichert, was another famous student of Johannes Müller. Thus, Waldeyer's fascination with cancer and the microscope can be traced directly to the professors' professor—Johannes Müller.⁷⁹⁸

Beginning with his early days at Königsberg and Breslau, Waldeyer exhibited a particular interest in the use of stains for the early diagnosis of cancer. He was perhaps the first, as early as 1867, to conclude that cancer cells developed from normal cells, and that invasion and metastasis resulted from the passage of these transformed cells through tissues, lymphatics, and the bloodstream.⁷⁹⁹ Waldeyer described the histopathology of the inter-tissue spread of cancer with an accuracy amazing for the time. His was indeed a very modern conception of cancer. In addition to his general penchant for investigations into the nature of cancer, Waldeyer further evinced a particular interest in throat diseases. Thus, the consultants' decision to select Waldeyer to replace the vacationing Virchow was eminently reasonable.⁸⁰⁰

The Fourth of March

During the first week of March, 1888, the consultants, led by Mackenzie, called upon Waldeyer to examine the Prince's expectorated sputum microscopically. On March 4, 1888, the

⁷⁹⁸The students of Johannes Müller constitute a pantheon of acclaimed nineteenth-century anatomists, physiologists, and pathologists. Even as the "Great Men" analysis of history has passed from sunlight to shadow in academe, it is difficult not to recognize the mark of Müller in his students and his students' students. Historians have recognized this extraordinary influence for some time. See Billroth, *The Medical Sciences in the German Universities*, 218, Malkin, *Out of the Mist*, 135, Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, 168.

⁷⁹⁹See Roderick E. McGrew and with the collaboration of Margaret P. McGrew, "Cancer," in *Encyclopedia of Medical History* (New York: McGraw-Hill Book Company, 1985), 50.

It is humbling to note that the idea that cancer cells develop from normal cells was not confirmed, strictly speaking, until the late 1970s. See Weinberg, *Racing to the Beginning of the Road*.

⁸⁰⁰Some might argue that Waldeyer should have been the first micropathologist to be asked to assess Mackenzie's biopsies. Virchow's prestige, however, coupled with his liberal turn, made him the initial pathologist of choice. In addition, Virchow was fifteen years senior to Waldeyer—a not-insignificant consideration at the time.

substitute micropathologist immediately concluded that the specimen was rife with “nest-cells.” Mackenzie finally received the tell-tale sign of cancer he had sought from the day he arrived in Berlin almost ten months earlier. Waldeyer left nothing to doubt. He claimed that his micropathological findings were “the result of a deep-seated destructive process” that had probably been present for some time.⁸⁰¹ True, this was cytological (cellular) rather than biopsy (tissue) material, but Virchow had also examined the Prince’s sputum less than six weeks earlier. Virchow had failed to find any evidence of cancer from a tumor that had grown large enough to obstruct the Prince’s windpipe.

Waldeyer presented Mackenzie with his positive cancer diagnosis even before he wrote his report. “Since Waldeyer had told me of the result of his microscopical examination,” acknowledged Mackenzie, “I had frankly accepted the cancer diagnosis as definitively established.”⁸⁰² Finally! There would be further quibbling or equivocation. No one—not even Mackenzie—harbored any residual indecision as to the true, fatal nature of Friedrich’s laryngeal tumor. The definitive diagnosis was cancer of the larynx. For Mackenzie, this was the “microscopic evidence”—the elusive confirmation—which he had been seeking from the beginning. He had unpopularly anchored his diagnosis and therapy on previous negative pathology reports. In the end, neither Mackenzie, nor Virchow, nor Gerhardt, nor the other German consultants established the definitive diagnosis of cancer. Waldeyer did. But it was too late.

Emperor Friedrich Wilhelm III

⁸⁰¹Stevenson, *Morell Mackenzie*, 109.

⁸⁰²Mackenzie, *The Fatal Illness of Frederick the Noble*, 181.

Five days later, on March 9, Friedrich's father, Emperor Wilhelm I of Germany, died just short of his ninety-first birthday.⁸⁰³ The Crown Prince immediately succeeded him as Friedrich Wilhelm III of Germany. Unfortunately, Friedrich's failing health tempered the hopes, aspirations, and dreams he had waited years to fulfill as Emperor. Persistent bleeding from his tracheostomy dashed his desire to ameliorate the harsh conservatism of Wilhelm I and Chancellor Bismarck. His plans to establish a more enlightened state with a more liberal agenda vanished through the tube feedings he received to bypass the cancer that was choking off his trachea and esophagus.

With a heavy heart and a vanquished soul, the rapidly-declining new Emperor dutifully attended to the affairs of state. Constant medical attention did nothing to restore his flagging strength. On June 10, barely three months into his reign, Friedrich could no longer take food by mouth. Shortly thereafter, he could not even swallow his own saliva—a symptom of total blockage of his food pipe (esophagus). Tube feedings and generous doses of cocaine—similar to what General Grant received across the Atlantic three years earlier—afforded only minimal comfort and did not halt the downward spiral of disease. Three days later he met with King Oscar of Sweden, but his breathing became so labored that it was clear to all in attendance that the new Emperor's end was near. The next day Friedrich's shortness of breath worsened and violent coughing led to a diagnosis of bronchopneumonia. This dire complication was probably secondary to the cancerous obstruction that prevented the normal traffic of secretions and excretions down and up the airways. At 11 A.M. on June 15, 1888—on the ninety-ninth day of his reign—Emperor Friedrich Wilhelm III died. Among those present, it was Sir Morell Mackenzie who “gently closed the blue eyes.”⁸⁰⁴

⁸⁰³Wilhelm Friedrich Ludwig was born March 22, 1797.

Backlash

The reader might assume that the consequences of the death of Emperor Friedrich have little relevance for the role of the microscope in the making of modern cancer. One could argue that the slander, libel, and scathing attacks hurled against Dr. Mackenzie by Germans and some British for not sustaining surgery on the Crown Prince in May, 1887 did not advance the use of the microscope in the diagnosis of cancer.⁸⁰⁵ Had Mackenzie not insisted on microscopic evidence that the Prince had cancer, they might argue that the outcome might have been different. Others might claim that Sir Morell's subsequent condemnation by the German press as a "political agent" and his ostracism by the Royal College of Physicians for unprofessional conduct—he resigned rather than undergo the ignominy of expulsion—have nothing to do with the history of cancer microscopy.⁸⁰⁶ Still others could allege that the Englishman's self-

⁸⁰⁴McInnis, Egan, and Aust, "Frederick William's Cancer," 520.

⁸⁰⁵Dr. Mackenzie's trials and tribulations following the death of Emperor Friedrich III warrant their own study in medical politics. A sketchy summary of the events that transpired from 1888 until Sir Morell's death in 1892—a broken man who also succumbed to bronchopneumonia (one of the most common causes of death at the time)—may be found in Stevenson, *Morell Mackenzie*, 21ff. and 161ff.

Less than a month following the death of Emperor Friedrich, the German consultants issued a sixty-two page black-bordered pamphlet that accused Mackenzie of excessive diagnostic and therapeutic optimism as well as poor judgment. Among their worst calumnies, however, was their accusation of "malpraxis." See Stevenson, *Morell Mackenzie*, 142. Most of their accusations were later found to be unwarranted if not untrue.

Incidentally, one of the major findings at the Emperor's autopsy as directed by both Virchow and Waldeyer was an acutely infected sinus tract probably caused by von Bergmann's probes. This pathology and certain contributor to Friedrich's morbidity and mortality was not dissimilar from President Garfield's acute infection in a time of Listerian controversy in America. The purulent cavity undoubtedly hastened the Emperor's demise. See Stevenson, *Morell Mackenzie*, 134. At autopsy, cancer was widely disseminated throughout the Emperor's body both grossly and microscopically.

Friedrich III's autopsy was the last ever performed by Rudolf Virchow. The eminent pathologist was about sixty-seven years old at the time and died when eighty. Whether or not the finality of the Emperor's autopsy speaks to Professor Virchow's mindfulness of personal complicity in the sovereign's death (parallel to Woodward with Garfield) is for the reader to decide.

⁸⁰⁶On June 26, 1888, the *Norddeutsche Kreuz-Zeitung* published a polemic highly critical of Mackenzie's medical "skills" and branded him "a political agent."

Sir Morrell was castigated in England as well as on the Continent, but for different reasons. The Royal College of Physicians reproved Dr. Mackenzie (laryngologists in Sir Morell's day considered themselves physicians rather than surgeons) for the unprofessional tactlessness he displayed in publishing his defensive tract, *The Fatal Illness of Frederick the Noble*, in October, 1888. Sir Morell resigned his diplomat status with the Royal College on

defense—that the potential radical “cure” of surgery could well be worse than moderate life-prolonging palliation—was a *post hoc* justification meant to assuage a guilty conscience rather than support the use of the microscope in the diagnosis of cancer.⁸⁰⁷ But they would all miss the larger point.

The Role of the Nineteenth-Century Microscope in the Making of Modern Cancer

The Problematic

At least one historian-surgeon concluded that the Friedrich controversy delayed the use of microscopy for the diagnosis of cancer. Dr. R. Scott Stevenson, a British otolaryngologist who carefully dissected the chronology of the Crown Prince’s travail, concluded in the 1940s that “the case of Crown Prince Frederick helped to retard the general acceptance of biopsy as an aid to precision in diagnosis.”⁸⁰⁸ In his “Summing-Up,” Stevenson found that “one of the most unfortunate effects of the notoriety of the case upon medical opinion was that the value of the removal of a specimen of living tissue for microscopic examination was discredited for several decades.”⁸⁰⁹

Dr. John A. Kirchner, an otolaryngologist who published a history on surgery of the larynx, wrote in *The Bulletin of the New York Academy of Medicine* in 1986 that “the negative reports submitted by Virchow on Crown Prince Friedrich’s laryngeal cancer had been widely

November 23, 1889. See Stevenson, *Morell Mackenzie*, 155. McInnis, however, claimed that Mackenzie was expelled. McInnis, Egan, and Aust, “Frederick William's Cancer,” 521.

⁸⁰⁷Sir Morell penned his best defense in Sir Morell Mackenzie, *Friedrich Der Edle Und Seine Arzte: Antwort Auf Die Berliner Broschüre: "Die Krankheit Kaiser Freidrich Iii."* (Leipzig: Ud. Spaarmann, 1888)., the main points of which are included in Mackenzie, *The Fatal Illness of Frederick the Noble*, Section II.—Controversial and Section III.—Statistical.

⁸⁰⁸Stevenson, *Morell Mackenzie*, 80. Dr. Stevenson wrote that routine pre-operative biopsy with microscopy to confirm the presence of a malignant laryngeal process did not become *de rigeur* until the 1930s. Stevenson, *Morell Mackenzie*, 79.

⁸⁰⁹Stevenson, *Morell Mackenzie*, 168.

reported, so that for several decades histologic examination was regarded as worthless.”⁸¹⁰ For evidence, Dr. Kirchner cited a 1926 quotation from J. E. MacKenty, “one of the leaders in the treatment of laryngeal cancer,”⁸¹¹ who wrote that “Unless grave reasons for haste exist, repeated and careful examination over a few weeks are recommended, and biopsy employed only when an impasse is reached and a positive diagnosis cannot be made by observation.”⁸¹² In addition to the unreliability of the microscopist’s interpretation, added Kirchner, some feared that biopsy could stimulate the growth of the cancer.⁸¹³ Mackenzie was one who so feared.⁸¹⁴

These warnings against the vicissitudes of clinical cancer microscopy, as we have seen, were hardly of recent vintage. Even Morell Mackenzie, who insisted on the micropathological confirmation of a suspicious tumor prior to its extirpation, admonished the practitioner in his 1871 textbook, *Growths in the Larynx*, to be wary “against relying too greatly on microscopical examination for differential diagnosis.”⁸¹⁵

Questions

The history of the treatment of cancer from General Grant to Crown Prince Friedrich to President Cleveland reveals a steady increase in reliance on the microscope to aid diagnosis and treatment. In the case of Grant, the use of the microscope was, at best, an afterthought. In the

⁸¹⁰Kirchner, "A Historical and Histological View of Partial Laryngectomy," 809.

⁸¹¹Ibid.

⁸¹²Ibid., citing J. E. MacKenty, "Cancer of the larynx," *Arch. Otolaryngol.* 3 (1926): 205-232.

⁸¹³Ibid.

⁸¹⁴Mackenzie charged, for example, that Professor Gerhardt’s fulgurations of the Crown Prince’s tumor either induced the transformation of a benign lesion into a malignancy, or “if it was malignant from the first, the disease was undoubtedly aggravated by the treatment.” See Mackenzie, *The Fatal Illness of Frederick the Noble*, 44. Speculation on the cause(s) of cancer and what would make a malignancy better or worse abounded in the nineteenth century. Unfortunately, much was conjectured, but little was known, about tumor origin and growth until the twentieth century.

⁸¹⁵Stevenson, *Morell Mackenzie*, 79.

case of Friedrich, diagnosis and treatment were stymied by conceptual conflicts despite an earlier role for microscopy. The study of the diagnosis and treatment of Cleveland's cancer showcases the modern use of the instrument as a primary participant in both the diagnosis and treatment of cancer.

Did the Crown Prince Friedrich debacle reverse the development of the application of the microscope to cancer medicine? Was the diagnosis of cancer by microscopic examination of biopsy tissue effectively banished from the thoughts and actions of late nineteenth-century clinicians? Was the confirmatory biopsy of General Grant's cancer near the end of his course, a mere afterthought, typical? Was Mackenzie's insistence on pre-extirpative microscopic proof of cancer outlandish? Was Dr. O'Reilly's rush to biopsy President Cleveland's mouth tumor for immediate microscopical diagnosis an unconventional act fraught with questionable judgment and a significant risk of inaccuracy?

As in most historical assessments, isolated examples do not a proof make.⁸¹⁶ For instance, upon deeper investigation the condemnatory quotations from Drs. Stevenson and Kirchner on cancer microscopy do not constitute more than a short-lived blemish on its value in the diagnosis of laryngeal cancer. Unsurprisingly, as the age of specialization dawned in the last years of the nineteenth century,⁸¹⁷ not all fields of medicine reacted in the same way to the promise (or censure) of medical microscopy. What was true for cancer of the larynx did not extend to cancers at other sites, for cancer is one of many diseases that can evolve over space as well as time—involving different organs in its course. In addition, the few years encompassed

⁸¹⁶Reality intervenes. In a fantasy world (as projected, for example, by the English philosopher David Hume) all examples might be available for testing and therefore constitute proof. The truth of this statement follows from the fact that if all evidence in the Universe sustained the validity of an assertion, then no examples would be available to contradict it. Since most of us live in the real world, historians generally use a few examples to support what in actuality is an allegation rather than a proof.

⁸¹⁷Stevens, *American Medicine and the Public Interest*, 53-54.

by the case studies of General Grant (1884-1885), Prince/Emperor Friedrich (1887-1888), and President Cleveland (1893) constituted one of the most rapidly-changing and transformative periods in the history of modern medicine. To appropriate William Sedgwick's famous quip on public health and apply it to cancer microscopy (and shift the time frame slightly), "Before 1880 we knew nothing; after 1890 we knew it all; it was a glorious ten years."⁸¹⁸

Evidentiary sources enabling one to evaluate the growth of the importance of the microscope in the diagnosis of cancer over the last years of the nineteenth century include a wealth of published (medical textbooks, scientific articles, newspaper stories) and unpublished (surgical reports) documents.

The Sources

Wellsprings of Support: The Importance of Texts and Other Writings

Textbooks of clinical medicine and the medical sciences provide excellent sources for the assessment of multi-year trends in the latter half of the nineteenth century in changing fields like microscopy. Compilation of these tomes requires years and, for economic reasons, statements and conclusions tend to be uncontroversial rather than polemical.⁸¹⁹ Further, texts of this nature usually restrict subject matter to the specific rather than the encyclopedic, thus ensuring focus rather than scatter. Furthermore, they are plentiful and constitute a rich diachronic mine for the historian of medicine. Thus, they are an excellent tool to assess clinical attitudes over time, including questions on the acceptance of diagnostic cancer microscopy in the late nineteenth century.

⁸¹⁸Elizabeth Fee, *Disease and Discovery: A History of the Johns Hopkins School of Hygiene and Public Health, 1916-1939* (Baltimore: The Johns Hopkins University Press, 1987), 19. Quoted by David Rosner, ed., *Hives of Sickness: Public Health and Epidemics in New York City* (New Brunswick: Rutgers University Press, 1995), 12.

⁸¹⁹But see the one-author exception of John Hughes Bennett immediately below.

Nineteenth-century texts were often penned by a single author rather than the many of today. As a result, texts sometimes argued in favor of ideas and methods before their general acceptance. John Hughes Bennett, an early example, insisted, in his 1849 text, that the microscope was essential to cancer diagnosis—but only when combined with clinical acumen.⁸²⁰ Only the microscope could accurately diagnose cancer, he wrote, but there were caveats as true then as now in both research and clinical practice. “Not that this instrument is in itself capable, even in the most expert hands, of doing any thing, but, conjoined with a knowledge of the symptoms, progress of the case, form and appearance of the morbid growth, it offers us an additional and most valuable means of prosecuting our inquiries.”⁸²¹

Scientific articles offer more up to date information than do textbooks. They are written in a much shorter time period and reflect more narrow analysis of a specific topic. Unlike textbooks, which often seek ecumenism rather than particularism, they often react to previous papers. As such, they yield insight into contemporaneous controversies that textbooks do not confer. Their deficiency, like newspaper articles, is lack of context.

In addition to topicality and lack of context, newspaper articles serve to give notice of the feelings and beliefs about cancer on the part of the non-medical establishment. Although newspaper editorials and feature writings may favor the parochial over the universal, certain papers like *The New-York Times* catered to a wide readership even in the late nineteenth century.

Surgical reports (the description of the operation by the operator) reveal the composite effect of theory, training, and experience on the actual application of knowledge to the goal—the treatment and/or cure of the cancer patient. Such reports are narrative and contemporary,

⁸²⁰Bennett, *On Cancerous and Cancroid Growths*.

⁸²¹*Ibid.*, 221.

although their formulaic style may obscure exceptions and deviations from the norm.

Nevertheless, surgical records provide the most basic evidence in favor of the adoption of cancer microscopy, for the future of the microscope for cancer diagnosis in the late nineteenth century depended largely on the surgeon as surgery became the optimal mode of treatment.

The Times

Watershed Years for Cancer Microscopy

Clinicians in Europe and American, despite years of exhortations promoting the use of the microscope in cancer by Bennett in Edinburgh, Francis Donaldson in Baltimore, Lionel Beale in London,⁸²² Oliver Wendell Holmes in Boston and others, remained skeptical of the merit of cancer microscopy. Dr. Mackenzie's 1871 admonition questioning the value added to clinical diagnosis by cancer microscopy, quoted above, is typical of the decade.⁸²³ Further, in his 1880 *Manual*, he failed to even mention the use of the microscope for the diagnosis of cancer of the pharynx or tonsil. He wrote that diseases in these sites should be diagnosed by clinical inspection.⁸²⁴ Less than seven years later, however, as evidenced by the case of the German Prince, he had clearly changed his stance on the microscope in the evaluation of neoplastic disease.

⁸²²Lionel S. Beale, *The Microscope in Medicine*, 4th ed. (London: J. & A. Churchill, 1878). Much, much more could be written about Lionel Beale's influence on the development of medical microscopy in the second half of the nineteenth century. My main focus in this chapter has been the German contribution to American medical microscopy. Nevertheless, I must note that upon Beale's death in 1906, William Osler, who had only recently removed to England, wrote that "Scores of men of my day...will always be thankful for the stimulating work which [Beale] did in Medical Microscopy." See Anton Sebastian, *A Dictionary of the History of Medicine* (New York: The Parthenon Publishing Group, 1999), 110.

⁸²³Stevenson, *Morell Mackenzie*, 79.

⁸²⁴Mackenzie, *Diseases of the Throat and Nose*, 82, 83. Nevertheless, he strongly urged the use of the microscope for postmortem confirmation of the ante mortem clinical diagnosis. See Mackenzie, *Diseases of the Throat and Nose*, 84. This venerable practice of diagnostic reinforcement, followed at least since the time of Hippocrates, provides positive and negative clinicopathological correlation (feedback) that remains a major pillar of medical education to this day.

From the 1880s to the 1890s, cancer microscopy (and medical microscopy in general) steadily gained favor. Those who valued the microscope in medicine extended its use far beyond that which had been contemplated by pioneers in optics, chemistry, and anatomic pathology. In part, this was due to the revolution from rational and empiric medicine toward scientific medicine. In essence, the acceptance of the microscope in cancer medicine resulted from a remarkable combination of new lenses, improved microtechniques, advances in medical education, renewed efforts toward the professionalization of medicine, and the rise of bacteriology. The 1880s opened with distrust and denial of the efficacy of cancer microscopy and ended with such widespread acknowledgment of its virtues that Cassandras warned of an overreliance on the microscope for diagnosis to the exclusion of clinical assessment.

There were many other factors that promoted the value of the cancer microscope at this time, for at its core the scientization of medicine included a revived interest in instruments like the microscope. Medical colleges began to offer courses in microscopy to attract students during an era of unprecedented growth in societal wealth—especially after the microscope became popular at the undergraduate level.⁸²⁵ The transmutation of medicine from word to science also had the consequence of increasing its complexity. No longer, in the famous words of eighteenth-century physician Dr. William Buchan, could “Every man [be] his own doctor.”⁸²⁶ The

⁸²⁵Stowell, "Microscopy in the University of Michigan."

⁸²⁶William Buchan, M.D., *Domestic Medicine; or, the Family Physician: Being an Attempt to Render the Medical Art More Generally Useful, by Shewing People What Is in Their Own Power Both with Respect to the Prevention and Cure of Diseases. Chiefly Calculated to Recommend a Proper Attention to Regimen and Simple Medicines.*, Special Edition, 1993 ed., 1 vols. (Philadelphia: Joseph Cruikshank, For R. Aitken, 1774; reprint, 2d. American edition, 1774; Special Edition privately printed for the members of The Classics of Medicine Library, 1993. The phrase might perhaps be better attributed to John Tennant, who published *Every Man His Own Doctor, or the Poor Planter's Physician* in 1734. The term may well be misconceived, for women—not men—did most of the homebound doctoring at the time.

Subsequent “editions” (mostly reprints) of Buchan’s text were published well into the nineteenth century. Paul Starr, following the lead of Francis Packard, wrote that *Domestic Medicine* was “the most influential book of its kind.” See Starr, *The Social Transformation of American Medicine*, 33, 452FN4.

instrumentation, education, and knowledge base requisite for the practice of medicine by the 1880s professionalized medicine and made it more difficult for non-physicians to utilize the microscope in medicine.⁸²⁷ Bacteriology united these different streams of interest and added the all-important element of pragmatism—for bacteria, the newly discovered cause of disease and target of therapy, could be visualized only with the aid of the microscope. So extreme was the turnaround in favor of the adoption of microscopy during these two decades that, by the end of the era, *not* to evince familiarity with the microscope and apply its newly-accepted benefits to medical practice was to appear unprofessional.

Explanation through Evidence

No single event during the final twenty years of the nineteenth century led to the mass adoption of medical microscopy by practicing physicians. The episodes chosen to illustrate the development of the history of cancer and microscopy during this era—the cancer case histories of General Grant, Crown Prince Friedrich, and President Cleveland—reflected, more than promoted, the role of the microscope in cancer medicine.⁸²⁸ Instead, incremental changes inspired by a handful of happenings related to the elements of the scientization of medicine—the movement of medical education from amphitheaters to the laboratory and clinic, and the revolutionary influence of microbiology on medical thought and practice—transformed the role

⁸²⁷Paul Starr entitled this era “The Consolidation of Professional Authority.” See especially Starr, *The Social Transformation of American Medicine*, 100-06.

⁸²⁸Indeed, it might be more accurate to write that the role of the microscope in the care of these three personages reflected *the worst* of cancer microscopy. The microscope served General Grant’s physicians as a confirmatory—if questionable—afterthought; Prince Friedrich’s as a misconstrued mandate that delayed a possibly curative procedure and (may have) unnecessarily cost him his life; and Cleveland’s, so shrouded in secrecy, that the microscope’s potential as a positive good in the diagnosis of the President’s cancer never received the publicity it deserved during his lifetime. In such analyses, it is necessary to remember that the microscope and those who interpreted its images were part and parcel of their times.

of the microscope in medicine from an enthusiast's plaything to an instrument of cancer diagnosis and the *sine qua non* of modern cancer medicine.

The 1880s began with clinician skepticism about the use of the microscope in clinical diagnosis and treatment. Review of the *Index-Catalogue of the Surgeon General* (today's *Index Medicus*) from its first year of publication in 1879 until 1887 reveals few entries for even an expanded definition of the meaning of "medical microscopy."⁸²⁹ A paucity of citations promoting the role of the microscope in medicine reflected indifference rather than antipathy, for the *Catalogue* during these years also lacked condemnatory writings. Instead, the turn toward medical microscopy, evident in later volumes, received impetus from a multiplicity of medical and societal sources.

In 1881, an editorial in *The New-York Times* urged improved diagnostic techniques to stem the growing plague of cancer deaths.⁸³⁰ "The popular dread of cancer," opined the *Times* editor, "is only equaled by the uncertainty of the medical profession in the diagnosis of that deadly disease."⁸³¹ What solution did the editor suggest? The microscope! The editorial cited Francis Donaldson's (misspelled as "Donalson") thirty-year-old work on the cancer cell and his strong promotion of the use of the microscope for cancer diagnosis. Reflecting the still-popular belief in constitutionalism, it urged the practitioner to "use the resources of science before the disease has become a deep-seated constitutional disorder."⁸³² Still, the editor had done his

⁸²⁹I reviewed all entries referring to "cancer," "microscope," and "microscopy" for the years 1879-1893 in the original *Index-Catalogue of the Surgeon General* volumes at the New York Academy of Medicine.

⁸³⁰New York Times, "Cancers—Microscopic Diagnosis: Donalson's and Smith's Papers on (Editorial)" 1881; 4:6-7.

⁸³¹Ibid.

⁸³²Ibid. Note the use of the word "constitutional" merely three years before General Grant bit into his peach of fate.

homework, for he acknowledged that microscopists had met “with only a measure of success.”⁸³³

The *Times* suggested that, despite the errors and misinterpretations attributed to the microscope in the past, practitioners should push forward on the study of cancer utilizing the microscope.

That same year, Carl Seiler, an American laryngologist, published the first indigenous American text on microscopy.⁸³⁴ Earlier American texts on microscopy and microtechnique pirated European editions or reworked basic German and British writings.⁸³⁵ Seiler’s *Compendium of microscopical technology* reveals that he had direct experience with microtechnique and microscopy. This pioneering American treatise hardly attained best seller status, but it did reveal that the *idea* of the microscopy had gained a foothold among some physician groups within the United States.

No fact in science is worthless; if we do not now see its practical bearing, it will, sooner or later, be brought forth.

—Francis Donaldson, 1853

In 1882 and 1883, Robert Koch announced a series of scientific discoveries that revolutionized the study and practice of medicine. Nevertheless, his associations of specific germs with human diseases initially received little notice on this side of the Atlantic. Koch’s 1882 identification of the “bacillus of tuberculosis,” for example, warranted nothing more than a brief notice in the *Boston Medical and Surgical Journal*.⁸³⁶ The American reviewer could not confirm Koch’s finding—nor did he discuss its enormous implications—but he did speculate that “our readers are likely to hear of this discovery again.”⁸³⁷ Why? Because although the

⁸³³Ibid.

⁸³⁴C. Seiler, *Compendium of Microscopical Technology* (Philadelphia: Brinton, 1881). Cited by Bracegirdle, *A History of Microtechnique*, 56FN88.

⁸³⁵Bracegirdle, *A History of Microtechnique*, 50.

⁸³⁶Boston Medical and Surgical Journal, "Bacillus of Tuberculosis."

nineteenth century was replete with purported causes of the “white plague,” the *Journal* reasoned that Koch’s laboratory and microscopical fastidiousness promised that if anyone could find the true agent of tuberculosis, he could.

The German microscopist’s discovery of the cholera bacillus the next year received only slightly more notice. Nonetheless, the continual parade of micropathogen discoveries by Europeans during the 1880s (and 1890s) transformed a trickle of American practitioner interest in medical microscopy into a torrent of excitement.⁸³⁸ Tumors and bodily fluids suddenly became targets for biopsies and collection. Indeed, some wondered whether the ideal nature of the microscope for the visualization of these tiny creatures was merely fortuitous or rather the result of heavenly design, for their size was perfect for identification under the corrected light microscope.

Short is the Life of an Idea without its Institutionalization

Popular calls for new efforts toward a solution to the waxing problem of cancer, contributions toward microtechnique, and scientific discoveries played major roles in the growth of medical microscopy. In the early 1880s, however, a major proponent was missing— institutional support. Individual scientists and pathologists proclaimed the value of the microscope in cancer medicine throughout the century, but rare were the organizations in the United States that transformed thought into action and promulgation. The first working session of the American Microscopical Society, for example, held in Chicago in 1883, trumpeted microtechnique and its application to investigations in botany, zoology, and even human

⁸³⁷Ibid.

⁸³⁸Kenneth M. Ludmerer delineated the year-by-year discovery of the “bacteriologic origin of certain diseases” during the years 1873 to 1905. See Ludmerer, *Learning to Heal*, 77 Table 4.1.

physiology. Even though, the boosters of this American microscopical establishment took little notice of its value to diagnosis in cancer or even medicine.⁸³⁹

Institutions originate from individual advocates of a cause. During the early 1880s, a ripple of isolated proponents of microscopic medicine swelled to a tidal wave. At first, a small but far-flung coterie of American supporters peppered medical journals and newspapers with calls for medical microscopy. They were the advocates and instigators of medical microscopy in the United States. Among their number were M. D. Mann,⁸⁴⁰ Carl Hempel Reed,⁸⁴¹ and George Duffield.⁸⁴² Mann, a practitioner in Buffalo, New York, can be considered as an outspoken advocate for cancer microscopy.

Mann, a gynecologist, was firmly grounded in the works of Johannes Müller and Rudolf Virchow. At a presentation to the Buffalo Microscopical Club in early 1883, he bewailed the fact that clinicians could not distinguish benign and malignant tumors on a timely basis.⁸⁴³ Whether or not there existed a unique cancer cell, nevertheless, he wrote, the microscope was the key to diagnosis because it permitted differentiation between the two most important types of malignancies—carcinomas and sarcomas.⁸⁴⁴ In conjunction with clinical features that could by themselves mislead diagnosis and postpone therapy, Mann found that certain characteristics of

⁸³⁹Gage, "Microscopy in America (1830-1945)," 84.

⁸⁴⁰M. D. Mann, "Some Points on the Histology of Malignant Tumors," *The Buffalo Medical and Surgical Journal* 22, no. 7 (1883).

⁸⁴¹Reed, "The Histogenesis of Carcinoma."

⁸⁴²Geo. Duffield, "Microscopical Diagnosis of Carcinomata," *Detroit Lancet* 7, no. 11 (1884).

⁸⁴³Mann, "Some Points on the Histology of Malignant Tumors," 300. The fact that Dr. Mann had a particular interest in diseases of women and showed a deep concern for cancer should not be a surprise. Prior to the advent of X-Rays and other internal imaging devices, the majority of premortem cancers detected by physicians were breast and cervicouterine—the special province of the gynecologist.

⁸⁴⁴*Ibid.*, 301-2.

the tumor tissue led to a definitive diagnosis of cancer, even without the invocation of a unique cancer cell. These included the number of cells in a given area under the microscope; their irregular, “malformed and misshapen” nature; and (long before tumor angiogenesis got its name) a “peculiar arrangement of the vessels.”⁸⁴⁵

Few accepted Mann’s insights. An unnamed “distinguished clinician” who, Mann wrote, had only a few days before “ceased to place any dependence on the microscope as a means of diagnosis,” was typical of practitioners.⁸⁴⁶ To him, Mann issued this cry for understanding and action. Only through an open-mindedness born of education and the humility that comes with experience could physicians realize the great potential of the microscope in the early diagnosis of cancer and its potential surgical cure.⁸⁴⁷ No, a diagnosis of cancer would not strike the eye fully formed from the biopsy’s microscopic image. “It has been thought by the uninitiated,” he wrote, “that we would see, with our lenses, the word ‘cancer’ printed on every cell and every fibre, and that all that were [sic] necessary was to have a small bit of a suspected growth to enable us to say absolutely as to its character.”⁸⁴⁸ The microscope could not and would not supplant the physician, surgeon, or pathologist, but it was an essential supplement to clinical acumen. Hence Mann’s impassioned “plea for the microscope, and for a proper understanding of its true position in reference to the very important matter, the diagnosis of tumors.”⁸⁴⁹ Dr. Mann’s institutional

⁸⁴⁵Ibid., 305, 04. One hundred and twenty years after Mann’s description, the Food and Drug Administration approved a drug (trade name Avastin; generic name bevacizumab) that inhibits the growth of blood vessels that sustain cancer cells.

⁸⁴⁶Ibid., 306.

⁸⁴⁷Ibid.

⁸⁴⁸Ibid.

⁸⁴⁹Ibid., 305.

affiliate, the University of Buffalo, was on its way to becoming a leader in American cancer medicine, to no small extent due to its emphasis on cancer microscopy.⁸⁵⁰

Medical Microscopy on Trial—1883

A case study from an unlikely source—the judicial system—highlights the dubious role held by the microscope in medicine in the early 1880s. The physician response to the decision handed down by the Pennsylvania court in *Commonwealth v. Dr. Samuel Gast* speaks volumes as to the low repute held by cancer microscopy at that time.

In 1883, the *Philadelphia Medical Times* reported on the trial of Sam Gast for manslaughter.⁸⁵¹ Dr. Gast—whose medical credentials, if any, went unreported—was an itinerant “cancer-doctor” reminiscent of William Avery Rockefeller. He traveled from town to town advertising his ability to cure cancer “without the use of the knife” in the local newspapers. Innumerable testimonials from unverifiable sources buttressed his claim.

The story began when a seventy-eight-year-old resident of Chester, Pennsylvania consulted her local physician for a small ulcer under her left breast. The practitioner decided that he could not be sure of the diagnosis, but since she appeared healthy it really did not matter. Nothing was to be done. He neither advised nor obtained a biopsy for microscopical examination. Indeed, no evidence was presented that he even considered a tissue diagnosis. Even if the lesion was malignant, concluded the local doctor, it “would not give [her] much trouble.” In words echoed throughout the century, the woman’s physician “further urged him

⁸⁵⁰Dr. Roswell Park and his laboratory at the University of Buffalo developed this leadership position in cancer and cancer research through their focus on cancer germs through the microscope in the 1890s and 1900s.

⁸⁵¹C. W. De Lannoy, “Cancer Cured without the Knife--the Operation a Success, but the Patient Dies--Report of the Trial of a Travelling Cancer-Doctor for Manslaughter,” *Philadelphia Medical Times* 13 (1883).

[the husband] never to mention the word cancer, as the resulting mental disturbance would affect her general health, which was at this time most excellent.”⁸⁵²

The woman, much to her misfortune, was dissatisfied with her physician’s pronouncements. She sought a second opinion. Enter Dr. Gast. He allegedly applied a “test medicine” that would turn the lesion black at its “roots” if cancer was present. Gast claimed that malignancies that reacted this way included “spider cancers, rose cancers, black cancers, and cauliflower cancers.”⁸⁵³ He concluded that the patient suffered from one of these cancers and wasted no time in applying his treatment—a caustic paste on and around the lesion that caused a “slough” (a chemical peel). A chemical dermabrasion of this nature can be excruciatingly painful, as the patient claimed. In fact, however, the cancer was, as advertised, “removed without the aid of the knife.” Gast treated her similarly for an ulcer under her right breast. It is unclear if she actually had such an ulcer. Shortly thereafter the patient died of “hemorrhage and exhaustion.”⁸⁵⁴ Gast absconded.

A Chester grand jury indicted the cancer-doctor on a charge of involuntary manslaughter and issued a warrant for his arrest. A posse of Chesterians apprehended him in Bellefonte, about one hundred and fifty miles away, where he was found to be “diligently working the same game.”⁸⁵⁵

At trial, Gast revealed that he had applied something to the patient’s ulcer to “burn it out.” By the coroner’s measurement, the ‘it’ amounted to seventy-eight square inches of flesh—

⁸⁵²Ibid., 531.

⁸⁵³Ibid., 533. I am not familiar with the histopathological nature of these purported malignancies under their given names. Nor have I come across them in my research for this paper. They are most likely descriptive terms coined by Gast to give a sense of authenticity to his work. That said, “cauliflower” is a word still used for a fungating malignancy. It does not, however, imply a specific cancer diagnosis.

⁸⁵⁴Ibid., 530.

⁸⁵⁵Ibid., 531.

many times greater than the tiny ulcer. Compounding the indictment, autopsy failed to reveal any evidence of cancer or anything that remotely resembled cancer. Of note, the coroner based this conclusion on both gross and microscopical evidence.

The case was a prosecutor's dream—an assured “guilty” verdict. C. W. De Lannoy, the author of the *Medical Times* article, performed the microscopy himself and provided the medical evidence against Gast. The microscopist confirmed the absence of any evidence of cancer and added that Gast had removed “twenty-five times [more tissue] than was necessary”—even if there had been cancer. The prosecution concluded that the self-proclaimed cancer curer had chemically cauterized nothing more than “a chronic ulcer” and murdered the patient in the process.⁸⁵⁶

The defense appealed specifically to the jury's mistrust of medical microscopy, claiming that De Lannoy used faulty microtechnique. They stipulated, for example, that his sections were cut “too thin” to diagnose cancer. In a remarkable display of “forensic eloquence,” the defense attorney appealed to the jury's inbred bias against the value of the microscope in medicine.⁸⁵⁷ Instead, he claimed that the case against the defendant was brought by jealous local physicians blind to Gast's amazing healing powers! The microscope was of no use in the diagnosis of cancer. Witnesses for the defense offered testimonial after testimonial affirming the cancer doctor's success in curing the dread disease. How, asked the prosecution, did the cured patients know they had cancer? Gast told them so. The prosecution retorted that none of the “cured” patients had shown any evidence—especially microscopical evidence—that they had cancer prior to Gast's treatment.

⁸⁵⁶Ibid., 532.

⁸⁵⁷Ibid., 533.

The plea fell on deaf ears. The jury acquitted Gast. The State had tried and failed to bring the medical microscope into the courtroom. Proponents of the microscopic analysis of disease had yet to convince the public of the diagnostic value of cancer microscopy. At the time, most American practitioners agreed.

First the Scientist-Physician

How was this bias reversed? First came the improvement of the microscope by scientist-physicians. By the mid-1880s, Ernst Abbé and other mechanical geniuses of the era had advanced the optical capabilities of the light microscope to a level comparable to that of today. Abbé's 1868 invention of the apochromatic lens was a great leap forward toward the fulfillment of the dream of three centuries of microscopists—an aberrationless lens.⁸⁵⁸ A decade later, Zeiss incorporated Abbé's apochromatic lenses, substage condensers, and oil immersion system into a new microscope—the modern light microscope. It is this marvel of physics and engineering for which Zeiss is famous, and for which modern versions of his light microscopes continue to be famous. Microtomal improvements and progress in other aspects of microtechnique also occurred during the 1880s to achieve this new system of microscopy.

At its core was a remarkably precise, available, and affordable “modern” microscope founded upon scientific progress in physics, lenses, and metallurgy.⁸⁵⁹ As one American microscopist noted in *The New York Medical Journal* in 1884, “few who are not constant readers of the literature pertaining to the physics of the microscope are aware of the great advances that have been made in the knowledge of the microscope as a physical instrument, and of the correspondingly great progress in the construction of the optical part due to such knowledge that

⁸⁵⁸<http://www.history.mcs.st-andrews.ac.uk/history/References/Abbe.html>: 2. Accessed March 30, 2003.

⁸⁵⁹As noted, microscope manufacturers constructed cheap scopes throughout the nineteenth century. Never before the 1880s, had precision, availability, and affordability come together in a single microscope.

has been made within the last ten years.”⁸⁶⁰ The roots of the modern microscope lay not in the late sixteenth or seventeenth centuries (where popular conception places it), nor in the early nineteenth century (when the lens improvements of Lister and others came to the fore), but in the late nineteenth century—and the 1880s in particular—when science, engineering, and manufacturing created an innovative instrumentology capable of investigating a new developing world of disease.

Venerable physician-scientists like Müller, Virchow, and Ehrlich needed no stimulus to integrate microscopy into their daily work. Their examination of the human condition from a medical perspective necessitated visualization of that which was too small to see with the naked eye. The new scientist-physician, among whose numbers may be included W. W. Kean and Joseph Bryant, was a practitioner who matured after the American Civil War and whose thoughts and actions followed a revolutionary methodology based on investigation and experience. Members of this new breed required a strong impetus to overcome the negative connotations of the microscope in clinical practice. Bacteriology provided that incentive.

Then Microbial Motivation

As an enzymatic reaction will not proceed without its substrate, so the microscope would not have had the impact it achieved late in the century without the impelling force of microbiology. Developments in the study of bacteria and other microbes gave the growing numbers of scientist-physicians the impulse to employ the microscope routinely. Links between bacteria and disease proceeded at a remarkable pace. So great was this influence upon all

⁸⁶⁰Hitchcock, "Recent Studies on the Theory of the Microscope," 337.

aspects of medicine and American society that the study of cancer became part and parcel of the microbiological revolution.⁸⁶¹

The timing of these discoveries in bacteriology is critical for an understanding of the making of modern cancer during the late nineteenth century.⁸⁶² Robert Koch's discovery of the tuberculous and cholera bacilli in 1882 and 1883, respectively, were not the first bacterial sightings, but they bolstered the idea that germs caused human diseases. In 1884, Edwin Klebs and F. A. J. Löffler identified *Corynebacterium diphtheriae*, the cause of the common and deadly childhood disease diphtheria.⁸⁶³ That same year, Nikolaier discovered *Clostridium tetani*, another bacterium whose toxin causes disease—in this case tetanus, a lock-up of the neuromuscular system. Eberth and Gaffky discovered the typhoid bacillus, the scourge of young children and adults alike, found in contaminated waters and tainted foods.⁸⁶⁴ Also in 1884, Fraenkel found the exciting cause of most pneumonias and named it *Diplococcus pneumoniae* after its microscopic appearance—two balls stuck together.⁸⁶⁵

Eighteen eighty-four was a watershed year in the history of medical microbiology for other reasons as well. Hans Christian Joachim Gram, a Danish physician, experimented with

⁸⁶¹See Nancy Tomes' wonderfully entertaining Tomes, *The Gospel of Germs*, Introduction and Chapter 7, "Antisepticconscious America".

⁸⁶²The dates cited in this section for the initial identification of various bacteria are commonly accepted. Nevertheless, other sources reveal that many of the microbes "discovered" during the 1880s and 1890s were first noted years earlier. The anthrax bacillus, for example, which Koch proved to be the cause of the disease in 1876, was first identified by Davaine and Pollender, French and German practitioners, respectively, in 1849. See Foster, *A Short History of Clinical Pathology*, 53. This recognition of these earlier discoverers is more than a trivial pursuit, for Louis Pasteur, a young man in the late 1840s, was greatly influenced by Davaine's finding. See Edwin Emerson, Jr., *A History of the Nineteenth Century Year by Year*, 3 vols., vol. 3 (New York: P. F. Collier and Son, 1901), 1379.

⁸⁶³I select *C. diphtheriae* in particular because of its tremendous medical and societal importance. In the 1880s, the mortality from diphtheria was about thirty-five (35) per cent. Emil von Behring's discovery of diphtheria antitoxin in the early 1890s reduced the death rate to about five (5) per cent. In 1901, von Behring won the first-ever Nobel Prize for Physiology or Medicine for his immunologic work on the *Corynebacterium*.

⁸⁶⁴Sigerist, *The Great Doctors*, 368.

⁸⁶⁵Current nomenclature uses the Genus-species taxonomy *Streptococcus pneumoniae*.

different chemicals to stain bacteria and concocted a process that he found particularly effective. Not long thereafter it became one of the most popular bacterial stains in the history of medicine—the Gram stain.⁸⁶⁶ In the Danish capital that same year, Louis Pasteur received high praise as the guest of honor at the meeting of the International Congress of Medicine.⁸⁶⁷ His work, which began with questions on the nature of fermentation, resulted in the creation of new industries and played a pivotal role in the acceptance of germ theory. Only a few months after Copenhagen, Pasteur applied concepts of germ theory to the development of a human vaccine against rabies that thrilled European and American medical-scientific communities alike.⁸⁶⁸ The success of Pasteur’s rabies vaccine, in combination with Koch’s proof of the causative nature of the tuberculous bacillus, thrust microbiology and the microscope to the forefront of medical as well as popular thought and practice. Media acclaim reinforced that practice.⁸⁶⁹ The micropathogenic mentality soon included cancer medicine as well.

Reinforced by a New Language of Cancer

⁸⁶⁶The Gram stain, taught to medical students and used by clinical microbiologists to this day, was one of many microtechniques for staining bacteria in the late nineteenth century. The result of Gram’s method—bacteria that retain the violet color and those that do not—gave rise to the well-known differentiation of bacteria into Gram-positive (stained) and Gram-negative (unstained) bacteria. The influence of this distinguishing characteristic has been so pervasive that contemporary antibiotics are often classified by their effects on “Gram-positive” and “Gram-negative” bacteria.

For Gram’s original citation, see C. Gram, “Über die isolirte Färbung der Schizomyceten in Schnittund Troken-präparaten,” *Fortsch. d. Med.* 2 (1884): 185-189.

⁸⁶⁷Coincidentally, Dr. Morell Mackenzie also attended the Copenhagen Congress. Naturally, he presided over the Section of Laryngology.

⁸⁶⁸In Copenhagen, Pasteur lectured on his canine experiments with rabies antiserum. On July 6, 1885, Pasteur inoculated Joseph Meister, the first patient to receive the anti-rabies serum. The young boy grew up to become a porter at the Pasteur Institute, but killed himself when the German Nazis entered Paris in 1940. See Stevenson, *Morell Mackenzie*, 47.

⁸⁶⁹For a perspective on the effects of Pasteur’s breakthrough on the non-scientific community, see Bert Hansen, “America’s First Medical Breakthrough: How Popular Excitement About a French Rabies Cure in 1885 Raised New Expectations for Medical Progress,” *American Historical Review* 103, no. 2 (1998).

Microbiology was not the only development to propel advances in cancer microscopy in the late nineteenth century. In 1885, as General Grant lay dying from metastatic epithelioma, Karl Friedländer, a young German pathologist, published a major treatise on medical microscopy that included cancer microscopy.⁸⁷⁰ His work encapsulated and augured the battles to come over the true nature of cancer into the twentieth century.

As late as the mid-1880s, the microscopic definition of cancer remained unsettled. Older microscopists like Virchow insisted that the diagnosis of cancer required the demonstration of tissue invasion and metastasis. Others disagreed, utilizing an updated version of the unique cancer cell concept that allowed a diagnosis of cancer based upon neoplastic characteristics of cells in and of themselves. Friedländer, for example, cited Waldeyer's definition of cancer as "an atypical proliferation of epithelium." This was a profoundly simple definition that required neither tissue invasion nor metastasis.⁸⁷¹ Nevertheless, the young Friedländer was sympathetic to the identification of tissue invasion, but only as a mark of aggressiveness, "*for the malignancy of the process is shown if it forces its destructive way through various tissues without hindrance.*"⁸⁷² Contiguous invasion, in this revised conception of cancer, was sufficient rather than necessary for its diagnosis. This was a major turnaround in thinking from the accepted wisdom of Virchow, for it permitted diagnosis at an earlier (and presumably more curable) stage of disease.

The real problem with cancer microscopy, Friedländer argued further, was not the definition of cancer. Rather, difficulty lay with the ability of the microscopist to recognize what

⁸⁷⁰Friedlaender, *The Use of the Microscope*.

In 1882, Karl Friedländer also identified another bacterial cause of pneumonia—Friedländer's bacillus. Today it is known as *Klebsiella pneumoniae*. Edwin Klebs, the co-discoverer of the diphtheria bacillus, independently noted the cause of this variant form of pneumonia in 1883.

⁸⁷¹*Ibid.*, 170.

⁸⁷²*Ibid.*, 171. *Italics* in the original.

he saw as cancer, an ability that depended heavily on the level of experience of the microscopist. Rather, difficulty lay with the degree of experience of the microscopist. Friedländer bemoaned the fact that too many cancer diagnoses were being made by microscope greenhorns. Education was the key, but hard-won knowledge remained the best assurance of accuracy. Until there came a time when both conditions were routinely achieved, only the experienced could be trusted to make a microscopical diagnosis of cancer. For Friedländer, unlike postmortem-driven pathologists of previous generations, the importance of the cancer diagnosis in the living patient was crucial. He recognized that (1) the “*immediate danger*” of a possible malignancy could be confirmed or denied microscopically;⁸⁷³ (2) an unequivocal microscopic diagnosis of cancer was essential prior to extirpative surgery (a theme that would be soon adopted by Mackenzie and others);⁸⁷⁴ (3) total excision of the cancer was mandatory because “if total extirpation is not performed the patient will die soon”;⁸⁷⁵ and (4) great danger lurked in the growing problem of the misidentification of cancer microscopically—for the pathologist, the practitioner, and, of course, the patient.⁸⁷⁶ As physicians became more reliant on the microscope for the diagnosis of cancer, the microscopist needed to be extremely careful that his diagnosis was accurate. The emphasis was shifting from whether the microscope should be used in the diagnosis of cancer to how it should be used.

⁸⁷³Ibid., 173. *Italics in the original.*

⁸⁷⁴Ibid., 172.

⁸⁷⁵Ibid., 173.

⁸⁷⁶Ibid., 1, 186-88. Friedländer argued that the best means to prevent “false positives” (seeing things that were not there; making diagnoses that were not true) was to have a firm grasp of the normal vs. the abnormal—the time-tested foundation of clinical education. As Friedländer warned, “*A discovery should never be regarded as pathological in its character unless the specimen has in every case been directly compared with the normal organ, which has been similarly treated.*” See Friedlaender, *The Use of the Microscope*, 186. Italics in the original.

The Imprimatur of Cancer Histories

History textbooks, in their academic sense as contemporary interpretations of the past, tend to appear only after their subjects are contextually coherent.⁸⁷⁷ As such, medical textbooks of the era offer a glimpse into the thought processes of those who wrote the histories, thus adding to the campaign in support of medical microscopy in the 1880s. Although many earlier microscopy textbooks included an introductory chapter on “the history of the microscope,” these essays tended to be timeline enumerations of names and dates with little context. It is therefore noteworthy that interpretive, contextual histories of microscopy and the microscope began to appear for the first time in the last two decades of the nineteenth century. E. M. Nelson produced such a work on “Historic Microscopy” for the famed Quekett Microscopical Club in 1885.⁸⁷⁸ Later that year, John Mayall, Jr. delivered the Cantor Lectures in London, on the history of the microscope.⁸⁷⁹ Mayall presented a series of five lectures over several weeks on the subject. He presented an in-depth historical analysis from the Ancient Greeks forward as to how lenses and microscopy had come, by the 1880s, to their stage of advanced development.

In 1891, J. H. Wilson published a two-part “History of the Microscope” in the *International Journal of Microscopy and Natural Science*, which itself had commenced publication only a decade before.⁸⁸⁰ In the celebratory fashion of popular history writings, his

⁸⁷⁷In other words, historical works tend to appear after their subjects have passed from the forefront of everyday consciousness.

⁸⁷⁸Nelson, "Historic Microscopy."

⁸⁷⁹Mayall, "Cantor Lectures on the Microscope".

During the 1880s, John Mayall, Jr., a long-time member of the Royal Microscopical Society, selected, purchased, and shipped more than one hundred and forty microscopes to what would become the Billings Microscope Collection of the Army Medical Museum in the United States. Today, it is the Armed Forces Institute of Pathology. See Blumberg, Smith, and Leeper, *Billings Microscope Collection*, v.

⁸⁸⁰Wilson, "The History of the Microscope."

essay commemorated the “tercentenary of the invention of the Microscope.”⁸⁸¹ Nevertheless, the bulk of his work concentrated upon the substantive advances in microscopy during the 1880s. With boundless optimism not uncommon in science-oriented treatises of the era, he projected that the microscope of the future would uncover “the ultimate elements of the material world.”⁸⁸² Further, judging from the enormous advances in microscopy he had witnessed in just the past few years, this future microscope, compared with the contemporary one, “will have little else than the name in common with it.”⁸⁸³ In closing, he noted that the microscope had become far more than “the instrument of strict scientific research.”⁸⁸⁴ In short, the microscope was no longer a “mere toy” of the natural philosopher.⁸⁸⁵ It had become, in essence, the preferred instrument of the scientist-physician and the physician-scientist. These late-nineteenth-century histories corroborate the coming of age of the microscope as the principle means of diagnosing modern cancer.

To Build More and Better Microscopes:

Manufacturing & the Dissemination of Medical Microscopy

As written works evidenced and celebrated the growth of the role of the microscope in science and medicine, so technical advances in manufacturing during the mid-1880s furthered the availability and appeal of the microscope for medicine. The tremendous rise in industrial techniques evident in the fields of transportation, communication, and weaponry in the latter half of the nineteenth century directly affected microscope manufacturing as well. Decreased

⁸⁸¹Ibid., 168.

⁸⁸²Ibid., 215.

⁸⁸³Ibid.

⁸⁸⁴Ibid.

⁸⁸⁵Ibid.

transport time and lower carrying costs allowed parts to flow to manufacturers and finished microscopes to ship to end-users more efficiently, quickly, and cheaply than ever before. Better gauges of supply and demand through improved communication between seller and buyer increased the efficiency of microscope manufacturing, as in many other industries. Technological improvements, common to other “take-off” economic scenarios, generated increased productivity through multiple efficiencies.

Interchangeability of parts was an idea whose time had come to microscope manufacturing only in the 1880s. In 1855, Samuel Colt opened an arms factory in Hartford, Connecticut. The Colt revolver became famous for its accuracy and the fact that its highly-machined parts were interchangeable. As Henry Ford’s assembly line—itsself highly dependent upon the concept of interchangeable parts—revolutionized the production of gasoline-driven automobiles half a century later, so Colt revolutionized the production of small arms and, in the process, inspired all manufacturers with the concept that reproducibility was a stepping-stone toward a mass market and increased profit. As Oscar W. Richards noted in his article on American microscope makers, the interchangeability of microscope parts in 1886 was “an idea only recently in extensive use.”⁸⁸⁶

Ernst Abbé’s apochromatic lens, fully integrated into the Zeiss microscope only in the mid-1880s,⁸⁸⁷ serendipitously contributed to the growth of medical microscopy. Abbé’s new lenses, “practically free from colour, and...clearer and sharper,” as Wilson exulted in his 1891 history, allowed the production of photomicrographs of a quality higher than anything Lebert or

⁸⁸⁶Richards, "American Microscope Makers," 125.

⁸⁸⁷Wilson, in his 1891 article, noted that Abbé’s “invention of a new type of optical glass,” occurred in the “last three or four years”—placing the date of lens incorporation around 1887. See Wilson, "The History of the Microscope," 213. Corinne Jacker situated the date for the new lens squarely in 1886. See Jacker, *History of the Microscope*, 175.

Woodward could have dreamed only a few years earlier.⁸⁸⁸ Medical journals began to replace timeworn line drawings with photomicrographs.⁸⁸⁹ As a result, medical education and information propagation in microscopy flourished, increasing the visibility and, with the benefit of experience demanded by Friedländer, the acceptability of the microscope in clinical medicine. The scientist-physician was accorded a higher degree of respect for his utilization of the microscope than ever before.

The Practitioners

Clinicians adopted medical microscopy more slowly than scientist-physicians like Virchow, Ehrlich, and Woodward. Nevertheless, by the last years of the 1880s, naysayers in the practice of medicine were fewer in number and less vocal in their condemnation of cancer microscopy than only a few years earlier. As the quality of individual instruments improved, education and experience increased, and accurate biopsy assessments followed, medical microscopy became more prevalent and better accepted among practitioners. Clinicians in America and their recalcitrant confrères in Europe began to embrace microscopy as an answer to the elusive quest for accurate pre-operative cancer diagnosis, a diagnosis that surgeons required and patients demanded.

The trajectory of practitioner acquiescence from the mid-1880s to the 1890s is evident from contemporary sources. As late as the Spring of 1886, Charles Sajous confirmed the still-prevalent skepticism toward medical microscopy in his *Lectures on the Diseases of the Nose and*

⁸⁸⁸Wilson, "The History of the Microscope," 214.

⁸⁸⁹Superb-quality photomicrographs taken through the apochromatic lens were only part of the reason for the revolution in medical-journal illustrating. Advances in photo-printing, led by the development of halftones, also contributed. Although *The Times* of London published the first photograph to appear in a newspaper in 1842, it was not until 1880 that the *New York Daily Graphic* published the first photographic illustration that utilized what became the industry-standard screened halftone. American photographer Frederick Ives had developed the first halftone photographic printing process only two years earlier.

Throat.⁸⁹⁰ These talks, delivered at the Jefferson Medical College in Philadelphia, taught that the diagnosis of cancer of the pharynx, General Grant's malignancy, was to be achieved solely by palpation—the clinical sense of touch. Palpation is a purely clinical undertaking.⁸⁹¹ Sajous found no need for microscopy in the diagnosis of cancer.

Nevertheless, advances in microtechnique were already beginning to influence the clinician's acceptance of diagnostic microscopy. In 1887, for example, certain textbook authors cautiously alluded to the use of the microscope in the *ante mortem* differential diagnosis of cancer. One was the Englishman Lennox Browne. In *The Throat and Its Diseases*, he wrote that he had “recently” employed the microscope in the case of a sixty-year-old man with a tonsillar lesion in order to differentiate a potential epithelioma from syphilitic gummata.⁸⁹² This need to differentiate was akin to the dilemma that confronted Crown Prince Friedrich's physicians. Whether Browne succeeded is unclear.⁸⁹³ Whether the micropathological findings aided his medical management is unknown. Nevertheless, his clinical use of the microscope to attempt to reach an early diagnosis of cancer reveals a growing interest by practitioners in that direction.

The late eighteen eighties were watershed years in the union of the diagnosis and treatment of cancer and the microscope, but for other reasons. As the idea that microscopic germs could cause disease gained a foothold in America, the number of publications that included medical microscopy as an essential element rose dramatically. From the first volume of

⁸⁹⁰Charles E. Sajous, *Lectures on the Diseases of the Nose and Throat, Delivered During the Spring Session of Jefferson Medical College* (Philadelphia: F. A. Davis, Att'y, 1886).

⁸⁹¹*Ibid.*, 276. Sajous, unlike Mackenzie a year later, suggested that the treatment of cancer of the pharynx was “extirpation, when practicable.” Sajous considered tumor excision even in the absence of confirmatory microscopy. See Sajous, *Diseases of the Nose and Throat*, 276.

⁸⁹²Lennox Browne, *The Throat and Its Diseases, Including Associated Affections of the Nose and Ear*, Second ed. (London: Bailliere, Tindall, and Cox, 1887), 246.

⁸⁹³Friedrich's physicians clearly did not succeed.

the Surgeon-General's *Index-Catalogue* (later the *Index Medicus*) in 1879 through volume six in 1884, cancer articles were highly descriptive and rarely mentioned microscopy.⁸⁹⁴ In 1885 (volume seven), articles that analyzed microscopical technique predominated over those of clinical microscopy. The majority of cancer-related clinical entries for that year consisted of surgical case reports *sans* microscopy. At the same time, however, the number of articles on medical microscopy far exceeded those of previous years. Almost all were in German.⁸⁹⁵

In 1886 and thereafter, a major change occurred in the number of *Index*-listed publications that interlaced microscopy with clinical aspects of cancer. More often than not, authors increasingly aimed these writings at the practitioner rather than the researcher. A noteworthy example is a series of interdisciplinary articles based upon a convocation of the Glasgow Pathological and Clinical Society held on February 3, 1886 and published in a major Scottish medical journal. The articles illustrate how far the notion of cancer microscopy had developed by the mid-1880s.

Glasgow Medical Journal Vols. 25-26 (1886)

The Pathologist

Several issues of the *Glasgow Medical Journal* during the Spring of 1886 contained remarkable articles on the value of cancer microscopy for the cancer clinician. In many ways, these publications constitute a window into the history of cancer in the late nineteenth century. As was common in the day, the series achieved a much wider readership than merely those who received the *Glasgow Medical Journal* by direct subscription, for many American publications

⁸⁹⁴I compiled this information from my personal extended review of each volume of the Surgeon-General's *Index-Catalogue* for the 19th century (1879-1900).

⁸⁹⁵Dr. John Shaw Billings, much to his credit in a time of growing nationalism, included medical publications from many foreign countries (although mainly Anglo-European) and languages in his compilation. He was the major force behind the *Index-Catalogue* at its inception.

(and those of other countries) appropriated the articles—with and without acknowledgment. The “Glasgow Cancer Series,” derived from meetings of the Glasgow Pathological and Clinical Society, proposed to encompass much of what was known clinically about cancer at the time. The series may have been inspired by the rapidly rising incidence of cancer—a societal concern that was just coming to light in medical and public circles. Specifically, as Dr. Joseph Coats remarked in the opening, the presentations sought to examine cancer’s “origin and mode of extension; recurrence; hereditary tendency; and how does cancer cause death.”⁸⁹⁶

Coats began his elucidation of the contemporary conception of cancer from the well-worn pathological perspective. He defined the disease in the Virchowian tradition as a tumor that “in its growth does not respect neighbouring structures.”⁸⁹⁷ Nevertheless, he embraced the more modern concept illuminated by microscopy that cancer was broader in scope than the malignancy of invasion and metastasis.⁸⁹⁸ Indeed, the microscope helped recognize that the disease known as cancer clearly included many different cell types and tissue origins with dissimilar degrees of aggressiveness.

Implicitly casting the old notion of constitutionalism aside, he also asserted that cancer was specific to its site of origin. The microscope, he claimed, proved that cancer was a local rather than constitutional disease, for metastases “breed true” to their location of origin rather than their site at discovery. Connective tissue cancers remain sarcomas. Epithelial tissue neoplasms remain epitheliomas (carcinomas).⁸⁹⁹ In words that could have been written a century

⁸⁹⁶Joseph Coats, "On Cancer in Certain of Its Pathological Aspects," *Glasgow Medical Journal* 25, no. 4 (1886): 250.

⁸⁹⁷*Ibid.*

⁸⁹⁸*Ibid.*

⁸⁹⁹*Ibid.*, 256.

later, Coats noted that they have “the same form and the same arrangement as that of the primary tumour.”⁹⁰⁰ Thus, the microscope taught the practitioner that he need not accept the appearance of cancer in different parts of the body as an innate property of the organism as a whole (constitutionalism). Rather, cancer originated at one place and spread to others while maintaining the characteristics of the primary tumor (localism with metastasis). Microscopic sections of blood and lymphatic vessels showed tiny bits of the original cancer en route to their deadly destinations. Thus, concluded Coats, cancer in its modern sense was local, retained its native cell type, and originated in either epithelial or mesodermal tissues. This new vision of cancer as a local disease, derived from and supported by cancer microscopy, had far-reaching advantages for both diagnosis and treatment, as the final two chapters of this dissertation will demonstrate.

The Surgeon

William Macewen, in the next article, explored surgical aspects of the treatment of cancer.⁹⁰¹ His key question addressed the mechanism by which cancer proliferated; viz., how do neoplasms spread? Knowledge of this process could aid its surgical excision—and stay the hand of the surgeon when the disease had outgrown the reach of the scalpel. Such foresight could avoid needless surgical complications and the loss of life resulting from vain operative interventions that so worried Samuel David Gross in 1853.

Macewen offered four pathways to explain the development of an increased cancer burden in the individual. These were (1) direct invasion of contiguous tissues;⁹⁰² (2) invasion of

⁹⁰⁰Ibid.

⁹⁰¹William Macewen, "Carcinoma in Its Pathological and Aetiological Aspects, with Remarks on the Principles of Its Surgical Treatment," *Glasgow Medical Journal* 25, no. 4 (1886).

⁹⁰²Ibid., 277.

the lymphatic system (with its own nexus of lymph nodes, glands, and vessels);⁹⁰³ (3) dissemination through the all-pervasive venous system⁹⁰⁴ and auto-inoculation—the direct spread of cancer by contiguous contact.⁹⁰⁵ Armed with knowledge of this pathophysiology of how cancer spreads throughout the body, the modern surgeon could dispose of a resectable cancer by following a few simple rules: do not cut into the cancer at surgery (for fear of auto-inoculation),⁹⁰⁶ and remove all adjacent and effected lymphatics and fat (to eliminate residual cancer that could lead to recurrence). Years before Halsted received credit for the radical mastectomy, Macewen taught that extirpative breast cancer surgery should excise more than just the breast in order to increase the probability of cure. “The mamma is then quickly detached and elevated in a piece with the flap of axillary adipose tissue. So that the primary tumour, the lymphatic vessels, and lymphatic glands, are removed *en masse*.”⁹⁰⁷

Macewen expressed contempt for those recalcitrant practitioners who clung to notions of constitutionalism, for such ideas precluded surgical treatment for potentially curable cancers. He could excuse laymen for harboring this outmoded concept, but not his fellow clinicians. “There is a prevalent opinion among the laity, reflected from and fostered by, many of the best members of our profession, that cancer is a constitutional or blood disease, and that any one becoming the subject of this affection is inevitably doomed. Logically, with such an opinion, there is little or no use of operating at any stage.”⁹⁰⁸ The erroneous belief in the constitutional nature of cancer

⁹⁰³Ibid., 278.

⁹⁰⁴Ibid., 279.

⁹⁰⁵Ibid., 280.

⁹⁰⁶Ibid., 289.

⁹⁰⁷Ibid., 290.

⁹⁰⁸Ibid., 291.

punished the innocent, for the very thought of cancer caused the patient to postpone a visit to the doctor. This fear-based procrastination, more often than not, insured his or her early demise.

Physicians steeped in traditional conceptions of cancer who demanded clear clinical evidence of invasion and/or metastasis prior to action compounded the tragedies of those patients fortunate to appeal for help early in their course. With such an additional delay, the diagnosis and prognosis of cancer as a death sentence became a self-fulfilling prophecy. Thus, innumerable patients and doctors waited until the disease became incurable. “The propagation of [a belief in the constitutional nature of cancer],” warned Macewen, “is productive of the most dire of results.”⁹⁰⁹ The microscope, through its support of cancer localism, taught that postponement of tumor diagnosis and treatment through foolish constitutionalism and other old ways of thinking about cancer was akin to manslaughter.⁹¹⁰ No longer was death from cancer the ineluctable consequence of punishment for sin.

The Senior Surgeon

Jonathan Hutchinson, Senior Surgeon to the London Hospital as well as Professor of Surgery and Pathology in the Royal College of Surgeons, also addressed the Glasgow Pathological and Clinical Society on that Wednesday in early February, 1886. He concurred with Coats and Macewen that the local nature of cancer was beyond question. Further, Hutchinson concurred that localism was the keystone for the immediate treatment of cancer, for it “enforce(s) upon the surgeon the duty of acting very promptly, very boldly, and, if need be, very perseveringly, in its operative treatment.”⁹¹¹

⁹⁰⁹Ibid.

⁹¹⁰Manslaughter is “the unlawful killing of a human being without express or implied malice.” <http://www.merriam-webster.com/dictionary/manslaughter> accessed March 7, 2008.

⁹¹¹Jonathan Hutchinson, “On Cancer as a Local Disease, and the Importance of Its More Detailed Clinical Study,” *Glasgow Medical Journal* 25, no. 5 (1886): 342.

To some extent, Hutchinson bemoaned the microscopic nature of cancer, because it left “the whole subject of new growths...for some time past almost exclusively in the hands of those who use the microscope.”⁹¹² Hutchinson complained that histologists “re-classified tumours for us (practitioners—LK), and have indeed in some instances almost written out their life-histories in the laboratory.”⁹¹³ Instead, he suggested that clinicians and microscopists should work hand in hand. Nevertheless, clinicians appeared uninterested in cancer microscopy when histopathologists seized the opportunity to create a new nomenclature based upon microscopical elements of the disease. The use of the microscope in the diagnosis of cancer, long the black sheep of a family dominated by constitutionalism, had swung from ‘nay’ to ‘yea.’ No longer could the cancer patient be adequately served without it. The microscope permitted a new classification for pathological growths in general, a new terminology of tumors, and a new conception of the nature of cancer. Somewhat to Hutchinson’s chagrin, the microscope had become essential to cancer diagnosis.

The Pathologist of Literature and Theory

A. Ernest Maynard showed amazement at the recent rapid growth in cancer literature. “Hardly a week passes,” he discovered, “but some journal either at home or abroad contains some reference to carcinoma.” Germany, France, and England were the major contributors to this expanding literature. The United States went unmentioned in Maylard’s observation, but this was not unreasonable. Dr. John Shaw Billing’s *Index-Catalogue* affirms the paucity of American contributions.⁹¹⁴

⁹¹²Ibid., 329-30.

⁹¹³Ibid.

⁹¹⁴This is my personal observation after review of the *Index-Catalogue* volumes for the years in question.

Maylard had another interest beyond cancer literature; viz., “the microbial theory of carcinoma.”⁹¹⁵ He was against it. Perhaps his enthusiasm for cutting-edge cancer studies led him to contemplate the notion that microscopic organisms caused cancer, but his condemnation of the idea was years ahead of his colleagues, for the germ theory of cancer was far from reaching its apogee. Nevertheless, Maylard recognized that the microscope was the key to finding “a little microbe comfortably curled up in a cancer cell.”⁹¹⁶ None, however, had yet been demonstrated to his satisfaction. He sadly concluded that although cancer bore a strong clinical resemblance to diseases of recently-proven microbial origin, he could not accept “this tempting theory,” for “there is (no microbe) in their histological structure.”⁹¹⁷ The microscope had an additional utility. It could also disprove theories of cancer’s origin.

The Practitioner's Perspective

John Glaister was a practitioner’s practitioner who penned his contribution to the *Glasgow Medical Journal* with the confidence and genius of a clinician who had first-hand cancer experience during his career. He presciently noted that although the microscope had become essential to the day-to-day care of the cancer patient, the true cure for the disease lay elsewhere.⁹¹⁸ He focused on bringing the cancer patient to the physician sooner and without shame—even women with breast tumors.⁹¹⁹

Not in theories, nor through microscopes, would the clinician find the solution to reducing the growing number of deaths from cancer. Instead, Glaister believed the answer lay in

⁹¹⁵Maylard, "Carcinoma Considered Chiefly in Its Pathological Aspects," 349.

⁹¹⁶Ibid.

⁹¹⁷Ibid.

⁹¹⁸John Glaister, "Cancer from the Family Practitioners Point of View," *Glasgow Medical Journal* 25, no. 6 (1886).

⁹¹⁹Ibid., 445.

increased public awareness of the disease. Glaister applied the somewhat abstract notions of cancer localism and diagnostic microscopy to the real woman with a breast lump, bloody vaginal discharge, or some other symptom or sign of disease. Although there was “no more terrible disease” than cancer, he wanted that at-risk individual to know that cancer was no longer—if it had ever been—incurable.⁹²⁰

Practitioners, newly enthusiastic about the use of the microscope for the diagnosis of cancer, learned that early diagnosis and treatment gave new hope to the cure of a disease shrouded, in the public psyche, in pain, suffering, and horrible, inevitable death. Twenty-seven years before the founding of the American Society for the Control of Cancer, Glaister predicted that “the remedy...is to spread widely the fact that cancer in its inception is purely a local lesion, and that extirpation of it at this stage will afford almost complete impossibility of return.”⁹²¹ Enlightened practitioners needed to promulgate the gospel of the culture of modern cancer to inform a disillusioned public still under the sway of traditional, pre-microscope clinicians. Still, Glaister’s main concern was the layman who perceived cancer in terms of sin rather than science. Practitioner knowledge of the new art and science of cancer microscopy was not enough to overcome these prejudices. Modern physicians needed to trumpet these new findings far and wide.

Glasgow Series, In Conclusion

In closing, these participants and others in the Glasgow series represented a new discourse on cancer and the microscope in the modern age. Not all the writings showered the microscope with praise. Indeed, some took the debate beyond cancer microscopy to ask why

⁹²⁰Ibid.

⁹²¹Ibid.

Clinicians founded the American Society for the Control of Cancer, which later became the American Cancer Society, in 1913.

modern theories of cancer that embraced it failed to yield better outcomes for patients. Specifically, they criticized the new microscope-derived terminology,⁹²² questioned why the local theory of cancer had not led to more cures,⁹²³ and complained that the Victorian “delicacy” of the gentle sex prevented women from seeking timely counsel from their (male) physicians.⁹²⁴ The Pathological and Clinical Society discussions involving cancer microscopy continued long after the papers that led to the 1886 Glasgow series were published. In sum, they reaffirmed the new but enduring clinical role of the microscope in the diagnosis and treatment of cancer—its triumphs and shortcomings.

The Burden of Proof Inverted: 1887-1893

By the late 1880s, the burden of proof had shifted from the scientist-physicians who urged the use of the microscope in the everyday care of cancer to those who condemned it. An avalanche of evidence accumulated in the late 1880s and early 1890s that sustained the efficacy of cancer microscopy. Nevertheless, it was more postscript than prologue, for scientists and physicians had already proclaimed the great ideas and consequences of the microscopic nature of the disease—the concept of the cancer cell, localism, and early surgery—to all who would listen. The turnaround from condemnation to attestation was so complete that, by the last years of the century, practitioners embraced the microscope with conviction and utilized the technology in their daily rounds.

Applications of cancer microscopy to new arenas of diagnosis and treatment aided its acceptance by the average practitioner. The trickle of cancer articles in the *Index-Catalogue* that involved microscopy in the early-to-mid 1880s became a torrent by the last years of the decade.

⁹²²Hector C. Cameron, "The Aetiological and Clinical Aspects of Carcinoma," *Glasgow Medical Journal* 25, no. 5 (1886): 355.

⁹²³Steven, "The Origin of Cancer," 426.

⁹²⁴Glaister, "Cancer from the Family Practitioners Point of View," 445.

Increasingly, clinicians adapted findings from one technique or organ system to another.⁹²⁵ The cell-based microscopical examination of sputum was a case in point. Attempts by Andral (1821) and Walsh (1843) to reliably diagnose lung cancer based upon the microscopy of sputum samples had failed. Improvements in microscopes and microtechnique by the late 1880s revived the old idea and made the cytological diagnosis of lung cancer reliable.⁹²⁶ In 1887, Hampeln demonstrated that the medical microscopist could consistently diagnose lung cancer from a sputum sample. This turn in diagnosis was a renaissance that fulfilled the nearly-forgotten promise of earlier nineteenth-century cytology.⁹²⁷

Practitioner opposition to cancer microscopy also melted away before a growing chorus of well-respected clinicians who supported cancer microscopy.⁹²⁸ Henry C. Coe, the surgeon at the fledgling New York Cancer Hospital who had enthusiastically reviewed Karl Friedlaender's textbook of microscopy in 1885,⁹²⁹ explicitly examined the risks and benefits of cancer microscopy in an 1887 article in *The New York Medical Journal*.⁹³⁰ He concluded that the

⁹²⁵The cross-pollination of ideas is one of the strongest contributors to the growth of knowledge.

⁹²⁶Sputum cytology greatly advanced the differentiation of lung cancer from tuberculosis. Röntgen discovered the X-ray on or about November 30, 1895, so internal imaging falls late in this period. See Wilhelm Konrad Röntgen, "Über eine neue Art von Strahlen," *Sitzungsberichte der physikalisch-medizinischen Gesellschaft zu Würzburg* (1895): 132. Although the "Röntgen Ray" was one of the most rapidly adopted technologies in medical history (and the public imagination), not until the first years of the twentieth century did clinicians routinely depend upon X-rays for the differentiation of various lung and other diseases. Until then, microscopic examination of sputum samples was the most specific method by which to diagnose lung cancer in the living patient.

⁹²⁷Onuigbo, "Lung Cancer in the 19th Century." Biopsy dominated cytology during the middle quarters of the century and, arguably, the final quarter as well. Today their relationship is complex and highly dependent upon the sampling method of the operator and the forte of the pathologist.

⁹²⁸The power of the authoritative medical voice in the Gilded Age and Progressive era is difficult to grasp for those of us who have lived through the last two generations of America's Age of Criticism (of authority). For a sociological and historical analysis of medical authority in the late nineteenth century, see Starr, *The Social Transformation of American Medicine*, Chapter 3 and especially pages 127-40.

⁹²⁹Friedlaender, *The Use of the Microscope*. Coe translated the work for D. Appleton and Company and donated his copy to the New York Academy of Medicine. I had the pleasure of reading it at the Academy's Malloch Rare Book Room.

instrument itself was not at fault for the errors of earlier diagnostic microscopy by surgeons and other practitioners alike, for there was “no real antagonism between the results obtained, unless truth is antagonistic to itself. It is the observers and not the observations that are in opposition.”⁹³¹ He strongly endorsed the use of the microscope for cancer diagnosis. Other medical masters of the day agreed.

Clinical thought leaders of the day threw their concerted support for medical microscopy into the founding of the Medical Microscopy Society in 1887.⁹³² Institutional validation, as in the case of the first cancer hospital, solidified the trend toward diagnostic microscopy and accelerated its growth. C. Heitzmann, one of the founders of the Society, served as its President two years later. In his Presidential address, he recalled that initially he had “serious doubts” about the ability of the Society to survive. After its founding, however, the number of microscopy courses in medical schools⁹³³ and the number of clinical pathology laboratories in hospitals⁹³⁴ increased dramatically. Thus, only two years after the establishment of the Society, Heitzmann no longer had any qualms as to its the durability.⁹³⁵ The profit potential of clinical

⁹³⁰The article is Coe, "The Clinical *Versus* the Microscopical Evidences of Malignant Disease." For more information, see the section above on “Obtaining the Specimen: The Autopsy of the Living.”

⁹³¹*Ibid.*, 681.

⁹³²C. Heitzmann, "The Future of Microscopy," *The Brooklyn Medical Journal* 3, no. 10 (1889): 597.

⁹³³Dock, "Clinical Pathology in the Eighties and Nineties," 673.

⁹³⁴*Ibid.*, 680, Morman, "Clinical Pathology in America, 1865-1915," 198. Dr. Morman’s analysis is specific to Philadelphia, but I believe many of his conclusions are generalizable beyond that city.

⁹³⁵Heitzmann, an Austrian immigrant who took up residence in Brooklyn, aimed his writing more toward those entering the new field of medical microscopy than toward patients who hoped to benefit from their work. Nevertheless, by 1889 he was able to answer his chief concerns (“Will there be a sufficient number of practitioners who are willing to be adepts of science?” and use the microscope for medical services) with a resounding ‘Yes!’ See Heitzmann, "The Future of Microscopy," 597.

histopathology, including cancer microscopy, was one of many factors that assured its longevity.⁹³⁶ Foremost, however, was the now-secure eminence of scientific medicine.

New Ideas, New Uses

When I began the use of the microscope, nearly twenty years ago, there were but few pathologic laboratories in the United States, and even the chairs of Histology and Pathology were 'more honored in the breach than in the observance' in at least nine-tenths of the first-class medical colleges. But now, what a happy advance. In every large city well equipped pathologic laboratories have sprung up to meet the professional demand; every first-class medical college can now boast of its laboratory equipments and 'show its faith by its works;' and thus in all directions we may discover the march of scientific medicine.

-James E. Reeves, 1894⁹³⁷

The role of the scientific impulse in everyday medicine and the microscope in medical research reinforced its application to practice through clinical pathology. Revival of a germ theory of cancer further promoted the microscope in cancer. In 1888, for example, the still-venerable Rudolf Virchow (who had only recently successfully side-stepped his probable culpability in the Crown Prince Friedrich debacle) announced that parasitic infection might cause cancer.⁹³⁸ This idea, in circulation through notions of infection and contagion long before Koch's identification of the anthrax bacillus in 1876, touched off a firestorm of debate on the credibility of a germ theory of cancer. Investigation of the controversy through tumor transplantation, diagnostic biopsy, and other methods all required microscopy.

By 1889, a marked increase in the demand for microscopes reflected the growth of medical and cancer microscopy through clinical pathology. The microscope trade grew rapidly

⁹³⁶Edward Morman elaborates on this point in his study of Philadelphia. See Morman, "Clinical Pathology in America, 1865-1915," 211.

⁹³⁷Reeves, *A Hand-Book of Medical Microscopy*, 21.

⁹³⁸John H. Woodburn, *Cancer: Search for Origins*, Holt Library of Science (New York: Holt, Rinehart and Winston, Inc., 1964), 102. Virchow's endorsement of a germ theory of cancer causation late in his career represented a major reversal from his long-standing belief that "irritation" was the exciting cause of cancer. Nevertheless, he may have rationalized that infection from germs was a form of irritation.

and capitalism entered the battle for market share. In the United States, the heady days of the early 1880s, which witnessed the largest number of microscope manufacturers in history, began to yield to consolidation—a sign of a profitable but maturing industry.⁹³⁹ Herbert R. Spencer, son of the American microscope pioneer, Charles A. Spencer,⁹⁴⁰ had established the Spencer Lens Company in Geneva, New York, in 1880. Nevertheless, it was not until 1889, when he moved to Cleveland with his renamed H. R. Spencer Optical Company, that business boomed. Two years thereafter, Spencer and Fred R. Smith formed the Spencer and Smith Optical Company, which remained a microscope-manufacturing institution until acquired by the American Optical Company in 1935.⁹⁴¹

Ernst Abbé Redux

In Europe, the last years of the 1880s were momentous times for the Zeiss works, the leading microscope manufacturer on the Continent. Although Carl Zeiss began the company that carried his name in 1847, it was not until the late 1880s that Zeiss microscopes enjoyed international repute. Ernst Abbé had much to do with both the research and corporate success of the firm. In the 1880s, he was responsible for both the optics and the production of the highly corrected apochromatic lens systems introduced by the Zeiss factory.⁹⁴² To a major extent, his corporate skill led to the establishment of Zeiss offices worldwide, an achievement that would have been difficult to imagine only a few years before.⁹⁴³

⁹³⁹Turner, *Great Age of the Microscope*, 14.

⁹⁴⁰Charles A. Spencer led C. A. Spencer & Sons for decades. His death in 1881 led to the dissolution of the firm, but the Gold Medal he won for his objective lenses at the international Paris Exposition of 1878 brought fame to his name. See Jacker, *History of the Microscope*, 120. Herbert R. Spencer capitalized on this publicity. See Purtle, "History of the Microscope," 258.

⁹⁴¹Padgitt, *Early American Microscopes*, 18, Purtle, "History of the Microscope," 258.

⁹⁴²Walton, Beeson, and Scott, eds., *Oxford Companion to Medicine*, 788.

Abbé first collaborated with Zeiss in 1866 when the latter approached the young professor with “various optical problems.”⁹⁴⁴ Zeiss made him a partner in 1876 and, beginning around 1887, manufactured the professor’s apochromatic lenses as an integral part of his microscopes.⁹⁴⁵ Abbé became sole owner of corporate Zeiss when his elderly partner died in 1888 after more than forty years in the optical business. The forty-eight-year old Abbé proceeded to expand the firm internationally. Abbé was in the right place with the right product at the right time. As the demand for microscopes for medical diagnosis grew, Abbé became a very wealthy man. In 1891, perhaps disillusioned by the inadequacy of Bismarck’s social reforms, Abbé founded the Carl Zeiss Foundation for research in science and social improvement.⁹⁴⁶ The marked growth in the microscope manufacturing industry, driven by the dynamic interplay between the adoption of scientific medicine, the acceptance of medical microscopy, and Abbé’s own contributions to the science and manufacturing of objective lenses, made Zeiss the premier microscope maker of its day.⁹⁴⁷

The Paradigm Shift toward Medical Microscopy Confirmed

Semantics

⁹⁴³<http://www.history.mcs.standrews.ac.uk/history/References/Abbe.html:2>. Accessed March 30, 2003.

⁹⁴⁴<http://www.history.mcs.standrews.ac.uk/history/References/Abbe.html:2>. Accessed March 30, 2003.

⁹⁴⁵Wilson, "The History of the Microscope," 213. Corinne Jacker subsequently gave the year as 1886. Jacker, *History of the Microscope*, 175.

⁹⁴⁶<http://www.history.mcs.st-andrews.ac.uk/history/References/Abbe.html:2>. Accessed April 1, 2003.

⁹⁴⁷Ernst Abbé, an amazing achiever on many fronts, did not end his Progressive endeavors with the establishment of the Carl Zeiss Foundation. In 1896, he inaugurated an early revolutionary form of welfare capitalism at Zeiss that included a cooperative corporate structure (where Zeiss management, employees, and the University of Jena all shared in the profits), an eight-hour work day, holiday pay, sick pay, and pensions. Upon his death in 1905, he left his estate to his beloved University of Jena and to the employees of Zeiss who had made him rich and famous. See <http://www.history.mcs.st-andrews.ac.uk/history/References/Abbe.html:2>. (Accessed April 1, 2003.) Interestingly, Abbé was born into a poor family and attended the University of Jena as a student only as the result of scholarships funded by his father’s employer.

Also around 1890, the modern semantics and conceptualization of cancer—now based upon cancer microscopy—took shape. Cancer terminology suffered from the widespread use of eponymous nomenclature, where the eponyms were not well known, and from torturing Latin to create names that bordered on the arcane as they failed to provide an understandable identity. This left physicians on different levels of a metaphorical Tower of Babel—unable to know if the words used to describe a tumor by two or more practitioners were a reasonable approximation of their thoughts and intended meanings. Under the new classification, practitioners and pathologists divided neoplasms (itself a recent neologism) into benign tumors and malignant cancers. Clinicians accepted the additional microscopically-determined subdivision of malignancies into carcinomas and sarcomas.⁹⁴⁸ Further, carcinomas were described as epithelial (thus serving as a transition from the old ‘epithelioma’ terminology based upon gross inspection) or glandular.⁹⁴⁹ Standardized terminology aided medical education and allowed investigators, practitioners, and pathologists to precisely communicate among themselves about patients and tumors.

Uniformity of terminology blended with experience to reduce the incidence of microscopical errors due to misinterpretation and misattribution. Accuracy increased. Practitioners lost their long-held contempt for microscopical diagnosis. At first, as evidenced by the General Grant case study, they used microscopy to confirm their own gross clinical opinions. Soon thereafter, however, the microscopical diagnosis dominated and framed the pathological diagnosis. Within the few years from the 1880s to the 1890s, microscopy became indispensable for the diagnosis of cancer. Indeed, practitioners rapidly became reluctant to diagnose cancers

⁹⁴⁸Henry Dickson Bruns, "The Pathological Aspect of Cancer," *New Orleans Medical and Surgical Journal* 16 (1889): 726.

⁹⁴⁹*Ibid.*, 728.

without microscopic confirmation—an amazing turnabout from their earlier resistance to medical microscopy. Previously unquestioned gross diagnoses yielded to conscious doubt as the number and types of tumor designations swelled.⁹⁵⁰ As Edward Schaeffer noted in an 1889 issue of the *Journal of the American Medical Association*, the microscope “often enabled (the clinician) to make a correct diagnosis when other signs fail.”⁹⁵¹ The universal call for the microscopic diagnosis of cancer was indeed a paradigm shift.

The Éclat of Medical Technology

The public, agog at the world-transforming, microscope-based medical and surgical achievements of the Pasteurs, Kochs, and Keens, developed a new faith in microscopical diagnosis. Perhaps for the first time in history, laymen sensed an almost palpable promise of a real *cure* for disease.⁹⁵² Practitioners used their new-found authority to nudge otherwise recalcitrant patients toward surgery. With a positive microscopical cancer diagnosis in hand, one writer noted in *JAMA* in 1889, “The surgeon is encouraged to act boldly where an operation is practicable, and the patient is induced to submit to an operation the arguments in favor of which might otherwise fail to carry conviction.”⁹⁵³

⁹⁵⁰Leukemia is a good example of the continuous differentiation of diseases into divisions and subdivisions in the late nineteenth century as a result of microscopic investigation. In the 1840s, Donn , Virchow, and Bennett wrote that leukemia (literally, ‘white blood’) should be distinguished from infection-related pyemia (the presence of copious numbers of white blood cells or leukocytes in the bloodstream). In 1891, Paul Ehrlich further subdivided leukemia into lymphatic and myelogenous types, a major distinction still used today. In the twentieth century, even more subdivisions resulted from microscopic, chemical, and genetic analyses. Today there are as many types of leukemia as there are different blood cells.

⁹⁵¹Schaeffer, “On the Microscopical Diagnosis of Cancer,” 403.

⁹⁵²Many authors make this point, although they rarely adequately credit the role of the microscope in the development of these revolutionary treatments. Pasteur’s rabies vaccine, Koch’s ill-fated (but still diagnostically useful) BCG (Bacillus Calmette-Gu rin), and Keen’s neurosurgical techniques serve as examples. See Hal Hellman, *Great Feuds in Medicine: Ten of the Liveliest Disputes Ever* (New York: John Wiley & Sons, Inc., 2001), 71-72.

⁹⁵³Schaeffer, “On the Microscopical Diagnosis of Cancer,” 404.

Within a few years, patients began to expect microscopical confirmation of their practitioners' now-considered-preliminary gross diagnostic "opinion." As expectations became demands, the physician who wanted to be viewed by his patients as up to date had no choice but to accept the primary role of microscopy in the diagnosis of cancer. This turned out to be no great sacrifice, for no matter how error-laden microscopical diagnosis had been in his youth, the physician of the late nineteenth century benefited enormously from the heightened authority and earning power afforded by his adoption of medical science and its new technique—microscopy.

The Growth of Cancer Research

The dynamic interrelationships between science, technology, medicine, and the public stimulated cancer research, which attracted inquiring youth to the field and further enhanced clinical practice. In 1890, David von Hansemann, who defended his doctorate under Jules Cohnheim (with whom Ehrlich studied) and worked as assistant to Virchow in Berlin, leaped beyond the first-order microscopical diagnosis of cancers to differentiate malignancies on the basis of their *dedifferentiation*—a key indicator of prognosis.⁹⁵⁴ His paper, published in *Virchows Archiv*, classified tumors on the basis of their degree of cellular regression—so-called anaplasia.⁹⁵⁵ The more anaplastic, the more deadly, the poorer the prognosis. The concept that malignant cells could "regress" and that this reversion to (what was believed to be) a lesser state of development could be identified and "graded" microscopically, formed the basis for much

⁹⁵⁴David von Hansemann, "Über asymmetrische Zellteilung in Epithelkrebsen und deren biologischer Bedeutung," *Virchows Arch. F. path. Anat.*, 119 (1890): 299-326. As James R. Wright, Jr. noted, von Hansemann published his article as a monograph three years later. See David von Hansemann, *Studien über die Spezificität den Altruismus und die Anaplasie der Zellen mit besonderer Berücksichtigung der Geschwulste* (Berlin: Verlag von August Hirschwald, 1893). Also see Wright, "Relationship of Surgical Oncology and Pathology in Early 20th Century America," 255 and 65 Footnote 35.

⁹⁵⁵'Anaplasia' is a term for cellular regression to what was believed to be a more primitive cellular state. The word is derived from the Greek, *ana-* backward + *plassein-* to form.

cancer research in the twentieth century as investigators explored cytological processes to discern “what went wrong” with renegade cancer cells.⁹⁵⁶

As cancer researchers discovered deeper insights from their microscopical investigations, microtechniques developed further. Progress in staining did not end with the young Paul Ehrlich. In 1890, Berthold Gustav Carl Giemsa, a Hamburg pharmacist, produced a new stain that particularly highlighted blood cells—including their nuclei and cytoplasm. Although Ehrlich had stained blood cells a decade earlier,⁹⁵⁷ the Giemsa stain was quicker to apply and yielded intracellular organelles in bolder outline.⁹⁵⁸ The very next year, Ehrlich, who had begun his investigations into the realm of cancer through chemistry, staining, and immunology, differentiated the two major types of leukemia using this stain. He based his myelocytic and lymphocytic varieties of blood cancer—named for their site of origin—on their microscopically-elucidated underlying cell type.⁹⁵⁹ Clinicians soon divided the dual leukemic designations into acute and chronic subtypes, which led to the four major variations of today—acute and chronic myelogenous leukemia; acute and chronic lymphocytic leukemia. Through science, research, and the transformation of the vocabulary of tumors in the late nineteenth century, the place of prominence for microscopy in the history of cancer was solidified.

Time Gained: Microscopy and the Intra-Operative Diagnosis of Cancer

⁹⁵⁶I borrow the word ‘renegade’ (more a value judgment than an indicator of scientific objectivity) with respect from Robert A. Weinberg, *One Renegade Cell: How Cancer Begins*, The Science Masters Series (New York: Basic Books, 1998). Weinberg’s story of the making of a cancer cell incorporates a historical biography of cancer researchers in the late twentieth century. Nevertheless, von Hansemann’s unmentioned notion of neoplastic anaplasia undergirds many of the later discoveries Weinberg elucidates.

⁹⁵⁷Clark and Kasten, *History of Staining*, 101.

⁹⁵⁸One of the most important early uses of the Giemsa stain was the diagnosis of the global scourge, malaria—a parasitical disease based upon the invasion of blood cells.

⁹⁵⁹Myelocytes emerge from the bone marrow (Gk. ‘muelos’: marrow); lymphocytes from the lymphatic system (New Latin ‘lymphā’: water).

As surgeons adopted the tenets of scientific medicine in the late nineteenth century, microscopy played a more important role in actual cancer operations as well as in clinical diagnoses. Until the 1880s, surgeons rarely removed biopsy tissue from the living patient for the purpose of diagnosis.

The reasons were clear. Prior to the advent of antibiotics, the dual threats of infection from “invasive” tissue removal (artificially bypassing the body’s natural microbial defenses by scalpel and other means) and lengthened operative time (increased microbial exposure) was significant. Instead, surgeons felt compelled to remove a tumor of ominous gross appearance in the here and now. Later, they would reconcile the clinical diagnosis with the micropathology later. The problem was the lengthy duration of slide preparation. Indeed, the total time from biopsy to tissue preparation to microscopical interpretation was so long that the patient might die before the surgeon received the confirming or refuting micropathology report. Clinical judgment in such circumstances was understandably paramount.

William Stewart Halsted’s role in the evolution of the operative treatment of breast cancer is illustrative of the changing attitude toward microscopy during cancer surgery. Halsted, who graduated from the College of Physicians and Surgeons in 1877 and returned to teach there after his post-graduate training with the famed Theodor Billroth in Europe, moved to the fledgling Johns Hopkins Hospital with William Henry Welch and William Osler in the late 1880s.

In 1891, standing firmly on the shoulders of his predecessors,⁹⁶⁰ Halsted took a further step when he performed the *en bloc* excision of a cancerous breast with the axillary contents

⁹⁶⁰The history of the mastectomy (breast removal) in general, and radical mastectomy (excision of the breast, axilla with lymph tissue, and underlying chest wall muscles) in particular, spans millennia. As early as 180 CE, Leonidas of Alexandria removed healthy-appearing tissue in addition to the lump in the breast, a conceptual

(including lymph nodes and vessels) and pectoral muscles attached. Not content with the implied theoretical assumptions of the operation—that cancer was a local disease that could disseminate through the lymphatics—Halsted sought the ability to discern between a benign and malignant tumor while the patient was still on the operating table. He and Welch reasoned that the dream of intraoperative diagnosis lay in rapid microtechnique.

Advances in microtomy, as noted above, were part of the solution, but faster total processing time of the biopsy was essential. Immediate microscopical diagnosis had to be quick and reliable to be diagnostically useful during surgery. Welch attempted to freeze Halsted's operative biopsy tissue for staining and inspection, but in 1891 his technique was so slow that Halsted completed the operation long before Welch could finish his micropathological analysis.⁹⁶¹ The necessity for rapid intra-operative diagnosis grew as the surgical treatment of cancer increased during the last decade of the century.

A young resident at Hopkins rose to the occasion four years later. In 1895, Thomas Cullen of the Johns Hopkins Pathology Laboratory rushed into publication an easy, rapid method

forerunner to the radical mastectomy of Halsted. In the eighteenth century, Henry Francois Le Dran, a Parisian surgeon, and Jean Louis Petit advocated the excision of the breast and its lymphatic drainage in the treatment of breast cancer to increase the probability of non-recurrence. In 1869, more than twenty years before Halsted's first reported radical mastectomy, Sweeting advocated removal of the lower portion of the pectoralis muscle in addition to the breast. In 1873, Richard von Volkmann, a German surgeon, added axillary (armpit) dissection to the treatment of breast cancer. He later claimed that by the late 1870s, this form of "radical" mastectomy was standard throughout Germany and Austria. In 1878, a year after his graduation from the College of Physicians and Surgeons, William Stewart Halsted sailed to Germany, like so many other American medical graduates in this history, to complete his training. He returned to the United States armed with the most modern ideas and techniques that the birthplace of scientific medicine had to offer.

For a more detailed explication of the history of the surgical treatment of breast cancer, see Michael B. Shimkin, *Contrary to Nature: Being an Illustrated Commentary on Some Persons and Events of Historical Importance in the Development of Knowledge Concerning.....Cancer* (Washington, D. C.: United States Government Printing Office, 1977).; Daniel De Moulin, *A Short History of Breast Cancer* (Boston: Martinus Nijhoff Publishers, 1983)., and from a richly-presented interpretation of Halsted and his legacy through the twentieth century, Barron H. Lerner, *The Breast Cancer Wars: Hope, Fear, and the Pursuit of a Cure in Twentieth-Century America* (Oxford: Oxford University Press, 2001)., Chapter 2, "Establishing a Tradition: William Halsted and the Radical Mastectomy."

⁹⁶¹Rosen, "Beginnings of Surgical Biopsy," 363. Welch was hardly the first to attempt rapid microscopical cancer diagnosis by frozen section. See Wright, "Surgical Pathology," 297.

of frozen section development at the instance of his mentor William Henry Welch.⁹⁶² Reminiscent of today's rush to publish, the now-venerated Hopkins pathologist feared that any delay on Cullen's part would jeopardize his claim to first discovery. Nevertheless, Louis B. Wilson of the Mayo clinic, despite the achievements of Cullen and Welch, developed and publicized a procedure for "fresh-tissue diagnosis" a decade later, a procedure that earned him acclaim as the discoverer of frozen-tissue diagnosis by those unaware of previous work in the field.⁹⁶³ The accomplishments of Welch, Cullen, and Wilson toward the dream of intra-operative tissue diagnosis forever linked between microscopy, surgery, and cancer. In the words of William Mayo, pathologists had finally achieved "a way to tell us surgeons whether a growth is cancer or not while the patient is still on the table."⁹⁶⁴ By the 1890s, it was clear to most that the path to improved cancer diagnosis and surgery required microscopy.

The World Expanded: Microscopy and Medical Education

The growing role of the microscope in research, clinical medicine, and surgery did not escape the attention of medical educators. Like other American physicians fortunate to receive post-graduate education abroad, Welch transplanted his German training across the Atlantic to his native country. In 1878, he established the first required laboratory course utilizing microscopy in a United States medical college at Bellevue in New York City.⁹⁶⁵ Columbia's College of Physicians and Surgeons followed with their own course the next year.⁹⁶⁶

⁹⁶²Thomas S. Cullen, "A Rapid Method of Making Permanent Specimens from Frozen Sections by the Use of Formalin," *Bulletin of the Johns Hopkins Hospital*, 6 (1895): 67.

In a reversal of the usually-conceived East to West trajectory of scientific development, Cullen also published his American article in a German journal of pathological anatomy. He entitled it "Beschleunigtes Verfahren zur Färbung frischer Gewebe mittelst Formalins," *Zentralbl. Allg. Path. Anat.*, 1895, 6: 448-50)

⁹⁶³Louis B. Wilson, "A Method for the Rapid Preparation of Fresh Tissues for the Microscope," *Journal of the American Medical Association* 45 (1905): 1737.

⁹⁶⁴Helen Clapesattle, *The Doctors Mayo* (Minneapolis: University of Minnesota Press, 1941; reprint, Pocket Books, 1968), 294.

During the nineteenth century, medical school proprietors of private institutions adopted a strong competitive spirit to attract paying students. Courses in medical microscopy became a drawing card and, as a result, a standard part of the curriculum. The cachet surrounding bacteriology was the initial impetus, but it was not long before the manifold applications of the microscope to medicine perpetuated coursework in microscopy in American medical colleges. Chief among these utilities was the new but rapidly growing field of clinical pathology, which drew many young physicians jealous of the fame achieved by many European and some American pathologists.⁹⁶⁷

Medical school proprietors and students also recognized the potential for new microscope-related occupations and the potential for increased income for practitioners. As George Dock reminisced on his education and early career in the late nineteenth century, he remembered that “obligatory laboratory courses were established in American schools in the eighties, patterned on the German models.”⁹⁶⁸ Nevertheless, as Dock wrote, it was really “in the nineties, it (the microscope) became more widely recognized as a valuable aid in diagnosis.”⁹⁶⁹ Indeed, Edward T. Morman credited Dock, then at the University of Michigan, with the founding of the first clinical laboratory in the United States in 1893—the year of Cleveland’s travail.⁹⁷⁰ Thus, in education as in clinical medicine and surgery, between the advent of the introduction of microscopy into the medical curriculum in 1878 and the establishment of the first permanent

⁹⁶⁵Morman, "Clinical Pathology in America, 1865-1915," 199.

⁹⁶⁶Ibid.

⁹⁶⁷Heitzmann, "The Future of Microscopy."

⁹⁶⁸Dock, "Clinical Pathology in the Eighties and Nineties," 673. As noted, the first such American courses were established in the late 1870s.

⁹⁶⁹Ibid., 680.

⁹⁷⁰Morman, "Clinical Pathology in America, 1865-1915," 199.

clinical laboratory in the United States in 1893, the attitude of the contemporary practitioner and future generations of practitioners toward medical microscopy morphed from rejection to skepticism to acceptance to necessity.

The Public Sees the Light

The adoption of medical microscopy by practitioners resulted from a long-term refinement of talents and techniques. The unflagging spirit of inquisitive American physicians led them to travel to the medical mecca that was Germany in the last half of the nineteenth century. From there they brought back new ideas and methods that had themselves only recently been invented or discovered by Europeans of many nationalities. As a result, these American/European trainees convinced everyday practitioners to use the microscope for the diagnosis and treatment of cancer and other diseases. In turn, what the clinician found in doing so was a more accurate and reliable means of differentiating tumorous diseases. Nevertheless, microscopy required positive popular opinion to establish a permanent place in the halls of medicine. The acceptance of medical microscopy within the community of practitioners was not enough by itself to sustain popular attention, for in the dynamic interplay between patient and physician, modern medicine provided a larger role for the patient than in earlier times. Had microscopy been welcomed by clinicians but not the general public, the microscope might never have become the icon of modern medicine.

The popularization of medical microscopy was neither spontaneous nor natural. Although wide-spread interest in the microscope among the curious and the wealthy spanned centuries, skeptics at least as long ago as John Locke in the seventeenth century sensed

something unnatural—even unholy—in the visualization of things too small for the unaided eye to see.⁹⁷¹

To a significant extent, Locke’s philosophy of moral anatomy persisted well into the nineteenth century. During the middle decades of that century, however, the mechanization of industry, the secularization of society, and the derivative scientization of medicine did much to transform the mindset of the interested masses from religious rejection toward worldly acceptance of the microscopic image as a true microcosm of macrocosmic reality.

John Harley Warner argued that from the 1850s to the 1870s, microscopes were used far more at popular gatherings than in medical laboratories.⁹⁷² In the years that followed, however, the adoption of microscopy by the scientific medical community fostered new terms, techniques, and specialized applications that bewildered and befuddled non-scientists. The public lost interest and scientific microscopy supplanted amateur microscopy. Gone were the days when the public participated in microscopical entertainments directly through soirées and other social gatherings. Nonetheless, the earlier fascination of the public with the microscope laid the groundwork for a vicarious appreciation of the instrument and of those who used it in the medical sphere.

Ideas—like merchandise—need to be sold. Proponents of the new present innovative concepts that are analyzed, tested, confirmed (or rejected), and adopted (or discarded). In this

⁹⁷¹Wolfe, "Sydenham and Locke on Anatomy," 209. John Locke, a philosopher by reputation but a physician by training, inherited to the belief of British empiricism that reality was derived from the senses. Something that could not be touched, tasted, smelled, heard, or seen was suspect. In medical terms, Locke did not equate the microscopic image with God-given vision. Instead, he held that the macroscopic and microscopic were unconnected—not part of a natural continuum of spacial girth and therefore untranslatable from one medium to another. In addition, the microscopic diverted the practitioner’s attention from the productive empiricism of bedside observation. Instead, it instigated a literally out-of-body experience that diminished patient-physician interaction. Stanley Joel Reiser presented an insightful analysis of Wolfe’s article and the seventeenth-century English philosophy of microscopy in Reiser, *Medicine and Technology*, Chapter 4, “The microscope and the revelation of a cellular universe,” and especially 73.

⁹⁷²Warner, "Popular Microscopy," 21-22.

case, advocates of medical microscopy advertised their offering through many of the traditional venues pioneered by professional promoters at the time. In 1890, for example, E. C. Hoyt, a microscopist unencumbered by immoderate boosterism, suggested in *The Microscope* that more practitioners and the public should be aware of the blessings of the instrument.⁹⁷³ How did he envision this to be accomplished? Hoyt suggested two age-old strategies: fame and riches. Long before the early-twentieth-century motion picture industry carefully constructed the star system for cineastes and voyeurs alike, the interests, yearnings, and passions of the famous and the infamous attracted the attention of the multitude. In the nineteenth century, these trend-setters included orators, pastors, and the wealthy. Hoyt suggested that the microscope community enlist the patronage of the celebrated Reverend De Witt Talmage to spread the good word about the coming of medical microscopy.⁹⁷⁴

Thomas De Witt Talmage was a Presbyterian preacher of the late nineteenth century whose fame extended from pulpit to pulp media. By 1890, when Hoyt suggested that Talmage be recruited as a spokesman for microscopy, the Reverend was orating in his third church—considerably larger than the first two.⁹⁷⁵ Talmage’s renown reached far beyond his pulpit, for he extended his trademarks—“eloquence and sensationalism”—to journalism and literature.⁹⁷⁶ In 1890, publishers reprinted his sermons in over three *thousand* journals. It was said that he

⁹⁷³E. C. Hoyt, "Microscopical Education in America," *The Microscope* 10, no. 2 (1890).

⁹⁷⁴*Ibid.*, 80.

⁹⁷⁵http://www.1911encyclopedia.org/T/TA/Talmage_Thomas_De_Witt.html Accessed May 5, 2004. Talmage’s third church held more than 5000 parishioners. Nevertheless, congregants deemed that capacity insufficient to include all who wished to attend. The first two churches burnt to the ground.

⁹⁷⁶http://www.1911encyclopedia.org/T/TA/Talmage_Thomas_De_Witt.html Accessed May 5, 2004.

reached more than 25 million readers!⁹⁷⁷ What better individual, wrote Hoyt, to propound the glories and miracles of the modern microscope to a public fascinated by science!

Hoyt's second brainstorm for the popularization of microscopy was an appeal to riches. He suggested that microscopists should be paid much more than their current 1890 fees.⁹⁷⁸ Besides the obvious self-interest contained in this plan, Hoyt believed that higher salaries for microscopists would attract more and better applicants to the new field. In addition, high salaries would draw the attention of "the common man." In an age dedicated to growing wealth, high remuneration for scientists of the microscope (especially in medicine) would spotlight the specialty and swell its ranks.⁹⁷⁹ In a "progressive" age of growing societal self-consciousness and scientific and medical miracles, the advantages of microscopy were becoming self-evident.

The Periodical Press and the Popularization of Microscopy

Another venue for the popularization of medical microscopy was the lay media. Articles written by physicians for public consumption and education attracted readers to the use of the microscope for medical diagnosis and treatment. Magazines and newspapers—long before motion pictures, television, and the internet transformed the bulk of Americans from a reading public to a viewing public—functioned as important channels of communication. To publish in *Harper's*, *McClure's*, or the *Ladies Home Journal* at the end of the nineteenth century was to reach a large, concerned, and attentive audience. As more individuals experienced cancer

⁹⁷⁷http://www.1911encyclopedia.org/T/TA/Talmage_Thomas_De_Witt.html Accessed May 5, 2004. Since the census population of the United States in 1890 was approximately 63,056,000, Talmage reached about 40% of the entire country! To put that percentage in perspective, a writer today who had an audience of 40% of the population of the United States would communicate with about 110,000,000 individuals, larger than the number of Super Bowl viewers in this country. U. S. Bureau of the Census, *The Statistical History of the United States*, A 1-16.

⁹⁷⁸Hoyt, "Microscopical Education in America," 80.

⁹⁷⁹More important than actual economic growth, measured, for example, by the gross domestic product, was the perception of increasing wealth. More so than today, the belief that a self-made man could rise to the fore through hard work and clean living to attain economic success was stronger then. Witness the enormous popularity of Horatio Alger's *Ragged Dick* (1867) and its sequels in the late nineteenth century.

through a family member or friend in their midst as the century wore to a close, notice of cancer-related articles grew and the press responded in kind with more such writings.

In late 1891, an article on cancer by B. Farquhar Curtis and William T. Bull, two New York physicians, appeared in *Harper's*. To a large extent, that publication served as a paean to the progress of microscopy and cancer science in the nineteenth century.⁹⁸⁰ Their five-page “Treatment of Cancer and other Tumors” summarized prevalent theories, diagnoses, and treatments unconceivable a few years earlier. Indeed, the mere presence of such a subject in a popular magazine trumpeted the importance of the topic to the general population as well as recent changes in the field. The goal of the article was clear: to induce patients with tumors to undergo biopsy for the purpose of microscopic analysis and then, if positive, to follow through with immediate surgery. The standard procedure for the definition and diagnosis of malignancy—six years after the death of General Grant—had become tissue-based microscopy.

First, Curtis and Bull built their case for the current diagnosis and treatment of cancer. “What is a tumor?” they asked. A tumor is “an abnormal growth of tissue in some part of the body...sharply demarcated from the surrounding tissues...not being due to the processes of ordinary inflammation.”⁹⁸¹ An inflammatory lesion, therefore, was no longer considered a tumor. This distinction, fostered by the microscope, represented a giant leap from the early nineteenth-century definition of tumors.

What causes tumors, they asked? In plain language, Curtis and Bull reprised the cancer causation theories of the nineteenth century in the light of the new microscope-based science of cancer. Did tumors derive from a “cancerous diathesis”—a hereditary predisposition to the

⁹⁸⁰B. Farquhar Curtis and William T. Bull, “The Treatment of Cancers and Other Tumors,” *Harper's New Monthly Magazine*, November 1891.

⁹⁸¹*Ibid.*, 919.

disease? This was their nod to constitutionalism and the notion of intrinsic inevitability that portended treatment failure and death. No, they responded, the microscope clearly revealed the local nature of cancer and, if excised before extension, its curability. Microscopy had revealed that even tumors in different parts of the body with similar characteristics were merely “secondary” derivatives of the first tumor—i.e., metastases. In short, they emphasized, “cancer is a local disease.”⁹⁸²

Is cancer hereditary? “Uncertain,” they concluded (failing to produce statistical evidence), because tumorous diseases are “so common that not many families are without a history of tumor development in some of their branches.”⁹⁸³ Common things are common—but not necessarily related causally. Does previous injury cause tumors? Maybe. But injuries are even more prevalent than tumors, so again it is difficult to establish cause and effect.⁹⁸⁴ Microscopy uncovered no direct link between injury and malignant formations.

Was cancer an ectopic miscue—a consequence of embryonic tissue that had lost its way during development and ended up in a part of the body where it did not belong? In asking this question, Curtis and Bull payed homage to Julius Cohnheim, student of Virchow and teacher of Ehrlich and Welch, who conceived the embryonal rest theory.⁹⁸⁵ Indeed, the authors called it “one of the most fascinating of all the theories which have been advanced.”⁹⁸⁶ However, Cohnheim’s theory, failing what logical positivists of the twentieth century would call

⁹⁸²Ibid., 921.

⁹⁸³Ibid.

⁹⁸⁴The double-blind, prospective randomized clinical trial (“RCT”), which seeks to establish causality and association through probability, did not become popular until after the Second World War.

⁹⁸⁵See Footnote 318 for an explanation of Cohnheim’s Embryonal Rest theory.

⁹⁸⁶Curtis and Bull, “Treatment of Cancers,” 921.

“testability,” had neither gross nor microscopic proof.⁹⁸⁷ Nevertheless, the attraction of the theory grew out of the intriguing nature of animal and human development advanced by biologists in the late nineteenth century.⁹⁸⁸ Since the embryonal rest conception of carcinogenesis derived from elements of anatomy, embryology, microscopy, and cancer medicine, it was truly interdisciplinary.

What about “recent discoveries as to the importance of bacteria in the causation of disease”?⁹⁸⁹ Did bacteria cause cancer? Curtis and Bull acknowledged that it was certainly possible that bacteria caused cancer—after all, plant gall tumors appeared to be generated by bacteria—but the best they could conclude from the available evidence was that “all is mere conjecture.”⁹⁹⁰

Regardless of the cause of cancer, however, its treatment was more important than theory and supposition. Had the advance of science throughout the nineteenth century added nothing to the control of this devastating disease? Curtis and Bull acknowledged that “the faint-hearted and the sceptical” among their readers would cry, “Nothing!”, but the authors strongly disagreed. No, no, no, they responded—surgery, surgery, surgery. Surgery early. Surgery complete. “Much has been accomplished...almost entirely by surgery.”⁹⁹¹

⁹⁸⁷Interestingly, the confluences between the pluripotential nature of embryonal rest cells and modern-day stem cells have carried the concept behind Cohnheim’s ill-fated carcinogenesis theory into the twenty-first century. See, for example, recent evidence that stomach cancer is caused by undifferentiated bone-marrow-derived cells in Jean-Marie Houghton et al., “Gastric Cancer Originating from Bone Marrow-Derived Cells,” *Science* 306 (2004).

⁹⁸⁸The history of embryology (from the Greek, ‘study of the swelling within’) is, of course, a multi-tome work in itself. Nevertheless, in short, embryology arose as a scientific discipline in the last quarter of the nineteenth century with the publication of Ernst Haeckel’s work in 1875 on the development of animal form (*Anthropogenie*) and the description of fertilization by August Hertwig in 1876. Thomas Hunt Morgan, a long-time Columbia Professor who linked genes and chromosomes, published the first American research on experimental embryology in 1897. See Sebastian, *A Dictionary of the History of Medicine*, 281-82.

⁹⁸⁹Curtis and Bull, “Treatment of Cancers,” 921.

⁹⁹⁰*Ibid.*, 922.

Surgeons Curtis and Bull saluted “experienced microscopists” who “learnt to distinguish the character of a tumor by its minute structure.”⁹⁹² Cancer diagnosis, however, regardless of how advanced it had become as a result of the microscope, was not treatment. Surgery was the proper therapeutic response to cancer. Every effort should be made to induce patients with malignancies to undergo “the knife.” “There is no hope of cure except by operation.”⁹⁹³ In their experience, fear of the knife engendered the greatest risk, for it led ineluctably to death by default.

By the end of the nineteenth century, surgery had become safer, more tolerable, and more successful than ever before. Anesthesia administration and morbidity had improved. Antisepsis had evolved. There was no longer any excuse, Curtis and Bull wrote, for patients “deceiving themselves as long as possible, and concealing their trouble from all their acquaintances, as if a refusal to acknowledge the existence of the tumor could prevent its growth.”⁹⁹⁴ “To delay,” they warned in the strongest possible terms, “is to make a deliberate attempt at suicide.”⁹⁹⁵

Curtis and Bull’s well-written article for public consumption unwittingly related the remarkable changes in the culture of cancer that had come about between General Grant’s death in 1885 and President Cleveland’s secret surgery in 1893. Although cloaked in their justifiable (if self-serving) promotion of early tumor surgery, Curtis and Bull had enumerated the

⁹⁹¹Ibid.

⁹⁹²Ibid., 920.

⁹⁹³Ibid., 923.

⁹⁹⁴Ibid., 922.

⁹⁹⁵Ibid., 923.

The next chapter will investigate the dynamic interplay between “the knife,” anesthesia, antisepsis, and the making of modern cancer.

developments in cancer biology, diagnosis, and treatment achieved with the aid of the microscope.

The Power of William Osler's *Principles*

Even when old theories die and biases are discounted, the language of description itself may form a final barrier to understanding nature.

-Stephen Jay Gould⁹⁹⁶

As articles in popular periodicals like that of Curtis and Bull swayed the public toward cancer surgery and the acceptance of microscopy for the sake of science and medicine, so did medical publications affect physicians. William Osler's 1892 *The Principles and Practice of Medicine*, a sterling example of an influential tome, reached a level of acclaim and durability rarely attained by textbooks of medicine.⁹⁹⁷ Indeed, it is said that Osler's text was so magisterial that it became the paradigmatic foundation for John D. Rockefeller's enormous financial support for the study of scientific medicine—including the establishment of the Rockefeller Institute for Medical Research in New York.⁹⁹⁸

The groundbreaking effect of Osler's 1892 first edition on the economics and politics of medicine notwithstanding, the text actually represents a transitional piece between traditional and modern cancer on both the clinical and microscopic levels. The physical examination constituted the mainstay of Osler's diagnostic model. He reserved description and analysis of the "histologic" findings—which may be termed tumor microscopy today—for those few cancers

⁹⁹⁶Stephen Jay Gould, "This View of Life: Bacon, Brought Home," *Natural History*, June 1999, 76.

⁹⁹⁷Harold Malkin praised Osler's monument to modern medicine as "the most popular book on internal medicine ever written, certainly until the middle of the twentieth century." Malkin, *Out of the Mist*, 383. Professor Osler's text went through several editions in the United States and around the world. On a personal note, my father used a later edition of Osler's *Principles* in medical school in Switzerland during the 1950s.

⁹⁹⁸*Ibid.*, 383-84. The Institute opened in 1901; its first laboratories in 1906. See Malkin, *Out of the Mist*, 384. The influence of Frederick T. Gates, who brought the idea of funding scientific medical research to Rockefeller, Sr., also had a far-reaching effect on John D. Rockefeller, Jr., as was evident in the story of Bessie Dashiell.

where, in his judgment, the history and physical exam provided insufficient clues toward a firm diagnosis. For example, Osler depicted the histology of stomach cancer (the second most common cancer at the end of the nineteenth century⁹⁹⁹) not for its clinical value, but for its elucidation of the important principle that different microscopical varieties of gastric carcinoma caused similar symptoms. To Osler in 1892, as to generations before him, the microscope was, in essence, a sometime supplement to clinical discovery.

Microscopic diagnosis aside, Osler's tumor nomenclature bridged the gap from traditional to modern tumor terminology. Time-worn terms like encephaloid and scirrhus and microscopical designations like "cylindrical-celled epithelioma."¹⁰⁰⁰ Contrary to what might be expected based upon Osler's relegation of microscopy to a secondary status in the diagnosis of cancer, he was one of the earliest advocates of medical microscopy in the United States.¹⁰⁰¹ Like William Welch shortly after him, Osler's interest in microscopy was part and parcel of his post-graduate training in German scientific medicine. Indeed, Osler trained in Berlin with Virchow at the end of 1873.¹⁰⁰² Back in the States, he owned the only available microscope at the University (of Pennsylvania) Hospital as late as 1884.¹⁰⁰³ Nevertheless, it is clear that physical

⁹⁹⁹Early epidemiologists deemed only cancer of the uterus (including cancer of the cervix at that time) more common than stomach cancer. See William Osler, *The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine* (New York: D. Appleton and Company, 1892; reprint, 1978), 376.

Despite a superabundance of hypotheses, the explanation for the decreased incidence of stomach cancer throughout the twentieth century is unclear. Today, it is not even the most common gastrointestinal malignancy.

¹⁰⁰⁰*Ibid.*, 376-77. Of all tumor histologies that Osler incorporated into his treatise, stomach cancer was the most internal and best described. Cancers of the brain (p. 918), esophagus (p. 343), lung (p. 556), and kidney (p. 770) drew no microscopical analysis in his original 1892 edition.

¹⁰⁰¹Harvey Cushing, *The Life of Sir William Osler*, Special ed., 2 vols., vol. 1, *The Classics of Medicine Library* (Oxford: Clarendon Press, 1925; reprint, 1982), 137.

¹⁰⁰²Malkin, *Out of the Mist*, 155. Sir William Osler wrote of his own experience in "Berlin Correspondence," *Canadian Med & Surg J* 2 (1873-1874): 308.

¹⁰⁰³George T. Harrell, "Osler's Practice," *Bulletin of the History of Medicine* 47 (1973): 550.

examination was his forte and primary diagnostic tool.¹⁰⁰⁴ For William Osler, as late as 1892, the microscope remained important but subordinate.¹⁰⁰⁵ In short, the old continued to influence the new for, as Osler illustrates, the history of medicine is, in the finest detail, more evolution than revolution.

Microscopy Ascendant

Other developments in 1892, more immediate but less enduring than Osler's clinical textbook, further propelled medical microscopy to the forefront of cancer diagnosis. A. P. Ohlmacher, a Chicago Professor of Biology and Embryology summarized their impact in an article he wrote for *The Medical News*. There he noted a hallmark that bespeaks acceptance and advance of a new technology—viz., competition with change. "Improvements in the methods of microscopic research," he noted, "have become so numerous that it confuses one to keep abreast of them. Scarcely is a method or formula proposed ere it is modified, extended, or superseded. The technique of the last year is becoming old."¹⁰⁰⁶

If research is the bedrock of clinical medicine, then no better example can be expressed than the application of Paul Ehrlich's differential staining techniques to the investigation of the diseases of white blood cells. In 1892, E. E. Goldman employed Ehrlich's 1877 research

¹⁰⁰⁴Sir William Osler's clinically-grounded diagnostic acumen is legendary. It remains the foundation of his well-deserved (in my opinion) hagiographical treatment to this day. The American Osler Society and numerous contemporary books and articles treat his writings and teachings with great respect and thus contribute to his lasting influence. Contrast the enduring positive image of Osler with that of J. Marion Sims, whose image has plummeted from saint to sinner in the writings of many historians of medicine.

¹⁰⁰⁵By 1913, Sir William's regard for the microscope in the diagnosis of cancer had grown as he incorporated the instrument as a primary tool for both clinical medicine and medical research. As he noted that year in the Silliman Lectures, delivered at Yale, "the introduction of the microscope in clinical work widened greatly our powers of diagnosis, and we obtained thereby a very much clearer conception of the actual processes of disease." See William Osler, *The Evolution of Modern Medicine: A Series of Lectures Delivered at Yale University on the Silliman Foundation in April, 1913* (New Haven: Yale University Press, 1921), 205-06.

¹⁰⁰⁶A. P. Ohlmacher, "Heidenhain's Modified Micro-Technical Methods and Their Advantages for the Physician," *The Medical News: A Weekly Medical Journal* 61, no. 21 (1892): 573.

histological techniques to stain leukocytes, perhaps for the first time in a histopathological setting.¹⁰⁰⁷ Laboratory findings like leukocytosis (excess quantity of white blood cells) and diseases like leukemia (cancer of white blood cells) came into sharper focus as clinical investigators used the microscope to pinpoint the source of their patients' problems and, in the process, to elucidate prognosis as well as diagnosis.¹⁰⁰⁸ The microscope was integrated ever more into the clinic as the century came to a close. The growth of clinical and surgical pathology affirmed this development and, in turn, dynamically expanded the role of the microscope in medicine.

In one of the most far-reaching (if initially unrecognized) microscopical advances of the era, Dmitri Alexievich Ivanovski, also in 1892, demonstrated that a 'virus' (a term derived from the Latin for 'poison') caused disease. Although it is highly unlikely that he actually saw the filterable agent (in this case the tobacco mosaic virus) with a light microscope, the concept that such disease-causing agents existed that were too small to be visualized with the light microscope caused a flurry of interest in the investigation of cancer and other disorders that extended well into the twentieth century and beyond.¹⁰⁰⁹

¹⁰⁰⁷E. E. Goldman, "Beitrag Zu Der Lehre Von Dem 'Malignen Lymphom'," *Centralblatt allgemeine pathologische Anatomie* 3 (1892). Cited by Rather, *The Genesis of Cancer*, 219 Footnote 138. Goldman himself alleged that he was the first to apply Ehrlich's research techniques to clinical medicine. Others, including Ehrlich, have every reason to dispute Goldman's claim.

¹⁰⁰⁸Leukocytosis is often secondary to a primary process like infection. Leukemia, even if engendered by a virus, is intrinsic to the white cell. Leukocytosis typically regresses with treatment of the primary infection; leukemia does not. Hence, the differentiation of histologically normal but abundant white blood cells from the microscopically abnormal cells found in cancer of the white blood cells is critical to the prognosis as well as diagnosis of the patient.

¹⁰⁰⁹Scientists did not actually visualize the first virus-type particles until the early 1930s. They are too small to see with the light microscope. In 1931-32, Max Knoll and Ernst Ruska at the University of Berlin developed the first transmission electron microscope that could discern these much-smaller-than-bacteria biological entities. For more, see Walton, Beeson, and Scott, eds., *Oxford Companion to Medicine*, 788. and Jacker, *History of the Microscope*, 175.

Thus, by the early 1890s, research and practice had become heavily dependent upon medical microscopy. Indeed, the pendulum swung so far in favor of the microscope that veterans, who well remembered a time not long ago when the attitude of community practitioners toward microscopy was aversion rather than attraction, warned that physicians had become *too* dependent upon the instrument. Thus, in 1896, Sir Dyce Duckworth admonished his fellow clinicians for following the allure of the microscope rather than focusing more attention on their patients. It was Duckworth who urged physicians to “lift our eyes from the microscope” and put the patient first and foremost.¹⁰¹⁰ Two years later, Virchow warned that histopathologists were also in danger of becoming mere “‘readers’ of glass slides.”¹⁰¹¹ Indeed, the role of microscopy in everyday medicine had become so important by the end of the century that the very title of “pathologist” had been magically transformed into that of “histopathologist” in recognition of the vital contributions of microscopy to the nature of disease.

A New Lease on Life for President Cleveland

By 1893, repudiation of the concept of medical microscopy had given way to acceptance and even necessity. In that year alone, landmark events in medical microscopy included the introduction of formalin as a tissue fixative by a German physician,¹⁰¹² the birth of *The Microscope* (subtitled *a monthly journal for naturalists, physicians, and druggists*),¹⁰¹³ and the

¹⁰¹⁰Sir Dyce Duckworth, "The Prognosis of Disease," *British Medical Journal* 2 (1896).

¹⁰¹¹Rather, *The Genesis of Cancer*, 155.

¹⁰¹²Hajdu, "Cytology," 674. Blum, a resident of Frankfurt-Am-Main, earned credit for the introduction of formalin. Formalin fixative combined with paraffin embedding (developed seven years later) became a standard method of tissue processing for over a century.

¹⁰¹³From *Index Medicus* vol. 15, 1893: 112. *The Microscope*, Volume I, Number 1 of was published in Washington, D.C. in January, 1893.

display of microscopes at the Columbian Exposition in Chicago, Illinois, for visitors from all around the world to see.¹⁰¹⁴

Even the government of the United States joined the bandwagon. On May 30, 1893, as President Cleveland scraped the potentially fatal “rough patch” on the roof of his mouth,¹⁰¹⁵ George Miller Sternberg, an eminent American bacteriologist,¹⁰¹⁶ received his commission to become Surgeon General of the United States Army. His fame rested firmly on his emphasis of the importance of scientific medicine, of which there was a paucity in the armed forces to that point, and his implementation of “a four-month course for all new medical officers, with laboratory classes that included instruction in bacteriology, clinical microscopy, and urinalysis.”¹⁰¹⁷ Thus, as William Henry Welch prepared to scrutinize President Cleveland’s unnamed biopsy slides, even the government of the United States officially recognized the importance of medical and cancer microscopy. In the short period of ten years, a major turnaround had occurred.

Coincidentally, 1893 also witnessed a major decline in the didactic system of medical school education with the opening of the Johns Hopkins Medical School. Hopkins was to play no small role in the furtherance of medical microscopy. William Henry Welch, fully convinced

¹⁰¹⁴American Microscopical Society, "Microscopes at the Columbian Exposition," *Proceedings of the American Microscopical Society* 15 (1893).

¹⁰¹⁵Quotation from A. E. Porritt, "Some Historical Surgical Operations," *St. Mary's Hospital Gazette* 42, no. 5 and 6 (1936): 107. Coincidentally, the term “rough patch” has become economic slang to refer to a period of short-lived recession or worse. In 1893, President Cleveland experienced both pathological and economic rough patches.

¹⁰¹⁶See Malkin, "Comparison of the Use of the Microscope in Pathology in Germany and the United States During the Nineteenth Century," 85. In 1892, Sternberg published his *Manual of Bacteriology*, the first major text on the subject written by an American. The interested reader can find much more on Sternberg’s fascinating life and adventures in Harold M. Malkin, "The Trials and Tribulations of George Miller Sternberg (1838-1915)--America's First Bacteriologist," *Perspectives in Biological and Medicine* 36 (1993).

¹⁰¹⁷Malkin, "Comparison of the Use of the Microscope in Pathology in Germany and the United States During the Nineteenth Century," 85.

of the value of medical microscopy through the German model of scientific medicine, was its first professor of pathology. Firmly based upon the Continental “learning by doing” methodology that is still prevalent in medical colleges today, Hopkins fostered the hands-on approach to medical education and the foundational principle that research and teaching complemented each other.

Medical microscopy followed naturally from both principles as a means toward the end of accurate cancer diagnosis and treatment. The ideational divide between laboratory and clinic narrowed. As a result, microscope-based clinical pathology became an essential weapon in the armamentarium of the cancer practitioner. Abraham Flexner’s early-twentieth-century choice of Hopkins as both the prototype and paragon for medical education reified the role of medical microscopy as it affirmed Hopkins’ teaching and research strategies.¹⁰¹⁸

The Crucial Element of Modern Cancer Medicine: Microscopy

The second half of the 19th century was the golden age of cancer pathology. It established the basis for all diagnostic endeavors, for the understanding of neoplastic processes including the metastasis, and for the activities of all branches of cancer science that came into being since 1900.

-Sigismund Peller¹⁰¹⁹

Thus, by 1893, the year of the President’s secret cancer surgery, the practitioner could no longer comprehensively—or even properly—evaluate the cancerous patient’s pathology without microscopy. The strategies of diagnostic microscopy and therapeutic surgery that dictated the course of Cleveland’s cancer reflected what had become the standards of the time.

Frank Huntington Bosworth’s *A Text-Book of Diseases of the Nose and Throat*, published in multiple editions throughout the end of the nineteenth century, effectively chronicled how the

¹⁰¹⁸Flexner, *Medical Education in the United States and Canada*, 12.

Ironically, Johns Hopkins Medical School, grounded in Germanic scientific medicine, made the *de rigueur* post-graduate educational excursions to the Continent unnecessary for post-Welchian generations.

¹⁰¹⁹Sigismund Peller, *Cancer Research since 1900* (NY: Philosophical Library, 1979), 21.

hard-won victory for microscopically-validated cancer had changed the landscape for the evaluation of the clinical aspects of the disease between the diagnostic years of Grant and Cleveland.¹⁰²⁰ Had the General's cancer of the faucial tonsil been diagnosed a decade later than it was, Bosworth's first vs. third editions make clear that Grant's consultants would have chosen a different course of diagnosis and treatment. An 1890s diagnosis would have marked the acceptance of cancer as a disease of local origins rather than the idea of a diffuse, whole-body constitutional process that persisted into the early 1880s. The transformation in the conception of cancer that radically altered the diagnosis and treatment of tumors rested squarely upon the results of microscopical investigations.

Although successful extirpative surgery in Bosworth's text remained limited to those few cancers diagnosed very early in their course, by the beginning of the 1890s surgery played an expanded role even in the palliation of such cancers. The *Text-Book* of 1896 found that there was "little question that such measures as snaring, curetting, and cauterization serve to postpone the fatal termination, and also add somewhat to the comfort of the patient."¹⁰²¹

Unlike in the days of Samuel David Gross's famous publication of 1853 warning of the risks of cancer surgery,¹⁰²² no longer was surgery a shortcut to death. Instead, Bosworth noted that, despite persistent limitations, "it must be borne in mind that in many cases the (surgical) patients survived the operation and were free from the disease for periods varying from three to five months before recurrence set in. Furthermore, a number of instances have been reported in

¹⁰²⁰Bosworth's texts on diseases of the nose and throat (under slightly different names) spanned the years from 1881 until the late 1890s.

¹⁰²¹Francke Huntington Bosworth, *A Text-Book of Diseases of the Nose and Throat*, Third ed. (New York: William Wood and Company, 1896; reprint, 1897), 568.

¹⁰²²Gross, "On the Results of Surgical Operations in Malignant Diseases."

which the operation was successful and the disease apparently completely eradicated.”¹⁰²³

During the years from the publication of Gross’s *On the Results of Surgical Operations in Malignant Diseases* until the 1890s, surgery for the treatment of cancer evolved from pariah to palliator and, more often than ever before, curer. Cancer microscopy was the facilitator.

Bosworth also echoed as well as supported the steps taken by Dr. Joseph Bryant in the diagnosis and treatment of President Cleveland. Diagnosis of tumors of the soft palate no longer rested solely on their clinical manifestations. Gross appearance and palpatory findings could mislead. Microscopy, Bosworth believed, did not.¹⁰²⁴ He listed the growths of the soft palate as papilloma, adenoma, fibroma, sarcoma, and carcinoma—all terms derived from medical microscopy that make up the modern medical lexicon. But, he added, “the points in the differential diagnosis (between, for example, adenoma and carcinoma—LK) need not be referred to, for the microscopic examination will at once settle the real character of the growth.”¹⁰²⁵ Furthermore, even in the most advanced cases, surgery yields benefits, for “yet we are scarcely warranted in concluding that operative measures have not been of service.”¹⁰²⁶ Thus, even in the most dire circumstances, surgery had become the angel of life for the cancer patient. Not to operate was to assure a horrid death. The microscope, now the final arbiter of cancer diagnosis, had become the foundation of therapeutic decision-making.

¹⁰²³Bosworth, *Diseases of the Nose and Throat*, 568.

¹⁰²⁴The interpretation of any visual form, including the appearance of a tumor under the microscope, was and is only as good as the skill of the interpreter. President Cleveland’s physicians chose the best “slide-readers” of their time. By the 1890s, microscopical education routinely began at the college level and progressed through medical school and post-graduate training. As with much of the history of the microscope in the nineteenth century, comprehensive education in medical microscopy began in Germany, traversed the Channel to Great Britain, and sailed across the Atlantic to the States.

¹⁰²⁵Bosworth, *Diseases of the Nose and Throat*, 563.

¹⁰²⁶*Ibid.*

CODA

From Plaything of Beauty and Wonder to Instrument of Science and Medicine

The classification most useful...is that founded upon the microscopic character of the neoplasm.

-John Reeves, 1894

By the early 1890s, the microscope, invented four centuries earlier, had become a fully medicalized instrument of science. As medicine turned to science for its process, the microscope became part and parcel of scientific medicine.

Raymond Williams, the mid-twentieth-century Welsh social critic/novelist of a socialist turn of mind, propounded the anti-McLuhanesque notion that technology follows rather than determines social and cultural change.¹⁰²⁷ Similarly, the application of the microscope to cancer medicine could not have occurred without the supportive culture of an accepted theory of cellular anatomy, physiology, and pathology; ideas about a microscopic cause of cancer; thoughts accepting a mechanistic nature of man and disease; and the testable notion that cancer could be recognized—even defined—*before* invasion and metastasis. Thus, theory fostered practice and practitioners accepted the microscope as an instrument of cancer medicine long after its invention in the sixteenth century and refinement in the nineteenth. In the long run, the most important finding was that the microscope did the job of diagnosis better than what had come before. It raised the accuracy of cancer diagnosis to previously unachievable levels. Early and accurate recognition of malignancies became the basic precept of cancer culture in the late nineteenth and early twentieth century.

The evolution and transformation of the microscope over the course of the nineteenth century spurred medical researchers of all persuasions to view cancer and medicine literally

¹⁰²⁷ Raymond Williams, *Television: Technology and Cultural Form* (Hanover, N.H.: Wesleyan University Press, 1974; reprint, 1992), 13.

through a new lens. In the process, the gaze of the medical eye encountered a previously-unseen world of beauty and horror. In the decades to come, new knowledge gleaned from the microscope led to innovative theories that fostered novel types of microscopes and imaginative perspectives on life and disease.

By 1893, the year of Cleveland's cancer surgery, the culture of cancer had embraced and valorized the microscope as a major weapon against the disease. The evolution of microscopy—from optics to microtechniques—yielded a rich harvest for cancer medicine. Physicians of all persuasions learned that the nature of the disease warranted examination at the microscopic level to define and refine the ambiguities of its macroscopic appearance. In the grand scheme of medicine's history, it was the temper of the times—the ascendance of science, the growing incidence of cancer, the expanding authority of the medical profession, the rise of specialization, the invigorated emphasis on instrumentation, the visualization and acceptance of the concept of disease-causing microorganisms, and the increased painlessness, safety, and success of surgery—that gave birth to modern cancer and made the microscope a *sine qua non* of modern cancer medicine.

Chapter 7

The Treatment of Cancer: From Ancient Antidotes to the Golden Age of Surgery

Surgery became the treatment of choice for cancer at the end of the nineteenth century. As the microscope revolutionized the diagnosis of cancer, surgery transformed the treatment of cancer.¹

The use of available treatments for cancer depends upon perceptions of the efficacy and safety of those therapies. If efficacy for a given treatment is believed to be low and safety concerns high, as they were with regard to surgery in the early- and mid-nineteenth century, patients and ethical physicians will avoid that therapy and seek alternatives that purport to offer more with less risk. During the last decades of the nineteenth century, both the efficacy and safety of certain cancer treatments improved. The rise of modern cancer surgery at that time – the result of the confluence of developments in disparate discipline – ushered in an era of greater success in the treatment of cancer than ever before.

Acceptance of the paramount role of surgery in cancer therapy was no small feat, for it followed on the heels of decades, nay, centuries, of skepticism and often downright rejection of the therapeutic value of cancer surgery. Witness Samuel David Gross's widely-accepted conclusion, published in 1853, that cancer was "incurable" by surgery.² Remember the consensual decision of General Grant's consultants in 1884 and 1885 that surgery would lead to

¹When I write that surgery became the treatment of choice for cancer in the late nineteenth century, I am referring to deep, internal cancers such as cancers of the chest or abdominal organs (for example, lung, stomach, kidney, uterus) or cancers in "superficial" organs like the breast that may harbor cancers deep within these organs. On the other hand, practitioners have recommended the "surgical" removal of skin growths and other tumors on the surface of the body since ancient times, as explained below.

² S. D. Gross, M. D., "On the Results of Surgical Operations in Malignant Diseases," *Transactions of the American Medical Association* 6(1853).

nothing more than horrid disfigurement.³ Reflect on Morell Mackenzie's 1888 analysis, even in the light of controversial microscopic evidence, that the operative excision of Crown Prince Friedrich's tumor would lead to a fate worse than death.⁴ Then contrast these studies of antipathy toward and avoidance of surgery with the remarkable reversal represented by the case of President Grover Cleveland, whose medical advisors, within the timeframe of a few weeks in 1893, took him with little hesitation or doubt from biopsy and microscopical diagnosis to the operative chair.⁵

Certainly, the natural histories of no two cancers—or the patients in whom they grow and invade—are identical, but the treatment of cancer in general underwent an enormous conceptual and therapeutic transformation during the last decades of the nineteenth century. This chapter relates and analyzes the history—part evolution and part revolution—of the rise of modern cancer surgery. It highlights the people and places, as well as the conceptual realizations and discoveries, that led to the metamorphosis of surgery from a dreaded last-ditch attempt to remove or palliate traditional cancer to the most desired first-line treatment for the excision and, hopefully, cure of modern cancer.

Oncologic Surgery—Past as Present: Cancer Treatment Today

The treatment of cancer today is multimodal and combinatorial. In general, diagnosis determines therapy, so clinical diagnosticians expend much effort on blood tests, X-rays, and a host of other investigations in addition to analyzing symptoms and physical examination findings to assure the most accurate diagnosis possible. As in the late nineteenth century, the microscopical interpretation of pathological biopsy tissue remains the unquestioned standard for

³See Chapter 3, "General Grant's Cancer."

⁴See Chapter 6, "New Visions, Newer Insights."

⁵See Chapter 4, "The 'Secret' Anxious Summer."

the diagnosis of most solid tumors. And although there are hundreds of different “types” of cancers that clinicians diagnose with tests and pathologists with biopsy tissue, each having its own specific treatment(s), therapies fall into a few general categories.⁶ These include surgery, radiation and hormonal, immunologic, chemical, and biologic therapies—either alone or, more commonly, in combination.

Whereas in the early nineteenth century, the discovery of the characteristic late-stage cancer often led to a seemingly short-lived (“acute”) disease ending in rapid death, chronic control or outright cure more and more often result from the multipronged attack on cancer today. The ultimate “cure of cancer” remains elusive as of this writing, but the individual cancer patient has a higher probability of a successful outcome today than ever before in the history of the disease.

Breast cancer serves as an excellent example. For most of the nineteenth century, women presented to their physicians with masses in their breasts typically described as the size of a walnut, lemon, or even grapefruit. Superficial ulceration above the tumor leading to the distinctive odor of dying flesh or bloody discharge was common, for women believed that treatment for the disease was worse than benign neglect. In consequence, most women died within a few months of such a clinical diagnosis of breast cancer. Today, women and their

⁶I emphasize cancer “type” because the nature and naming of cancer are still in flux. Historically, cancer was—and, largely, still is—defined by its site of origin. Thus, there are brain cancers, breast cancers, and bladder cancers.

However, what if the molecular processes that underlie the cancer are the same—regardless of organ of origin? And what if process determines treatment? Should descriptive or analytical findings serve as the basis of cancer terminology? Analytical naming yields an advantage toward treatment, for tyrosine kinase inhibitors, for example, tend to more precisely target the underlying process of chronic myelogenous leukemia (CML) more than cell cycle inhibitors, which, in turn, are more specific than other chemotherapeutic agents in current use. As knowledge of the basic science of cancer increases, it is my hope and expectation that cancer terminology will identify molecular signatures rather than gross pathologies. If so, accurate definition of cancer may lead to more targeted therapies. And more targeted therapies may encourage more a more precise nomenclature of cancer. CML is a case in point. Oncologists speak of treating constitutive tyrosine kinase (myelogenous) leukemia, now labeled Chronic myelogenous leukemia in the blast phase, with tyrosine kinase inhibitors instead of current, less specific therapies.

physicians diagnose breast tumors much earlier in the natural course of the disease, either because of self-examination techniques publicized by organizations like the American Cancer Society, or through imaging studies like mammograms that are widely promoted as screening tests. Earlier diagnosis, named by Dr. Paul Marks, former President and Chief Executive Officer of the Memorial-Sloan Kettering Cancer Institute as the single most important advance in cancer medicine during the twentieth century, plays a major role in more successful treatment outcomes today, for numerous studies have shown that earlier diagnosis yields better therapeutic results.⁷

Mammography, for example, first developed in 1913, has become a breast cancer detection examination that often leads to longer and healthier lives than cancer patients could have expected in the nineteenth century and before.⁸ Thus, a suspicious breast lesion spied on a routine mammogram of an asymptomatic patient—or even a breast X-ray performed on a patient with a suspicious palpable nodule—leads to further diagnostic tests. These may include breast ultrasonography, xeroradiography, and a host of other new and old imaging studies that culminate in an image-directed biopsy. The goal of the diagnostic studies is to define the type as well as the “stage” of the cancer—i.e., to establish its extent and likely severity so as to try to predict the outcome of *this* patient’s cancer treatment. And this patient’s treatment is a set of modalities derived from experience gleaned from the treatment of similarly-staged cancers in the past. If the diagnosticians judge the breast tumor to be amenable to surgery, the imaging studies may also serve as road maps to guide the surgeon’s hand.

⁷I interviewed Dr. Paul Marks, then President and Chief Executive Officer of Memorial-Sloan Kettering Cancer Institute, on July 14, 1999. He emphasized that the greatest advance in cancer medicine during the twentieth century was the earlier diagnosis of cancer, not the chemotherapeutic agents for which Memorial was and is famous.

⁸For a comprehensive medical history of mammography, see R. H. Gold, “The Evolution of Mammography,” *Radiologic Clinics of North America* 30, no. 1 (1992).

Such precision enhances the probability that surgery will remove the entire tumor and leave uninvolved breast tissue intact. If the cancer is too large or widespread to allow for surgical excision, then various combinations and permutations of other treatment modalities mentioned above come into play. Often, depending upon the stage of the disease, surgeons combine supplementary therapies with operative removal in the initial treatment plan. Thus, diagnosis determines therapy and, together, they both *probabilistically* predict prognosis.

Recent statistics reveal that a woman with a breast cancer discovered at a relatively early stage has a better than eighty percent probability of surviving five or more years.⁹ Even the most life-threatening stage of breast cancer (Stage IV), which involves metastases to body sites well beyond the breasts, has a 20% five-year survival rate. As a result, death rates from breast cancer continue to decline overall, as they have for many years.¹⁰

Despite this Panglossian assessment, I do not wish to leave the impression that the consistent cure of breast cancer is near or even that optimal cancer therapies exist, for surgery often disfigures and treatment failures devastate patients and physicians. Advanced cancers, those in higher stages, are still the most difficult to treat as well as cure.

Even today, rare is the adult who has experienced no personal loss from cancer. Still, progress in the understanding, treatment, and cure of breast and other cancers during the twentieth and early twenty-first centuries has been astounding, and each day brings new ideas, findings, and practices likely to benefit cancer patients. As one of the most active fields of medicine, the push toward a/the cure of cancer is strong. Modified optimism reigns.

⁹<http://imaginis.com/breasthealth/statistics2.asp#5> accessed January 22, 2007. Current staging depends upon the size of the tumor (T), as well as the presence or absence of tumor in lymph nodes (N) or at sites distant to the breasts (M). Five-year survival statistics for a Stage II breast cancer, which include spread to lymph glands in the axilla (but not beyond), exceeds 80%.

¹⁰ See <http://www.cdc.gov/MMWR/preview/mmwrhtml/mm5103a1.htm> accessed January 22, 2007.

A Treatment of a Different Kind—Historical Treatment

At this juncture, I would do well to capture the manner in which historians have written the story of cancer surgery—from its beginnings until the end of the nineteenth century. Historians from the late 1800s until the last quarter of the twentieth century wrote the history of cancer surgery predominately in terms of “Great Mens’ History.” Even Henry Sigerist, an ardent proponent of socialized medicine who succeeded William Henry Welch as director of the Johns Hopkins University Institute of the History of Medicine in 1932 and wrote several articles related to cancer, structured his (arguably) most famous book, *The Great Doctors*, around the medical biographies of great men.¹¹ His biographees include some of those discussed in previous chapters (Müller, Virchow, Koch, and Ehrlich), as well as others to be considered in this chapter (Semmelweis, Pasteur, Lister, and Billroth).

In 1977, Michael Shimkin, M. D., then Chief of the Laboratory of Experimental Oncology in San Francisco, published *Contrary to Nature*, a marvelously-illustrated paean dedicated to a Whiggish development of the history of the treatments of cancer—especially surgery.¹²

Occasionally before Shimkin, but, more commonly, after him, historians examined other agents of change—institutions, minorities, and women—in their contextual settings to paint the history of cancer on a richer, more enlightening canvas. Nevertheless, the focus on “great men”

¹¹Henry E. Sigerist, *The Great Doctors: A Biographical History of Medicine*, trans. Eden and Cedar Paul (Garden City, NY: Doubleday & Company, Inc., 1933; repr., 1958). One of Sigerist’s most direct articles on cancer was “The Historical Development of the Pathology and Therapy of Cancer,” *Bulletin of the New York Academy of Medicine* 8, no. 11 (1932).. Therein, he claimed that the problem of cancer belonged to “the realm of philosophy.” *Ibid.*, 653..

¹²Michael B. Shimkin, *Contrary to Nature: Being an illustrated commentary on some persons and events of historical importance in the development of knowledge concerning Cancer* (Washington, D. C.: United States Government Printing Office, 1977). Dr. Shimkin’s marvelously illustrated and progress-filled tome, was itself derived from the works of Dr. Henry Sigerist. Sigerist, *The Great Doctors*. and Dr. Esmond R. Long Esmond R. Long, *Selected Readings in Pathology*, Second ed. (Springfield, IL: Charles C. Thomas, 1961).. An overview of the history of cancer could well begin with Shimkin’s text.

continues to exert significant influence on the history of cancer in general and cancer surgery in particular.

Nevertheless, it is patently unfair to begin and end the story with such a restricted cast of actors. Only to point the spotlight at “great *men*” omits the contributions of others less well known but foundationally important to transitions and transformations in the culture of cancer. This focus will, in time, change. As the number of women physicians in oncology increases, for example, I fully expect that their influence in the field and their role in the history of cancer medicine—and the way that history is written—will increase substantially. Fairness and equality in the study of the history of cancer will prevail when, at some future, hoped-for time, descriptors pigeon-holing men, women, black, and white will no longer dominate historical tomes. In the meantime, I will attempt to broaden the field of contributors to the history of the treatment of cancer.

Perspective—The Context of Historical Understanding

If perspective means the breadth and depth of understanding, then knowledge of the past helps to embrace the present and prepare for the future. As such, to grasp the rise of surgery for the treatment of cancer in the late nineteenth century requires a look back to what had come before.

Throughout history, concepts of disease circumscribed and informed the treatment of traditional cancer. Patients who believed that disease generally and cancer specifically were God’s punishments for sin felt no need for diagnosis and treatment. Circumventing God’s Will could only make a bad situation worse. A lump was a bump, and if it killed the stricken soul, so be it. Undoubtedly, cancer was the underlying cause of many early-to-mid-nineteenth-century deaths listed in censuses as “old age” or “cause of death unknown.” Further, the widespread

belief in the inherited nature of cancer appeared to make curative attempts futile, if not heretical. The Bible was unambiguous. God “does not leave the guilty unpunished; He punishes the children and their children for the sin of the fathers to the third and fourth generation.”¹³ If cancer had a familial genesis, then patient and progeny had no recourse, for the successful treatment of malignancies would surely lead to their resurrection again and again. The common observation that tumor removal from one part of the body only led to its reappearance elsewhere strongly supported the Biblical warning.

Physicians who accepted the predominant early-nineteenth-century notion of constitutionalism, an idea aligned with patients’ acceptance of inherited cancer (as pathophysiology, in modern terms, relates to genetics), also viewed extirpative therapy as hopeless. Why should the patient suffer to postpone the inevitable when the very makeup—the “constitution”—of the patient’s own body doomed him to recurrent horrors? Empiricism, the prevalent methodology of the early-to-mid-century, strongly supported constitutionalism, for patients and physicians commonly observed cancer recurrence and the failure of therapies to cure the disease. Cancer diagnosed was life defeated, for who or what could prevail against God’s will and wrath? To alter this world-view required a complete reassessment of the workings of the Universe, a transformation wrought by secularization.

The Treatment of Traditional Cancer: Many Choices, Many Failures

Gloom and doom prevailed over the treatment of traditional cancer. Honest men admitted ignorance and predicted failure while charlatans preyed on empty hopes. As Dr. Herbert Snow quipped regarding the potpourri of treatments for cancer in 1893, “*populus vult*

¹³Punishment for sin is a repeated theme in the Pentateuch. For this quotation, see Exodus 34:7, Numbers 14:18, Deuteronomy 5:9.

decipi et decipiatur.”¹⁴ Different strategies dominated therapy. These included medical (i.e., non-surgical) as well as surgical modalities. The goal of treatment was to make the cancer disappear from sight; i.e., to remove all visible traces of the disease. For out of sight was the measure of cure.

Traditional efforts toward palliation and cure included environmental changes, dietary modifications, exercise, poultices, potions, and pills.

Regardless of treatment, however, outcomes were uniformly poor. Direct comparison of Samuel David Gross’s 1853 tabulated outcomes with twenty-first century cancer treatment statistics is impossible, for terminological, diagnostic (palpability in the mid-nineteenth century; pathology and imaging in the 21st), and staging (superficial, deep) criteria were very different. Also problematic is the definition of cure, for it varied over time. Shortly after the opening of the New York Cancer Hospital in the late 1880s, for example, a “cure” implied discharge alive from the Hospital or even merely survival of an operation. The notion of the five-year disease-free survival rate, a common standard today, did not dominate the concept of cure until the twentieth century.¹⁵

Thus, pessimism ruled the mindset of traditional cancer patients and their physicians for most of the nineteenth century. Outcomes were so dreadful that surgeon Gross rationally concluded that the surgical treatment of cancer often led to results worse than no treatment at all.

¹⁴“The people wish to be deceived, so let them be deceived.” Herbert Snow, *A Treatise, Practical and Theoretic on Cancers and the Cancer-Process* (London: J. & A. Churchill, 1893). 199.

¹⁵Dr. James Ewing (*Neoplastic Diseases, A Textbook on Tumors*, 1919) of the Cornell Medical College and the General Memorial Hospital, the new name of the New York Cancer Hospital as of 1898, may have been the first to propose the five-year survival rule as the standard of cancer cure. Francelia Butler, *Cancer Through the Ages: The Evolution of Hope* (Fairfax, VA: Virginia Press, 1955)., 392

Given the various definitions of “cure,” Ewing attempted to standardize its definition. Standardization of medical terminology, medication ingredients, and the dosages of “ethical” medicines, among other things, was a major interest of early twentieth-century physicians and, after the Food and Drug Act of 1906, a broad swath of the American population.

For the majority of patients and their physicians, however, no treatment was not an option. Then, as now, the duty of the physician was to treat without doing harm. A host of cancer therapies, non-surgical and surgical, old and new, became available to meet the needs of the growing numbers of cancer patients.

Non-Surgical Traditional Cancer Therapies

Theory

Carried too far

Can become a burden

For future generations.

The nineteenth century was the heyday of the belief in climatological and meteorological influences on human diseases. Cancer was no exception. As in the case of tuberculosis, with which cancer was often confused, physicians prescribed a change of climate for patients who had the means to follow this advice.¹⁶ Practitioners counseled patients in cold climates to seek warmer environments; patients in wet climates to seek drier environs; and patients living at low altitudes to vacate to higher altitudes. Sea-faring voyages were an especially-popular prescription, and solar therapy (sun exposure) was the sometime accompaniment of the admonition to breathe clean, fresh “open” air—especially for those increasing numbers of laborers who had spent most of their lives indoors.¹⁷

¹⁶Sheila M. Rothman, *Living in the Shadow of Death: Tuberculosis and the Social Experience of Illness in American History* (Baltimore: The Johns Hopkins University Press, 1994), 19-22

¹⁷The literature on non-surgical therapies for cancer in early-to-mid nineteenth century is vast. Although medical textbooks offer a wide view of possible treatments for patients with cancer, volumes by physicians intended for laymen yield a powerful perspective on such therapies. One especially-popular work was William Buchan’s *Domestic Medicine; or, The Family Physician*, first published in 1769, yet enjoying a vast audience over its more than one hundred forty editions and translation through the course of the nineteenth century. On this particular subject of the environmental treatment of cancer, see William Buchan, M.D., *Domestic Medicine; or, the Family Physician: Being an Attempt to render the Medical Art more generally useful, by shewing people what is in their own power both with respect to the Prevention and Cure of Diseases. Chiefly Calculated to recommend a proper*

Dietary modifications were as popular in the eighteenth and nineteenth centuries as they are today. Dr. William Buchan, for example, who penned an extremely popular how-to text for laymen, echoed today's oft-heard advice that a cancer diet should be "wholesome" and "light, but nourishing."¹⁸ Of course, "all strong liquors, high-seasoned and salted provisions, are to be avoided."¹⁹ Buchan offered no evidence to support his proscriptions, for the wisdom of the admonition was plain to those who heeded it.²⁰

Clinicians valorized programmed exercise as larger segments of the populace expended less physical labor than prior generations due to industrialization and a general decline in outdoor activities. Following the concept of the prescription of opposites, as in suggestions for climatological and environmental change, practitioners urged exercise for those who received little, and rest for those who labored much.

Traditional practitioners commonly applied treatments directly to the cancer itself. Poultices that contained various chemicals, especially caustics, dominated local cancer therapy. Poultices were soft, usually warmed, pastes spread on cloth or linen and placed directly on the cancer sore. These innocuous-appearing pastes often harbored irritative caustics like iron perchloride and sulfuric acid that burned the tissues beneath them. In the process, poultices killed all cells—normal and malignant—within their reach.²¹ Skin reacted to this destruction by forming an eschar—a thick, coagulated crust or slough of dead tissue. Caustics and escharotics

attention to Regimen and Simple Medicines, vol. 127, The Classics of Medicine Library (Philadelphia: Joseph Cruikshank, For R. Aitken, 1774; repr., 1993), 364, 365

¹⁸Ibid., 362.

¹⁹Ibid., 365, 362

²⁰The science of medical proof is very much a twentieth and twenty-first century endeavor. Nonetheless, pioneers P.-C.-A. Louis (see below) published statistical analyses of medical outcomes in the 1830s, and inchoate attempts at proof appear in works attributed to Hippocrates.

²¹Snow, *On Cancers*: 204.

were popular cancer treatments from ancient times. They appeared effective because they often left no visible cancer in their wake. Indeed, Snow noted that many of the miraculous cancer cures of the nineteenth century were actually “mild escharotics of vegetable origin, principally the acrid juice of plants” that produced little cancer cure but much chemically-burned skin.²² Unfortunately, seemingly salutary appearances can be deceiving, for invasive disease returned elsewhere and the practitioner was obliged to repeat the process over again as long as the patient could tolerate it. Internal cancer dissemination, the ultimate spread of malignancy, however, was beyond the reach of burning poultices.

The most common cancer-treating ingestibles were potions and pills. Potions were liquids that commonly contained alcohol as one of their many ingredients. Alcohol served to dissolve the other component compounds and met with patients’ approval because of its agreeable taste, pain-numbing property, and other pleasurable effects of inebriation. John D. Rockefeller’s father, William Rockefeller, regularly sold these elixirs to desperate but unsuspecting cancer patients.²³ Proprietary potions, many based on “secret” formulae,²⁴ led the list of specifics, for practitioners often profited more from the medicines they sold than from attending the patient. Indeed, it appears that the greater the hope (and hype), the higher the price. A good example was “Plunkitt’s plaister,” a proprietary mishmash for cancer noted by John Hunter in the late eighteenth century that persisted well into the nineteenth, which was priced much higher than justified by the cost of its simple, individual components.²⁵

²²Ibid., 205. Cundurango, the South American cancer “cure” of the early 1870s touted by Schuyler Colfax, Grant’s first Vice President (1869-73), was probably nothing more than another example of a skin-burning chemical caustic that led to eschar formation. See Chapter 3, page 32.

²³Ron Chernow, *Titan: The Life of John D. Rockefeller, Sr.*, First Vintage Books Edition ed. (New York: Vintage Books, 1998). 6.

²⁴Typically, the formulae were secret but the ingredients common.

Pills, unregulated in the United States before the twentieth century, contained a host of ingredients and led to variable and often unpredictable short-lived responses in those who took them. Pills that purged stool and urine were among the most common. These included diarrheics and diuretics—chemicals that induced watery stools or excessive urination, respectively. The objective was to rid the system of whatever poison caused the cancer. Mercury-containing pills were frequently-prescribed purgatives. Buchan’s treatment of scirrhus tumors, for example, was “to take twice of thrice a-week a dose of the common purging mercurial pill.”²⁶ Further, on the theory that disastrous diseases require dangerous remedies, physicians prescribed hemlock extracts, in various forms, to their cancer-ridden patients. So as not to kill the patient outright, Dr. Stork, a highly-touted Viennese cancer authority of the eighteenth century, advised small initial doses followed by graduated increments. He also warned that the deadly nature of the disease required years-long treatment to achieve the best results.²⁷ Dr. Stork’s successes with hemlock, like many other eighteenth- and nineteenth-century therapies for cancer, are anecdotal and hyperbolic rather than statistical.

Phlebotomy was the predominant treatment of cancer by heroic physicians until the latter decades of the nineteenth century.²⁸ The removal of blood for salutary purposes was an

²⁵Jessie Dobson, "John Hunter's Views on Cancer," *Annals of the Royal College of Surgeons of England* 25(1959): 179.

²⁶Buchan, *Domestic Medicine*, 127: 362. Mercury was particularly advantageous because it could be prepared in many forms—pills, potions, ointments.

²⁷*Ibid.*, 363-5.

²⁸One could argue that phlebotomy was a surgical procedure, for prior to the adoption of needled syringes in the late nineteenth century, blood was typically removed by cutting into the vein; i.e., vein sectioning or venesection. In the eighteenth century, William Buchan certainly believed that “bleeding” was a surgical procedure, for he wrote that “no operation of surgery is so frequently necessary as bleeding.” *Ibid.*, 421. Then again, he also believed that “every man (including “Midwives, Gardeners, Blacksmiths, &c.”—LK) is in some measure a surgeon whether he will or not,” thereby confounding the differentiation between surgery and non-surgery. *Ibid.*, 420.

Heroic physicians were the so-called “regulars” or “traditionalists” who used time-worn methods like phlebotomy to extremes. Their treatment algorithms contrasted with those of the “irregulars” or “empirics” who

attractive strategy, for practitioners utilized it to treat cancer and other ailments. It was, in a sense, all-purpose, and required little knowledge of individual diseases. Belief in constitutionalism was the foundation of general applicability of blood-letting, for regular physicians envisioned blood as the transporter of humors as well as the seat of diseases. If the cause of cancer was an imbalance of Galenic humors, with a particular excess of black bile, removal of blood via venesection might restore the harmony of the humors and reverse illness. Unfortunately, phlebotomy rarely cured. Instead, it often rendered a patient substantially weaker or even induced cardiovascular collapse, depending upon the patient's underlying condition and the quantity of blood removed. George Washington, for example, may well have died in 1799 from his phlebotomies rather than the upper respiratory illness that led to them.²⁹ Because of the dangers of phlebotomy, empirics and other "irregular" physicians eschewed it for the treatment of cancer and focused instead on more localized therapies with less potential for harm.

When all else failed, the "treatment" of cancer led ineluctably to opium and other narcotics. General Grant, for example, received cocaine—a very new "therapy" at the time. The poppy extract and coca plant derivatives assuaged pain, dulled the senses, and allowed the sufferer a modicum of respite before death. Few believed that opium affected the malignancy, for cure was not the objective at this late stage. Buchan, for example, knew well that opium was "a kind of solace" that would not "cure the disease, but it will ease the patient's agony, and render life more tolerable while it continues."³⁰

rarely resorted to blood-letting. Samuel Thomson, *New Guide to Health; or, Botanic Family Physician. Containing a Complete System of Practice, upon a Plan entirely new; with a description of the vegetables made use of, and Directions for preparing and administering them to cure disease* (Boston: E. G. House, 1822). 5, 9. Not surprisingly, patients often preferred the treatments of the empirics to those of the regulars.

²⁹P. Stavrakis, "Heroic medicine, bloodletting, and the sad fate of George Washington," *Md Med J* 46(1997).

³⁰Buchan, *Domestic Medicine*, 127: 365.

Although the non-surgical treatment of traditional cancer offered many specifics, almost none withstood the tests of time and modern medicine.³¹ Indeed, of the various evidence-based, non-surgical therapies used today—radiation, hormones, immunologics, chemicals, and biologics—none existed during the twilight of traditional cancer treatments when General Grant enjoyed his last full summer on the Jersey shore in 1884.

On the Uses and Abuses of Surgery for the Treatment of Traditional Cancer

Treatments for both traditional and modern cancer included surgery. Nevertheless, surgery at the end of the nineteenth century was a world apart from what had come before. To no small extent, this was because physicians and medical scientists of the modern era learned to mitigate the twin evils of traditional cancer surgery—pain and infection—which had previously led many cancer patients to forgo surgery and others to suffer from it.

An Ancient Endeavor

Surgery is one of the miracles of mankind—like language, the cumulative nature of human knowledge, and the arts. The etymology of the word trumpets its meaning, for surgery is a skill that derives from the Greek for “work of the hand.”³²

By the late nineteenth century, surgery was already an ancient treatment for cancer. The Edwin Smith Papyrus, which dates to the seventeenth century BCE and is the earliest known medical-surgical treatise, describes among its forty-eight cases at least one that would seem to be

³¹“Specifics” is the key word, for methods of discovery for new anti-cancer agents still include the investigation of natural substances from plants and animals. It is also likely that some chance cancer-treatment ingredients from the age of traditional cancer medicine included agents still in use today. Vinca alkaloids, originally isolated from the periwinkle plant, may be one example.

³²From the Greek *cheir* ‘hand’ and *ergon* ‘work.’

Dr. Harvey Cushing, famed Harvard neurosurgeon and Pulitzer-prize-winning biographer of the clinician Dr. William Osler, distinguished the surgeon from other physicians as follows: “The physician requires a special combination of head and heart; the surgeon of head, heart and hand – a rare combination which comes partly by gift and partly by training.”

a malignant tumor.³³ The unknown author of the Papyrus instructed that for the treatment of these multi-focal, swollen, cold, fluid-less masses “there is nothing”—meaning that the best treatment is no treatment.³⁴ For superficial growths, however, the surgical therapy of choice was excision or cauterization—especially if they were hot and draining.³⁵ Noteworthy is the fact that the Smith papyrus evinces a keen awareness of human anatomy, the foundation of all surgery. Archeologists have since discovered metal surgical tools dated to the Homeric era and later from the early first millennium BCE. These sharp and pulling implements could cut and remove the symptomatic, superficial tumors described in the Smith Papyrus. (See fig.)

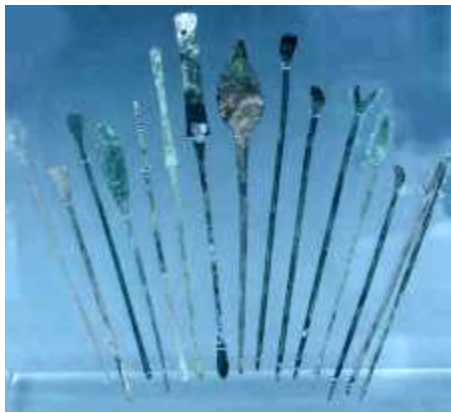


Figure 5. Surgical Utensils - Roman period (1st Century CE)³⁶

³³James Henry Breasted, ed. *The Edwin Smith Surgical Papyrus*, Two vols., vol. One & Two, The University of Chicago Oriental Institute Publications (Chicago: The University of Chicago Press, 1930; reprint, 1984), 403-06. I refer to Case Forty-Five, which Breasted translated as “Bulging Tumors on the Breast.” Case Forty-One may describe a necrotic ulcer related to another breast malignancy. *Ibid.*, 374-91. It is doubtful to me that the other six breast lesion cases (XXXIX, XL, XLII, XLIII, XLIV, and XLVI) involved cancers, despite what others have written. These alternate pathologies seem to be mainly inflammatory “tumors”—abscesses—caused by wounds and other traumatic insults to the breast. As I have noted previously in this dissertation, practitioners used the term ‘tumor’ to include infectious lesions well into the nineteenth century.

³⁴*Ibid.*, 405. Interestingly, the ancient papyrus that Smith purchased in Egypt during the mid-nineteenth century also noted that the physician should not treat tumors that were hard, painless, cool, and without drainage, for surgery would likely render the disease worse. This was a lesson emphasized by Samuel David Gross three and a half millennia later. *Ibid.*, 404-05.

³⁵*Ibid.*, 363-69. Case Thirty-Nine.

The Hippocratic writings of the late fifth and fourth centuries BCE affirm the Ancient Egyptian advice to abstain from the surgical treatment of non-superficial tumors. One of the Hippocratic aphorisms specifically admonished the reader that “it is better not to apply any treatment in cases of occult [deep—LK] cancer; for, if treated, the patients die quickly; but if not treated, they hold out for a long time.”³⁷ On the other hand, physicians, as in Ancient Greece and Egypt encouraged the removal of superficial growths by knife and burning.³⁸

Aulus Cornelius Celsus, who lived during the first century CE, wrote what was probably the first systematic treatise on medicine. This work, *De medicina*, was part of his much larger encyclopedia.³⁹ He may have been one of the first to conflate inflammatory and malignant growths, for he described the four cardinal features of inflammation as rubor (redness), calor (heat), dolor (pain), and tumor (swelling, growth). Like the Egyptians and Greeks before him, the Roman Celsus stressed that the surgeon must show forbearance when dealing with a deep cancer.⁴⁰ On the other hand, Celsus also prescribed the *early* excision of superficial cancerous lesions and, as a result, reported the first known cases of surgery for lip and other facial cancers. He was also among the first to advocate caustic pastes. As noted, these skin-burning agents persisted well into the nineteenth century. Finally, he wrote much on the pain-killing properties

³⁶ From http://www.bordet.be/en/presentation/history/cancer_e/cancer2.htm accessed 2/17/07. These are copper alloy utensils.

³⁷ Francis Adams, ed. *The Genuine Works of Hippocrates*, Special ed., 2 vols., vol. 2, The Classics of Medicine Library (London: The Sydenham Society, 1849; reprint, 1985), 758. Section VI, number XXXVIII by the modern pagination. Also see Hippocrates, *The Aphorisms of Hippocrates*, trans. Thomas Coar, Special ed., The Classics of Medicine Library (London: A.J. Valpy, 1822; repr., 1982). 177., where the previously-translated term ‘treatment’ is replaced by ‘cure’; i.e., “Better not to cure hidden cancers, for they who are cured quickly perish”—a most disturbing thought!

³⁸ Adams, *The Genuine Works of Hippocrates*, 758.

³⁹ T. Clifford Allbutt, *Greek Medicine in Rome; The Fitzpatrick Lectures on the History of Medicine Delivered at the Royal College of Physicians of London in 1909-1910*, Special ed., vol. 180, The Classics of Medicine Library (London: Macmillan and Co., 1921; repr., 2001). 202.

⁴⁰ http://www.bordet.be/en/presentation/history/cancer_e/cancer2.htm accessed 2/20/07.

of the poppy—in case other cancer treatments failed.⁴¹ In short, his recommendations set the tone and the standard for the treatment of cancer well into the nineteenth century.

Galen, a Greek physician who served the Roman Emperor Marcus Aurelius in the 2nd century, rejected the empiricism of Hippocrates (c. 460-c. 370 BCE) and Celsus. Instead, he based his treatment of cancer on the humoral theory of disease causation. His rational-deductionist approach to treatment advocated the re-balancing of excessive humors. Cancer, characterized by an excess of black bile, or *melan chole*, required the removal of blood via venesection in order to achieve harmony and health.⁴² Although Galen performed surgery, it is unclear from his work on cancer, *De tumoribus praeter naturam (Swellings Contrary to Nature)*—the only known treatise from antiquity specifically devoted to tumors—under which circumstances he would operate on tumors.⁴³ Perhaps the omission is understandable, for Galen's objective was the systematization of disease and the derivation of treatment from causation.⁴⁴ Neither goal in his philosophy provided for excisional surgery. Therefore, if, as Galen believed, black bile caused cancer, then treatment and cure followed removal of the

⁴¹Sherwin B. Nuland, *Doctors: The Biography of Medicine*, Special ed., The Classics of Medicine Library (New York: Alfred A. Knopf, 1988). 267.

⁴²Jeremiah Reedy, "Galen on Cancer and Related Diseases," *Clio Medica* 10, no. 3 (1975): 234.

⁴³Philip W. Moss, "Galen on Cancer: How Ancient Physicians Viewed Malignant Disease," (1989), <http://www.cancerdecisions.com/speeches/galen1989.html> accessed February 21, 2007. It should be noted that Cancer, as defined in this dissertation, warranted only a small space in Galen's treatise on tumors. Obesity and inflammatory lesions made up the bulk of his discussion.

⁴⁴The idea of causation informed much of Galen's oeuvre. In the polytheistic Roman world, causation was a problem for intellectuals. Christianity, which the Roman Empire did not officially adopt until two centuries after Galen, appeared to solve the problem of causation by investing causation in the ultimate Prime Mover. The effect of this shift of agency from Man to God reduced the need for those living from Late Antiquity until the Renaissance to seek the causes of things such as cancer—a philosophy detrimental and generally fatal to those with growths "contrary to nature."

malicious excessive bile via bloodletting.⁴⁵ Blood was the seat of disease. Direct removal of the tumor played no role in this philosophy.

Galen's prescription for the treatment of growths "contrary to nature" overshadowed that of Hippocrates and especially Celsus until at least the sixteenth century. Andreas Vesalius (1514-1564) showed that many of Galen's hypotheses and directives lacked a verifiable anatomical basis.⁴⁶ The centuries between Galen and Vesalius saw few new directions in the treatment of cancer, for the development, progress, and innovation of human enterprise was not highly valued during an era when Man was no longer the focus of culture. The Renaissance in medicine as well as culture brought renewed emphasis on Man. The Scientific Revolution of the sixteenth through eighteenth centuries refocused on the physical nature of the world and imagined a mechanical universe. In medicine, these advances in understanding promoted new knowledge of the structure of the human body through the dissections of Vesalius,⁴⁷ the circulation discoveries of William Harvey (1578-1657),⁴⁸ and the pioneering investigations of the pathologist, Giovanni Morgagni (1682-1771).⁴⁹ The ground-breaking knowledge of anatomy

⁴⁵Reedy, "Galen on Cancer," 234.

⁴⁶Whether Galen's enormous hold on the theory and practice of medicine for more than a millennium related to his teleological approach to medicine, as Singer suggested, or his Christian-friendly beliefs, as McGrew wrote, is difficult to assess. Charles Singer, *A Short History of Scientific Ideas to 1900* (New York: Oxford University Press, 1959). 101; Roderick E. McGrew and with the collaboration of Margaret P. McGrew, *Encyclopedia of Medical History* (New York: McGraw-Hill Book Company, 1985). 121. Suffice it to say, Galen wrote the book on tumors "contrary to nature," named sub-types of cancer such as scirrhus (*skirros*), and linked cause to treatment and cure.

⁴⁷Especially *De humani corporis fabrica (On the Workings of the Human Body)*, published 1543.

⁴⁸Especially *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus (An Anatomical Exercise on the Motion of the Heart and Blood in Living Beings)*, 1628.

⁴⁹Especially *De sedibus et causis morborum (The Seats and Causes of Disease)*, 1761.

contributed by these and other investigators of nature in peace and war established the framework for the surgical treatment of cancer in the nineteenth century.⁵⁰

Traditional Cancer Surgery in the Nineteenth Century

The lapse of centuries of civilization has done no more, in respect to the question of operation [for cancer], than to furnish elements for demonstrating what the observant genius of one man [Hippocrates] had, in an era of comparative barbarism, so acutely divined.⁵¹

—Dr. W. H. Walshe, 1846

Despite the great increase in the knowledge of human anatomy and pathology beginning in the sixteenth century, the ancient paradigm of bloodletting, caustic pastes, and the occasional removal of superficial growths continued to dominate the treatment of cancer well into the nineteenth century.

Even in the case of breast cancer, one of the most common and ancient of the known cancers (and a lesion that often bordered between superficial and deep), surgery in early-to-mid nineteenth century America was little different from that of Ancient Greece or Rome.⁵² In 1889, for example, George Jackson Fisher wrote an article on “A History of Surgery” for Ashhurst’s comprehensive *International Encyclopedia of Surgery*.⁵³ Therein he quoted from the writings of Leonides, a first-century Roman surgeon of Greek heritage, to show that the method of performing breast cancer surgery had changed little in eighteen hundred years:

⁵⁰The importance of wartime injuries to the changing landscape of anatomy and surgery cannot be overemphasized. The wars of religion that punctuated the sixteenth and seventeenth centuries in Europe provided a surplus of human disasters from which physicians like Ambroise Paré could expand surgical and anatomical knowledge through their treatment of the wounded and dying. Many of these techniques, including the use of post-operative applications and bandages, carried over into cancer treatments, including surgery.

⁵¹W. H. Walshe, *The Nature and Treatment of Cancer* (1846). 95.

⁵²The first case study of a tumor in the oldest known medical-surgical text, *The Edwin Smith Papyrus*, written, as noted above, around the 17th century BCE, examines the treatment of breast tumors. Thus, it is reasonable to state that breast tumors are the oldest reported tumors in history. See Breasted, *The Edwin Smith Surgical Papyrus*, Case 39..

⁵³John Ashhurst, Jr., ed. *The International Encyclopedia of Surgery, A Systematic Treatise on the Theory and Practice of Surgery by Authors of Various Nations*, Revised ed., VI. vols., vol. VI. (New York: William Wood & Company, 1889).

I make the patient lie upon her back, then I cut upon the sound part of the breast above the cancer, and burn in the incision with a red-hot iron sufficient to arrest the flow of blood; I immediately incise again and dissect up from the deepest part of the mamma, and again burn the incised parts, and after this I repeat the cutting following it with the red-hot iron sufficient to arrest the hemorrhage. The first burning is for the arrest of the hemorrhage, but afterwards the burning is for the removal of every vestige of diseased tissue. But often also when the indurated cancerous tumor is situated less deep in the breast, the entire operation is performed without the cautery, for in such cases it is sufficient to amputate to the sound parts, as there is no danger from hemorrhage.⁵⁴

In sum, the knife cuts and the iron burns. Following the ancient algorithm that continues to provide the foundation for medical practice today, the physician made a clinical diagnosis as to the cause of the patient’s problem (“indurated cancerous tumor”), decided what needed to be done (“incision,” “dissect[ion]”, and “removal”), and followed the technique he thought—based upon learning and experience—would best ameliorate the condition. Nevertheless, it is instructive to note that Leonides mentioned nothing about the patient’s ability to tolerate the pain of the procedure. Nor did he comment on the patient’s post-operative condition in terms of infection or bleeding, let alone survival.

From the facts, figures, and inferences now brought forth, the conclusion is inevitable and imperative, that extirpation of cancerous growths with the knife can neither be regarded as a means of curing cancer, nor of prolonging the existence of persons afflicted with the disease.⁵⁵

—Dr. W. H. Walshe, 1846

At the beginning of the nineteenth century, cancer surgery was a quick, dirty, and dangerous affair. Setting aside the problem of errors made in the diagnosis of cancer,⁵⁶ tumors deemed operable by the surgeon caused consternation on the part of patient and physician alike. The woman operated upon for a breast tumor underwent the procedure without general anesthesia but with the ever-present fear of complications that caused more suffering than the

⁵⁴Ibid., 811.

⁵⁵Walshe, *The Nature and Treatment of Cancer*: 94-95.

⁵⁶There are many types of diagnostic errors. The error of most concern is the “false positive,” whereby a diagnosis of cancer is made although the patient, in retrospect, did not have cancer.

tumor itself and, perhaps, an earlier demise than the tumor would have caused. In addition to the pain and suffering of the operation and its aftermath, patients and surgeons feared excessive bleeding, infection, circulatory collapse, and even intra-operative or post-operative death.

The Appalling Ratio

Thirty years ago, taking all operations together, fully one-third of our patients died, many of them often from slight operations.

—W. W. Keen, 1901⁵⁷

The operative mortality rate for all surgeries taken together was unconscionably high. In addition, the average post-operative mortality rate in a hospital approached 25%.⁵⁸

“Uncomplicated” vaginal deliveries of newborns by physicians or medical students led to maternal death rates that were also one in four.⁵⁹ Soldiers wounded in the American Civil War and earlier wars suffered a similar fate, for operations to set bones and amputate limbs frequently led to rapid, horrible deaths.⁶⁰ Perhaps the greatest operative mortality of all was associated with the treatment of compound fractures, where broken bones punctured the skin. Barely one in ten survived!⁶¹ In 1872, Marcus Beck, a cousin of Lister, called this “the appalling ratio.”⁶² Compare this flagrant mortality rate with “watchful waiting”—essentially non-operative observation—where the survival was three of ten.

⁵⁷William Williams Keen, "The Progress of Surgery in the Nineteenth Century," in *Addresses and Other Papers* (Philadelphia: W. B. Saunders & Company, 1905), 340-41.

⁵⁸Charles E. Rosenberg, *The Care of Strangers: The Rise of America's Hospital System* (Baltimore: The Johns Hopkins University Press, 1987; repr., 1995). 126.

⁵⁹C. D. Haagensen and Wyndham E. B. Lloyd, *A Hundred Years of Medicine* (New York: Sheridan House, 1943). 292. and Nuland, *Doctors*: 245. These mortality rates in previously healthy mothers were the stimulus behind Ignaz Semmelweis' enormously important contributions to the problem of childbed fever, as we shall see.

⁶⁰W. W. Keen, "Before and After Lister: Lecture I, Before Lister," *Science New Series*, 41, no. 1067 (1915): 851. In many wars, the number of combatants dead from disease exceeded those killed in battle.

⁶¹*Ibid.*; "Before and After Lister: Lecture II, After Lister," *Science New Series*, 41, no. 1068 (1915): 887.

⁶²Sir Rickman John Godlee, *Lord Lister*, Special ed., vol. 205, The Classics of Medicine Library (Oxford: At the Clarendon Press, 1924; repr., 2005). 133.

Mortality rates among cancer-surgery patients were little better. Patients who underwent operations for cancers within the abdomen had, at best, a fifty-fifty probability of survival.⁶³ As a result, common knowledge and experience taught that *no* operation was often better for the patient than operating—especially with internal malignancies.⁶⁴ One of Dr. William W. Keen's mentors declared in mid-century that "any man who dared to open the abdomen to remove an ovarian tumor should be indicted for murder!"⁶⁵ Keen himself expanded the number of body sites that were off limits to cancer surgeons during the traditional era when he declared in 1901 that "to open the head, the abdomen, or the chest thirty years ago was almost equivalent to signing the death warrant of a patient."⁶⁶

Why was Traditional Cancer Surgery so dangerous?

Thirty years ago...the surgeon never dared to interfere until he was obliged to do so. Hence, not only were many modern operations not even thought of, but in obscure cases we had to wait until time and disease developed symptoms and physical signs such that we were sure of our diagnosis and then, knowing that death would follow if we did not interfere, we ventured to operate.

—W. W. Keen, 1901⁶⁷

Cancer surgery was fraught with enormous dangers before the final decades of the nineteenth century. In addition to the intolerable pain and suffering that accompanied operations before the advent of surgical anesthesia, surgical risks included intra-operative death, life-threatening post-operative infection, and an extremely high cancer recurrence rate. This last

⁶³Keen, "Progress of Surgery," 99.

⁶⁴Keen, "Before Lister," 851.

⁶⁵Keen, "Progress of Surgery," 99.

⁶⁶*Addresses and Other Papers*, Special ed., The Classics of Medicine Library (Philadelphia: W. B. Saunders & Company, 1905; repr., 1998). 328. Keen first published the essay in which he first made this chilling observation, "The Progress of Surgery in the Nineteenth Century," in 1901.

⁶⁷"Progress of Surgery," 339-40.

peril was especially likely if patient and/or physician procrastinated on surgery until the disease had spread beyond its local confines—as they often did.

Cancer patients who underwent surgery for cancer or other indications suffered an alarmingly high operative mortality rate. Given the general belief that cancer surgery was a treatment of last resort, it is not surprising that many patients who found themselves on the way to the operating room suffered from poor general health and advanced disease. The oft-debilitated condition of the patient by the time that surgery was agreed to was a major contributor to this egregious death rate. Excessive alcohol intake, a common intemperance in the nineteenth century⁶⁸ and a cheap, readily-available source of cancer pain amelioration, further reduced operative survivability.⁶⁹

In the early years of the nineteenth century, before the advent of surgical anesthesia, operators sedated patients with various soporifics, including alcohol and different forms of opium. Long before the standardization of drug doses and ingredients beginning in the early twentieth century, none of these agents was easy to quantify or titrate. In addition, given non-uniform patient tolerance levels, surgeons often found their patients under-sedated, over-sedated, or non-sedated. Even after the advent of surgical anesthesia in the 1840s, the administration of just the right amount of consciousness-altering drug was difficult to achieve. Catastrophes resulted, for patient restiveness due to inadequate sedation during a fine-hand procedure could easily lead to miss-placed incisions and slashed arteries. Worse, excessive patient sedation could translate into an operative death by overdose.

⁶⁸W. J. Rorabaugh, *The Alcoholic Republic: An American Tradition* (Oxford: Oxford University Press, 1979). As Rorabaugh makes clear, the consumption of alcohol by Americans before the Second Great Awakening of the 1830s-1840s far exceeded today's robust imbibition levels.

⁶⁹Stephen Paget, *Essays for Students* (New York: William Wood & Company, 1899). 73.

Intra-operative and post-operative bleeding was another major concern. Whether by errant incision, an increased propensity to bleeding,⁷⁰ or a vascular tumor,⁷¹ hemorrhage was a major concern during traditional cancer surgery that could lead to circulatory collapse and death. Traditional cancer surgeons stanching bleeding by direct pressure to the blood vessel, cautery, and ligatures. Direct pressure was a stop-gap measure with little hope of long-term control of hemorrhage, for bleeding often recurred after the release of the pressure. Cauterization, an ancient practice by which the operator burned the bleeding source directly with heated metal, followed the observation that burnt tissue stopped bleeding. Unfortunately, the cautery also caused severe tissue damage,⁷² which could itself lead to an increased incidence of infection or even recurrent hemorrhage. In 1552, Ambroise Paré (c. 1510-1590), a French military surgeon, introduced the idea of tying off the bleeding vessel to provide an alternative to cauterization. Ligatures, which are thin filaments of various materials tied tightly around a vessel, were effective during the operation, but could lead to post-operative bleeding as the tie completely cut through the vessel over time. Further, ligatures could induce post-operative infections, for these unsterilized strings, often stored around the button of the surgeon's bloody coat and left hanging outside the patient's wound so that the operator could pull them gradually over time to remove them as the tissues healed from within, provided a nidus and pathway for infection directly into the wound.⁷³

⁷⁰Bleeding risk is increased in heredity diseases such as hemophilia and von Willebrand's disease as well as in acquired conditions, such as excessive recent alcohol intake.

⁷¹Increased numbers of blood vessels and total blood volume (vascularity) are common features of malignancies. Enlarged blood vessels are so inherent to 'cancer' that the term itself may derive from the crab-like appearance of the tumor's vascularity.

⁷²Cell proteins are denatured by heat, causing them to lose their functionality.

⁷³Haagensen and Lloyd, *A Hundred Years of Medicine*: 25.

Indeed, post-operative infection was yet another major fear, for many who survived the cancer operation succumbed to infection days and weeks later. Before the antiseptics, asepsis, and sterilization of the modern era, any insult to the integrity (especially of the integument) of the human body—traumatic, surgical, or otherwise—increased the risk of infection. The standard treatment for the surgical site post-operatively, at least since the days of the Ancient Sumerians and Hippocrates, was wound irrigation with wine followed by bandaging and the soaking of the bandages with more wine.⁷⁴ Prior to the acceptance of the causative explanations of bacteriology in the late nineteenth century, many surgeons took comfort in the promise of “laudable pus”—the notion from Galen that the creamy, yellow-white excrescence seeping from the wound was a good and essential sign of healing.⁷⁵ Indeed, the prevalent belief until the late nineteenth century was that those who developed such pus three to five days after surgery would live.⁷⁶ Those who did not were doomed to the horrible death of sepsis. Among surgeons, pus became a preeminent topic of conversation. “Pus,” wrote Sir Frederick Treves about this era, “was the most common subject of converse, because it was the most prominent feature in the surgeon’s work.”⁷⁷

Statistics that surgeons began to compile in the mid-nineteenth century supported their trepidation toward post-operative infections. Most of the ninety percent mortality rate for

⁷⁴Jason T. Miller, Scott Y. Rahimi, and Mark Lee, "History of infection control and its contributions to the development and success of brain tumor operations," *Neurosurgical Focus* 18, no. 4 (2005): 2. accessed online 3/19/07 at <http://www.aans.org/education/journal/neurosurgical/apr05/18-4-4.pdf>.

⁷⁵ Ibid. accessed online 3/19/07 at <http://www.aans.org/education/journal/neurosurgical/apr05/18-4-4.pdf>.

⁷⁶Surgeons often divided pus into three types. “Laudable pus,” as noted, was the most sanguine. “Sanious pus” was a thin, blood-tinged excrescence of mixed but portentous prognosis. “Ichorous pus was the worst for its smell could be overwhelming and its contents abominable.” (after Sir Frederick Treves as quoted by Nuland, *Doctors*: 347.)

⁷⁷Ibid. Sir Treves became a prominent member of the medical literati upon his retirement from surgical practice. He is the author of *The Elephant Man and Other Reminiscences* (1923).

compound fractures, for example, resulted from post-operative infections. Cancer surgery patients fortunate to survive their operative procedures suffered the same fear of such infections.

The high post-operative recurrence rate was another bar to traditional cancer surgery and another reason to delay surgical intervention as long as possible. Recurrence was not the result of shoddy cancer surgery, for even the best of operators had prodigious numbers of long-term failures. In his seminal work on *Operations for the Cure of Cancer of the Breast*, published in 1895, William Halsted (1852-1922) surveyed the post-surgical breast cancer recurrence rates of the best operators in Europe.⁷⁸ Richard von Volkmann, who added survival-enhancing axillary dissection to breast cancer surgery even before Halsted graduated from medical school, had a fifty-nine percent recurrence rate during the 1870s. The celebrated Vincenz Czerny (1842-1916), who did so much later in the century to advance oncologic surgery, noted a sixty-two percent recurrence among his breast cancer patients. Fischer's failure rate was seventy-five percent. And Theodor Billroth, the most famous of all and the pioneer of so many modern cancer surgeries, had a cancer recurrence rate during the same period of eighty-five percent!⁷⁹

These atrocious results followed the nature of traditional cancer surgery, for with the risk of intra-operative complications, post-surgical infections, and high recurrence rates, surgeons sought to operate only when absolutely necessary and, even then, as expeditiously as possible.⁸⁰ Thus, palliative procedures dominated curative efforts, surgeons removed as little of the tumor as would provide at least some relief, and all hoped that the operation would prolong life rather than

⁷⁸William S. Halsted, "The Results of Operations for the Cure of Cancer of the Breast Performed at The Johns Hopkins Hospital from June, 1889, to January, 1894," *The Johns Hopkins Hospital Reports* IV, no. 6 (1895).

⁷⁹Ibid., 6-7. Unfortunately, Halsted did not clarify the case selection criteria, thus creating the possibility that many of these cancer operations were on non-cancerous (including inflammatory and infectious) conditions.

⁸⁰John Marshall, "The Morton Lecture on Cancer and Cancerous Diseases Delivered at the Royal College of Surgeons of England on Monday, the 18th November, 1889," in *Hunter-Beekman Tracts* (1890), 23.

shorten it. Traditional cancer surgery was, in essence, a vicious circle of self-fulfilling prophecies that led to a premature end.

So Why Even Consider Traditional Cancer Surgery at All?

The tragedies of traditional cancer surgery aside, it was and is the duty of the physician to treat his/her patients with the best *available* means possible—always keeping in mind the ancient admonition *primum non nocere*—“Above all, do no harm.”⁸¹ But “harm” is a fluid concept that means different things to different people at different times and in different places. In general, the standard of “harm” was much more severe in the nineteenth century than today. Tolerability appears to have been much greater then than now. Witness, for example, the excruciating pain of Fanny Burney’s pre-anesthetic-era breast surgery, the torture of General Grant’s daily throat examination, and the fulgurations of Crown Prince Friedrich’s vocal cord—and the evocation of horror and disbelief that they visit on today’s readers.

Still, surgery—despite all its attendant risks and sufferings—was, for the traditional physician, the only accepted possible cure for cancer.⁸² Cancer patients heeded the ancient wisdom that drastic times called for drastic measures. Some would risk everything, including their lives, for the chance to be free of cancer. Others would not, and they sought to temporize by less dire means.

Thus, there was a tendency to seek therapies—when patient’s sought treatment and physicians provided it—that often sacrificed efficacy for acceptance. Hence, the plaster, piaster, and salve were born. Nevertheless, it was clear to many physicians by the nineteenth century

⁸¹The exact origin of the phrase is uncertain, but a close paraphrase may be found in Hippocrates’ *Epidemics*, Bk. I, Sect. V.

⁸²The absence of verifiable alternatives to cancer surgery stimulated the growth of the alternative cancer treatments industry of the nineteenth century that physicians today often call “Quack medicine.” ‘Quack,’ from a Dutch term that means “boaster who applies a salve,” probably derives from the common non-surgical application of such unguents of the nineteenth century and before.

that such therapies were themselves dangerous, for they did little to assuage the predictable as well as manifest ravages of advanced cancer and gave the patient and his kin false hope.⁸³ Non-surgical temporizing only traded immediate expediency for later disaster.

There were, however, some bright spots on this gloomy landscape, for some had the foresight to capitalize on these treatment differences to forge an environment more conducive to the successful surgical treatment of cancer.

Where to Operate?

Given the procrastination that led patient and physician to postpone cancer surgery until little or no hope remained, given the diagnostic inaccuracy that led to many unwarranted operations, and given the intra-operative and post-operative risks of the era, it is noteworthy that some patients enjoyed better outcomes than others. To no small extent, improved results depended upon the surgical venue.⁸⁴

Surgeons and other operators performed early nineteenth-century operations in several different locales.⁸⁵ Surgeons usually operated upon the wealthy in the privacy of their own homes. Dr. Dominique Jean Larrey, for example, operated upon his private patients like Fanny Burney in the comfort, cleanliness, and supportive surroundings of their own homes.⁸⁶ In

⁸³Snow, *On Cancers*: 204.

⁸⁴Note that the location at which cancer surgery occurred has built into it a number of critical factors, including economic and social as well as environmental.

⁸⁵I added the term “other operators” because there were many whose formal training and experience were quite limited. To entitle them “surgeons” would be problematic.

In addition, please note that I will focus on the domestic residence and the institution rather than other venues of surgery. Military field operations, commonly performed on soldiers wounded in battle, were critical for developments in the history of surgery, but not directly to cancer patients.

⁸⁶Dr. Larrey did not always have the luxury of residential operations, for he was above all a military surgeon. Nevertheless, as Napoleon’s Surgeon-in-Chief from 1797 to 1815, he inaugurated “flying ambulances” with skilled attendants to bring the wounded and dying to field hospitals where he improved soldiers’ quality of care—and probability of survival—by making the facilities more like specialized medical-surgical “private” residences.

contradistinction, the poor and dispossessed, confined to institutions such as almshouses and hospitals, received care where they lay. The operative suite, the twentieth-, and twenty-first-century locus of surgery, was rare before the end of the nineteenth century.⁸⁷

The best general site for a surgical operation in the early-to-mid nineteenth century, based upon outcomes, was the private home of the well-to-do patient.⁸⁸ Statistical evidence, gathered especially after mid-century, bolstered this commonly-held belief and made it incontrovertible.⁸⁹ Amputations performed in the private home, for example, led to a mortality rate one fourth of that in hospitals.⁹⁰ Deaths following obstetrical procedures in hospitals exceeded those in private residences by eight hundred percent.⁹¹

Physicians offered many reasons for this enormous discrepancy in surgery-related morbidity and mortality, but causation and proof are difficult to validate. In the era of traditional cancer, scriptural, socioeconomic, hygienic, and miasmatic concepts dominated the debate. Each implies much about the underlying beliefs of patients and their physicians at the time.

The Bible was the book most commonly owned and referenced by Americans during the nineteenth century. Leviticus, the third book of the Pentateuch, which focused on legal concerns

⁸⁷Keen, *Addresses*: 246.

A prominent exception to this timeline was the surgical amphitheater, which can be traced back to the Pennsylvania Hospital in 1804 in the United States. See <http://www.uphs.upenn.edu/paharc/collections/exhibits/amph/>. (Accessed October 22, 2007) Nonetheless, the number of patients operated upon in this venue was small, despite images of Warren and Morton at the Massachusetts General Hospital (1846) and Thomas Eakins' *The Gross Clinic* (1875).

⁸⁸Godlee, *Lister*, 205: 124.

⁸⁹As noted below, Pierre-Charles-Alexandre Louis greatly expanded the accumulation of medical knowledge through aggregated collections of patient statistics beginning in the 1830s. Statistical methodologies and "numbers crunching" have played a major role in the history of cancer from the nineteenth century to the present.

⁹⁰Keen, "Before Lister," 849. from Sir James Y. Simpson, *The Works of Sir James Y. Simpson, Bart.*, vol. II (Edinburgh: Adam and Charles Black, 1871). 345..

⁹¹Keen, "Before Lister," 849.

and priestly rituals, mandated the separation of the diseased from the healthy.⁹² Hospitals and almshouses in the nineteenth century served this purpose because these long-term facilities segregated their residents from the healthy citizens of the outside world.⁹³ Indeed, institutions of this sort not only promoted quarantine rather than patient isolation, but the paltry sums spent on upkeep led to limited numbers of personnel and unsanitary conditions. Reused wound bandages, toiletless facilities, and unwashed blankets that covered many sick and dying patients in succession exemplified these shortcomings. Benjamin Rush (1745-1813), the best-known American physician of the late eighteenth and early nineteenth century, called these institutions “the sinks of human life.”⁹⁴ Cancer, long believed to be just punishment for sin, fit well into this milieu of Christian orthodoxy because of the prevalent notion throughout most of the nineteenth century that cancer, like leprosy, was contagious.

Socioeconomically, the well-heeled tended to blame the poor and ill as instigators of their own fate. This conflation of theology and materiality asked why should a man be poor and/or ill unless found wanting in the eyes of a judging God? Thus, this explanation warranted that the rich enjoyed better surgical outcomes than the poor because those with wealth were more deserving or, alternatively, that the rich were less sinful “in the hands of an Angry God”, not

⁹²Leviticus 13: 43-46. The priest was to make the diagnosis of leprosy based upon a reddish-white “sore.” The non-specificity of such a lesion may have led to many false positives and the exclusion of “unclean” and “defiled” individuals who could not in fact communicate the “plague” that this dictum meant to prevent.

⁹³Note that although Leviticus charged that the “unclean” and “defiled” “shall dwell alone,” Christian charity made it a blessing to care for the sick. Thus, those who cared for the poor and sick in these early institutions inhabited an intermediary position in the eyes of the healthy, for Christian ethics elevated their calling while society denigrated it as a job for prostitutes and others of similar repute. Florence Nightingale in Great Britain and Clara Barton in the United States are often credited with improving the image of one type of caregiver—viz., the nurse.

⁹⁴Haagensen and Lloyd, *A Hundred Years of Medicine*: 23.

because—as twenty-first-century eyes see it—their homes were cleaner (for cleanliness is a luxury that requires time and money) and less infested.⁹⁵

Hygiene, an ancient idea,⁹⁶ gained additional currency in the nineteenth century with the advent of indoor plumbing and, decades later, the fear of germs.⁹⁷ Hygiene included much more than personal cleanliness, for fresh air, pure water, adequate drainage, and ample light also added to its meaning. Cleanliness, a notion of self-care that blossomed in the United States beginning the 1830s, found acceptance in the home long before the institution.⁹⁸ Owners of private homes could afford the self-indulgence of personal hygiene. The poor and ill could not. Charitable institutions of the early to mid-nineteenth century, like hospitals and almshouses, reeked of noisome odors. At the time, hospital hygiene was an oxymoron.

Noxious smells formed the basis of miasma theory, a belief popular during the nineteenth century that postulated foul air as the cause of disease.⁹⁹ Popular lore blamed miasmatic influences for the recurrent cholera epidemics in the Western world during the middle third of

⁹⁵Jonathan Edwards linked the ephemerality of health and the eternality of sin several times in his 1741 sermon “Sinners in the Hands of an Angry God.” See, for example, <http://www.ccel.org/ccel/edwards/sermons.sinners.html>. (Accessed October 22, 2007)

⁹⁶The Greek goddess of health, Hygeia, was the daughter of Aesculapius, Greek god of medicine.

⁹⁷In 1829, the Tremont Hotel in Boston became the first hotel in the United States with indoor plumbing. According to one source, it sent “ripples of awe throughout the country.” The White House acquired indoor plumbing with running water in 1833. The construction engineer planned to fashion the original pipes from dug-out wooden logs, but changed to iron for fire protection. See <http://www.theplumber.com/usa.html> Accessed April 4, 2007.

⁹⁸Suellen Hoy, *Chasing Dirt: The American Pursuit of Cleanliness*, 1st ed. (New York: Oxford University Press, 1995). 23.

Note the charged Biblical term “unclean” as a designation for a person as well as a state of being. That first meaning has been lost since the advent of bacteriology and the acceptance of the notion that the individual was not necessarily the maker of his own fate, especially once medical scientists determined that disease could infect an unerring innocent as well as a deserving sinner.

⁹⁹See, for example, *ibid.*, 31.

“Miasma” has Greek roots in stain and defilement. (*Oxford English Dictionary* online) Malaria, another disease linked to miasma, etymologically means “bad air”—mal-aria.

the century.¹⁰⁰ Miasma theory serves as an example of a retrospectively false belief in medicine with salutary consequences, for the municipal efforts of mid-century to rid the environment of corrupted air led to the public cleanliness movements called sanitation.¹⁰¹ Indeed, sanitation turned out to be a self-fulfilling prophecy, for sanitized water and air did indeed reduce the incidence of epidemic diseases—just not by the means conceived.

Physicians rarely ascribed the cause of cancer to miasma, for they linked pollution to acute ailments rather than to usually chronic afflictions like cancer. Nevertheless, foul air played a significant non-causative role in cancer surgery, for smell was one of the signs used by physicians to diagnose disease, whether it was an ulcerating cancer or a post-operative infection. Indeed, post-operative infection was the greatest fear, short of death, harbored by patients who survived surgery in the age of traditional cancer. It was also a compelling reason for patient and physician to avoid surgery as a treatment for cancer, for there was no good, safe, dependable anti-infective. The possibility of death from infection was ever-present.

The FOUR HORSEMEN of Death¹⁰²

From the beginning of time until the middle of the nineteenth century, surgery of any kind was liable and even likely to be followed by infection, and infection was liable, and even likely, to prove fatal.

-Guy Williams¹⁰³

¹⁰⁰For a classic study of the “Cholera Years,” especially in their social and historical context, see Charles E. Rosenberg, *The Cholera Years: The United States in 1832, 1849, and 1866*, 1st ed., 1 vols. (Chicago: The University of Chicago Press, 1962)..

¹⁰¹Formally, sanitation has more to do with water and sewage than air, but odors connected the various components thought to govern health and disease well before the acceptance of bacteriology.

Sanitary fairs, i.e., women’s efforts to aid the sick and wounded, reached their height of popularity during the American Civil War. They were a tacit admission that pestilence was an evil equal to combat in leading to the loss of lives.

¹⁰²“The four horsemen” of Death is my label for the major types of infection in the age of traditional cancer. I derived this designation, of course, from *Revelation 6*, which presents the white, red, black, and pale (green?) horses with their riders. The New Testament names only the rider of the pale horse, and his name is Death. The other riders went unnamed, although subsequent interpreters have titled them with the *means* by which the riders caused death—pestilence, war, and famine. It is quite appropriate to name the pale horse’s rider Death, for paleness-inducing anemia of acute or chronic disease often precedes death.

Before the end of the nineteenth century, the possibility of post-operative infections was a major reason for avoidance of surgery.¹⁰⁴ This fear led to procrastination or evasion of surgery because it provoked trepidation in potential cancer surgery patients and inhibited physicians from suggesting such a “radical,” risky therapy as surgery. Post-operative infections were a source of confusion because, although physicians utilized many modes of treatment, there was scant evidence that any one therapy worked consistently. Moreover, it was impossible to predict who would get an infection post-operatively and who would not.¹⁰⁵ In an era when religious beliefs often provided the answer to the question of why one individual suffered and died while another did not, the differentiating factor appeared to those at the time to be a consequence of the individual’s personality and deeds—or, more likely, misdeeds. Even secular surgeons naturalized their superstitions by speaking of “times of disaster” and “blind Nemesis.”¹⁰⁶ Beyond fears and irrationalities, however, the main actors in this theater of surgery, infection, and dread were the four horsemen of Death.

The four horsemen of Death were septicemia, hospital gangrene, erysipelas, and pyemia. They were much more common in hospitalized patients than in patients treated in their own

¹⁰³Guy Williams, *The Age of Miracles: Medicine and Surgery in the Nineteenth Century* (London: Constable and Company Ltd, 1981). 57.

¹⁰⁴The history of infectious diseases is vast, but I would like to emphasize that the identification of microscopic germs as a cause of disease preceded Pasteur, Koch, and others of the nineteenth century by hundreds of years. Girolamo Fracastoro, for example, was an Italian physician who proposed the notion that diseases are spread through microscopic bodies in his seminal 1546 work, *De contagione et contagiosis morbis et curatione* (*On Contagion and the Cure of Contagious Disease*). Even earlier, the great Roman genius of the first century BCE, Marcus Terentius Varro (116 BCE-27 BCE), wrote that invisible particles could enter the body and cause disease. (*On Agriculture* 1, xii) One of many excellent sources on the history of infectious diseases is Fielding H. Garrison, "Fracastorius, Athanasius Kircher and the Germ Theory of Disease," *Science* 31, no. 796 (1910).. For Varro, Fracastoro, and others, please see below on “Etiology—The Cause of Things.”

¹⁰⁵Even in the extreme case of open fractures, where the post-operative infection rate approached ninety percent, it was impossible to predict which one of ten patients would not succumb.

¹⁰⁶Godlee, *Lister*, 205: 134.

residences. As a result, practitioners often called them “hospitalisms.”¹⁰⁷ Each had somewhat different manifestations, clinical courses, and proposed therapies, but cancer surgery patients risked all—as well as a deadly outcome—because they appeared especially likely to follow operations.¹⁰⁸ It is difficult to exaggerate their importance in the decision-making process to undergo or forgo surgery in the era of traditional cancer. Thus, I will briefly describe them individually to try to convey a sense of the real risks and horrors that governed the decision for or against cancer surgery before the end of the nineteenth century.

Septicemia—Hot Poisoned Blood

Septicemia, the most consistently deadly of these potentially fatal infections, was (and is) an extremely dangerous condition that appeared to result from a “corruption” of the blood.¹⁰⁹ Sharp-eyed observers called it “blood poisoning,” because its characteristic sudden onset of high fevers, rigors, and, ultimately, circulatory collapse and shock mimicked poisoning.¹¹⁰ The fact that sepsis even occurred in some patients who developed laudable pus made the risk of septicemia and the predictability of a post-operative course all the more uncertain.¹¹¹ Physicians and surgeons in the era of traditional cancer diagnosed a septic patient with ease, for its hallmarks were widely appreciated although both cause and cure remained unknown.

¹⁰⁷Sir James Y. Simpson published a series of articles on “Hospitalisms” in 1871. See Simpson, *The Works of Sir James Y. Simpson, Bart.*, II.

¹⁰⁸Godlee, *Lister*, 205: 125.

¹⁰⁹For example, autopsy records from the Woman’s Hospital in New York City revealed that the most common cause of death in J. Marion Sims’s cancer surgery patients was septicemia. (Memorial Hospital Archives, Record Group 500 Hayes Martin Collection, Box 2, folder 35 “Cancer Therapy, Early Treatment, 1847-1930,” page 30)

¹¹⁰Godlee, *Lister*, 205: 126.

¹¹¹Sepsis and septicemia, despite their equivalence in common parlance, are not identical. Septicemia is the presence of sepsis-producing agents (usually toxin-producing bacteria) in the bloodstream. Sepsis is the toxic condition itself.

Despite this lack of knowledge (or, perhaps, because of it), practitioners offered many therapies to thwart the ravages of sepsis. These included cold compresses, cool or ice baths, fanned air, and a host of potions and pills. Unfortunately, physicians conflated symptoms and disease, for they treated the symptom *as* the disease. Meanwhile, the underlying infection (cause) continued unabated to its natural conclusion. The unpredictability and seemingly capricious appearance of septicemia in post-operative cancer patients helped drive them and their physicians to consider surgery as nothing more than a treatment of last resort.¹¹²

Hospital Gangrene—Plague of Place

Hospital gangrene, the most mysterious of the Four Horsemen, appeared to be peculiar to public institutions for the care of the sick. In essence, it represented the death and decay of tissue with infection in a hospitalized patient—especially after surgery.¹¹³ Its enigmatic nature followed from the unpredictability of its appearance in a given patient, the strange clinical course from bed sore to death, and its apparent propensity to attack those in a hospital environment.

It may have been the greatest affliction of hospitalized post-operative patients in the age of traditional cancer, for, based upon my review of case reports from the early to mid-nineteenth

¹¹²Physicians have since catalogued a host of infectious agents that cause septicemia. Staphylococcus with its toxins (and the body's excessively exuberant immune reaction to those toxins) is a great offender, but it is only one of many. ("MRSA," which stands for Methicillin-Resistant Staphylococcus aureus, is a growing offender.) If recognized early, the clinician attempts to define the offending agent with samples taken from potential entry sites of the pathogen into the body (skin, lung, bladder, gastrointestinal tract, blood), "cultures" these samples to discover which organism(s) proliferate in a growth-stimulating environment (e.g., agar gel), and then treats the hospitalized patient with intravenous antibiotics shown to kill the disease-producing agent. Nonetheless, despite antibiotics and a host of supportive therapies, the probability of death remains unacceptably high, exceeding fifty percent in severely compromised patients.

¹¹³The term "hospital gangrene" is today rarely used outside its historical medical context. Modern equivalents might be bed sores, decubitus ulcers, and pressure sores. These more recent expressions implicate the origin of hospital gangrene in the skin over the bony prominences of patients immobilized by disability and disease. Attendants frequently turned well-cared-for patients in bed to avoid these pressure-related sores. (General Grant received such care after falling on his hip outside his New York City home on December 24, 1883. He was bedridden for many weeks thereafter.) Patients in charity institutions, however, did not often receive such intensive care. Before the advent of antisepsis in the late nineteenth century and antibiotics in the twentieth, ulcers that developed over these pressure points and became infected led, ultimately, to sepsis.

century, the incidence of hospital gangrene appears to have exceeded that of the other three post-operative scourges.¹¹⁴

No one could be sure why such tissue decay was more common in the institutional setting, but neither could anyone dispute the fact.¹¹⁵ In mid-century, clinicians believed that hospital gangrene followed dirt, pollution, and overcrowding—ideas all consistent with the miasmatic theory of disease.¹¹⁶ The smell of hospital gangrene was apparent from a great distance, for ambling along the streets of Paris in mid-century, wrote W. W. Keen, “one could recognize at a distance a surgical hospital owing to the stench of the human putridity it contained.”¹¹⁷ Even the youthful Joseph Lister, then well on his path toward becoming known as the “Father of Antisepsis” before the end of the century, adhered to the tenets of miasma as late as 1868. His experiments on wound infections at the time show that he believed that hospital gangrene “was brought about somehow or other by the impure state of the atmosphere produced by the overcrowding of patients with decomposing sores.”¹¹⁸

The then-perceived causes of hospital gangrene led to a variety of ultimately insufficient treatments. Hospital attendants, when time permitted, cleansed dirty and polluted surfaces with

¹¹⁴The notoriety of hospital gangrene may have led physicians to report it more often than post-operative infections of lesser consequence, but the spotlight thrown on hospital gangrene by Joseph Lister, James Y. Simpson, and others at least supports its importance, if not its statistical dominance.

¹¹⁵Godlee, *Lister*, 205: 124.

¹¹⁶*Ibid.*, 128.

¹¹⁷Keen, “Before Lister,” 848-9.

¹¹⁸Godlee, *Lister*, 205: 127.

This “impure state” was as much a comment on the low social and economic status of the hospitalized patient in the world of traditional cancer as it was on a disease-generating atmosphere.

Three years after this comment, as we shall see, Lister no longer held this belief. In the interim, he learned that it was not the air per se that caused infection, but minute particles within it. He called them “floating ferments.” Joseph Baron Lister, *The Collected Papers of Joseph, Baron Lister*, 2 vols., vol. 1, The Classics of Medicine Library (Oxford: Clarendon Press, 1909; repr., 1979). 205.

soap and water.¹¹⁹ Charitable institutions for the sick remedied overcrowding with patient isolation, ventilation, and fresh air—where space permitted.¹²⁰ Those who cared for the sick and poor in the institutional setting tempered the putrid smell of hospital gangrene with a variety of agreeable agents. Alcohol and benzoin were most common, but myrrh, glycerin, and even honey appear on hospital treatment lists from the time.¹²¹

The lack of time and space in the non-private setting distinguished the hospital from the private home. Nevertheless, those at the time believed that it was the hospital itself, not the nosocomial horrors associated with economic and social disadvantages, that caused gangrene in post-operative cancer patients.

Unfortunately, improving the cleanliness of the patient's surroundings or the nose's sensibility to the foul stench did not improve the patient's condition. The persistence and spread of hospital gangrene in a given patient led ineluctably to personal tragedy. Physicians and their patients knew this well, adding yet another reason to avoid surgery as a treatment for cancer.

Erysipelas—The Red Disaster

Erysipelas was a common but less fatal disease than hospital gangrene or septicemia. As late as 1872, Martin Beck, Lister's cousin, recorded twenty-one cases of erysipelas among the patients in the eighty surgical beds (26%) at the University College Hospital in London. Four died of the disease (19%).¹²² Thus, more than one in four developed erysipelas, but *only* about one in five died of it. Nonetheless, dread of the disease was widespread. Decades earlier, in 1820, when the renowned and experienced surgeon Astley Cooper removed a small wen from

¹¹⁹Godlee, *Lister*, 205: 124.

¹²⁰*Ibid.*, 330.

¹²¹*Ibid.*, 157-8.

¹²²*Ibid.*, 132.

the head of the newly-crowned King George IV, it was said that his hands trembled for fear that the monarch would die from erysipelas.¹²³

Erysipelas, etymologically, means “red skin.” For centuries, healers called it St. Anthony’s fire, for they thought the intercession of the Saint curative against this and other diseases deemed infectious.¹²⁴ Erysipelas usually began as a small, innocent-appearing, red patch on the skin of the head or leg. If it progressed, as it often did, it became an “angry blush.”¹²⁵ In the early-to-mid nineteenth century, physicians diagnosed the disease by its characteristic red, indurated (hardened “soft” tissue), painful, hot-to-the-touch skin.

Today, clinicians believe that erysipelas is generated by a break in the skin that circumvents the cutaneous barrier and allows bacteria to proliferate beneath it. The causative agent remained unknown, however, until Pasteur in 1880 discovered what microbiologists later called *Streptococcus*.¹²⁶ Physicians then and now realized that the redness and other signs of the disease could spread like wildfire. If the signs worsened, the patient became at risk for tissue necrosis and gangrene, often followed by systemic infection that ended in septicemia and death.

The weaker and more debilitated the patient, the greater the probability that the small red patch would enlarge, become gangrenous, and lead to death. Traditional cancer patients, especially in the later stages of their disease, were usually weak and debilitated. If such patients underwent surgery as a last-gasp measure, their debilitation increased and their resistance to the

¹²³Keen, "Progress of Surgery," 347.

¹²⁴Some believe that the term “St. Anthony’s fire” should be properly restricted to ergotism rather than erysipelas, but it is likely that the observers appended the name of the saint of infectious and communicable diseases to many diseases. See M. W. Carlton and D. B. Kunkel, "St. Anthony's fire: an eponym for ergotism, not erysipelas," *American family physician* 52, no. 1 (1995).

¹²⁵Godlee, *Lister*, 205: 125.

¹²⁶The bacteria are usually Group A *Streptococci*. GAS can also cause “Strep” throat, scarlet fever, pneumonia, and a host of other infectious diseases.

spread of erysipelas weakened further.¹²⁷ Practitioners knew this and sought to avoid adding erysipelas to the list of their cancer patients' post-operative, end-of-life woes.

Pyemia—Staph of Death

In the age of traditional cancer, clinicians considered pyemia and septicemia, now closely related, to be separate entities. Before the rise of bacteriology, physicians thought that pyemia was a manifestation of pus-corpuscles in the blood rather than the organisms that produced the toxins, hence the literal translation of its name “py-emia.”¹²⁸

Histologically, pyemia began after a wound (surgical or otherwise) set up a nidus for infection. In essence, this initiation of disease was similar to that of the other three major hospitalisms. However, if this local infection involved veins, of which there are rich networks underneath the skin, pus-filled blood clots could develop. If the septic clot dislodged from its valvular mooring, the venous circulation carried it to the heart and, from there, wherever the heart pumped—brain, lung, liver, kidneys, etc. Once wedged into a new location, the septic clot burgeoned into an abscess similar to the growth of a metastatic cancer.¹²⁹

Clinically, the disorder began with the development of pus from a local insult induced by an operation, obstetrical delivery, or trauma.¹³⁰ Shaking chills and profuse diaphoresis

¹²⁷Compromise of the immune system plays a major role in this increased “debilitation,” but scientists knew little of immunity until the beginning of the modern cancer period in the late nineteenth century. For example, one of the earliest pioneers in immunology, Paul Ehrlich, began his seminal investigations into the nature of the antigen-antibody complex only in 1889.

¹²⁸Greek: ‘Py-’, pus and ‘-emia’, blood. Staphylococcus is the predominant cause of pyemia. “Staph,” a popular shortening of Staphylococcus, is a common resident on normal and abnormal skin. Anything that broke the protective barrier of the skin could lead to local and then systemic infection. In retrospect, Staphylococcal species were a major cause of hospital diseases in the era of traditional cancer. Nevertheless, Friedrich Julius Rosenbach did not describe the yellow (Staph. aureus) and white (Staph. alba, now Staph. epidermidis) colony-forming bacteria until 1884.

¹²⁹Even today, clinicians and pathologists sometimes refer to pyemia as a “metastatic infection.”

¹³⁰I specifically mention parturition because Ignaz Semmelweis, one of the progenitors of germ theory, discovered that physicians spread a form of pyemia, called childbed fever, from one woman to another.

(sweating) heralded the acute onset of pyemia. Body temperature during the rigors could exceed 104° Fahrenheit.¹³¹ Thereafter, the chills disappeared until the next day or the day after. In between fever spikes the patient exhibited the cardinal signs of systemic infection—loss of appetite, nausea, vomiting, and rapid weight loss.¹³² Sir Rickman Godlee, a British surgeon best known during the early twentieth century (and nephew to Lord Lister), wrote that “Recovery is rare after the second shiver.”¹³³ The site of the new abscess location often determined the course of the disease. Metastatic infections of the brain caused headaches, fever, and encephalitis. Lung involvement led to difficulty breathing and the hemoptysis (coughing blood). Infection in the liver initiated jaundice (yellow eyes, skin, and dark urine) and pain over the right upper quadrant of the abdomen. Occasionally, milder forms of pyemia could persist for months, but in the age of traditional cancer, death often followed swiftly after evidence of infective metastases.

In 1874, William Cadge of Norwich, England, noted in his address to the British Medical Association that pyemia was, like the other Four Horsemen of death, endemic to hospitals. For pyemia, “if it does not find its birth-place, does find its natural home and resting-place in hospitals; and although a hospital may not be the mother of pyaemia, it is its nurse.”¹³⁴ The nurse may literally have been the agent who transferred the seeds of pyemia from one patient to another, for cleanliness was far from godliness in most institutional settings at this time. Cancer patients harbored an additional risk for pyemia because of the proclivity of their disease to cause

¹³¹Forty degrees Celsius.

¹³²In the first edition of his classic textbook of medicine, William Osler provided a compelling description of pyemia during the age of bacteriology—but before antibiotics. William Osler, *The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine*, The Classics of Medicine Library (New York: D. Appleton and Company, 1892; repr., 1978). 117..

¹³³Godlee, *Lister*, 205: 126.

¹³⁴William Cadge, “The Address in Surgery, Delivered before the Annual Meeting of the British Medical Association at Norwich, August, 1874,” *The Lancet* 104, no. 2659 (1874): 238. Quoted by Godlee, *Lister*, 205: 136.

open sores with ulcerations. Post-surgical cancer patients were at even greater risk. Not only did they sustain open wounds in the normal course of their operations, but their surgeons may have unwittingly filled those wounds with the very germs that led to their patients' demise. In light of the debilitation suffered by most cancer patients in general, pyemia was an ever-present threat to their lives. Cancer surgery only increased their liability and the hospital was a runway to death.

The Problem with Traditional Cancer Treatments, including Surgery

The treatment of traditional cancer with medicines and surgery lacked accountability and credibility. In essence and in retrospect, it was not "scientific." What do I mean by that? Scientific medicine implies a degree of systematization, conceptualization built upon cumulative knowledge, experimentation in the broadest sense, and an ongoing analysis of generated data. The scientific method demands a systematic process from hypothesis to experimentation to collection of results to analysis and rejection, confirmation, or reformulation of the hypothesis. In the main, such process and analysis were absent in medicine and surgery before the last decades of the nineteenth century.

To no small extent, knowledge of 'what' without an understanding of 'how' and (within the limits of science and philosophy) 'why' was an integral component of the pre-scientific era, when didacticism and empiricism ruled medical education and the practice of medicine.

Physicians in the traditional era depended upon received wisdom and punctuated observations during episodic epiphanies. Those who would be surgeons made diagnoses of cancer on growths found and described by sight and palpation (touch). Practitioners paid little attention to the characteristics of a tumor other than its location and consistency. Terms like encephaloid, scirrhus, encephaloid, cerebriform, colloid, fungus hæmatodes, and sarcoma led

the list of cancer names.¹³⁵ Radically different cancers such as those of the breast and stomach could receive the same epithet—scirrhus—for both displayed a hard consistency to the touch of the pathologist’s dissecting instrument. Clinicians labeled disparate cancers in the uterus or breast sarcomatous or even encephaloid, for they were of a fleshy nature. Practitioners thus described tumors through their own senses and rarely published information that compared the same disease in different patients. Individual case studies predominated in the medical literature. Any link between microscopic tumor analysis, operative procedure, and outcome was exceptional until late into the nineteenth century. Traditional cancer treatment in general, and surgery in particular, was an individualized, regionalized, scattershot affair.

Transitions

As the last quarter of the nineteenth century began, the successful treatment of cancer was rare indeed. Muddled notions of cancer causation, medical therapies of proprietary but unproven value, and surgery laden with risks that far outweighed benefits, all added to the woe of the cancer patient. Expressions of hopelessness and depression peppered the writings of cancer patients and their physicians. Cancer quacks preyed on the human spirit. Nevertheless, powerful winds of change began to blow from East to West, as fundamental European revolutions spread to an America in its medical infancy.

Progress is a consequence that builds on itself. Like a snowball rolling down a wet slope, advances in fields like science, technology, and medicine rapidly accrete new ideas and practices to enlarge the sphere of knowledge and create yet newer concepts and actions. Yet, the original nidus is still recognizable as a descendant of the past. Given their strange and enticing differences, those at the time often see these developments as new—but not always. Resistance

¹³⁵As noted in Chapter 1, these terms in their translated-from-Latin-to-English forms would be, respectively, hard, brain-textured (encephaloid, cerebriform), gelatinous, bloody, and fleshy.

to change is as fundamental to human nature as is change itself—be it in science, medicine, or other endeavors of human activity.

Such was the beginning of the rise of modern cancer surgery in the late nineteenth century. It started with acknowledgment of the problems and deficiencies of traditional cancer treatments (especially surgery) and then built upon seeds of ideas first presented decades—even centuries—earlier to address those failings. It reaped the fruits gleaned from other disciplines and applied them to its own. And, in the late nineteenth century, began to coalesce and synthesize those developments to become a most powerful force for the treatment of cancer.

First Inklings—Types and Origins of Cancer

Despite the sameness of the surgical treatment of traditional cancer for much of the millennium prior to the late nineteenth century, it is critical to note that ideas that would water the roots of change could be found in the theories and practices of a few European physicians long before then.

Religious strife, highlighted by the Italian Inquisition, economic warfare between Italian City-States, and a malaise of disease evident in Mannerist painting, ravaged Italy during the sixteenth and seventeenth centuries. In this hostile climate, Marcus Aurelius Severinus (1580-1656), a surgeon who lived and worked under the ever-present threat of excommunication and death from the Italian Inquisition,¹³⁶ constructed what was probably the first workable differentiation between benign and malignant tumors, in his tome *De Recondita Abscessum Natura* (*The Obscure Nature of Tumors*, 1632).¹³⁷ During an age when physicians conflated

¹³⁶Inquisitors did indeed exile Severinus from Naples, but he returned at the request of the townspeople to continue his medical work.
<http://worldwideschool.org/library/books/sci/history/AHistoryofScienceVolumeII/chap27.html>, accessed 2/28/07.

¹³⁷Josiah C. Trent, "Five Letters of Marcus Aurelius Severinus To 'The Very Honourable English Physician, John Houghton'," *Bulletin of the History of Medicine* 15(1944); C. Espinel, "The portrait of breast cancer and Raphael's La Fornarina," *The Lancet* 360, no. 9350 (2002).

inflammatory lesions like abscesses with malignancies like terminal breast cancer under the rubric of “tumors,” it is noteworthy that an individual under enormous personal duress could systematize and distinguish such growths as he found in his clinical practice.

More than a century later, at the height of the *Ancien Régime* in mid-eighteenth-century France, a Parisian surgeon, Henry Francois Le Dran (1685-1770), conceived the remarkable proposition that cancer was a localized rather than a constitutional disease. He believed that the initial tumor spread via the vessels of the body—especially the lymphatics—to involve other areas. In the case of breast cancer, this idea led Le Dran and his somewhat older colleague, Jean Louis Petit (1674-1750), to advocate the excision of regional lymph nodes—a century and a half before Halsted suggested a more extensive version of the same—in order to forestall the spread of cancer. Le Dran’s notion of original localization directly contradicted Galen’s theory of constitutional humors and gave pause to those who would rethink the nature of cancer a century later.

Transformations—Better Solutions based on a New Methodology

By the middle of the nineteenth century, investigators and practitioners from established and emerging disciplines on both sides of the Atlantic world built upon the work of those before them to transform the theory and practice of cancer medicine. The impetus was clear. As the microscope allowed a more accurate diagnosis of cancer, and as early statistical analyses displaced anecdotal and experiential collections of patients’ histories, physicians and surgeons learned that no treatment at all was often better than any available therapy. Some physicians, like the distinguished William Osler (1849-1919), who is often called “the Father of Modern Medicine,” embraced therapeutic nihilism, thus putting into practice the notion that nothing

could be better than something in the treatment of cancer.¹³⁸ Samuel David Gross (1805-1884), like other surgeons at the vanguard of their profession, earlier propounded the idea that cancer surgery, in particular, was a high-risk, low-reward gamble.¹³⁹ Nevertheless, larger movements in the context of culture and society were beginning to influence medicine in general and cancer medicine in particular.

Surgery would not have come to dominate the treatment of cancer over the course of the nineteenth century without the acceptance and growth of the application of science to medicine. “Science” is an interesting word of many meanings. It descends etymologically from the Latin “scientia”—knowledge. In common parlance, science was and is a process and its conclusions are said to be scientific. Today, the term science is loaded with positive connotations. In the mid-nineteenth century, however, its import was more ambiguous, like a ship emerging from a fog bank, for science was a threat to the established methodologies of didacticism and empiricism. By its very nature, the process of science carried with it a revolution in education, theory, and practice. Before the last quarter of the nineteenth century, no one could know which of these approaches—didacticism, empiricism, science—would triumph as the underpinning of medicine. Then, over the next decades in the West, the new scientific process that reduced the morbidity and mortality from cancer trumped its older rivals.

It is difficult to pinpoint a beginning for medical science. Was it the rationalizations and observations of Hippocrates and his followers? Could it have been the descriptions and dissections of Galen and his devotees? Or was it earlier than both, perhaps when the first mortal,

¹³⁸William Osler, *The Evolution of Modern Medicine: A Series of Lectures Delivered at Yale University on the Silliman Foundation in April, 1913*, The Classics of Medicine Library (New Haven: Yale University Press, 1921; repr., 1982). 21.

¹³⁹Gross, "On the Results of Surgical Operations in Malignant Diseases."

Prometheus, noted that fire effected consistent and reproducible changes in human flesh? Or should we seek a more subtle beginning? For is it possible to gauge intent versus event, because medical science (like all science) requires conscious control, while happenings may be chance and unrecognized until (re)discovered generations or millennia later as if for the first time. And when did wonder about the natural world become thoughtful and purposeful manipulation of the natural world—or does medical science assume both? For the science of medicine, in its essence, is the appreciation and analysis of wonder leading to knowledge and understanding.

Regardless of origins, the seventeenth century is labeled, in the West, as the age of “Scientific Revolution.” During that century, Astrology gave way to Astronomy and Constellations lost their anthropomorphic identities and became no more than orbiting planets and luminous stars that followed discernible laws. Those laws allowed early astronomers and physicists to make verifiable predictions. In short, observations became systematized. As the violence and devastation of European religious conflagrations of the 17th century gave rise to secularism as the dominant *modus operandi* of society, the scientific method of thesis-experiment-results-conclusion-altered thesis began to replace the venerable but now-inadequate methods of didacticism and empiricism. In their wake, the treatments of disease also changed.

Medicine was neither the first field of study to favor the scientific method nor the discipline that most rapidly adopted its principles, once accepted. Andreas Vesalius working in Padua in the sixteenth century and William Harvey in London during the seventeenth applied a scientific methodology to their investigations of human anatomy and circulation, respectively.¹⁴⁰

¹⁴⁰I must note that decades before Harvey’s *Exercitatio anatomica de Motu Cordis et Sanguinis in Animalibus* (1628), Michael Servetus, the great Spanish savant, wrote a reasonably accurate description of the closed-loop cardiopulmonary circulation. Unfortunately, his work was unknown well into the eighteenth century (Latin publication, 1790; English, 1953), for he was burned at the stake for heresy in 1553 and all but three copies of his major (non-medical) work, *Christianismi Restitutio*, were destroyed shortly thereafter. See John Farquhar Fulton, ed. *Selected Readings in the History of Physiology*, Special ed., vol. 210, The Classics of Medicine Library (Springfield, IL: Charles C. Thomas, 1930; reprint, 2006), Chapter 2.

Nonetheless, most medical instruction and practice continued to valorize didactic history, with its timeworn texts and personal anecdotes of therapeutic successes over scientific approaches, until deep into the nineteenth century. In addition, clinicians used microscopy sparingly for the investigation of cancer, and, even then, often questioned its results. Surgeons continued to follow the ancient prescriptions of Galen and Medieval physicians for venesection and other techniques despite the continued presence of intractable pain and deadly infections. As a result, the treatment of cancer changed little conceptually until after the revolutionary open-mindedness of secularism that began, for the most part, in the late eighteenth century. This turn from a faith-based acceptance of the world as it is to a pro-active investigation of nature for the benefit of mankind established the foundation for a scientific approach to surgery in general and cancer surgery in particular. John Hunter was a prime mover in laying that scientific and medical groundwork.

THE BEGINNINGS OF MODERN CANCER SURGERY

John Hunter – Natural Genius and Genius of Nature

Historians and physicians justifiably honor the eighteenth-century Englishman John Hunter (1728-1793) as the “Father of Scientific Surgery”¹⁴¹ and “Surgery’s First Scientist.”¹⁴² Even beyond surgery, he was a true genius, for genius begins with curiosity, fascination, and awe; embraces disrespect for tradition; sates on reinforcement from Nature; and blossoms in transferable wisdom. Hunter applied these traits to his studies of nature and medicine, for curiosity was his motive force, science his method, and an understanding of nature his goal.¹⁴³

¹⁴¹Shimkin, *Contrary to Nature*: 86. Dr. Sherwin Nuland noted that the Royal College of Surgeons placed a plaque near the tomb of John Hunter in Westminster Abbey that proclaimed him “the founder of scientific surgery.” Nuland, *Doctors*: 198.

¹⁴²See <http://www.hunteriansociety.org.uk> and *Doctors*: 175.

¹⁴³Although, it seems, his wit tilted more towards intelligence than humor. *Ibid.*, 179.

Like those who transcended the conventions of their age to create new ways of seeing and doing, Hunter refused to accept what others took for granted. He was, indeed, a renegade, for he consciously went against the tenets of his time to forge new links between nature, science, and medicine.¹⁴⁴ In addition, he was considered uncouth by his contemporaries and lacked the formal education of his day (he never attended medical school).¹⁴⁵ These anti-traditional leanings gave colleagues and competitors still other excuses to cast a wary eye on the man and his teachings. But Hunter's role as outsider served him well, for it allowed him to pursue his own interests without deference to others.

Hunter's interests lay in Nature, for the natural world was his playground. He collected, classified, and correlated biological specimens as children do with pebbles on a beach. Through the knowledge he gleaned from these specimens, Hunter developed a profound interest in comparative animal anatomy and human pathological anatomy. He then applied that knowledge and meticulous method to human surgery. A contemporary described Hunter at his dissection table as "standing for hours, motionless as a statue, except that, with a pair of forceps in each hand, he was picking asunder the connecting fibers of some structure he was studying."¹⁴⁶

By the time of his death, in 1793, Hunter had amassed a collection of almost fifteen thousand animal specimens. Dr. John Ashurst, who compiled one of the most distinguished and extensive surgical texts of the late nineteenth century, eulogized Hunter when he wrote that he "was, unquestionably, the most distinguished anatomist and surgical pathologist of the

¹⁴⁴The etymology of 'renegade,' from the Spanish, derives from one who negates (again) or denies accepted wisdom.

¹⁴⁵Sigerist, *The Great Doctors*: 207.

¹⁴⁶Williams, *The Age of Miracles*: 8.

eighteenth century.”¹⁴⁷ It comes as no surprise that Hunter came to serve King and students under the title of “Surgeon Extraordinary.”¹⁴⁸

Hunter’s interest in nature and its processes, befitting his mien, began when he was a child. His brother William, ten years his senior, was a polished and articulate anatomist who became physician to Queen Charlotte in 1764. How much of an influence William had on John may never be fully known, but, some years after little John marveled at the colors of leaves and the antics of ants, he joined his elder brother in the Dissecting Room to become a superb anatomist in his own right.¹⁴⁹ What John gained from William and their dissections was invaluable, for John applied his knowledge of gross anatomy and pathology directly to surgery. Certainly others had explored the human corpus before Hunter, but he did it better because he insisted on proof through experimentation.

Thus, John Hunter was a medical scientist, for while others offered abstract theories and expostulations to support their surgical undertakings, he demanded detached objectivity through investigation. A famous exchange between Hunter and his most famous student, Edward Jenner (who was later credited with the discovery of the smallpox vaccine and, by extension, the field of immunology), illuminates this critical difference between Hunter and his contemporaries. When Jenner, asked Hunter a question about hedgehogs in 1775, Hunter famously replied “Why do you ask me a question by the way of solving it? I think your solution is just; but why think? Why not try the experiment? Repeat all the experiments upon a hedgehog as soon as you receive this,

¹⁴⁷Ashhurst, *Encyclopedia*, 843.

¹⁴⁸King George III appointed Hunter “Surgeon Extraordinary” in the *Annus mirabilis* of 1776. Some of John Hunter’s other accumulated titles include “Surgeon-General of the Army,” “Inspector-General of Regimental Hospitals,” and, after the death of Sir Percival Pott in 1788, “First Surgeon of Great Britain.”

¹⁴⁹Nuland, *Doctors*: 175.

and they will give you the solution.”¹⁵⁰ Experimentation, not rationalization or random observation, was Hunter’s mantra. Hunter was a thinker ahead of his time in an Age of Enlightenment and Reason.

John Hunter believed in the interdisciplinary nature of science as well as the science of nature. In the realm of medicine, his studies of anatomy, pathology, and surgery extended his foundational interest into a single consistency—the nature of Man. “Nothing in nature stands alone,” wrote Hunter, “but that every art and science has a relation to some other art of science, and that it requires a knowledge of these others...to become perfect.”¹⁵¹ To investigate the structure of the human body was to open a window onto disease that led seamlessly, through experimentation and careful analysis of its findings, to its amelioration. Surgery became, more often than not, that treatment which led to improvement. In cancer medicine, as in his other scientific pursuits, Hunter’s interdisciplinary inquiries—objective, dispassionate, and detached—confirmed the Enlightenment belief that the whole was greater than the sum of its parts.

John Hunter – Cancer as Inflammation

Perhaps because cancer defied simplicity and easy classification, Hunter evinced a special interest in it. He proved himself, in retrospect, a transitional figure in the history of cancer, for while his methods were revolutionary, his conclusions were more conventional. He insisted on a scientific approach to the study of human disease but held that contagion motivated its spread.¹⁵² He believed that cancer began locally, but eschewed the use of the microscope (which could have lent a scientific underpinning to his belief in localism) as a “tool of dangerous

¹⁵⁰Letter from John Hunter to Edward Jenner, August 2, 1775.

¹⁵¹Sigerist, *The Great Doctors*: 188.

¹⁵²Dobson, "Hunter's Views," 177.

deception.”¹⁵³ Thus, his estimable status in the history of cancer derives from the method of his approach to the disease, rather than his acceptance of new cancer technologies, interpretations, or conclusions. Nevertheless, Hunter’s idea that cancer could be something other than constitutional and non-surgical opened the way to new thoughts and meanings about the nature of the disease.

Hunter classified diseases, which he called “unnatural dispositions,” into three types based upon their duration. One group encompassed afflictions that resolved rapidly, like the common cold. A second included conditions that developed over time, like callused hands after rough handiwork. Third were diseases of a “more lasting” nature.¹⁵⁴ Cancer resided in Hunter’s last category, for this group included pathologies for which, as he noted, “we have no specific nor even a palliative.”¹⁵⁵

Hunter expanded the knowledge of cancer by showing that more bodily organs could be involved with cancer than previously thought. Whereas most of his contemporaries listed the female breast and uterus along with the lips and face as the major cancer sites, Hunter’s pathological dissections allowed him to see sites of origin—usually beyond the scope of his fellows—that lay hidden within the corpus. These included cancer of the pylorus of the stomach and the pancreas.¹⁵⁶ Time would prove the importance of Hunter’s scientific, dissection-based insights, for these deep malignancies did not achieve their proper place among the array of human cancers until the nineteenth and twentieth centuries.

¹⁵³Nuland, *Doctors*: 352.

¹⁵⁴Dobson, "Hunter's Views," 176.

¹⁵⁵*Ibid.*

¹⁵⁶*Ibid.*

Beyond nosology and organ involvement, cancer for John Hunter was a condition of inflammation. He joined the traditional physicians of his time by recognizing imbalances as causes, for inflammation is characterized by hot over cold and wet over dry.¹⁵⁷ Hunter's career spanned the era from an emphasis on Morgagni's organ-based pathology of *De Sedibus* (1761) to the beginnings of Marie François Xavier Bichat's (1771-1802) emphasis on tissue-based disease. Cells, the basic units of late nineteenth-century medicine, went unheralded in Hunter's world of aberration-filled microscopical images. The modern neoplastic, "cell-reproduction-out-of-control" model, popular in the twentieth century, would have been incomprehensible to an anatomist like Hunter. His frame of reference encompassed organs and tissues rather than cells.¹⁵⁸ Inflammation and cancer were gross diagnoses in Hunter's day. The two have much in common on the macroscopic level—tumor, rubor, calor, dolor—so it is not surprising that Hunter situated cancer within the inflammatory conditions.

Still, Hunter's conception of cancer went beyond mere inflammation when he added that cancer spread by "contamination"—implying an infectious nature. This centrifugal dissemination of tumorous tissue encompassed three forms; viz., sympathy, remote sympathy, and the "communication of its matter to other parts by contamination."¹⁵⁹ In view of the fact that a firm understanding of cancer metastasis lay many years in the future, Hunter's idea of communication via contamination of other organs and tissues was prescient.¹⁶⁰

¹⁵⁷Traditional humoralism paired blood (sanguine temperament) with hot and wet, yellow bile (choleric) with hot and dry, black bile (melancholic) with cold and dry, and phlegm (phlegmatic) with cold and wet. Ancient Greek humoralists considered cancer an excess of black bile—thus, cold and dry.

¹⁵⁸Rudolf Virchow, in the mid-nineteenth century, honed in on cells as the basis of disease rather than the previously paradigmatic organs (Morgagni) or tissues (Bichat). Twentieth-century neoplastic theory is, above all else, a cell-based explanation. Interestingly, Virchow, whose fame rests on the pathologic cell, concentrated on non-cellular and extra-cellular etiologies for the development and proliferation of cancer.

¹⁵⁹Quotation from Dobson, "Hunter's Views," 177.

Nevertheless, the mechanism of cancer dissemination and the cause(s) of cancer were much less clear to Hunter than its inflammation-like expression—and much less likely to lead to viable therapies. Hunter believed that the main causes of cancer were “age, parts and hereditary disposition; perhaps climate also.”¹⁶¹ We might prefer to label Hunter’s causes as associations or predispositions, but from the perspective of treatment, his causes left little to be done. Neither age nor hereditary could be reversed, and climates could be changed only by those limited few endowed with the wherewithal to do so. As far as specific remedies were concerned, Hunter mentioned Plunkitt’s “secret remedy”—arsenic, and, especially, surgery.¹⁶² Surgery was Hunter’s cancer treatment of choice.

Why Surgery? The Logic of Localism with a Hope of Cure

Hunter’s notion of cancer as inflammation aside, his greatest claim to fame in cancer medicine was his belief that tumors began locally. Shunning the systemic constitutionalism of his day, Hunter’s localism was a revolutionary and counter-intuitive departure from accepted medical thought, derived ultimately from his application of the scientific method to medicine and surgery.

Mixing old concepts of cancer spread by contamination with new models of local origin, Hunter’s belief system envisioned a cure for cancer by means of surgery, but if and only if

¹⁶⁰As early as 1773, Bernard Pehrilhe, a Parisian physician, intimated that cancer could be a local process that invaded the lymphatics to become generalized throughout the body. Nonetheless, it was not until 1829, decades after the death of John Hunter, that J.C.A. Recamier (1774-1852), in *Récherches sur le Traîtement du Cancer, par la compression Méthodique simple ou Combinée, et sur l’Histoire Generale de la Meme Maladie* (vol. 2, p 110, lines 3-7), named “metastasis” (etymologically, a “change of position”) and propounded the essentials of the modern concept of cancer metastasis. Recamier was a French gynecologist and obstetrician. See H. S. J. Lee, ed. *Dates in Oncology*, Landmarks in medicine series (Pearl River, NY: The Parthenon Publishing Group Inc., 2000).

¹⁶¹Quotation from Dobson, "Hunter's Views," 177.

¹⁶²Plunkitt’s remedy was a proprietary mishmash of variable ingredients with questionable efficacy. Arsenic, in Hunter’s view, was *too* inflammatory. *Ibid.*, 179.

surgery could completely and irrevocably extirpate the growth.¹⁶³ If cancer began in a specific site rather as merely one focus of many within a generally predisposed body, then surgical eradication of the growth could be curative. This model, however, required radical shifts in the traditional treatment paradigm, for it mandated that late tumor discovery yield to diagnosis at the earliest stage, and that last-ditch surgery must be replaced by immediate surgery. Both diagnostic and therapeutic transformations in traditional cancer medicine required changes in behavior that few patients and physicians at the time could accept, to no small extent because of the inherent risks of surgery.

Although undaunted by the risks attendant upon increased numbers of surgical procedures as the logical consequence of localism, Hunter held fast to the traditional notion of disposition. He hoped for a medicine that would alter the propensity of the tumor to grow and spread, but found none. Certainly, surgery could not change the disposition of the tumor, for surgery was by its very nature a local procedure that did nothing for the body as a whole. Thus, he believed that operative cancer excision could not be the final or ideal treatment.

Nevertheless, Hunter believed that surgery was the best available treatment for cancer and could, at times, be almost as salutary as a hoped-for, non-existent, disposition-changing elixir. “But as we have no such medicine, we are often obliged to remove cancerous parts; which extirpation, however, will often cure as well as we could do by changing the disposition and action.”¹⁶⁴ Thus, surgery became Hunter’s greatest hope for the cure of cancer.

¹⁶³Ibid.

¹⁶⁴Williams, *The Age of Miracles*: 178.

**The Distinction between Abstract Theory and Real-World Practice—Surgery, yes –
but for Whom? What? Where? When? and How?**

To Hunter, theoretical support for the surgical treatment of cancer was compelling, but the decision to operate did not come without practical concerns. Age, disposition, and climate influenced the choice of candidates for surgery as well as the extensiveness of the procedure itself. The physical examination contributed information on the feel of the tumor (palpation) and its location, both of which further informed the judgment for or against surgery. When Hunter added to these considerations the question of *which* surgery should be performed, the simplest of cases could become most complicated. In essence, there were no easy solutions, for neither diagnosis nor treatment was clear or straightforward.

The process of patient selection for cancer surgery was daunting and humbling. First, the clinician needed to assess the overall condition of the patient. If the patient was already severely weakened and debilitated prior to surgery, predictable surgical disaster would surely be followed by the condemnation hurled by the I-told-you-sos of the age of traditional cancer.

Next, the would-be operator must accurately appraise the extent of disease. The physical examination was critical to this diagnostic determination for, to Hunter and others who found the distortions of the eighteenth-century microscope “deceptive,” there were few tools beyond the examiner’s senses. The physician carefully palpated the area of concern to determine whether the tumor was “within proper reach” and ascertained that the overlying skin was moveable.¹⁶⁵ If so, the growth became approachable by surgery and dissectible from its surrounding tissues—both auspicious findings for a potential cure. The potential operator then noted the condition of the lymph glands into which that region of the body drained (e.g., the axilla/armpit in the case of breast tumors). If downstream lymph nodes were enlarged, hard, and/or immovable, it was

¹⁶⁵Quotations from Dobson, "Hunter's Views," 180.

likely that the cancer had spread beyond its site of origin and that its excision was no longer within “proper reach.”¹⁶⁶ Distant even more than local propagation doomed an operative undertaking to failure.

The surgeon had to be neither shy nor timid in this clinical examination, for the patient’s well being and life depended upon it. “We cannot be too nice in our examination, nor often too rough-handed in the operation,” wrote Hunter. “In cases where the original and consequent tumours are circumscribed, and sufficiently moveable, the operation has generally been successful.”¹⁶⁷

Even if Hunter decided on the basis of the clinical examination that the growth warranted surgery, questions remained. How extensive should the surgery be? Too little, and the tumor could recur, an apparent vindication of traditional constitutionalist beliefs. Too much, and the patient might suffer an increased risk of death from intra-operative hemorrhage, post-operative infection, or other vicissitudes of extensive surgery.

Nonetheless, Hunter, in general, opted for more extensive surgery rather than less. Complete removal of the tumor was essential, for failure to eradicate the “whole disease” was unsatisfactory. Inadequate resection and “the sore [surgical incision] either does not heal, or if it does, the cicatrix [scar] breaks out [in cancer] again.”¹⁶⁸ Furthermore, removal of only the sensorial disease was often insufficient, for “after the visible disease is removed, we should minutely examine the sore so as to feel and press every part, and if anything is hard or irregular, remove it.”¹⁶⁹

¹⁶⁶Ibid.

¹⁶⁷Ibid.

¹⁶⁸Ibid.

Hunter's belief in localism, despite his traditionalist, anti-microscopic approach to the extent of disease, thus led him to take a very aggressive stance toward cancer surgery in general and tumor extirpation in particular. In the case of breast cancer, he concluded, "I considered that the bad success arising from amputation of the breast arose from not taking away enough. I was resolved to take away much more than seemed necessary. I removed then at once all that seemed diseased and along with it near an inch thick of fat."¹⁷⁰ Hunter's excision of more than just the palpable and visible elements of breast cancer preceded Halsted's popularization of the "radical" mastectomy by more than a century.¹⁷¹ Both followed the same theory of localism to come to understand that surgery could be mankind's best answer to the problem of cancer.

The Legacy of a Transformative Figure

In the final analysis, John Hunter held fast to many of the beliefs of his day even as his work led him to then-heretical notions of localism and a preference for surgery as the treatment of choice for cancer. His notions of "dispositions," inflammatory causation, spread by contamination, and gross inspection of tumors (to the exclusion of the microscope) were consistent with the tenor of his time. On the other hand, his genius and radicalism lay in revolutionary attacks against ingrained notions of constitutionalism, the postponement of cancer surgery, and technical minimalism.

¹⁶⁹Ibid. Note also that Hunter's tradition-bound distaste for the microscope relegated him to the recognition of residual, palpable, and "visible disease." The microscope allowed a more careful analysis of residual tumor cells, for the microscopist could see not only the absence of cancer cells, but also the presence of normal tissue.

¹⁷⁰Ibid.

¹⁷¹Halsted, of course, radicalized breast cancer surgery by what he removed as well as by how much tissue he removed. My point, however, is that the idea that the operative excision of more than just the palpable tumor was a tenet of cancer surgery long before Halsted.

The concept that the surgeon should remove more tissue than can be seen as grossly visible or microscopic pathology continues to be enshrined to this day in the surgical principle that excised tumor specimens should have "clean margins"—i.e., that the tissue surrounding the cancer should be free of any and all microscopic disease to minimize the risk of local recurrence.

His stalwart quest for scientific investigation led to careful anatomical dissections and analysis. When combined with a penchant for inquiry into the nature of cancer, his findings caused him to embrace localism its logical necessity to take an anti-traditional approach to the treatment of the disease with surgery—despite the known risks.

Many of his students carried his concept of localism into future generations. When the Medical Committee of the Society for Investigating the Nature and Cure of Cancer met in the first years of the nineteenth century to formulate a series of questions on the disease (only a few years after Hunter's death), the seventh of their thirteen queries was "May cancer be regarded at any period, or under any circumstances, merely as a local disease?"¹⁷² Five of the eight members of the committee had trained with John Hunter and propounded his belief in localism.¹⁷³

Thus, John Hunter applied science to medicine and localism to cancer. As a result, he fostered a new direction for investigations into the nature of cancer and elevated the surgical treatment of cancer to a higher plane. Decades after Hunter's passing, Joseph Lister, a surgeon who contributed much to assuaging one of the great risks of the increased use of cancer surgery that Hunter promoted, spoke of his inquisitive predecessor with reverence.¹⁷⁴ In fact, an engraving of Joshua Reynold's masterful portrait of John Hunter—showing the eighteenth-century naturalist/surgeon deep in thought amidst his anatomical specimens—hung in Lister's study.¹⁷⁵ And Lister was averse to letting anyone remove it from its place of honor.¹⁷⁶

¹⁷²Bruce S. Schoenberg, "A Program for the Conquest of Cancer: 1802," *Journal of the History of Medicine and Allied Sciences* 30(1975): 12.

¹⁷³*Ibid.*, 5.

¹⁷⁴Dobson, "Hunter's Views," 599, 600.

¹⁷⁵http://upload.wikimedia.org/wikipedia/commons/d/df/John_Hunter.jpg Accessed 11/3/07.

Transitions to Science

The decades following John Hunter's death in 1793 were filled with countless technological innovations and scientific developments. Although built upon earlier discoveries and developments, the rate of innovation increased.

Following the political, social, and economic upheavals fostered by the American and French Revolutions, the idea that the fruits of human knowledge could wrest a man's destiny from blind fate swept slowly over Europe and America. Industry joined the revolution early on, creating both demand and supply for new inventions. Larger and faster means of production synergized with more rapid means of communication to change everyday lives, profiting its proponents greatly and spurring yet more innovation. Governments enabled new forms of business ownership through joint stock and corporate structures that stoked the fires of industry fueled by state grants and loans from ever-more-numerous banks. Many individuals, especially in urban areas, benefited from a rise in the standard of living in general—better food, clothing, and shelter—and specific transformations in politics (more inclusive, democratic forms of government), economics (greater opportunities in everyday life that allowed individuals to focus on what they did best rather than serving only as producers of all necessities for their families), and society (the emergence of a new order of persons—a middle class—who neither labored in pits nor owned them, but instead managed, administered, and executed their employers' wishes).

Science provided both a methodology and a framework for these transformations, for science offered a means and an end for products and producers. Entrepreneurs in arms and other manufactures adopted the fruits of science quickly, but physicians and surgeons were slow, at first, to apply science to medicine. Only years after chemistry and physics had yielded new

¹⁷⁶Godlee, *Lister*, 205: 600.

forms of energy (steam, followed decades later by electricity) to power industry and striking, fast colors to add zest to life, did men of science and then medicine merge these findings to discover chemicals that offered painlessness and magic bullets to counter physical suffering and infection. Nonetheless, the adoption of a scientific approach to medicine was a powerful force, for once it began to show its power through diagnosis (for example, the microscope, 1820s and later;¹⁷⁷ thermometer, 1867;¹⁷⁸ sphygmomanometer, 1881¹⁷⁹) and treatment (anesthesia, antisepsis) the archaic elements of pre-scientific didacticism and empiricism were swept away.

Scientific medicine was difficult to resist because it came as part of the industrial revolution and because it worked. When physicians, surgeons, patients, and the general public began to appreciate the ability of the new medicine to lengthen and improve the quality of life, pre-scientific and alternative forms of therapy popular in the early-to-mid nineteenth century began to disappear in favor of novel and/or improved treatments—including surgery.

John Hunter was one of the most prominent eighteenth-century natural philosophers to conceptualize and pioneer the application of science to medicine and surgery to cancer. Nevertheless, he could not predict the avalanche of innovation that led to and fostered scientific

¹⁷⁷Although invented in the 1590s, the microscope did not become a conventional instrument of medicine until after the advent of aberration-free lenses in the 1820s-1830s and the acceptance of prognostic histopathology in the United States in the 1880s. See Chapter 6 for details.

¹⁷⁸Sir Thomas Allbutt invented the first medical thermometer used for taking the temperature of a person in 1867. The Ancients probably used heat-measuring devices. Nevertheless, Galileo invented a water-based temperature measuring instrument in 1593 and the German Daniel Gabriel Fahrenheit (1686-1736) the first mercury-based precursor of the modern thermometer in 1714. Anders Celsius (1701-1744), a Swede, suggested the 0-100° scale used for the freezing and boiling points, respectively, of water in 1742. (The term “Celsius” was adopted by an international conference on weights and measures only in 1948.) Lord William Thomson Kelvin expanded Celsius’s temperature scale to extend to absolute zero (-273° Celsius) in 1848. See <http://inventors.about.com/library/inventors/blthermometer.htm> accessed November 23, 2007.

¹⁷⁹Samuel Siegfried Karl Ritter von Basch invented a water-bag-filled version of the modern sphygmomanometer in 1881. Certainly many instruments for measuring blood pressure preceded (and followed) von Basch’s device, but his was one of the first non-invasive methods to do so. Not surprisingly, the sphygmomanometer was slow to gain wide acceptance “many physicians of the time being skeptical of new technology, claiming that it sought to replace traditional ideas of diagnosis.” Quotation from http://www.medphys.ucl.ac.uk/teaching/undergrad/projects/2003/group_03/history.html accessed November 23, 2007.

medicine, for in his time science was not as integral to society as it would become in the nineteenth century. Nor was surgery as safe as it would be. Certainly the use of surgery for the treatment of cancer in John Hunter's time was problematic and could never be widely adapted—no matter how compelling on a theoretical level—because it was too painful and its results too unpredictable and fraught with danger. Over the decades that followed his death, however, the application of science to medicine induced transformations that eased both the pain and the suffering attendant upon cancer surgery. As such, these changes illuminate the dynamic influence of society on science as well as science on society.

The Birth of Modern Cancer Medicine

Society and Science

They all believed that ideas are not “out there” waiting to be discovered, but are tools—like forks and knives and microchips—that people devised to cope with the world in which they find themselves. They believed that ideas are produced not by individuals, but by groups of individuals—that ideas are social. They believed that ideas do not develop according to some inner logic of their own, but are entirely dependent, like germs, on their human carriers and the environment. And they believed that since ideas are provisional responses to particular and unreproducible circumstances, their survival depends not on their immutability but on their adaptability.

—Louis Menand, *The Metaphysical Club*¹⁸⁰

Louis Menand's brilliant encapsulation of the thinking of some of the titans of nineteenth-century American intellectualism (Oliver Wendell Holmes, Jr.; William James; Charles Sanders Peirce, and John Dewey) is a fitting introduction to a discussion of the influence of society on the development of cancer medicine in the last decades of the nineteenth century, for it reveals the interconnectedness of people, environments, and ideas. Although notions of progress, advance, and achievement in medicine are often portrayed as the work of individuals (“pioneers,” “giants,” “trailblazers”), nothing could be further from the truth. Isaac Newton (1643-1727) was correct to note that “If I have seen a little further it is by standing on the

¹⁸⁰Louis Menand, *The Metaphysical Club* (New York: Farrar, Straus and Giroux, 2001; repr., 2002). xi-xii.

shoulders of Giants,” but he was only half right, for those Giants must be placed *in situ*—i.e., in the context of their time and place.¹⁸¹ Rare is the honest inventor whose work is truly *sui generis*.

Transformations in Thought

Modern advances in science alter, and often destroy, traditional ways only when the philosophical assumptions underlying new scientific theories are accepted by society.
—Werner Heisenberg, *Physics and Philosophy* (1958)¹⁸²

The nineteenth century in America witnessed some of the most epochal intellectual transformations in the history of mankind. The idea that man and his environment were fixed and unchanging became an interrelationship of constant dynamism and alterability. Collective ideologies gave way to individualisms, founding institutionalism in its wake. Predominant pessimism and resignation toward life and living became guarded optimism as Americans of different walks of life had more longevity and something more to live for. Each of these radical notions tempered, modified, transfigured, and/or revolutionized the approach to health and disease that had dominated thinking for centuries. A focus on transformative ideas presages and explains change in the treatment of cancer.

Secularization—From Fixity to Change

“Transformation” becomes a key word in this period....Taking on meaning in the new worlds of physics and modern biology....Transformation seemed to be what the new culture was all about.

—Warren Susman, *Culture as History*¹⁸³

¹⁸¹Newton’s famous phrase, which was actually “*Pigmaei gigantum humeris impositi plusquam ipsi gigantes vident*,” was written by him to Robert Boyle in a letter dated February 5, 1676. The remark is actually a working of a much older metaphor dated to the twelfth century. See http://en.wikipedia.org/wiki/Standing_on_the_shoulders_of_giants (accessed 1/5/08). I have little doubt that the true basis of the phrase—an expansion on “two can see better than one”—has more ancient origins.

¹⁸²Werner Heisenberg, *Physics & Philosophy*, ed. Ruth Nanda Anshen, vol. XIX, World Perspectives Series (New York: Harper & Row, 1958; repr., 1962). Back cover.

¹⁸³Warren I. Susman, *Culture as History: The Transformation of American Society in the Twentieth Century* (New York: Pantheon Books, 1984). xxvii.

Until the middle of the nineteenth century, the lives of individuals in the West typically followed an unchanged and unchangeable pattern. It is difficult to conceptualize the ideologically rigid, unchanging world accepted by much of pre-nineteenth-century America. From cradle to grave, sons' lives paralleled their father's as did their forefathers; daughters followed mothers in the milestones of marriage, childbirth, and domestic chores, as had their mothers before them. Surely not everything was fixed, for the sun rose and set and the seasons changed with the pages on the almanac—yet even here was a quality of repetitious sameness. In general, what was would always be, for God had created Man in His image, and God is changeless.¹⁸⁴

The wall of fixity buttressed by the medieval Church crumbled with increased speed in the eighteenth century and collapsed with hastened purposefulness during the nineteenth. A degree of naïve optimism engendered by Gottfried Wilhelm Leibniz's (1646-1716) belief that God's unchanging world was the best possible was attacked by Voltaire (*Candide, or Optimism*, 1759) and other Enlightenment intellectuals who refused to accept the notion that plagues and other natural disasters were for the good of Mankind.¹⁸⁵ Thomas Malthus's *An Essay on the Principle of Population* (1798), David Ricardo's *On the Principles of Political Economy and Taxation* (1817), and Karl Marx's "Communist Manifesto" (1848) in the fields of economics, politics, and beyond, fostered the belief that the acceptance of things as they were did not have to be. Man, they argued, could change—no, had to change—or the consequences would be dire. Even the great American religious revivals of the 1730s-40s and 1830s-40s touted awakenings toward perfectionism that required change for implementation.

¹⁸⁴Genesis 1: 27.

¹⁸⁵Scholars emphasize that Voltaire's *Candide* was directly inspired—provoked?—by the Lisbon Earthquake of 1755 and the Seven Years' War that began soon thereafter. Ira O. Wade, *Voltaire and Candide: A Study in the Fusion of History, Art, and Philosophy* (Princeton: Princeton University Press, 1959). 88.

Scientists, being of society as well as in it, slowly but surely relinquished belief in the fixity of life and adopted principles of change. Although the intellectual notion of change surely began long before Heraclitus argued that a man cannot step into the same stream twice,¹⁸⁶ nineteenth-century scientists *qua* natural philosophers began to describe the world and life within it as a study in change rather than constancy.

Charles Lyell's (1797-1875) investigations into the geological forms around him led him to conclude by the early 1830s that the world was ever-changing—albeit slowly.¹⁸⁷ The long-accepted dates of the Bible—the creation of the Earth (approximately 5768 years ago, or 3760 BCE), the flood of Noah (approximately 2304 BCE), etc.—could not possibly account for the changes he witnessed on the Earth's surface using fossils and other evidence. Interestingly, Lyell—caught in a time-wise between immutability and change—believed that plants and animals were the same from God's Creation to Lyell's time.¹⁸⁸ On the question of whether the surface of the Earth had changed, however, he had no doubt. As Galileo had supposedly quipped on the relation between the Earth and the Sun—"It moves!"—so Lyell's observations led him to a similar conclusion on the nature of the planet—It changes!

¹⁸⁶Plato, in *Cratylus*, credited Heraclitus (c. 535 BCE-475 BCE) with what is today titled the Doctrine of Flux. A fragment suggests that the original quotation might have been "You could not step twice into the same river; for other waters are ever flowing on to you." <http://www.iep.utm.edu/h/heraclit.htm> (Accessed 1/7/08) My favorite variant is "No man ever steps in the same river twice, for it's not the same river and he's not the same man."

¹⁸⁷Charles Lyell, *Principles of Geology, Being An Attempt to Explain the Former Changes of the Earth's Surface, by Reference to Causes Now in Operation*, Special ed., 3 vols., vol. 1, The Classics of Science Library (London: John Murray, 1830; repr., 1997); *Principles of Geology, Being An Attempt to Explain the Former Changes of the Earth's Surface, by Reference to Causes Now in Operation*, Special ed., 3 vols., vol. 2, The Classics of Science Library (London: John Murray, 1832; repr., 1997); *Principles of Geology, Being An Attempt to Explain the Former Changes of the Earth's Surface, by Reference to Causes Now in Operation*, Special ed., 3 vols., vol. 3, The Classics of Science Library (London: John Murray, 1833; repr., 1997).

¹⁸⁸Lyell lived long enough to witness Darwin's extension of Lyell's geological work to biological forms. When confronted with Darwinian theory, he reportedly said, "I now realize I have been looking down the wrong road." Lyell accepted Darwin's conclusions and, in his remaining years, became a major Darwinian proponent. <http://users.hol.gr/~dilos/prehis/prerm1.htm> (accessed 1/7/08)

Many before Charles Darwin (1809-1882) had suggested that biological forms change over time,¹⁸⁹ but none had supported his conclusion with the intensity of thought, level of evidence, and beauty of expression put forth in his *Origin of Species* (1859) and other works. Darwin, whose early education included training in medicine,¹⁹⁰ gave voice to change and made it legitimate.¹⁹¹ He also lent science an aura of truth and validity in the public mind that, when added to the psychological trauma of the American Civil War, called into question the belief-driven religious underpinnings of society. Scientific objectivity gained a foothold in a secularizing world that had begun to value technology and its contributions to the improvement of everyday living.

Recurrent plagues and the rise of total war served to further the assumption of changelessness in popular religiosity.¹⁹² Secularization and nineteenth-century positivism—the

¹⁸⁹For a compelling series of lectures available to the public on Darwin's intellectual heritage and beyond, see Edward J. Larson, *The Theory of Evolution: A History of Controversy, The Great Courses* (Chantilly, VA: The Teaching Company, 2002), Videocassettes, 12 Lectures, Course No. 174. Edward Larson preceded this lecture series with his investigations into the history of evolution in his Pulitzer Prize-winning book, *Summer For The Gods: The Scopes Trial and America's Continuing Debate over Science and Religion* (Cambridge, MA: Harvard University Press, 1997; repr., 1998).

Indeed, one of Darwin's predecessors in the historical chain of evolutionary thought was his own grandfather, Erasmus Darwin (1731-1802). In the elder's final poem, *The Temple of Nature* (1803, a year after his death), originally titled *The Origin of Society*, Erasmus Darwin focused on the Chain of Being from microscopic organisms to Man in society. Therein he adumbrated much of his grandson's Theory of Evolution—except for the process of natural selection. See http://en.wikipedia.org/wiki/Erasmus_Darwin#Poem_on_evolution (accessed 1/7/08). Of course, Charles never knew his grandfather, for Erasmus had died years before his birth, but he certainly knew of him and of his work with plants and animals.

¹⁹⁰Robert Darwin, Charles's father, was a physician.

¹⁹¹ As Darwin made change legitimate, Einstein made it relative—relative to what was, is, and/or will be.

¹⁹²Major cholera epidemics spread over the United States in 1832, 1849, and 1866. Rosenberg, *Rosenberg, Cholera Years*. Other diseases, like diphtheria and pneumonia, routinely carried off “innocent” newborns and children.

Total war, which encompasses all the people and resources of a nation, was recognized as a “new” form of warfare by Clausewitz Carl von Clausewitz, *On War*, ed. Michael Howard and Peter Paret, trans. Michael Howard and Peter Paret, The Center of International Studies at Princeton University (Princeton: Princeton University Press, 1832; repr., 1989). after the Napoleonic Wars, but undoubtedly dates back at least to ancient China, as aphoristically taught by Sun Tzu Sun Tzu, *The Art of War*, trans. Thomas Cleary, Shambhala Dragon Editions (Boston: Shambhala, 6th Century BCE; repr., 1988). In the United States, total war that involved soldiers and citizens alike

application of scientific principles to society—appeared *prima facie* to offer more viable solutions to the problems of the day. And what was the basis of secularism—as opposed to religion—if not change? By the late nineteenth century, change had become the accepted, if not wished for, order of the day.

If change had become good, then efforts to combat poverty, ignorance, and disease—including the growing problem of cancer—had become laudable. The acceptance of change in the United States by the late nineteenth century helped legitimize medicine, for what is medicine if not an attempt to change the “natural” course of disease? Change also fostered new developments, innovations, and approaches to old medical problems like cancer. In the process, it transformed the culture of cancer from fear of interference with God’s Will to an all-out endeavor to use the resources of scientific knowledge and medical science to combat an ancient inexorable foe. Only then, promised this radical notion that change is good, could man contribute to his own fate and make the future better than the past.

I must note that despite the belief of some at the time, science ended neither religion nor sin—it only changed them in the public perception.¹⁹³ Religion did not disappear.¹⁹⁴ Instead, religion became *a* source of support during trying times rather than *the* source of support; *a*

began with the Civil War. As with recurrent diseases, so did war engender disillusion with the religious underpinnings of society.

¹⁹³William K. Clifford (1845-1879), a British mathematician and philosopher, offers an excellent example of pro-scientific, anti-ecclesiastical stance of the late nineteenth century. In his 1877 essay, “The Ethics of Belief,” he noted that “It is wrong always, everywhere, and for anyone, to believe anything upon insufficient evidence.” William Kingdon Clifford, *The Ethics of Belief and Other Essays* (Prometheus Books, 1999).

¹⁹⁴Contrast Clifford’s dogmatic denigration of faith and religion with his contemporary, William James (1842-1910), who seems to have spent much of his life searching for the nexus between science and religion—and finding it in the mind, through the science of psychology and the philosophy of pragmatism. William James, *The Varieties of Religious Experience: A Study in Human Nature* (New York: Penguin books, 1902; repr., 1985); *Psychology - Briefer Course*, A Limited ed., 100 vols., vol. 89, The 100 Greatest Masterpieces of American Literature (Franklin Center, PA: The Franklin Library, 1892; repr., 1983); *Pragmatism - A New Name for Some Old Ways of Thinking*, A Limited ed., 100 vols., vol. 75, The 100 Greatest Masterpieces of American Literature (Franklin Center, PA: The Franklin Library, 1907; repr., 1982).

source of understanding rather than *the* source of understanding; *an* approach to living rather than *the* approach to living. To this day, most hospitals include chapels. Why? As a source of comfort; to explain the unexplainable; to rationalize the irrational. For many, religion takes over where science and medicine end.

Out of Many, One

Man is not only a contributory creature, but a total creature; he does not only make one, but he is all; he is not a piece of the world, but the world itself; and next to the glory of God, the reason why there is a world.

—John Donne (c. 1572–1631)¹⁹⁵

The former generations acted under the belief that a shining social prosperity was the beatitude of man, and sacrificed uniformly the citizen to the State. The modern mind believed that the nation existed for the individual, for the guardianship and education of every man....The individual is the world.

—Ralph Waldo Emerson (1803-1882)¹⁹⁶

The cultural acceptance of secularism in late nineteenth-century America and its attendant valorization of change ushered in a host of political, economic, and social transformations that encouraged changes in the treatment of cancer. No longer was acquiescence in one's fate after a diagnosis of cancer the only acceptable option. Instead, physicians and patients alike sought to alter the natural course of the disease from death to cure. Intrinsic to this new approach to the treatment of cancer was a re-focused societal emphasis on the individual rather than the community.

The “top-down” early modern hierarchies of European and American societies, with King as head or father and everyone else arranged neatly and permanently below, was questioned with increased vigor in the seventeenth century and continued into the eighteenth and beyond.¹⁹⁷ The

¹⁹⁵*Sermons*, No. 35, 1625.

¹⁹⁶From "Historic Notes of Life and Letters in New England" (1880) in Perry Miller, *The American transcendentalists, their prose and poetry* (Garden City, N.Y.: Doubleday, 1957), 5.

beheading of Charles I in 1649, the English Glorious Revolution of 1688, the American Revolution, and the French Revolution are only the most salient milestones in a torrent of political, social, and economic metamorphoses that transformed King and country into nineteenth-century Constitutional monarchies and national democracies.

The Republicanism of eighteenth-century America—born of a long-standing European Enlightenment and tempered by an expanding land base, a paucity of labor, and a political foundation mostly independent of the military—became a nineteenth-century democratic Republic of disparate voices, leveling social stratifications, and economic rugged individualism. Even slavery, the most inhuman and base element of traditional hierarchy, was outlawed by Western governments throughout the nineteenth century.¹⁹⁸ All in all, collective constitutions began to emphasize the one rather than “the people” as the fundamental unit of society.

This ideological shift in emphasis from community to individual during the nineteenth century influenced the theory and practice of medicine in general and cancer in particular. Greater focus on the individual led to a new view of the patient *as* individual rather than as representative or example of a time or region.¹⁹⁹ The physician’s concern in the early 1800s America with an individual’s time of birth, place of birth, climate, and family, as cogently revealed in the works of Sheila Rothman and John Harley Warner,²⁰⁰ for example, shifted to a

¹⁹⁷Richard L. Bushman and Institute of Early American History and Culture (Williamsburg Va.), *King and people in provincial Massachusetts*, Paperback ed. (Chapel Hill: Published for the Institute of Early American History and Culture Williamsburg Va. by the University of North Carolina Press, 1992).

¹⁹⁸Haiti, 1804; Argentina, 1813; Colombia, 1814; Chile, 1823; Central America, 1824; Mexico, 1829; Bolivia, 1831; Great Britain, 1834; British Colonies, 1838; Uruguay, 1842; French and Danish Colonies, 1848; Ecuador, 1851; Peru and Venezuela, 1854; Dutch Colonies, 1863; United States, 1865; Puerto Rico, 1873; Cuba, 1886; Brazil, 1888. Source: <http://www.antislavery.org/breakingthesilence/> accessed 1/20/08.

¹⁹⁹Michel Foucault makes this point with different emphasis in an alternate location. Michel Foucault, *The Birth of the Clinic: An Archaeology of Medical Perception*, trans. A. M. Sheridan Smith (New York: Vintage Books, 1963; repr., 1994).

concentration on individuals in the aggregate through statistical studies. The goal was to see what could be learned from a series of ones collected into a picture of many.

The history of traditional cancer's constitutionalism followed this ideological pattern. Until the mid-to-late nineteenth century, physicians emphasized the interconnectedness of the whole organism rather than the separateness of its individual parts. Traditionalists explained the recurrence of cancer in a distant organ after removal of its primary manifestation as a confirmation of the dominance of the whole over its parts. Morgagni in the eighteenth century and Bichat and others in the early nineteenth spotlighted parts—organs and tissues—rather than the whole. Nevertheless, it was not until after Virchow's emphasis on the cell as the fundamental unit of life that an ideological shift called increased attention to the parts—now organs, tissues, cells—rather than the whole.

Charles Darwin, in his *Origin of Species*, also contributed to this seismic ideological change. Darwin emphasized quantized modifications in the species as the backbone of evolution. Natural selection, the great contribution of Darwin, created new species, but the process began at the level of the individual. In addition, Darwin posited a “common ancestor” from which all organisms evolved. Application of this idea to cancer medicine combined with the ever-increasing valorization of localism over constitutionalism in the late nineteenth century, postulated that even the largest of cancers developed from a single cancer cell—the unit of cancer. Since then, the unit of selection and of cancer has devolved to smaller and smaller parts of the organism. Today, it is the molecule (DNA base; enzyme). Tomorrow it will be the atom and then, depending upon the effectiveness of treatments derived from that paradigm shift, the

²⁰⁰Rothman, *Living in the Shadow of Death.*; John Harley Warner, *Against the spirit of system : the French impulse in nineteenth-century American medicine* (Princeton, N.J.: Princeton University Press, 1998).

unit may be constituents of the atom such as the quark—and beyond.²⁰¹ In sum, even the concept of “individual” is evolving.

Institutionalism—Surrogate for Community and Care

The [New York Cancer] Hospital had its beginning in a meeting which was held at the residence of Mrs. General Cullum on February 7, 1884....The object of that meeting [was] to found a hospital for the treatment of such cases of cancer as were susceptible of relief. It was believed that a well-equipped institution for the purpose...was a much-needed charity in this city....It was hoped that in this way not only might the cure or relief of many sufferers from cancer be accomplished, but that thus invaluable opportunities for the study of this disease by skilled surgeons might be afforded, with a scientific advance such as no ordinary experience in a general hospital could hope to bring about.

-New York Cancer Hospital, *First Annual Report*, 1885²⁰²

Institutionalism, which emphasizes synergy through organization, expanded during the nineteenth century in the vacuum of diminishing republicanism and the evolution from community to individual. In the discipline of medicine, institutionalism encouraged implementation of the methodologies and tools of discovery offered by science in new settings.

In the United States, nineteenth-century institutions tended to be of three types: corporate (for profit), charitable (non-profit), and government. The number of corporations grew during the century as laws and money flows favored increased levels of capitalization and economies of scale multiplied profits. Government institutions were held back by a popular mindset that placed responsibility on the self rather than the system. In addition, history and the American Federalist system emphasized local over central government. As a result, municipal organizations tended to play a much bigger role in the life of the individual than those at the

²⁰¹Increased knowledge, of course, does not necessarily translate into improved well-being or happiness. I present this rosy scenario of change leading to progress to emphasize that modern cancer treatment evolved from traditional therapeutics under the umbrella of cultural transformations that occurred during the nineteenth century. These same cultural transformations fostered physical and psychological deracinations. In medicine, the emphasis on the part over the whole created specialization and led physicians to view patients as organs (“the lung patient in Room 666”), tissues (“the contact dermatitis in Exam Room 2”), and cells (“the Philadelphia chromosome-positive patient in for chemotherapy”) rather than as whole beings with essences comprised of families, relations, and histories.

²⁰²1885,p. 7.

national level.²⁰³ Institutions that cared for the poor and sick tended to be charitable, non-profit organizations supported financially and managerially by people of wealth.

The adoption of scientific medicine by physicians and patients in the late nineteenth century changed the character, methods, and goals of the hospital—the institution for the care of those afflicted with disease. As David Rosner revealed in his *A Once Charitable Enterprise*, much more than “science” was involved, for social, economic, and political factors weighed heavily on the old charitable institutions such as almshouses to compel them to change into the locus of choice for the sick and dying.²⁰⁴

As a result, hospitals, which had been residences of last resort for the needy and afflicted, became venues of choice for rich and poor alike. The influx of middle- and upper-class patients into the hospital in the late nineteenth century removed the musty seediness of the almshouse and replaced its sense of abject hopelessness with clean, modern amenities and an attitude of expectant optimism. The number of hospitals burgeoned. Dr. William W. Keen wrote that “this growth of hospitals has been within the last twenty years [1877-1897] one of the striking features of our civilization.”²⁰⁵

The method of care also changed, as the everyday sameness of the early nineteenth century chronic care institution evolved into a facility for active intervention. Surgery became the treatment of choice for cancer and, about the same time, the hospital became the home of surgery. Surgery, by its very nature, creates change, for what *was*—as a result of the surgeon’s blade—is no longer what *is*. In addition, transformative nineteenth-century concepts in patient

²⁰³The Civil War markedly increased the role of the national government in the lives of veterans and instituted pension, disability, and health care benefits that became the rule rather than the exception in the twentieth century. See <http://www1.va.gov/opa/feature/history/history1.asp> accessed January 24, 2008.

²⁰⁴David Rosner, *A once charitable enterprise: Hospitals and health care in Brooklyn and New York, 1885-1915* (Princeton: Princeton University Press, 1982; repr., 1987).

²⁰⁵Keen, *Addresses*: 247.

care—active nursing, cleanliness, post-operative observation—made the hospital a more vibrant institution than it had ever been. Indeed, it is a misnomer to equate early and late nineteenth century “hospitals,” which is why historians sometimes refer to the former as asylums²⁰⁶ and the latter as citadels of science. The goals of hospital care also underwent a major metamorphosis. Cure was always the dream, but until late in the century it was more a faith-based wish than prospect.²⁰⁷ Surgery offered the possibility of cure rather than the seeming endlessness of chronic care or certain death.

A Sense of Optimism

Where there is no hope, there can be no endeavor.

-Dr. Samuel Johnson²⁰⁸

Mental attitude is hard to gauge and even more difficult to generalize among a large and diverse population. Nevertheless, there are often clues available to the historian that signal the tenor of the times. During the late nineteenth century, a sense of optimism pervaded medical research and practice as well as large swaths of society.

The most discernible indications of optimism were social and economic. Immigrants in unprecedented numbers flocked to American shores, firm in the belief that life was better here than there.²⁰⁹ Parents sent their children to public schools, confident that education would “Americanize” them and lead them onto the road to success.²¹⁰ Women, the unenfranchised half

²⁰⁶I use “asylum” in the general sense of providing sanctuary or shelter as well as the more specific sense of a site of care for the destitute, including the insane.

²⁰⁷The quest for cure remains a wish for many today, but is more a reality than ever before.

²⁰⁸Quoted by President Cleveland’s Dr. Joseph Bryant, Joseph D. Bryant, “A History of Two Hundred and Fifty Cases of Excision of the Superior Maxilla,” *Transactions of the Medical Society of the State of New York for the Year 1890* (1890): 71.

²⁰⁹John Higham, *Strangers in the land : patterns of American nativism, 1860-1925* (New Brunswick, N.J.: Rutgers University Press, 2002). 159.

of the population in the late nineteenth-century United States, strove for greater political, economic, and social equality as newly-admitted states like Wyoming offered suffrage and vibrant countrywide organizations like the National Woman Suffrage Association and the more conservative American Woman Suffrage Association fought for gender-blind voting rights.²¹¹ Dreams of Life, Success, and Equality buoyed optimism.²¹²

Miracles of science pervaded society. In addition to the inventions of Bell and Edison, less renowned but culturally important innovations changed the landscape of late-nineteenth-century America. Levi Strauss patented his eponymous “waist overalls” in 1873; Waterman his fountain pen in 1884; Eastman his portable camera in 1888; Theophilus Van Kannel the revolving door in 1888, an invention that allowed easy access to skyscrapers and other large buildings whose natural vacuum made (and make) traditional doors difficult to open; Johann Valler’s lowly but functionally critical paper clip in 1890; and Whitcomb L. Judson’s zipper in 1893.²¹³ In medicine, Pasteur’s foundational research into the problems of spontaneous generation and putrefaction led to concepts of “germs,” new vaccines, and furtherance of the

²¹⁰The United States Americanization Department began at the conclusion of the First World War and published its best-known works in 1925. Nevertheless, the notion of Americanization—acculturation, assimilation, and accreditation (citizenship)—began much earlier (probably when Colonies became States and Patriots no longer considered themselves British Americans).

²¹¹Wyoming embraced suffrage rights for women as a territory in 1869 and continued them intact upon achieving statehood in 1890.

²¹²Of course, I am aware that not all Americans shared this optimism. Historians have penned volumes on the plight of the poor, the ill, the African American, the laborer, the farmer, and, in general, “the excluded” and “the other.” Certainly the cancer patients of whom I write were not optimistic—unless and until new developments in the treatment of cancer turned their feelings. These new developments, many of which brought hope instead of despair and life instead of death, are the subject of this chapter and thus explain my emphasis on optimism.

²¹³A brief selection from <http://www.enchantedlearning.com/inventors/1800b.shtml> accessed January 31, 2008.

belief that the application of science to society could improve the human condition without limits.²¹⁴

Economic revolutions, often augmented by science and scientific management, stirred dreams of success at all levels of society.²¹⁵ Novels by Horatio Alger, Jr. that sanctified hard work, honesty, and determination as ingredients for comfortable prosperity reached large numbers of readers. Revolutions in capitalism helped make large companies into larger corporations and, for a limited but highly visible few, brought unimaginable wealth.²¹⁶ Tabloids and increasing numbers of popular magazines gave hope even to the destitute and distraught that they, too, could join the ranks of the well-to-do.²¹⁷ Purposeful changes in managerial style streamlined business decision-making processes and augmented corporate profit margins through the ability to implement actions swiftly, take advantage of increasing pools of available capital, and implement ever more efficient manufacturing processes.²¹⁸ The success of these conscious

²¹⁴The late nineteenth-century novels of H. G. Wells and Jules Verne capture and romanticize the growing cultural belief in the endless potential of science to better the human condition. Like all great and popular novels, however, they also establish a tension between good and evil, for science can be used to engender darkness as well as light.

²¹⁵Frederick Winslow Taylor published his work on “Scientific Management” in 1911, but the idea of the rational application of scientific methods to business can be found much earlier in Adam Smith’s description of the division of labor in the eighteenth century. See Frederick Winslow Taylor, *The Principles of Scientific Management* (New York: W. W. Norton & Company, 1911; repr., 1967), *Shop management* (New York, London,: Harper & Brothers, 1905), and Adam Smith, *An Inquiry into the Nature and Causes of The Wealth of Nations*, ed. Edwin Cannan, 2 vols. (Chicago: The University of Chicago Press, 1776; repr., 1976).

²¹⁶Even today, after decades of inflation, the wealth of some of these capitalists is staggering. In 1918, Forbes estimated that the assets of John D. Rockefeller (son of cancer quack William Avery Rockefeller) amounted to \$1,200,000,000. “His income is estimated to work out at \$2,739,726.02 a day, \$114,155.25 an hour, \$1,902.58 a minute and \$31.70 a second....Mr. Rockefeller's wealth, if it could be turned into cash and distributed equally--which it couldn't--would give every man, woman and child in the United States \$1 each. His total equals approximately one-fourth of all the money in circulation in the country.” See http://www.forbes.com/2002/09/27/0927richest_print.html accessed January 30, 2008.

²¹⁷*The New York Times* Quotation of the Day for January 26, 2008, echoed this long-held sentiment: “Americans don’t dislike wealthy people; they want to be wealthy people.” (expressed by Senator John McCain of Arizona during the 2008 Presidential Campaign)

²¹⁸Alfred D. Chandler, *The visible hand : the managerial revolution in American business* (Cambridge, Mass.: Belknap Press, 1977).

changes, over time, led to corporate managers who were more professional and technically savvy than ever before. In turn, they were more able to control markets than be controlled by them. Control replaced luck and whim as it lent a sense of optimism to entrepreneurial and enterprise spirits.

At the interface between manufactures and medicine, some of the diagnostic and surgical instruments introduced during the late nineteenth century included the hypodermic syringe, aspirator, clinical thermometer, hæmostatic forceps, laryngoscope, rhinoscope, otoscope, and the ophthalmoscope—all of which are used today in minimally modified form.²¹⁹

These achievements and the positive psychological aura that accompanied them were not lost on those who practiced medicine. Medical schools affiliated with hospitals and hired physicians to research and teach.²²⁰ The specialization that resulted from increased professionalism and focused procedures altered the landscape of cancer medicine. The new microscopically-derived histopathological nomenclature for cancer, now a requirement for technical expertise, and the growing numbers of patients with cancer in the late nineteenth century set into motion a new enterprise dedicated to the diagnosis and treatment of the diseased, based upon novel methods of investigation and treatment that founded and sustained modern cancer medicine. The transformative effects of social and economic change on society aided and abetted the evolution from traditional to modern cancer medicine.

Science and Society Revisited

As societal transformations lent new directions to the contexts of science, so scientific ideas became incorporated into the workings of society and medicine. Transformations in

²¹⁹Keen, "Progress of Surgery," 342.

²²⁰Kenneth M. Ludmerer, *Learning to Heal: The Development of American Medical Education* (New York: Basic Books, Inc., 1985).

mathematics fostered new means of measuring change through statistics. Transformations in biological theory fostered new ways of interpreting developments in plants and animals over time. Transformations in medicine, utilizing these new ideas from statistics and biology and elsewhere, initiated novel approaches to the treatment of diseases. Transformations in cancer medicine, founded upon new applications from all of these forces, compelled changes in the treatment of cancer.

Statistics – Medical Science through Numbers

Mathematics is the language of the natural sciences. This truly amazing correlation—for it is far from intuitive²²¹—is most obvious for physics and astronomy, but applies with increasing realization to chemistry and biology as well.

For the Ancient Greeks, mathematics, philosophy, and the natural world were inextricably intertwined. They viewed mathematics as the height of rational thinking and sought to apply its principles to activities of daily life. Pythagoras (580-500 BCE) conceived of mathematics as a “purifier of the soul” and noted almost mystical connections between lines, shapes, and the harmonics of musical instruments.²²² Likewise, Plato (c. 424-c.348 BCE) believed that the Cosmos was suffused with a harmony derived from ideal forms and analyzable contents best discerned by mathematics through philosophy.²²³ Since then, countless mathematicians have applied extensions and new formulations of the knowledge of the Ancients to everything from the bending of light around enormous astronomical bodies to calculations of

²²¹For a brilliant exposition on the inexplicable yet powerful explanatory and predictive power of mathematics in physics, see Eugene Wigner, "The Unreasonable Effectiveness of Mathematics in the Natural Sciences," *Communications in Pure and Applied Mathematics* 13, no. 1 (1960).

²²² <http://www.thebigview.com/greeks/pythagoras.html> accessed 2/9/2008

²²³There is an old tradition that claims that above the entrance to Plato's Academy hung a sign that read "Let No One Un-versed in Geometry Enter." <http://community.middlebury.edu/~harris/Philosophy/Plato.html> accessed 2/9/2008.

the number of Americans likely to die from an Avian Influenza epidemic.²²⁴ In the process, statistics, a relatively new field of mathematics, was born where the whole had more meaning than the sum of its parts.²²⁵

Statistics is a branch of mathematics that involves the collection, analysis, interpretation, and presentation of masses of numerical data.²²⁶ Thus, because history is so much more than a compilation of facts in time, so statistics is more than a group of numbers that share a common theme.²²⁷ Edmund Halley (1656-1742), friend of Isaac Newton and first known discoverer of the comet that bears his name (1682), has received the moniker “Father of Vital Statistics” because of his pioneering collection and analysis of Parisian demographics in the late seventeenth century.²²⁸ Nonetheless, another Englishman, John Graunt (1620-1674), although much less heralded, deserves more credit because he preceded Halley’s demographic work by almost two decades.²²⁹ The important point is that natural philosophers and then scientists began to think of people as units to be studied in the aggregate. Study results could then be interpreted and applied

²²⁴The discovery of light bending in 1919 confirmed Albert Einstein’s General Theory of Relativity. Influenza deaths depend upon the probability—another derivative from ancient mathematics—that certain viruses will mutate into forms that can attach to human cell receptors, especially in the lining of the lungs, and spread from one human to another.

²²⁵It is difficult to pinpoint the origin of statistics (as opposed to statistical thinking, which undoubtedly precedes the Bernoullis by millennia), but credit, at least in the social sciences, is often given to (Lambert) Adolphe (Jacques) Quetelet (1796-1874), who, educated in mathematics, applied his knowledge of probability, astronomy, and mathematics to human properties (like height, weight—and racial divides) and, in the process, greatly influenced the direction of European social studies.

²²⁶ <http://www.merriam-webster.com/dictionary/statistics> accessed 2/9/2008.

²²⁷The etymology of “statistics” derives from politics, not mathematics. English *statistics* comes from German *statistik*, meaning the study of political facts and figures, and is itself derived from the Latin *status*, meaning state. <http://www.merriam-webster.com/dictionary/statistics> accessed 2/9/2008.

²²⁸Halley’s statistical project laid the foundation for the business of life insurance and annuities, but its purpose may have been the “Increase of Mankind,” to which he concluded that less fear of marriage was the key. He married shortly thereafter and had three children, thereby replacing himself and more. http://www.historynet.com/exploration/science_engineering/3025646.html accessed 2/9/2008.

²²⁹Major Greenwood, *Medical Statistics from Graunt to Farr* (Cambridge: Cambridge at the University Press, 1948).

to the whole. In the field of medicine, the analysis of efficacy of disease treatments took a giant step forward with the “numerical method” of Pierre-Charles-Alexandre Louis (1787-1872).

Louis was a French physician who graduated from medical school in Paris in 1813 and then left Napoleonic France to work in Russia for seven years.²³⁰ Upon his return, he became disillusioned with French Enlightenment medicine that was derived from theory and observation applied on a case-by-case basis. Instead, he began a multi-year project that collected information about patients and their outcomes that included data on their families, backgrounds, course of disease, and, if applicable, their autopsies. By 1825, he had amassed enough data to publish a treatise, *Récherches Anatomico-Pathologiques sur la Phthisie*, that revealed the increased knowledge about a disease that could be obtained from the study of aggregated data.²³¹ His conclusions, although hardly embraced by the establishment for their opposition to “the spirit of system”—he was never elected to a medical faculty, for example—attracted enough attention, especially from some of the younger physicians and foreign students, that he applied his method of quantification to studying the results of the popular treatment of bloodletting.²³² The 1835 publication of his results, *Récherches sur les Effets de la Saignée*, presented compelling evidence to heroic venesectionists that their treatment accomplished more harm than good.²³³

²³⁰http://www.pbs.org/wnet/redgold/innovators/bio_louis.html accessed 2/15/08.

²³¹Pierre-Charles-Alexander Louis, *Researches on Phthisis: Anatomical, Pathological and Therapeutical*, trans. Walter Hayle Walshe (London: The Sydenham Society, 1844). This is the first English translation of the 1825 French publication.

²³²The definitive work on revolution from the theoretical didacticism of the “spirit of system” to post-French Revolution medical empiricism is John Harley Warner, *Against the Spirit of System: The French Impulse in Nineteenth-Century American Medicine* (Princeton: Princeton University Press, 1998)..

²³³Pierre-Charles-Alexander Louis, *Researches on the Effects of Bloodletting in some Inflammatory Diseases*, trans. C. G. Putnam, The Classics of Medicine Library (Boston: Hilliard, Gray, & Company, 1836; repr., 1986). This is the first English translation of the 1835 French publication.

Louis's teachings and monographs neither cured tuberculosis nor caused physicians to cease venesection, but they invited questions about then-current medical theories and empiricism. Further, those who supported Louis's methodology, including American students in Paris like Oliver Wendell Holmes, Sr. (1809-1894), carried his statistical methods to other European countries and to America.²³⁴ Today, P.- C.- A. Louis is known as the Father of Medical Statistics. His great achievement was to quantify the study of medicine and the treatment of patients beyond the personal and the anecdotal. With his "numerical method," he constructed meaningful aggregates of medical knowledge based upon scientific methodology, deductive reasoning, and the wisdom gained from analyses that drew insights for one out of many, thus helping to transform the Case Report into the Clinical Trial.

Statistics regarding the results of operations have never been collected on a sufficiently large scale.

-George F. Shrady, 1887²³⁵

In the late nineteenth century, cancer surgeons grudgingly extended Louis's methodology to operative outcomes. Earlier, during the era of traditional cancer, surgeons defined a cancer cure as discharge from the hospital or even mere survival of the cancer operation. Thus, long-term statistics of the kind compiled by Louis were rare.

By the closing years of the 1880s, however, this short-term notion of "cure" failed to satisfy patients and physicians alike. Patients consented to undergo the pain, suffering, and risks of cancer surgery if and only if they had a reasonable chance for post-operative palliation and/or cure. Physicians and surgeons sought to learn which procedures had the greatest probability of success. As a result, pioneer surgeons such as Sir Henry Trentham Butlin (1845-1912) began to urge their colleagues to observe their cancer surgery patients post-operatively "sufficiently long

²³⁴<http://www.enotes.com/public-health-encyclopedia/louis-pierre-charles-alexandre> accessed 2/15/08.

²³⁵George F. Shrady, "The Curability of Cancer by Operation," *The Medical Record* 31, no. 4 (1887): 86.

to discover how far the operations have had the effect of delaying the course of the disease or of completely arresting it.”²³⁶ Butlin, the “Father of British Head and Neck Surgery,” urged the compilation of long-term cancer surgery statistics that included both site-specific and grade-specific outcomes.²³⁷ How else could cancer physicians learn the best treatments for their patients?²³⁸

Biology – A New History of Life

Knowledge of living organisms exploded during the nineteenth century. In Europe and the United States, cultural transformations such as secularization and the refocus on the individual placed new emphasis on the study of life as an ever-changing and comprehensible form of nature rather than a complete and completed work of God.

Natural philosophers became scientists, and scientists became biologists, chemists, and a host of other specialists dedicated to the study of nature.²³⁹ In biology, comparative anatomy revealed that Man was not the unique Creation once thought. The loss of human exceptionalism was compensated for, in part, by the salutary cross-application of knowledge gleaned from the study of plants and animals to human biology. Increased familiarity with human anatomy stimulated investigations into correlations between structure and function—i.e., anatomy and physiology. Scientists and physicians began to explain human disease in terms of abnormal human biology rather than punishment for sin or even one-system disorders (humors, blood).

²³⁶Henry T. Butlin, *On The Operative Surgery of Malignant Disease* (Philadelphia: P. Blakiston, Son & Co., 1887). 2.

²³⁷*Ibid.*, 3. The “site” is the location of the original cancer. The “grade” is the probable deadliness of the cancer based upon its histological appearance.

²³⁸Large, randomized, controlled trials today often include non-blinded committees devoted solely to the analysis of statistical data derived from those studies. Regardless of the size of the study, statistical analysis of the results is the cornerstone of their interpretation.

²³⁹Natural philosophers, a term that reaches back to the Middle Ages, speculate as to the nature of things; scientists use the scientific method to investigate the nature of things.

Specific treatments developed that sought to restore physical normalcy for specific conditions rather than assuage the psychological effects of sin or apply one-remedy-for-all solutions. In cancer medicine, as in other fields, Fate became science and Nature became nature. The world of life became a giant puzzle open to exploration, investigation, solution, and change.

The term ‘scientist’ was born during this era. William Whewell (1794-1866), co-founder of the British Association for the Advancement of Science, coined the term in 1833, although, consonant with other transformations discussed in this dissertation, the term did not come into general use until the last years of the nineteenth century.²⁴⁰ A new language to replace that of the ‘natural philosopher’ was necessary, because the world was opened anew to secular exploration and because the methods of investigation had changed. As the approach to science—the scientific method—evolved over the course of the nineteenth century, observational didacticism and empirical experientialism became scientific investigation and clinical examination. In essence, science changed the philosophy of medicine as well as its methodology.

Declarations by authorities became testable hypotheses subject to independent verification and reproducibility. That which was assumed to be true in the past became subject to question in the present. In the process, science opened doors to the study of the natural world that Natural philosophers never saw.

Biology is the study of change—change in the domain, kingdom, phylum, division, class, order, family, genus, species. (Medicine, in this cladistic hierarchy, involves the study of change in the individual or population.) All change occurs in time. Thus, biology is the change in life over time—change in the species from inception to extinction; change in the organism from conception to vigor to demise. If time is unidirectional, then so is biological change, but there is

²⁴⁰<http://www.victorianweb.org/science/whewell.html> accessed February 18, 2008.

sufficient variation within a population or within an individual that the trajectory of life can be changed.

The history of Charles Darwin's voyage on the H. M. S. Beagle and the longitudinal conclusions he derived from his cross-sectional investigations of variations in plants and animals are well known.²⁴¹ For medicine, however, Darwin's investigations into animal husbandry convinced a wide readership of the truth that many already knew; viz., that Man could change animals by selective breeding (i.e., unnatural selection).²⁴² And if Man could alter the natural history of animals, and animals had in many ways been found to be comparable to humans, then why could not Man apply this knowledge to change the natural history of the human species and benefit individuals in the process?

Modern Science, Biology, and Medicine

Cell theory, the introduction of compound microscopes with corrected lenses, and the rapid development of organic chemistry had completely changed the face of the biological sciences by the middle of the nineteenth century.

-L. J. Rather, Patricia Rather, John B. Frerichs²⁴³

As developments in general science fundamentally altered biology, new approaches to biology transformed the theory and practice of medicine. In consequence, medical traditions that extended back in time through the Renaissance and Middle Ages changed over the course of the

²⁴¹Thomas J. Barloon and Russell Noyes, Jr., "Charles Darwin and Panic Disorder," *Journal of the American Medical Association* 277, no. 2 (1997); Charles Darwin, *The Voyage of the Beagle*, ed. Leonard Engle, The Natural History Library (Garden City, NY: Doubleday & Company, Inc., 1860; repr., 1962); *Journal of Researches into the Natural History and Geology of the Countries Visited during The Voyage of H. M. S. Beagle Round the World under Captain Fitz Roy, R. N.*, Third ed. (London: The Folio Society, 1860; repr., 2003); Francis Darwin, ed. *The Autobiography of Charles Darwin* (New York: Dover Publications Inc., 1958).

²⁴²Shepherds, goatherds, cowherds, and swineherds etc. had practiced the breeding (and raising) of livestock for millennia. Darwin sought to learn from their experience by classifying and analyzing the results of answers to questionnaires he sent them. Few responded, but what he learned bolstered his belief in natural selection as the force of evolution.

²⁴³L. J. Rather, Patricia Rather, and John B. Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*, trans. L. J. Rather (Canton, MA: Science History Publications, 1986). 1-2.

nineteenth century with the assumption of new methodologies, terminologies, and practices that differed so radically from the old as to warrant a new name—modern medicine.

The transformative elements of nineteenth-century culture—including secularization, individuation, institutionalization, and optimism—influenced the practice of medicine directly through biology and its allied sciences. The notion that disease could be altered to restore health without committing a sin against God’s Will gave impetus and legitimacy to increasingly scientific attempts to improve therapeutics. Traditional didactic assumptions and observations that had guided the practice of medicine for many years yielded to a scientific method that, with the help of statistical analyses and experimentation, sought to test new and different strategies for the treatments of disease. The acceptance of change also affirmed this quest to restore health from disease. Thus, following the transformation in the ideology of disease from sin to science, practitioners used the tenets of cell biology in concert with new technologies offered by chemistry and microscopy to discover and apply better medical therapies.

The professional authority of physicians shifted from an allegiance with tradition to an allegiance with scientific progress.

-Lilli Sentz²⁴⁴

In the early nineteenth century, the practice of medicine was a product of natural philosophy, ancient Galenic teachings, astrology, and early modern, Renaissance, and Medieval medicine. It was, in short, an outgrowth of the confluence of Enlightenment rationalism, Church theology, and neo-Classical empiricism. The advance of the late nineteenth century from empiricism to science was the testing of hypotheses on a scientific framework. In addition, the economic and social successes of the applications of science to the public sphere helped to

²⁴⁴Lilli Sentz, *Medical History in Buffalo 1846-1996* (Buffalo: State University of New York at Buffalo, 1996). 146.

encourage the development of yet more technologies that offered medicine ever-widening therapeutic possibilities.

In chemistry, the products of the scientific methodology led to direct, visible improvements in daily living. The fundamental elements of living—food, clothing, and shelter—benefited from new processes of preservation (e.g., pasteurization), dyeing (e.g., William Perkin’s mauve), and glass making (e.g., mass production of sheet glass for residential windows) that derived from chemistry. The transference of these technologies to medicine led, for example, to increased knowledge and applications in the medical fields of bacteriology (treatment of bacterial overgrowth), pathology (tissue stains), and medical microscopy (glass slides and mass-produced lenses). In a strange confluence, secularization and advances in chemistry also fostered a new view of the human being, for, with greater knowledge of anatomy and physiology over the course of the nineteenth century, organisms began to be conceptualized less in terms of God’s instantaneous, unitary Creation, and more as chemical systems.²⁴⁵ This notion of human as chemistry allowed further synergies between science and medicine that opened more avenues of thought and practice into the nature of disease and its treatment.

In physics, discoveries in magnetism and electricity by William Gilbert (1544-1603), Benjamin Franklin (1706-1790), Luigi Galvani (1737-1798), Michael Faraday (1791-1867), and others, formed the bases of Thomas Edison’s experiments that led to the creation of the light bulb and the electric generator that sustained its luminosity. By the last two decades of the nineteenth century, medical scientists and physicians increasingly used mobile, clean electricity as a source of power for everything from microscopes to cauteries. Further, as in chemistry, life

²⁴⁵Human “chemical systems,” like the chemical industry, needed raw materials (food and water), synthesized new products (such as hair, skin, and urine), and broke down over time (such as bone fractures and disease).

in general and human action in particular, was found to follow the laws of physics—Divine or otherwise.

New developments in biology, chemistry, and physics contributed theory and technology to the industrial revolution, and industrialization produced more and better products for the practice of medicine. Instruments, formerly crafted individually by the hands of the physician and his assistant, became available in much greater numbers with improved tolerances and the interchangeability of parts. From pens to smocks to microscopes, the standardization and uniformity of mass production lent reliability and predictability to the practices of medicine. In the field of medical literature, book-making took on a new life as steam presses and halftone pictures increased the quantity and quality of volumes printed at the same time that they decreased unit costs.²⁴⁶ Medical students purchased American and other texts that only the wealthy could previously afford. W. W. Keen wrote, for example, that Samuel David Gross's *System of Surgery*, first published in 1859, "has probably had a wider influence in educating the profession than any other general surgical text-book issued up to the present time."²⁴⁷ Physicians in practice read more recent journals published at lower cost than ever before. The *Index-Catalogue of the Library of the Surgeon General's Office*, begun by John Shaw Billings (1838-1913) in 1879, endeavored to provide a compendium of medical literature that present and future generations could keep current for the education of medical students, researchers, and practicing physicians.²⁴⁸

²⁴⁶It is believed that the first halftone photograph printed in a newspaper was in the March 4, 1880 edition of New York's *The Daily Graphic*.

²⁴⁷Keen, *Addresses*, 247.

²⁴⁸The printed *Index Medicus* ceased publication with the December 2004 edition, replaced by *MEDLINE/PubMed* and a host of other online sources of "virtual" medical information. <http://www.nlm.nih.gov/hmd/about/collectionhistory.html> accessed March 3, 2008.

Laboratories mark the difference between the scientific and the empirical method.

-W. W. Keen²⁴⁹

Science, industry, and education combined to create mechanisms whereby new ideas for diagnosis and treatment could be tested in a neutral, unbiased environment unfettered by the prejudices of individual observation and empiricism. This “place of labor”—the laboratory—was the locus of scientific creation, testing, and practice. Born in the days of alchemy and early modern Europe, the laboratory was usually a distinct site, separated from places of other human activities such as eating and sleeping.²⁵⁰ As such, it permitted an area for thoughtful reflection and meticulous testing in which experimenters could pose questions and seek answers to those questions.

The laboratory also provided an interface between pure and applied science. Scientists took ideas, theories, and constructs and determined whether they generated positive (or negative) results in an atmosphere with one variable—the subject at hand. Initially the province of the private residence, the laboratory over the course of the nineteenth century became a staple of the institution—the scientific laboratory in the University or industrial research facility (such as Thomas Edison’s industrial laboratory at Menlo Park, New Jersey); the medical laboratory in the hospital or affiliated research unit. In medicine, it was, in essence, a place where the research scientist or physician could gather his thoughts, papers, books, and equipment—with relatively little distraction—and test hypotheses that could later be applied in the clinical setting. Louis Pasteur, Robert Koch, and Paul Ehrlich all worked in such an environment. Thus, the laboratory incorporated the great cultural waves of the nineteenth century—secularization, individuation, and institutionalization—as well as the technological advances derived from advances in

²⁴⁹Keen, *Addresses*: 324.

²⁵⁰The Oxford English Dictionary lists the first use of the word “laboratory” in 1605.

chemistry and physics, to create a synergistic environment for the conduct of medical research in the scientific manner and the discovery of new medical and surgical treatments for the benefit of mankind.

Science, Society, and Modern Cancer Medicine

The treatment of cancer benefited from the cultural, technological, biological, and medical transformations of the nineteenth century. Beyond the psychological acceptance of Man's ability to change the God-given course of the natural history of cancer, came the desire to do so. Industry provided new forms of power such as electricity that offered steady, (usually) reliable, transportable,²⁵¹ and (eventually) cheap sources of energy to enable laboratories, medical offices, and surgical suites to carry on their work without the dangers attendant upon earlier energy sources. Industry manufactured tools and vessels of great standardization and durability that enabled hospitals to become bastions of medical science at the same time that the prohibitive cost and expertise required for the one-time or sporadic use of such instruments outside the hospital made it the place of choice for certain forms of medical treatment, like cancer surgery.²⁵²

Science and scientific medicine are cumulative and eclectic enterprises. They are cumulative in that each verified finding becomes a piece of a puzzle that grows asymmetrically until the whole puzzle becomes but a piece in a still larger and more complex puzzle. They are eclectic in that scientists sift through problems and select the questions to be asked about those

²⁵¹In 1859, Gaston Plante, a Frenchman, invented the first practical lead-acid storage battery, similar to those used in today's automobile. A great advantage of Plante's battery was that it could be recharged. Thomas Edison invented the alkaline storage battery in 1901. <http://inventors.about.com/library/inventors/blbattery.htm> accessed March 15, 2008.

²⁵²The need for sterility was another major reason that drove surgery into the hospital, but, in most facilities, sterility was not a significant concern until the end of the nineteenth century.

problems from an infinite universe of limitless possibilities, using intelligence and experience to seek solutions based upon the acquired knowledge at hand.

This was as true in cancer medicine in the late nineteenth century as it is in particle physics today. In oncology, the hard-fought victory of localism over constitutionalism, the adoption of the microscope for cancer diagnosis over the clinician's resolute belief in diagnosis by gross examination,²⁵³ the increasing incidence of cancer in the United States and Europe over the course of the nineteenth century,²⁵⁴ and the consequent advantage of earlier rather than later diagnosis and treatment, all encouraged the development of new and better forms of cancer therapy.

Modern Cancer Surgery

Surgery won the role as the cancer treatment of choice by the end of the century, but it was not without a struggle. Non-surgical therapies continued to vie for the attention of patients and those who treated their cancers. Nevertheless, it was developments ancillary to cancer medicine and surgery that propelled the surgeon and his knife into the forefront of the treatment of cancer.

²⁵³As late as 1892, Daniel Lewis, a New York surgeon, wrote that "The sense of touch, when educated by experience, is the almost infallible diagnostician of cancer." An experienced clinician, he continued, will correctly diagnosis cancer "with his index finger ninety-nine times out of a hundred. It is more unerring than the microscope." Daniel Lewis, *Cancer, and Its Treatment* (Detroit: George S. Davis, 1892). 34.

Nevertheless, Dr. Lewis concluded that even if gross examination yielded a more accurate diagnosis of cancer than microscopical examination, the microscopic findings could be the critical element in predicting the patient's future. As he wrote, "As an aid to correct *prognosis*, all tumors should be classified by microscopical examination after removal," for it would reveal if any cancer fragments had been left behind to grow into a recurrent cancer. *Ibid.*, 8-9. This realization of impending surgical failure was commonly appreciated by the end of the nineteenth century. Francis J. Shepherd, *A Retrospect of Surgery: January 1886-January 1890* (Montreal: Gazette Printing Company, 1890). 230.

Despite the above, it should be noted that the American College of Surgeons did not require the microscopical examination of all surgically-excised tissue until 1926!

²⁵⁴There are innumerable sources for this stipulation, including Frederick Bowreman Jessett, "The Alleged Increase of Cancer," *The Lancet* 132, no. 3408 (1888). and Unknown, "Cancer in Medical Examinations," *The Sanitarian, a Monthly Magazine devoted to the Preservation of Health, Mental and Physical Culture* XX(1888)..

The turn toward a belief in the local nature of cancer (aided by the microscope), as well as the fruits of industrialization such as chemical stains, manufactured instruments, surgical smocks, autoclaves, new power sources, and many, many others, could not by themselves surmount the negativity toward surgery that resulted from its unbearable pain and often lethal outcome. Until these obstacles could be overcome, surgery had little chance to become anything more than an occasional solution for an unusually docile, willing, and/or desperate patient.

The great advances in scientific medicine during the nineteenth century peculiarly and serendipitously benefited the diagnosis and treatment of cancer—perhaps more so than any other disease to which human beings are susceptible. These developments included revolutions in microscopy, pain management, and infection control. Each impacted, directed, and, ultimately, elevated the surgical treatment of cancer.

During the course of the nineteenth century, the discovery and evolution of anesthesia, antisepsis, and then asepsis provided remedies for the colossal problems of traditional cancer surgery that, together with statistical methods (that conjoined results into a comprehensible and disseminative whole) and experimental cancer medicine (to be addressed in the next chapter), brought the treatment of cancer into the modern era and made surgery its leading light.

ANESTHESIA, or Painless Surgery

A new encouragement is open for surgeons in the different methods of operating at present as compared with those of former days.

-George F. Shrady, 1887²⁵⁵

The excruciating pain suffered by Fanny Burney during her breast surgery in 1811 was not an isolated event. In fact, the pain of surgery affected the operator as well as the patient. One interesting “what if” of history relates to the aforementioned Charles Darwin, who, during his medical student days at Edinburgh (1825-8), decided against the profession of medicine—at

²⁵⁵Shrady, "The Curability of Cancer by Operation," 88.

least in part—because he could not tolerate the screams of patients during surgery.²⁵⁶ What if, instead of his naturalist explorations, he had attended medical school after the advent of surgical anesthesia—when the piercing cries were replaced by silence—only a few decades hence and well within his lifetime?

From Ancient Egyptian times until at least the second half of the nineteenth century, pain was an assumed and major consideration in the contemplation and execution of any surgical undertaking. In fact, for much of the last two millennia in the West, pain was such a commonplace experience of daily life that it was deemed God's Will, and therefore sacrosanct and immutable. During the Middle Ages, in particular, pain was accepted as a manifestation of God's Judgment, The Fall, and the utter sinfulness of he who suffered the pain.²⁵⁷ As such, its treatment was, at times, off limits.²⁵⁸

Nevertheless, the desire to cure pain is as old as the quest to cure disease, because, for much of mankind's history, pain and disease were conceived to be inseparable. Pain was disease.²⁵⁹ The ability to dissociate cause and effect is primarily a derivative of modern anatomical and pathophysiological knowledge, which itself benefited from the application of scientific principles to the theory and practice of medicine.

²⁵⁶David Christian, "Big History," (Videotape) *The Teaching Company* (2008), Lecture 13.

²⁵⁷As Dr. Henry Bigelow wrote in a famous monograph published shortly after the discovery of the anesthetic properties of ether and chloroform, "The moralist proclaims [pain] as the impending retribution of terrestrial sin." Henry Jacob Bigelow, *Ether and chloroform : a compendium of their history, surgical use, dangers, and discovery* (Boston: David Clapp, 1848). 4.

²⁵⁸Note the similarity between cancer as punishment for sin and pain as a manifestation of God's Will and therefore inviolable. The conjunction is pain as a common symptom of cancer. The treatment of either was at times considered heresy.

²⁵⁹The distinction between symptoms, signs, and disease is predominantly a nineteenth- and twentieth-century phenomenon. Fever—whether from plague or pox—was a disease. Pain from cancer was a disease as was pain from a boil. Hence the traditional therapeutic objective to quell the pain (the symptom) rather than the more modern attempt to treat the underlying cause of the pain (the disease).

Ancient Roots

Divinum est opus sedare dolorem.²⁶⁰

-Hippocrates

Attempts to quell pain—from cancer or any other source—surely preceded written history. Alcohol, the mandrake, and the poppy seed, to mention three examples, were all well known in ancient times to induce a soporific state.²⁶¹ The drunkenness of Noah, “the first to plant a vineyard,” and the incestuous relations of Lot’s daughters with their drunken father, bespeak of alcohol’s long-known power to induce an altered state of consciousness in sickness or in health.²⁶²

The mandrake, the common name for members of the genus *Mandragora* in the nightshades family, yields properties long thought to be magical by virtue of the anthropomorphic shape of its forked roots and its poisonous nature.²⁶³ From Rachel and Leah to *The Golden Ass* to Shakespeare and present-day Wiccan rituals, the mandrake is an earthy plant used for centuries to induce sleep and painlessness in those daring or foolhardy enough to welcome the potential in its bifurcated root.²⁶⁴ The immortal goddess Aphrodite, who had no

²⁶⁰From a Latin translation of Hippocrates’ Greek words. In English: “Divine is the work to relieve pain.”

²⁶¹In 1983, Dr. Sherwin B. Nuland published a marvelous compendium of primary sources related to the history of anesthesia. Filled with his own wonderful comments and many illustrations, it is a necessary text for anyone with an interest in the discovery and emergence of surgical anesthesia during the nineteenth century. Sherwin B. Nuland, *Origins of Anesthesia*, Special ed., The Classics of Medicine Library (Birmingham, AL: Gryphon Editions, 1983).

²⁶²Noah (Genesis 9: 20-21) and Lot (Genesis 19:32-36) are only the earliest of Adam’s descendants to have had their histories recorded to include the influence of alcohol. Interestingly, the account of Eden does not mention the fruit of the vine, perhaps foreshadowing its Janus-like dual nature in the Old and New Testaments—a drink of joy and rapture (Jewish celebrations, the Eucharist) and a potion for evil (intemperance, curse, rage).

²⁶³For a fantastically moving depiction of the root and its magical properties, see Ofelia’s use of the mandrake root as instructed by Pan in the film “Pan’s Labyrinth,” 119 min., Picturehouse (USA), 2006.

²⁶⁴Rachel and Leah (Genesis 30: 14-16); Apuleius et al., *The Works of Apuleius* (London: George Bell and Sons, 1878). 203, *The Golden Ass*, Book X.; Shakespeare, *Antony and Cleopatra* I. v.

fear of its life-threatening effects, was said to have cast herself on a bed containing *Mandragora* to repress her grief over the death of Adonis.²⁶⁵

The opium poppy, *Papaver somniferum*, is the third and potentially the most potent of the major narcoleptics that are older than recorded history.²⁶⁶ Long used for both its painkilling as well as somnolent effects, opium and its derivatives (morphine, codeine) have somewhat different properties from alcohol and the mandrake root in terms of their onset of action, duration of action, and side effects. Evidence of the long-standing knowledge of these sleep-inducing analgesics can be found in the *Materia Medica* of Dioscorides, a first-century surgeon in Nero's army and today considered the father of botanical medicine, written about 65 C.E. Aulus Cornelius Celsus also wrote extensively on the poppy and its actions during the first century C. E. and opium was further popularized during the Middle Ages with its use in the concoction of many uses, the *Spongia somnifera*.²⁶⁷

The ancient origin of these agents makes clear that analgesia and anesthesia were not new to the nineteenth century.²⁶⁸ The difficulty with these early analgesics was that dosing was hard

²⁶⁵Carroll Woolsey Allen, *Local and Regional Anesthesia*, Second ed. (Philadelphia and London: W. B. Saunders Company, 1920). 18.

²⁶⁶Archeologists have unearthed images of opium poppies from the remains of ancient Samaria, over six thousand years old, as well as around the lakes of modern-day Switzerland. See http://en.wikipedia.org/wiki/Opium_poppy#History accessed March 26, 2008 and Owen H. Wangensteen and Sarah D. Wangensteen, *The Rise of Surgery: From Empiric Craft to Scientific Discipline* (Minneapolis: University of Minnesota Press, 1978). 291., respectively.

A narcotic (Gk., 'narke'), by the way, is that which induces stupor. Thus, a narcoleptic is a sleep-inducing agent. The distinction among these terms is often lost in common parlance.

²⁶⁷Nicholas Salernitanus (Nicholas of Salerno), who flourished during the twelfth century, elaborated on the uses of the *Spongia somnifera* for various surgical and non-surgical purposes. The *Spongia* was a sponge soaked in the juice of the mandrake, poppy, mulberry, and lettuce plus other ingredients. It could then be dried, transported without losing its potency, and then reconstituted when soaked. Nuland, *Doctors: 267, 70*.

²⁶⁸Many other forms of anesthesia, even non-medicinals, were known long before the nineteenth century. The induction of sleep—or fainting—via significant loss of blood was one very interesting form. Wangensteen and Wangensteen, *The Rise of Surgery*: 287-88. Perhaps this “relaxing” feature of venesection was one of the reasons for its popularity among the regular physicians of the eighteenth and early-mid nineteenth centuries. Larrey,

to quantify, so their effects tended to be unpredictable, of variable duration, and, sometimes, dangerous. Further, the purification of the active agents of these plant-derived agents and their ability to induce a controlled state of painlessness during surgery based upon principles of chemistry and physiology are products of the nineteenth century.²⁶⁹ That state of scientific refinement, beginning in the nineteenth century, helped surgery become the treatment of choice for cancer by the last years of the century.

Analgesia and Anesthesia

Analgesia and anesthesia are not the same. Although both imply a loss of sensation to painful stimuli, the difference between them lies in the ability to ‘perceive.’²⁷⁰ Patients under the influence of analgesics sense pain remotely, if at all, but they are not unconscious. Patients under anesthesia have no perception of pain and may be unconscious. The term ‘general anesthesia’ specifies unconsciousness. Neither phenomenon should induce a loss of vital functions such as the cessation of respiration or heartbeat.

A poem by the 4th-century Roman Christian poet, Prudentius, entitled “Before Sleep,” beautifully captures the feeling produced by analgesics:

The still Lethean waters
Now steal through every vein,
And men no more remember
The meaning of their pain.²⁷¹

surgeon to Napoleon and Fanny Burney, learned the use of blood loss and even shock on the battlefield as a powerful agent of anesthesia.

²⁶⁹In 1806, for example, Sertürner reported the first isolation of morphine from opium. John Walton, Paul B. Beeson, and Ronald Bodley Scott, eds., *The Oxford Companion to Medicine*, 2 vols., vol. 2 (Oxford: Oxford University Press, 1986; reprint, Gryphon Editions, Inc., 1988), 1299.

²⁷⁰The root of analgesia is ‘algos,’ meaning pain, so that the etymology of an-algesia is ‘without pain.’ On the other hand, the root of anesthesia is ‘aisthanesthai,’ meaning ‘to perceive,’ so anesthesia relates to an absence of perception—unconsciousness. <http://www.merriam-webster.com/dictionary> accessed March 31, 2008.

²⁷¹Quoted by Wangensteen and Wangensteen, *The Rise of Surgery*: 291.

Nonetheless, there is overlap between the two concepts. Although the alcohol, mandrake, and opium of the ancients are, strictly speaking, analgesics in that they can reduce the sensation of pain without loss of consciousness, larger doses of these agents may render a patient unconscious and therefore fit the definition of an anesthetic. Indeed, one of the great problems that plagued administrators of anesthesia during the nineteenth century was the determination of the proper dose of anesthetic that would render a surgical patient unconscious and insensitive to pain without suppressing their respirations—and inducing death.

This paper has already discussed several analgesics, including the topical cocaine used to treat General Grant during the final months of his life. This part of the chapter on the treatment of cancer will highlight anesthesia.

Anesthesia – The Word, Its Meaning, and Its History

Oliver Wendell Holmes, Sr. is often credited with creating the neologism ‘anesthesia,’ but this is not true.²⁷² The word was in use long before he suggested it to William Thomas Green Morton (1819-1868) in 1846. Dioscorides was probably the first to use the term in reference to surgery.²⁷³ Johann Bernhard Quistorp (1692-1761) used the term in his doctoral dissertation in 1718.²⁷⁴ Nathan Bailey further defined the word in 1721.²⁷⁵

²⁷²For example, the Wikipedia entry for “anesthesia” claims that Oliver Wendell Holmes, Sr. “coined” the word “in 1846.” See <http://en.wikipedia.org/wiki/Anesthesia> accessed March 31, 2008.

²⁷³Essence of mandrake, wrote Dioscorides in *Materia Medica*, is “given to those who are going to be cut or burnt (cauterized) and wish to have anesthesia.” Helen MD Askitopoulou, PhD, DA, FRCA, Ioanna A. Ramoutsaki, PhD, and Eleni Konsolaki, DMD, "Analgesia and Anesthesia: Etymology and Literary History of Related Greek Words," *Anesthesia & Analgesia* 91, no. 2 (2000): 489.

²⁷⁴Ray J Defalque and Amos J Wright, "Quistorp and "anaesthesia" in 1718," *Bulletin of Anesthesia History* 24, no. 1 (2006). Defalque and Wright give a detailed history of the word before Holmes, as well as an English translation of Quistorp’s dissertation. See www.anes.uab.edu/aneshist/quistorpmain.doc April 8, 2008.

²⁷⁵

http://dictionary.oed.com.arugula.cc.columbia.edu:2048/cgi/entry/50007802?single=1&query_type=word&queryword=anaesthesia&first=1&max_to_show=10 accessed March 31, 2008.

Nevertheless, Holmes is justly recognized for his connection to the word—he never claimed that he invented it—because he did more than anyone to publicize it. In his letter to Morton, the dentist who demonstrated use of such an agent on a patient undergoing surgery, Holmes noted that “The state [induced by the drug] should, I think, be called ‘Anæsthesia’. This signifies insensibility....The adjective will be ‘Anæsthetic’. Thus we might say the state of Anæsthesia, or the anæsthetic state.”²⁷⁶ Note that Holmes used anesthesia (the modern spelling) to refer to a state of being rather than the drug that produced it. Nonetheless, physicians and others used the word almost immediately to refer to the agent that induced the insensible state as well as the state itself.

The Origins of Surgical Anesthesia

Medicine’s greatest single gift to suffering humanity.

-Sir William Osler²⁷⁷

WHAT surgeon is there, who has not felt, while witnessing the distress of long painful operations, a sinking of the heart, to which no habit could render him insensible! What surgeon has not at these times been inspired with a wish, to find some means of lessening the sufferings he was obliged to inflict !

-John C. Warren, M.D.²⁷⁸

Surgical anesthesia should be distinguished from other types of anesthesia and is thus a consideration unto itself. Surgical anesthesia is used “for the purpose of permitting performance of an operative procedure.”²⁷⁹ As such, it may be general, regional, or local anesthesia. Anesthetics may also be used for diagnostic (e.g., breast biopsy) and non-surgical therapeutic procedures (e.g., many gastrointestinal endoscopies, like colonoscopy with polypectomy). In

²⁷⁶Dr. Holmes made these statements in a letter to William Morton dated November 21, 1846.

²⁷⁷Walton, Beeson, and Scott, *Oxford Companion to Medicine*, 997.

²⁷⁸John Collins Warren, *Etherization; with surgical remarks* (Boston: William D. Ticknor, 1848). 87.

²⁷⁹*Stedman’s Electronic Medical Dictionary*, v. 5.0, (Lippincott, Williams & Wilkins, 2000), “surgical anesthesia.”

this section, I will focus on the history of surgical anesthesia as it applies to the treatment of cancer.

The myth of the history of surgical anesthesia is that Morton discovered that ether, a common chemical, eased his dental patients' distress during procedures; that Morton suggested to the famous Dr. John Collins Warren of the fledgling Massachusetts General Hospital²⁸⁰ (MGH) that his secret formula, when inhaled by the patient, would render him senseless and pain free during an operation; and that when, on October 16, 1846 ("Ether Day" forever after), Morton administered his mystery drug to Warren's surgical patient, it was such a success—"Gentlemen," cried Warren, "this is no humbug"—that a miracle happened there and the world would never be the same.

In truth, surgical anesthetics were born in the seeds, flowers, and roots of the field. So many medicines have originated in nature that it is difficult to quantify their contributions to nineteenth- or even twenty-first century medicine. Roots, stems, flowers, and petals have served medicine for millennia.²⁸¹ Dioscorides' *Materia Medica* is just one example of this record—albeit one of the best—of a long tradition explicating the healing powers of select ingredients from the bounty of nature.

During the nineteenth century, to a large extent, these gifts were refined in the chemistry lab; unwittingly savored for other purposes in early nineteenth-century salons and private parties; and attained their greater good in the achievement of painless surgery in the operative suite. Although the exact origins of chemicals termed anesthetics may be debated, what is not disputed

²⁸⁰Founded 1811.

²⁸¹Why plant parts should benefit the treatment of human disease and the maintenance of health is a fascinating question in itself. The theory of evolution yields rewarding answers, in part because the relationship between Man and his environment (including roots, stems, flowers, and petals) is more entwined than presently thought of.

is that surgical anesthesia is one of the greatest (some say, *the* greatest²⁸²) contributions by Americans to humanity.²⁸³

Chemistry and Anesthesia

Chemistry has been a force in the treatment of cancer for centuries, but they became much more closely intertwined in the early nineteenth century. To meet the requirements of the Pure Food and Drug Act (United States, 1906), chemists purified and synthesized the medicinal products of nature into more standardized and refined products. In addition, the ability of chemists to combine different compounds and observe resultant new compounds and their properties lies at the foundation of pharmacology.

Ether

In the history of the development of anesthetics for the surgical treatment of cancer and other diseases, Valerius Cordus (1515-1554), a German botanist and physician, provided a major step forward in 1540 when he described the synthesis of “sweet oil of vitriol”—(diethyl) ether—from the mixture of (ethyl) alcohol with sulfuric acid (vitriol). Cordus was probably not the first to recognize ether, which is easily synthesized from the two common compounds, is a volatile liquid,²⁸⁴ and has a distinctive smell, but his description of the chemical process for its synthesis forever linked his name to the origins of surgical anesthesia in general and ether in particular.²⁸⁵

²⁸²Nuland, *Anesthesia*: 39.

²⁸³Even in this seemingly ironclad statement, controversy lurks. Japanese historians claim that Seishu Hanaoka (1760-1835) developed Tsusensan, an active component of which were anesthetizing anticholinergic alkaloids (especially atropine and scopolamine), long before Long, Wells, Jackson, and Morton came on the scene. See <http://www.general-anaesthesia.com/images/seishu-hanaoka.html> and <http://www.general-anaesthesia.com/images/chosen-asagao.html> accessed May 25, 2008.

For every discoverer, there is often an earlier originator. Definitions become critical, as this study of the beginnings of surgical anesthesia will illustrate.

²⁸⁴Volatile liquids vaporize at relatively low temperatures, so that ether—although predominately liquid at room temperature—could be sniffed or breathed in from the bottle in which it was contained.

²⁸⁵Chauncey D. Leake, "Valerius Cordus and the Discovery of Ether," *Isis* 7, no. 1 (1925): 22, 23.

Nitrous Oxide

In 1772, Joseph Priestley (1733-1804), a British theologian and natural philosopher, described the synthesis of the second foundational agent in the history of anesthesia—nitrous oxide. He used a glass apparatus filled with mercury and heated by a “burning lens” (magnifying lens that focused the sun’s rays on an object²⁸⁶) to produce nitrous oxide (N₂O), which he described in his seminal work, *Experiments and Observations on Different Kinds of Air* (1774-1786).²⁸⁷ Of greatest import was Priestley’s conclusion that air, rather than being an element of nature, was comprised of several different elements. This insight opened minds to the radical ideas that (1) the components of air deserved investigation in their own right, and (2) that other presumptive a-tomic elements of nature might also be divisible, thereby laying the theoretical foundations of nineteenth- and twentieth-century science. Nitrogen and oxygen, two major constituents of air, for example, constituted nitrous oxide. One of Priestley’s intellectual descendants later commented of him that “No single person ever discovered so many new and curious substances.”²⁸⁸ That commentator was the prodigy Humphry Davy (1778-1829).

In 1800, at the tender age of twenty-two, Davy, a pioneering chemist in his own right, penned a seminal work on the chemistry of nitrous oxide and foreshadowed its efficacy as a surgical anesthetic. In his *Researches, Chemical and Philosophical*, Davy discovered a method to purify the gas from the “oxide of azote.”²⁸⁹ Shortly thereafter, he inhaled “sixteen quarts of it

²⁸⁶Burning lenses are also known as “burning glasses.” See Chapter 6.

²⁸⁷Priestley synthesized nitrous oxide two years before his discovery of oxygen (August 1, 1774), but after his finding that plants inspire carbon dioxide and expire oxygen. See <http://www.historyguide.org/intellect/priestley.html> accessed April 19, 2008.

²⁸⁸John Davy, *Memoirs of the life of Sir Humphry Davy, bart, LL. D., F.R.S., foreign associate of the Institute of France, &c* (London,: Longman, Rees, Orme, Brown, Green & Longman, 1836). 527.

²⁸⁹Humphry Davy, *Researches, chemical and philosophical*

for nearly seven minutes.”²⁹⁰ The result was that “it absolutely intoxicated me. Pure oxygen gas produced no alteration in my pulse...; whereas this gas raised my pulse upwards of twenty strokes, made me dance about the laboratory as a madman, and has kept my spirits in a glow ever since.”²⁹¹ Appropriately, he named it “laughing gas.”

It was but a short leap for the brilliant Davy to conclude that nitrous oxide could quell the pain of surgery. In his own words, he wrote that “As nitrous oxide in its extensive operation appears capable of destroying pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place.”²⁹² Although Davy seems never to have used nitrous oxide as a surgical anesthetic, he was clearly enamored of its properties and continued to inhale it until he breathed his last.²⁹³

In 1815, Michael Faraday (1791-1867), Davy’s most famous pupil and one of the most renowned scientists of the nineteenth century for his work in chemistry and electromagnetism, discovered that ether induced many of the same giddy effects as nitrous oxide. But ether had a significant advantage over nitrous oxide in that it was much cheaper and easier to produce. The

chiefly concerning nitrous oxide, or dephlogisticated nitrous air, and its respiration. By Humphry Davy, (London: printed for J. Johnson. By Biggs and Cottle, Bristol, 1800), <http://www.columbia.edu/cgi-bin/cul/resolve?clio5208766>

http://books.google.com/books?hl=en&id=jhUAAAAAQAAJ&dq=davy+researches+chemical+and+philosophical&printsec=frontcover&source=web&ots=KjKktyIfzQ&sig=weA5R7f_e0-ruFM8ECYsc34izB8. 141-42; Davy, *Memoirs of the life of Sir Humphry Davy, bart, LL. D., F.R.S., foreign associate of the Institute of France*, &c: 55-56.

²⁹⁰*Memoirs of the life of Sir Humphry Davy, bart, LL. D., F.R.S., foreign associate of the Institute of France*, &c: 56.

²⁹¹*Ibid.*

²⁹²John Walton, Paul B. Beeson, and Ronald Bodley Scott, eds., *The Oxford Companion to Medicine*, 2 vols., vol. 1 (Oxford: Oxford University Press, 1986; reprint, Gryphon Editions, Inc., 1988), 45. Based upon his observation quoted above that nitrous oxide hastened the pulse, Davy was concerned that its use during a bloody operation would, because of the hastened pulse, lead to even more blood loss.

²⁹³Many presume that Sir Davy’s death at an early age had something to do with the numerous gases, including nitrous oxide, that he took into his lungs over the course of his lifetime. See, for example, <http://www.who2.com/humphrydavy.html> accessed April 23, 2008. True or not, it’s the stuff of legend.

synthesis of nitrous oxide required the cumbersome equipment and scarce chemicals utilized by Davy. Ether, unlike nitrous oxide, was readily available.²⁹⁴

Chloroform

The molecule that would become the third major anesthetic of the nineteenth century, chronologically, was chloroform. Chloroform, like ether and nitrous oxide, is a simple molecule. It consists of only five atoms—one carbon, one hydrogen, and three chlorides—written CHCl_3 in chemical shorthand. Like ether, it was produced by mixing two relatively common molecules (alcohol and chlorine bleach) to obtain a third with different properties, as in the phenomenon known as emergence.²⁹⁵ Samuel Guthrie (1742-1848), an American physician (rare for the time in the annals of historical firsts), received credit for the discovery of chloroform as a result of his 1831 paper.²⁹⁶ Guthrie performed the above-noted haloform reaction to produce chloroform only a few months before the Frenchman Eugène Soubeiran (1797-1859) and the German Justus von Liebig (1803-73).²⁹⁷ As bacteriologists would discover many pathogenic bacteria in the 1880s after Pasteur and Koch gained acceptance for germs as causative agents in the genesis of disease, so chemists discovered new molecules—like chloroform—at a frenetic pace during the 1820s and 1830s.²⁹⁸ Jean-Baptiste Dumas (1800-1884), a Frenchman, named and chemically

²⁹⁴N. A. Bergman, "Michael Faraday and his contribution to anesthesia," *Anesthesiology* 77, no. 4 (1992).

²⁹⁵Emergence, which describes the appearance of new properties after the combination of individual components that lack those properties (for example, the water molecule $[\text{H}_2\text{O}]$ from a combination of hydrogen $[\text{H}]$ and oxygen $[\text{O}]$ atoms), was a key concept for the development of chemistry and medicine in the nineteenth century and beyond.

²⁹⁶S. Guthrie, "New Mode of Preparing a Spiritous Solution of Chloric Ether," *American Journal of Science and Arts* 21, no. 1 (1831).

²⁹⁷J Wawersik, "History of chloroform anesthesia," *Allerg Immunol (Paris)* 30, no. 5 (1998).

²⁹⁸The process of scientific evolution, like biological evolution, often begins with a new finding—like the composition of chemical molecules or the pathogenicity of bacteria—followed by a burst of new explorations, discoveries, and innovations, in many new directions over a short period of time.

characterized the “chloroforme” molecule in 1834 as part of his much larger body of work on the haloform series.²⁹⁹

Through an eerie confluence of events, Dr. Guthrie had the opportunity to conceptualize a connection between his new compound and sleep induction—perhaps even surgical anesthesia—more than a decade before Crawford Long’s first experience with ether in 1842. One day, after working to decipher the properties of his new chemical, Guthrie left a sample in one of his rooms. His adventurous eight-year-old daughter happened by and, being by dint of age and inclination an explorer (like her father), decided to taste some of the very enticing stuff. She quickly fell asleep and slept—and slept. Her father could not awaken her despite vigorous attempts. It is likely that the young daughter had no primary recollection of the event, but Dr. Guthrie did.³⁰⁰ Unfortunately, as in the case of ether, the scientist failed to make the conceptual leap from agent of narcosis to anesthetic for surgery. Good luck is preparedness meeting opportunity, but chance, as Pasteur said, favors the prepared mind, and Guthrie, unlike Pasteur a generation later, was not thinking along these lines.³⁰¹ Thus, as in the past, the potential of this

²⁹⁹Others haloforms include iodoform, which Dumas introduced for the treatment of goiter, and bromoform. Through these experiments, Dumas found that halogens like chlorine, bromine, and iodine could substitute for hydrogen atoms in chemical compounds. (In fact, caustic bromine was used as a wound disinfectant during the American Civil War.) Dumas’ findings contributed to Dmitri Mendeleev’s 1869 construction of the Periodic Table of the elements. In addition, Dumas’ research in halogen substitution played a significant role in the development of modern inhaled anesthetics. Theodore A. Alston, "Nitrous or nitric? Same difference. Molecular formulas in the 1840s," *Journal of Clinical Anesthesia* 19, no. 2 (2007): 159.

³⁰⁰R. W. Patterson, “The First Human Chloroformization,” in R. S. Atkinson and T. B. Boulton, *The History of anaesthesia*, International congress and symposium series ; (London ; New York Carnforth, Lancs., U.K. ; Park Ridge, N.J., U.S.A.: Royal Society of Medicine Services ; Parthenon Pub. Group, 1989). as cited by Meyer Friedman and Gerald W. Friedland, *Medicine's 10 greatest discoveries* (New Haven: Yale University Press, 1998). 109.

³⁰¹The “good luck” aphorism is my paraphrase by way of Ovid (43 BCE-17 CE), *Metamorphoses* (completed 8 CE). The “chance” quotation is credited to Louis Pasteur (1822-1895).

chemical compound to be used for the induction of anesthesia during surgery went unrecognized for years thereafter.³⁰²

Ironically, this American discovery, chloroform, would be used as an anesthetic much more in the United Kingdom and Europe than in the States, primarily, as we shall see, for historical reasons. Chloroform, like its congener ether, is sweet to the smell and easy to synthesize, but it is more potent than nitrous oxide and much less volatile than ether. Unhappily, it is also more deadly in that there is much less margin for error (lower LD₅₀) in the dosing of chloroform than ether for surgical anesthesia.³⁰³

Suspended Animation

Despite the advent of ether, nitrous oxide, and chloroform by the early nineteenth century, the use of these agents as surgical anesthetics required something more than a knowledge of chemistry—viz., the application of these agents to the treatment of pain in general and surgical pain in particular. Davy's prescience led him to make this connection, at least theoretically, based upon his own experiences with nitrous oxide in the early nineteenth century, but it was the English physician Henry Hill Hickman (1800-1830) who first described the stupor-inducing effects of a chemical compound on an organism.

Dr. Hickman was a surgeon by training and an experimenter by nature. Around 1823, he began to use "carbon acid gas" (carbon dioxide) or asphyxiation (akin to suffocation, which produces the same effect) to render animals impervious to pain. He then performed all manner of incisions, including amputations, to assess their responses. Encountering little or no reaction

³⁰²<http://www.general-anaesthesia.com/images/chloroform.htm> accessed April 27, 2008.

³⁰³Medically, I am alluding to the Therapeutic Index or Therapeutic Ratio of chloroform v. ether. These measurements divide the lethal dose of a chemical for fifty percent of the population (LD₅₀) by its minimal effective dose for the same population (ED₅₀). The closer the lethal dose to the minimal effective dose, the closer the ratio is to 1.0 and the more dangerous the drug. Ether's therapeutic ratio is about 2.0. Chloroform's is much less.

from the puppies and mice on which he operated, he believed he had found the key to the prevention of surgical pain. He called it “suspended animation.”³⁰⁴ In 1824, he wrote up his findings and sent them to a Fellow of the Royal Society of London, hoping for just recognition for his discovery from Sir Humphry Davy and other members of the Society. Instead, he received no response until he read a scathing attack on his “sapient puff” in the very popular British medical journal, *The Lancet*, two years later.³⁰⁵ Hickman was distraught but unbowed. He continued to believe in his method for achieving painless surgery and turned for support, following his rejection by the English establishment, to Charles X of France in 1828.

In the end, his work was no more accepted in France than in England, but there was at least one French supporter who believed in Hickman’s findings. Dr. Dominique-Jean Larrey, surgeon to Napoleon and Fanny Burney, had noted that wounded soldiers felt much less pain during surgery performed in frozen fields than in warmer climes and astutely connected his observation with Hickman’s state of suspended animation.³⁰⁶ After Hickman’s efforts to convince the French Royal Society of the value of his research floundered, Larrey offered to

³⁰⁴Roger Maltby and Royal Society of Medicine Britain, *Notable Names in Anaesthesia* (RSM Press, 2002). 91.

³⁰⁵Antiquack, “Surgical Humbug,” *The Lancet* 5, no. 127 (1826): 647. The article, signed “Antiquack,” reads, in part: “Now giving this learned Theban full credit for his charitable intentions towards that unfortunate portion of his fellow creatures who may be doomed to come under his care, or to solicit his advice in any surgical case, can he for a moment suppose that any medical man of sense and judgment will be so far led away by a proposal so utterly at variance with all he has ever heard, saw, or read, of the deleterious effects of respiring the fixed air, even for a short time, as to believe, for a moment, that this letter was published with any intention of benefiting mankind.”

³⁰⁶Charles T. Jackson, *A manual of etherization : containing directions for the employment of ether, chloroform, and other anaesthetic agents, by inhalation, in surgical operations [...] / by Chas. T. Jackson* (Boston: J. B. Mansfield, 1861). 8-9. Charles Thomas Jackson, an important figure in the history of surgical anesthesia, wrote comprehensively on “former experiments” with painkillers in this 1861 monograph.

observe Hickman's work himself. The demonstration never occurred.³⁰⁷ Unfortunately, Hickman died soon thereafter and his efforts went unrecognized for many decades.³⁰⁸

From Party Drugs to Surgical Anesthetics

Neither the prescience of Davy nor the discoveries of Faraday nor Hickman's concept of suspended animation led directly to the use of inhaled gases for the induction of surgical anesthesia. Instead, alcohol, leading to a state of inebriation, remained the surgical anesthetic of choice for the early decades of the nineteenth century. For those who shunned the disorienting effects of alcohol, there was always mesmerism.³⁰⁹

Nevertheless, in a twist of fate reminiscent of the history of the microscope, these potentially medicine-altering compounds became the "recreational drugs" of party-goers for nearly two generations after the discovery of their chemical properties, for their ability to induce various levels of intoxication was evident even if their potential medicinal uses were not. Eager participants, upon learning of the happy effects of ether, inhaled it at "ether jags" and "ether frolics."³¹⁰ Others sniffed nitrous oxide at "laughing gas side shows."³¹¹ Still others inhaled chloroform during "chloroform binges."³¹² Revelers, including medical students, sat around

³⁰⁷Maltby and Britain, *Notable Names in Anaesthesia*: 93.

³⁰⁸Victor Robinson, *Victory over pain, a history of anesthesia* (New York,: Schuman, 1946). The Wellcome Historical Medical Museum honored Hickman posthumously on the centenary of his death in 1930. Ironically, the Royal Society of Medicine was chosen to award the Henry Hill Hickman medal and has bestowed it for research in anesthesia every three years since 1935.

³⁰⁹Short-lived "anesthetics" like mesmerism ("animal magnetism"), named after Franz Mesmer (1734-1815), were especially used to aid women through childbirth. Mesmerism was also attempted to calm patients for surgical procedures during its heyday in the 1830s.

³¹⁰Haagensen and Lloyd, *A Hundred Years of Medicine*: 229.

³¹¹Williams, *The Age of Miracles*: 45.

³¹²<http://www.general-anaesthesia.com/images/chloroform.htm>, accessed July 1, 2008.

inhaling and sniffing these chemicals with no thought of tomorrow. The effects could be riotous.³¹³

Strange and devious are the paths to discovery. Not only does the road to anesthesia now turn from Europe to the United States, but the idea of surgical anesthesia becomes an American endeavor and a uniquely American discovery. Along the way, however, were many missed opportunities. In 1836, for example, Morrill Wyman (1812-1903), a medical student at Harvard who went on to an illustrious professional career, participated in ether frolics at the Massachusetts General Hospital in Boston. Based upon his personal experiences with ether, Wyman routinely used ether to put his laboratory rats to sleep. Neither he nor his colleagues, however, ever thought of using it as a surgical anesthetic for humans. Years later, he called this “a great oversight.”³¹⁴

Nevertheless, one of the merry-makers at another American institution who participated in both laughing gas parties and ether frolics did play a critical role in the history of surgical anesthesia. His name was Crawford Long and he was a Southerner who did much of his medical training in Yankee territory.

Crawford Williamson Long, M.D.

The histories of cancer and surgical anesthesia became irrevocably linked through the actions of Dr. Crawford W. Long (1815-1878) on March 30, 1842, when he purposefully used “sulphuric ether” to induce a state of anesthesia in a patient, James Venable, from whom he

³¹³See the cartoon at <http://www.general-anaesthesia.com/images/ether-frolics.html>, accessed April 23, 2008.

³¹⁴Wyman wrote this in 1877. Wangensteen and Wangensteen, *The Rise of Surgery*: 277-8. Wyman would later be intimately involved in the Ether Wars as to who should receive credit for the discovery of surgical anesthesia. Richard J. Wolfe, *Tarnished idol : William Thomas Green Morton and the introduction of surgical anesthesia : a chronicle of the ether controversy* (San Francisco, Calif.: Norman Pub., 2001). 270.

painlessly removed a half-inch neck tumor.³¹⁵ Indeed, so painless was the operation that Venable refused to believe that surgery had been performed. Only when Long actually displayed the excised tumor to Venable did he believe it!³¹⁶ Thus, the first purposely induced state of anesthesia during surgery was for the removal of a tumor.

Long was an inquiring student, a conscientious practitioner, and, much to his detriment, a belated author. He trained in a number of institutions, searching for a rigorous medical education that was so elusive in the United States at the time.³¹⁷ During his student days, like many others, he participated in the laughing gas parties and ether frolics that enjoyed great popularity at the time. Also like others before him, Long noted that the sniffers and inhalers at these get-togethers became oblivious to all manner of bruises, falls, and injuries to which they were disproportionately vulnerable in their altered state of mind.³¹⁸ Unlike others, however, he conceived that these same agents could be applied to prevent the pain of surgery.

In fact, Long's use of ether for surgery followed directly from its recreational use.³¹⁹ According to Long's own testimony, late one night during the winter of 1841-2, a group of boys in Long's village of Jefferson, Georgia, decided that they wanted to inhale nitrous oxide for its

³¹⁵A second neck tumor was similarly excised from the same patient a few months later on June 6, 1842. <http://www.general-anaesthesia.com/images/crawford-long.html> accessed April 28, 2008.

³¹⁶Crawford W. Long, "An account of the first use of Sulphuric Ether by Inhalation as an Anaesthetic in Surgical Operations," *Southern Medical and Surgical Journal* 5, no. 12 (1849): 708, 09. The exact pathology of the lesion that Dr. Long removed from the neck of young Venable is unknown. I have never seen a pathology report and it is unlikely that Long, in 1842, would have dreamed of submitting an excised tumor for pathological examination. Some authors termed the lesion a cyst, but most use the term tumor in its general sense of swollen mass.

³¹⁷His medical education began with an apprenticeship under Dr. George R. Grant in Georgia, continued at Transylvania University in Kentucky, continued at the University of Pennsylvania (from which he graduated in 1839), and ended with post-graduate training thereafter during a year and a half in New York. Nuland, *Anesthesia*: 41.

³¹⁸George A. Degenshein, "This Golden Age of Surgery," in *Surgical Clinics of North America* (1978), 932.

³¹⁹I derived the following account directly from Long's personal recollections of his first use of ether in the early 1840s. Long, "First Use of Sulphuric Ether."

exhilarating effects.³²⁰ They approached Dr. Long to prepare the gas for them, but Long did not have the cumbersome equipment to do so and suggested, based upon his knowledge of chemistry and personal experiences, that the more-easily-obtained ether would produce a similar effect. One of the boys agreed with him, claiming to have had a good time with ether previously. In short order, Dr. Long procured some ether and passed it around. “They were so much pleased,” he wrote, “that they afterwards inhaled it frequently, and induced others to do so, and its inhalation soon became quite fashionable in this county.”³²¹

The ensuing popularity of ether in his county played a critical role in Long’s recognition of its potential as a surgical anesthetic. Long noticed that both he and his acquaintances, “while etherized, received falls and blows, which I believed were sufficient to produce pain on a person not in a state of anæsthesia, and on questioning them, they uniformly assured me that they did not feel the least pain from these accidents.”³²² During this time, he saw young Venable, another ether aficionado, in consultation for neck tumors. James wanted the tumors removed, but, despite numerous visits, always postponed surgery “from dread of pain.”³²³ At length, Long, all of twenty-six years old, reasoned that, given Venable’s recreational response to inhaled ether and Long’s knowledge of its pain-nullifying effects, “while under the influence of the vapour of ether...the operations might be performed without pain, and proposed operating on him while

³²⁰Jefferson, Georgia is about sixty miles northeast of Atlanta and about twenty miles north-northwest of Athens, Georgia, the home of the University of Georgia. Jefferson County, Georgia, with which Long’s Jefferson, GA is sometimes confused, is more than one hundred twenty miles southeast of Atlanta.

³²¹Long, "First Use of Sulphuric Ether," 707.

³²²Ibid.

³²³Ibid.

under its influence.”³²⁴ The operation was performed that evening, March 30, 1842, in front of several witnesses. It was a great success.

In the years that followed, Crawford Long utilized ether to induce anesthesia for obstetrical and dental as well as surgical procedures.³²⁵ At times, he would utilize a scientific approach to surgical anesthesia through his “controlled experiments.” Therein he would administer ether to a patient for one operation but not for a similar operation on the same patient. Not surprisingly, during the second operation the patient “suffered severely.”³²⁶

Given his measured, cautious, and non-promoting mien, however, he hesitated for years before publishing a narrative of his original work with ether. Indeed, Long delayed the publication of his 1842 discovery of ether as a surgical anesthetic until 1849, more than seven years after the fact and more than three years after it had been “discovered” up North in 1846.³²⁷ (By contrast, the Massachusetts General Hospital surgeons published their first publication on surgical anesthesia the very next day after their first use of ether!) Even then, Crawford Long did so only after others sought the credit—and the prize money—for the discovery that he deemed rightly belonged to him.³²⁸

Up North

³²⁴Ibid.

³²⁵In fact, Long delivered his wife of their second child with the aid of ether anesthesia on December 27, 1845, more than a year before James Y. Simpson introduced “obstetrical anesthesia” to the world in Great Britain.

Ironically, Dr. Long died from a massive stroke at the age of 62 shortly after administering ether to a woman in labor. Reportedly, his dying words were “Care for the mother and child first.” See <http://www.general-anaesthesia.com/images/crawford-long.html> accessed April 28, 2008.

The anniversary of Dr. Long’s first administration of anesthesia, March 30, was selected as the date on which physicians, first in Barrow County, Georgia, and ultimately in the entire United States, were to be honored with Doctors’ Day.

³²⁶<http://www.sma.org.sg/smj/4611/4611ms1.pdf> accessed May 11, 2008.

³²⁷Long, “First Use of Sulphuric Ether.”

³²⁸Ibid., 706.

The quest to achieve painless surgery was even more convoluted in the North than in the South. Certainly there were many more laughing gas parties and ether jags in Boston than in Jefferson. Nevertheless, the conceptual and practical leap from nitrous oxide and sulphuric ether as party drugs to surgical anesthetics took longer and involved many more twists and turns in Massachusetts than in Georgia.

It must also be noted that it was not by chance alone that many of the inaugural uses of surgical anesthesia were performed on patients with tumors, for these patients often required a depth and duration of anesthesia that alcohol and other relatively mild soporifics (sleep-inducing drugs) could not provide. Having stated the importance of anesthetics to cancer surgery, however, in the North it was initially through the mouth rather than the skin (and the treatment of cancer patients) that anesthesia made its way into surgery.

New England

The deep intellectual roots and scientific enthusiasm of New England made it ripe for the invention of surgical anesthesia. In all the United States, it had many of the best-trained scientists—including chemists and biologists—physicians, and apothecaries. The Northeast also served as home to some of the oldest and most renowned scientific and medical institutions of the day. In Boston, Hartford, and environs, for example, the focus of the New England development of surgical anesthesia, the Harvard Medical School was founded in 1782 and the Massachusetts General Hospital in 1811. By the 1840s, both were well established. Despite all these advantages, however, the spark to achieve the conceptual link between chemistry, human biology, and surgical anesthesia was still missing when Dr. Long used ether to remove a tumor from the neck of James Venable.

This was not for a lack of colorful characters. The New England contenders in the race to “discover” surgical anesthesia were Horace Wells (1815-1848), Charles T. Jackson (1805-1880), and William T. G. Morton (1819-1868). Gardner Colton (1814-1898) had an opening role in the drama. Renowned surgeon John Collins Warren (1778-1856) of the Harvard Medical School and a founder of the Massachusetts General Hospital and junior surgeon Henry Bigelow (1818-1890) also played critical parts, but, like Colton, they laid no claim to the title of “discoverer.”

Indeed, the path to surgical anesthesia in New England was a drama from which any student of life could profit—be he an M.B.A. candidate studying models of entrepreneurship or a casual theatergoer searching for entertainment—for it encompassed a panoply of personalities, an octave of emotions, a quest for self-aggrandizement, and a determination to be the first to accomplish what no one yet had seemed to achieve in the history of mankind, viz., painless surgery. Their biographies, foibles, and contributions to the development of surgical anesthesia during its early years have been documented in countless books and articles.³²⁹ My purpose, however, is to integrate these personalities (so compelling and important in the race to claim the prize!) and the culture of their time into the interface between chemistry, surgery, and the treatment of cancer.

Dentistry

Surgical anesthesia in New England began not with the excision of tumors or the amputation of limbs, but with dentistry. It was there in the treatment of rotten teeth that the paths of chemistry, recreational drug use, and surgery first converged.

³²⁹Two relatively recent in-depth analyses are Julie M. Fenster, *Ether Day: The Strange Tale of America's Greatest Medical Discovery and the Haunted Men Who Made It* (New York: HarperCollins Publishers, 2001; repr., 2002); Wolfe, *Tarnished idol : William Thomas Green Morton and the introduction of surgical anesthesia : a chronicle of the ether controversy* (2001). A slightly older but landmark contribution to the field is Martin S. Pernick, *A calculus of suffering : pain, professionalism, and anesthesia in nineteenth-century America* (New York: Columbia University Press, 1985).. Sherwin B. Nuland published an excellent source book with background chapters. Nuland, *Anesthesia*.

Dentistry was an ideal branch of medicine for the beginnings of surgical anesthesia.³³⁰ Today, anyone who has ever had his teeth drilled without the benefit of anesthesia (fortunately, now a rare event—at least in the United States!) is fully aware of the severe, lancinating, focal-to-radiating pain that the treatment of decayed teeth entails. Such pain in the usually-fully-alert (and primed) patient is often of a crescendo nature, peaking rapidly and subsiding gradually. Painkillers for this type of pain pattern are a gift from Heaven because of their acute, limited nature and therefore lack of concern for the long-term side effects caused by chronically-administered drugs. Such pain relievers, as in the case of non-dental surgery, had been sought for centuries, but by the beginning of the 1840s, no panacea had been recognized.³³¹

Gardner Quincy Colton

“Professor” Gardner Quincy Colton was a cross between a chemistry teacher and a showman—perhaps the P. T. Barnum (Colton’s contemporary and friend³³²) of natural

³³⁰Lest the reader be tempted to separate dentistry from medicine, note that their histories are closely intertwined. During the Early Middle Ages, for example, monks performed much of the practice of medicine, surgery, and dentistry. In the twelfth century, however, a series of papal edicts prohibited monks from continuing to perform these services. In their stead, barbers, who had assisted monks during their operations and had the tools to continue to do so, assumed many of the monks’ surgical-dental functions. Well into the sixteenth century, Ambroise Paré (“the Father of Surgery”), a prominent figure in the history of medicine, included in his *Collected Works* (1575) much practical information on teeth as well as general surgery.

http://www.ada.org/public/resources/history/timeline_midlage.asp accessed May 12, 2008.

In the 1770s, John Hunter wrote and published a comprehensive study of human teeth, once again revealing the close association between dentistry and medicine. John Hunter, *The Natural History of the Human Teeth: Explaining Their Structure, Use, Formation, Growth, and Diseases*, Second ed., The Classics of Medicine Library (London: J. Johnson, 1778; repr., 1980).

³³¹It is difficult to provide evidence for an increasing prevalence of dental caries and gum disease during the nineteenth century that would require increased numbers of extractions with their concomitant pain. Nonetheless, it is theoretically possible to posit such an increase because (1) caries are associated with carbohydrate (e.g., “sweets”) fermentation by mouth organisms, (2) the production and importation of carbohydrates in the United States increased after the War of 1812 (with a decline during the Depression of 1837-1843), and (3) dental hygiene at the time left much to be desired. See, for example, D. Beighton, A. Adamson, and A. Rugg-Gunn, “Associations between dietary intake, dental caries experience and salivary bacterial levels in 12-year-old English schoolchildren,” *Archives of oral biology* 41, no. 3 (1996)..

³³²Gary B. Smith Smith, BM, FFARCS and Nicholas P. MB Hirsch, BS, FFARCS, “Gardner Quincy Colton: Pioneer of Nitrous Oxide Anesthesia,” *Anesthesia & Analgesia* 72, no. 3 (1991): 389.

philosophy in general and chemistry and nitrous oxide in particular.³³³ He began medical school in 1842 at the College of Physicians and Surgeons on Crosby Street in New York,³³⁴ but learned before he graduated that giving public lectures and demonstrations on the effects of nitrous oxide were more lucrative and entertaining than practicing medicine. In 1844, he “threw physic to the dogs,” as he exclaimed, and dropped out of the Columbia medical school after grossing the enormous sum of \$535 during his first public demonstration (on March 19th in New York City at the Broadway Tabernacle, which was designed by Charles Finney) of the riotous effects of nitrous oxide on ordinary people.³³⁵

Having tasted the sweet flavor of success, Colton, like others of his day, then took his show on the road. Without a doubt, he performed his most history-altering demonstration in Hartford, Connecticut on December 10, 1844, when he staged his “Great Exhibition of the effects of inhaling nitrous oxide” to an eager crowd at Union Hall.³³⁶ The demonstration itself was not so different from those that he had given on many prior occasions, for there were the usual “forty gallons of gas,” “young men volunteers” to inhale the nitrous oxide, and the “strong men...engaged to occupy the front seats to protect those under the influence of the gas from injuring themselves or others.”³³⁷ It could have been the perfect con in an age of imposture, but Colton was no charlatan and this was no ruse. The laughing gas really did exhilarate, excite, and

³³³ <http://www.general-anaesthesia.com/images/gardner-colton.html> accessed May 12, 2008.

³³⁴The Columbia College of Physicians and Surgeons was located on Crosby Street, near Broadway and the Bowery in lower Manhattan, from 1837 to 1856. <http://ps-handbook.com/node/25> accessed May 12, 2008.

³³⁵Smith and Hirsch, "Gardner Quincy Colton: Pioneer of Nitrous Oxide Anesthesia," 382-3.

³³⁶*Ibid.*, 383.

³³⁷From the *Hartford Courant*, as quoted by *ibid.*, 383-4.

entrance those who inhaled it. No, what was different was the presence in the audience of a young dentist who would change the course of history as a result of Colton's demonstration.³³⁸

Horace Wells - The Seminal Connection

The young spectator in the audience that chilly evening was Horace Wells, who at the age of twenty-nine would become the first to reason that the chemical properties of nitrous oxide could be used to induce a pain-free state in a patient undergoing a dental procedure *and* the first patient ever to undergo such an operation under its influence. He thus became both the discoverer of nitrous oxide as a surgical anesthetic as well as the first patient to inhale it for that purpose.

Wells moved to Hartford in 1836 after he obtained his dentistry degree in Boston. He had many students. At some time during 1842-44, he taught and later partnered with an aspiring dentist a few years his junior, William T. G. Morton.³³⁹ Their business association, however, was “unremunerative” and the two went their separate ways in October, 1844, after about six months.³⁴⁰

Exactly what Wells expected from Colton's laughing gas extravaganza on that Tuesday evening in December is unclear, but since he attended with his wife, he may well have gone to

³³⁸Interestingly, Gardner Colton never claimed that he was the discoverer of surgical anesthesia. He did, however, use nitrous oxide as a dental anesthetic again and again—reportedly without any deaths—for the removal of “nearly a million teeth” during a career that extended via his Colton Dental Association into seven United States cities and well into the 1890s, as *The New York Times* wrote in his 1898 obituary. "GARDNER Q. COLTON DEAD," *New York Times (1857-Current file)* 1898. It is possible that Colton enjoyed more pecuniary gain from nitrous oxide than any of the declared contenders for the discovery of surgical anesthesia.

³³⁹Fenster, *Ether Day*: 55-57.

In 1840, Morton actually attended the Baltimore College of Dental Surgery—“the world's first dental school”—but he never graduated. <http://www.general-anaesthesia.com/images/william-morton.html> accessed May 19, 2008.

³⁴⁰Wangensteen and Wangenstein, *The Rise of Surgery*: 658 Footnote 8. The dissolution of the partnership was formally announced in Boston newspapers on October 18, 1844. Fenster, *Ether Day*: 56.

Note that as late as 1845, Morton remained financially indebted to Wells for “operations on teeth and instruction in the Art of Dentistry per agreement \$50.00” per an entry dated March 4, 1844. <http://library.uchc.edu/hms/daybook.html> accessed May 16, 2008.

the Exhibition to be entertained. From that day on, however, the exact happenings in the chronology of surgical anesthesia—as recorded years later by Colton, Wells, and others—become even less clear.³⁴¹ It appears likely that either Wells witnessed the antics of a young apothecary's assistant, Sam Cooley, who became injured while under the influence of Colton's nitrous oxide yet felt no pain (as described by Colton in his 1897 memoirs³⁴²), or that Wells inhaled the gas himself “and ran against a bench, and bruised his leg severely, but, as he said, was not conscious of pain while the effect of the gas lasted.”³⁴³

Horace Wells then experienced a eureka moment. “Why cannot a man have a tooth pulled while under the gas and not feel it?” he asked Colton.³⁴⁴ The Professor seems to have been oblivious to the prodigious implications of Wells' question, but, shortly thereafter, Wells proceeded to arrange for the extraction of his own aching tooth under the influence of Colton's gas.

On or about December 11, 1844, Wells asked Dr. John M. Riggs, a former student of his³⁴⁵ and then a neighboring dentist in Hartford, to remove his decayed molar while under the influence of nitrous oxide. Colton supplied the gas and Riggs removed the tooth. Wells' disbelief after the extraction was akin to that experienced by James Venable in Crawford Long's office more than two years earlier. “A new era in tooth pulling!” Wells exclaimed. “It is the

³⁴¹Colton, Wells, Samuel A. Cooley, and John M. Riggs all gave different accounts of the events of December 10th and 11th, 1844, for example. Smith and Hirsch, “Gardner Quincy Colton: Pioneer of Nitrous Oxide Anesthesia,” 384.

³⁴²G. Q. Colton, *Boyhood and manhood recollections. The story of a busy life.* (New York: A. G. Sherwood, 1897).

³⁴³Gardner Q. Colton, “THE INVENTION OF ANAESTHESIA,” *New York Times* (1857-Current file) 1862.

³⁴⁴Smith and Hirsch, “Gardner Quincy Colton: Pioneer of Nitrous Oxide Anesthesia,” 384.

³⁴⁵Fenster, *Ether Day*: 55.

greatest discovery ever made. I didn't feel it so much as the prick of a pin!"³⁴⁶ The good news spread rapidly about Hartford. By the end of the month Wells had painlessly extracted more than a dozen teeth from his eager patients and, with Cooley, had great plans to extract many more.³⁴⁷

From Hartford to Boston

Horace Wells rapidly extended his insight beyond dentistry to include any surgery. In fact, it may even have gone beyond nitrous oxide, for later evidence supports the Wells' claim that he occasionally substituted ether for nitrous oxide—although he readily admitted that he preferred the latter in dentistry due to its better safety profile for shorter procedures.³⁴⁸

Soon after his December, 1844 epiphany, Wells took his gas and his idea (which, remember, Humphry Davy had suggested to a clueless readership two generations earlier) from Hartford to Boston to attempt to induce his colleagues to treat their patients while under the influence of nitrous oxide. His plan, according to Cooley, was to create “a large and lucrative business” through the production and administration of nitrous oxide to dental patients, but Wells denied this.³⁴⁹ Convincing practitioners to use nitrous oxide was not an easy task, for the common perception at the time from the personal recollections of laughing gas party participants was that the effects of the molecule were at best unpredictable and at worst violent and

³⁴⁶Colton, "THE INVENTION OF ANAESTHESIA."

³⁴⁷Fenster, *Ether Day*: 61.

³⁴⁸Colton, "THE INVENTION OF ANAESTHESIA."

³⁴⁹Fenster, *Ether Day*: 62.

In December, 1846, Wells wrote that in Boston he planned to disseminate knowledge of the anesthetic effects of nitrous oxide “into the hands of proper persons, without expecting to derive any pecuniary benefit therefrom.” *Hartford Courant*, December 7, 1846, as reproduced by Nuland, *Anesthesia*: 55.

As Fenster notes, the veracity of Cooley's statement is suspect in light of Wells' rapid and wide dissemination of knowledge of the anesthetic properties of nitrous oxide for the practice of dentistry.

catastrophic.³⁵⁰ Nevertheless, Wells would not be deterred. One of those he called upon in Boston was William Morton, with whom he had partnered in Connecticut the year before. Morton expressed “incredulity” at Wells’ claim, but Wells made clear that “I *have* done it, and can do it again.”³⁵¹

Wells must have ultimately convinced Morton of his sincerity—if not the value of his discovery—for Morton, now a medical student at Harvard,³⁵² arranged for Dr. John Collins Warren, Chief of Surgery at Massachusetts General Hospital, to meet Wells in Boston. Wells lectured to Warren’s Medical School class on the virtues of painless operations. Warren must have been impressed, for he invited Wells to give a demonstration in the Hospital amphitheater.

Wells’ Failure and Decline

On January 15, 1845, in front of numerous medical students, physicians, and his own former dental student, William T. G. Morton, Wells proceeded to demonstrate the anesthetic properties of nitrous oxide on a patient—barely a month after he first noted its effects and began using it on his own patients.³⁵³

³⁵⁰Even Dr. Riggs, who extracted Wells’ wisdom tooth that December, 1844, openly remarked that by using nitrous oxide “We knew not whether death or success confronted us.” Fenster, *Ether Day*: 60.

Sam Cooley claimed that he and Wells would keep the nature of their magic gas secret, which would have obviated concerns about its known deleterious effects, but, again, Wells hardly kept nitrous oxide a secret. See *ibid.*, 62.

³⁵¹Colton, “THE INVENTION OF ANAESTHESIA.” Italics in the original. The words are those of Mrs. Esther W. Walton, as quoted by Colton. Mrs. Walton was an ear witness who testified as to the conversation that transpired between Wells and Morton on this occasion.

³⁵²Some claim that Morton matriculated at Harvard Medical School to win the favor of a young woman rather than achieve the education necessary for a profession. Regardless, the conclusion of Morton’s time at Harvard Med was the same as at Baltimore Dental School—he never graduated. <http://www.general-anaesthesia.com/images/william-morton.html> accessed May 19, 2008.

³⁵³Fenster, *Ether Day*: 63.

The highly-anticipated event was a disaster. First, the initially-scheduled patient refused to undergo the planned amputation and left the Hospital.³⁵⁴ Then, since “no other operations were scheduled for the week,” Warren asked for a student volunteer to have a tooth pulled.³⁵⁵ One agreed.³⁵⁶ Wells administered the nitrous oxide and began the extraction. The patient moaned or groaned or, in the vernacular of the day, “halloed.”³⁵⁷ Regardless of the patient’s exact vocalization, the crowd had had enough. Whether they were primed for failure and derision, perhaps based upon their own experiences with laughing gas, or whether the height of their expectations set up too big a fall, the students jeered. Again and again they hurled the epithet “Humbug!” at Wells. It was more than the usually-respected and admired Wells could tolerate. He slunk out of Boston the next day and began a downward slide that ended in his death in 1848, three years later, at the age of thirty-three.³⁵⁸

The cause of the failure of Wells’ nitrous oxide to induce an adequate level of anesthesia is a matter of some controversy and conjecture. Wells claimed that “the bag was by mistake

³⁵⁴Ibid.

³⁵⁵Ibid. The fact that there were so few scheduled operations at one of the most respected hospitals in the United States in 1845 is at once extremely important for understanding the history of cancer treatments as well as the role of anesthesia in the history of surgery, in general. As we shall see, the development of surgical anesthesia was a major force in the enormous increase in the number of surgeries by the end of the nineteenth century.

³⁵⁶I doubt that a similar request at Harvard Med or any other medical school today would elicit such a volunteer—even from an audience of medical students. In the early-to-mid nineteenth century, however, when oral hygiene left much to be desired and alternatives to extraction were few, it would not have been unusual to have numerous students in the class who might be willing to undergo such a procedure—especially with the promise of painlessness.

³⁵⁷Fenster, *Ether Day*: 63-64.

³⁵⁸Within months of the nitrous oxide debacle, Wells closed his practice in Hartford, gave up his practice entirely, and attempted other projects without success. Nuland, *Anesthesia*: 56-57. In early January, 1848, he began to use chloroform. Wells became addicted to it and mentally unstable. Now in New York, he doused two prostitutes with sulphuric acid. He was convicted and incarcerated in the notorious Tombs Prison. After detoxification in prison, he committed suicide by slitting open an artery in his leg—after inhaling chloroform to kill the pain. <http://www.general-anaesthesia.com/images/horace-wells.html> accessed May 19, 2008.

withdrawn much too soon”; i.e., that the patient received too small a dose of the anesthetic.³⁵⁹ Julie Fenster, analyzing the event from the perspective of more than a century and a half later, concluded that the “quality” of the nitrous oxide Wells obtained in Boston may have been quite different from that which he received from Colton or made with Cooley.³⁶⁰ Indeed, both could be true. I would add that perhaps the student-patient—a likely a reluctant, last-minute substitute—felt a heightened level of excitement that might have required a higher dose of gas, and/or that he may previously have attained a level of tolerance to nitrous from inhalations at laughing gas parties that would have also necessitated a larger induction dose to achieve the desired anesthetic effect.³⁶¹

Professor Charles Thomas Jackson

Horace Wells’ disastrous demonstration in January, 1845, with nitrous oxide failed to attain for Wells the recognition for which he yearned. Nevertheless, his journey to Boston to induce others to use anesthesia and reflect on the possibility of painless surgery was not a failure, for, although most gave up on the possibility of painless surgery, a few had their interest piqued.

One of the latter was Charles Thomas Jackson, a Boston Brahmin, Harvard Medical School graduate (1829) and now (1844-5) professor and chemistry teacher of Morton. Jackson, after giving up the practice of medicine not long after his return from post-graduate studies in Paris (1836), actually opened the first laboratory for research and instruction in analytical

³⁵⁹Wells, *Hartford Courant*, December 7, 1846, as reproduced by *ibid.*, 55.

³⁶⁰Fenster, *Ether Day*: 63.

³⁶¹Douglas S. Ramsay et al., "Nitrous oxide analgesia in humans: Acute and chronic tolerance," *Pain* 114, no. 1-2 (2005). It is also possible that the student was more frightened than hurt, for the student-patient later claimed that “he had experienced almost no pain.” Fenster, *Ether Day*: 64. Unfortunately, no one seemed to care.

chemistry in the United States (1838), but his interests ranged far beyond chemistry into mineralogy and geology.³⁶²

Wells had also called upon Jackson during his visit to Boston in early 1845.³⁶³ It was Jackson—Jackson who knew so much, Jackson who craved respect, Jackson who could not bear the thought that Morton might win sole credit for the discovery of surgical anesthesia—who added the chemical link in the interface between chemistry, human biology, and painless surgery and became one of the contenders for the coveted title of Discoverer of Surgical Anesthesia.

Wells avowed that while in Boston he had conversed on the subject of painless surgery with Jackson as well as Morton, “both of whom,” according to Wells, “admitted it to be entirely new to them.”³⁶⁴ Jackson later claimed that Wells’ contention could not have been further from the truth.³⁶⁵ In 1861, Jackson wrote that he had put himself to sleep with ether and, in “the

³⁶²To this day, Charles Jackson’s undisputed fame rests upon his geological work in New England and Lake Superior. His contributions to the advent of anesthesia are more problematic.

³⁶³This was not Wells’ first meeting with Jackson. In October of 1844, two months before Wells’ epiphanic experience with Coulton’s nitrous oxide, Wells and Morton sought Jackson’s professional opinion on the dental plates that had led to their partnership—as sought as well as to receive the eminent Jackson’s endorsement. They received both. Fenster, *Ether Day*: 56. Thus, Charles Thomas Jackson was known to Wells and Morton well before their forays into surgical anesthesia using nitrous oxide and ether.

³⁶⁴Horace Wells, *Hartford Courant*, December 7, 1846, as reproduced by Nuland, *Anesthesia*: 55. Wells presented his complete response to the claims of Jackson and Morton in his 1847 monograph, Horace Wells, *A History of the Discovery of the Application of Nitrous Oxide Gas, Ether, and other Vapors, to Surgical Operations* (Hartford: J. Gaylord Wells, 1847). 6-11. The quotation is from page 6 of the monograph.

³⁶⁵Jackson, *A manual of etherization : containing directions for the employment of ether, chloroform, and other anaesthetic agents, by inhalation, in surgical operations [...] / by Chas. T. Jackson*: 20.

In fact, Jackson may (I emphasize the “may”) have known more about ether anesthesia than he admitted to, for at least one author wrote that Jackson and William Morton visited Crawford Long’s home town, Jefferson, Georgia, during the spring of 1842. This was just about the time that Long began to use ether for surgical anesthesia and the two Northerners may have heard of Long’s discovery at that time. Frank Kells Boland, *The first anesthetic; the story of Crawford Long* (Athens, GA: University of Georgia Press, 1950). Chapter VII.

I did not include this potentially controversy-revising trip to Long’s 1842 town of practice in the body of the text because the author, Frank Kells Boland (1875-1953), had too little evidence and too much self interest in this purported visit to justify its inclusion. Boland, a Georgia physician, was President of the Crawford W. Long Memorial Association, published his book through the University of Georgia, and clearly had no love lost for Charles T. Jackson. More damning, however, is Boland’s lack of hard evidence—it is circumstantial at most—to back up his claim that Jackson and Morton stole Long’s great discovery. See, for example, John Duffy, “Review: The First Anesthetic - The Story of Crawford Long,” *The Journal of Southern History* 16, no. 4 (1950).

winter of 1841-2,” made the conceptual leap from ether as a soporific chemical to a surgical anesthetic. The timing of his recollection was conveniently a few months earlier than Crawford Long’s first documented use of nitrous oxide anesthesia!³⁶⁶

Jackson’s *post hoc* description of this potentially groundbreaking event in the history of anesthesia—Jackson immodestly labeled it “the experiment from which the discovery of anæsthesia was deduced”³⁶⁷—is so compelling and so reminiscent of the descriptions of others as to warrant quotation, for his words both capture the sensations and convey the emotions that etherized humanity would experience forever after.

I took a bottle of that ether and a folded towel, and having seated myself in a rocking-chair, placed my feet in another chair so as to secure a fixed position as I reclined in the one in which I was seated. Soaking my towel in ether I placed it over my nose and mouth, so as to allow me to inhale the ether vapor mingled with air, and began to inhale the vapor deeply into my lungs. At first it made me cough, but soon that irritability ceased, and I noticed a sense of coolness followed by warmth, fullness of the head and chest, with giddiness and exhilaration, numbness of the feet and legs, followed by a swimming sensation as if afloat in the air. This was accompanied with entire loss of feeling, even of contact with my chair. I noticed that all sensation of pain had ceased in my throat, and the sensations which I had were of the most agreeable kind. Much pleased and excited I continued the inhalation of the ether vapor, and soon fell into a dreamy state, and then became unconscious of all surrounding things. I know not how long I remained in that state, but suppose that it could not have been less than a quarter of a hour, judging from the degree of dryness of the cloth which during the stage of unconsciousness had fallen from my mouth and nose, and lay upon my chest.

As I became conscious, I observed that there was no feeling of pain in my throat, and my limbs were still deeply benumbed, as if the nerves of sensation were fully paralyzed. A strange thrilling now began to be felt along the spine, but it was not in any way disagreeable. Little by little sensation began to manifest itself, first in the throat and body, and gradually it extended to the extremities; but it was some time before full sensation returned and my throat became really painful.

Reflecting on these phenomena, the idea flashed into my mind that I had made the discovery I had for so long a time been in quest of—a means of rendering the nerves of sensation temporarily insensible, so as to admit of the performance of a surgical operation on an individual without his suffering pain therefrom.³⁶⁸

³⁶⁶Jackson, *A manual of etherization : containing directions for the employment of ether, chloroform, and other anaesthetic agents, by inhalation, in surgical operations [...] / by Chas. T. Jackson*: 18.

³⁶⁷Ibid. The occasion for Jackson’s epiphanic “experiment” was his accidental inhalation of chlorine gas—an extremely irritating, noxious gas—and his attempts to assuage the resultant pain in his throat and lungs by inhaling “ether and ammonia.”

³⁶⁸Ibid., 19-20.

If only he had published those sentences before 1842—or even 1845! If only the date 1841-2 could be verified! There are simply too many questionable occurrences in Jackson’s lifetime to accept his statement—and certainly the date of occurrence—at face value. Notice, for example, how Jackson also expediently recalled that the duration of anesthesia “could not have been less than a quarter of an hour.”³⁶⁹ Is it coincidental that fifteen minutes was the great divide between dental and surgical anesthesia³⁷⁰—between the relatively short-duration (but safer) nitrous oxide of Long (whom Jackson visited in 1854 and apparently believed to be the discoverer of nitrous oxide surgical anesthesia by virtue of Long’s history and affidavits³⁷¹) and the longer-duration, deeper-anesthetic state inducible by ether? There is little doubt that Jackson knew that sulphuric ether could cause loss of consciousness, for he demonstrated that fact before his chemistry classes in 1844.³⁷² Nevertheless, he never seems to have made the ideational connection between the consciousness-altering properties of ether and its potential use as a surgical anesthetic.

Jackson’s claim to the discovery of ether anesthesia was not the only controversial, uncorroborated discovery in his history. Jackson alleged that in 1832 he gave Samuel F. B. Morse (1791-1872), at the time a painter and newly-appointed art professor at the fledgling New York University,³⁷³ the idea for an “electro-magnetic telegraphic apparatus.” Three years later, Morse alone received a patent for the device.³⁷⁴ No doubt Jackson and Morse conversed about

³⁶⁹Ibid., 19.

³⁷⁰Ibid., 14.

³⁷¹Fenster, *Ether Day*: 209-11.

³⁷²<http://www.general-anaesthesia.com/images/william-morton.html> accessed June 4, 2008.

³⁷³New York University was then known as the University of New York. It was officially renamed in 1896.

electromagnetic signal transduction during their voyage, but later adjudication found no credible evidence to support Jackson's claim to the invention of the telegraph.³⁷⁵

Jackson may well have played a part—even a formative one—in Morse's conceptualization of the telegraph as well as in the advent of surgical anesthesia, but his claim was insufficient in both cases to warrant the title "Discoverer." Indeed, the pattern of his claims over his lifetime reveals either amazing bad luck through lack of corroborative evidence or megalomania.³⁷⁶

³⁷⁴The occasion for their 1832 meeting was a chance encounter aboard a trans-Atlantic voyage from Europe to New England when Jackson returned from his post-graduate studies in Paris. Fenster, *Ether Day*: 133-7.

³⁷⁵Jackson sued for patent rights for many years after Morse received the patent, but lost.

The invention of the telegraph and the discovery of anesthesia were only two of Jackson's self-announced claims to fame. Others included his claim on the discovery of the mechanics of digestion, whereby Jackson attempted to gain exclusive access to William Beaumont's gastric fistula patient, Alexis St. Martin, and the synthesis of guncotton, the highly flammable compound nitrocellulose.

³⁷⁶Jackson was deeply and irrevocably affected by his recurrent near encounters with lasting fame. His dejection over the lack of recognition for the invention of the telegraph was assuaged only by the diversion offered by William Morton's attorney in 1846 when R. H. Eddy, Esq. suggested that Jackson and Morton co-patent sulphuric ether as a surgical anesthetic. Fenster, *Ether Day*: 99-100. Even the idea of co-patency, however, was doomed to failure, for ether was too ubiquitous to sustain a patent [ether anesthesia was immediately used during the Mexican War (1846-8)], state medical associations prohibited restrictive "secret remedies," *ibid.*, 75, and Morton was too difficult a personality for any partner to tolerate.

Decades later, after years of struggle and failure to achieve what Jackson considered his just recognition and reward, it is said that the old Professor happened upon Morton's grave in the Mount Auburn Cemetery in Cambridge, Massachusetts. The engraving on the "Morton monument" erected by the people of Boston less than a year and a half following Morton's death in July, 1868, credited Morton grandiosely as "Inventor and Revealer of Anesthetic Inhalation. BEFORE WHOM In all time Surgery was Agony. BY WHOM Pain in Surgery was averted and annulled. SINCE WHOM Science has control of pain." (For a photograph of the monument, see http://www.asahq.org/Newsletters/2006/06-06/zeitlin06_06.html accessed May 28, 2008. Note that the "Ether monument" in Boston's Public Garden, the first sculpture in the Public Garden's history, should not be confused with the "Morton monument" in Mount Auburn Cemetery. The Ether monument, according to the New England Society of Anesthesiologists, "is the world's only monument to a drug." <http://www.nesa.net/NESA/ethermon.html> accessed July 1, 2008).

According to legend, the apotheosis of Morton was more than Jackson could bear. Jackson reportedly cried a primal, inhuman scream and was carried away by Union soldiers to the McLean Hospital (for the mentally insane). He was incarcerated there until he died seven years later, in 1880. Alex Beam, *Gracefully insane : the rise and fall of America's premier mental hospital* (New York: Public Affairs, 2001). 38-39.

Jackson's own gravestone (*not* a monument), also at Mount Auburn, gave him credit for both the discovery of and the epiphany that led to surgical anesthesia, for the engraver wrote that "Through his observations of the peculiar effects of sulphuric ether on the nerves of sensation and his bold deduction therefrom the benign discovery of painless surgery was made." If only History had been so kind to him while he was still alive! For a photograph of the stone, see http://en.wikipedia.org/wiki/Image:Charles_Jackson_grave.jpg accessed May 28, 2008.

Professor Charles Thomas Jackson's role in the history of the discovery of surgical anesthesia was not that of Discoverer, but, rather, of Facilitator, for his deep knowledge of chemistry, far-ranging intellect, and communicative inclinations led him to suggest to William Morton—at his student's request—that ether was preferable to nitrous oxide for the induction of anesthesia.

William Thomas Green Morton

Morton followed Jackson's suggestion to substitute ether for nitrous oxide and, in the process, gained credit for the publicization of surgical anesthesia and, in some minds, the discovery itself. Within a few months of Morton's public demonstration of his concoction³⁷⁷ under the Bulfinch Dome of the Massachusetts General Hospital on October 16, 1846—Ether Day—the word and the method of administration spread to Bostonians, other Americans, and Europeans as well as other surgeons, physicians, dentists, and the public around the world. Nevertheless, the developments before and after October 16th were not without rancor and controversy. Ultimately, they led to the destruction of Morton himself.

Even before partnering with Wells in 1844, Morton had sought a variety of schemes to achieve wealth and recognition. He had borrowed money to purchase goods, sold them, and never repaid the loan.³⁷⁸ He had devised one flimflam after another to fleece the unsuspecting of their earnings and savings. He had even taken money from his partner, Horace Wells, to promote a new type of gold dental work, and sought the endorsement of Professor Charles Jackson in Boston, but spent the money on himself.³⁷⁹ Morton must have exuded a trusting and

³⁷⁷Morton's Letheon was not simply sulphuric ether. He added oil of orange to mask the obvious smell of the ether as well as to increase the probability of receiving a patent for his "compound" under law. Fenster, *Ether Day*: 76.

³⁷⁸*Ibid.*, Chapter 7, "The Confidence Man".

³⁷⁹*Ibid.*, 55-56.

hard-working personality, for the unwary in the West, South, and Northeast of the United States continued to be scammed by him. Even Wells, following the failure of their partnership in the fall of 1844—and Morton’s principal role in that failure—continued to regard Morton as “a friend.”³⁸⁰ Nevertheless, Morton’s disreputable history would come back to haunt him in the end.

Regardless of his history, however, Morton seemed deeply motivated to improve on Wells’ anesthesia and to apply it during surgical operations. Throughout 1845 and 1846, heeding Jackson’s suggestion, Morton experimented diligently with sulphuric ether. He anesthetized fish, other animals, and himself—all under the cloak of secrecy to avoid losing a potential windfall.³⁸¹ The ether worked well without major drawbacks. By the fall of 1846, about a year and a half after witnessing Wells’ apparent failure to anesthetize a patient with nitrous oxide, Morton was ready to use his masked ether on a fellow human. The opportunity presented itself on September 30, 1846, in the person of Eben Frost, “a man residing in Boston...suffering great pain, and wishing to have a tooth extracted.”³⁸² The remainder of Morton’s description of his first patient to receive ether anesthesia was related through the dentist’s son, who wrote that Mr. Frost

was afraid of the operation, and asked if he could be mesmerized. I [William Morton] told him I had something better, and saturating my handkerchief, gave it to him to inhale. He became unconscious almost immediately. It was dark, and Dr. Hayden held the lamp while I extracted a firmly-rooted bicuspid tooth. There was not much alteration in the pulse and no relaxing of the muscles. He recovered in a minute and knew nothing of what had been done to him.³⁸³

³⁸⁰Ibid., 56.

³⁸¹<http://www.general-anaesthesia.com/images/william-morton.html> accessed June 4, 2008.

³⁸²Americanization Department, *The Mexican War and Slavery 1845-1861*, ed. Americanization Department, XII vols., vol. VII, *America: Great Crises In Our History Told by Its Makers, A Library of Original Sources* (Chicago: Veterans of Foreign Wars of the United States, 1925). 64-65.

³⁸³Ibid., 65.

Recognition

This event, by itself, might have led no further than had Long's operation on Venable or Wells' private extractions under nitrous oxide. But Morton had an enormous advantage over the other two, for he was either so sure of his ether or so confident that he had invited a journalist, Albert G. Tenney, to observe the entire procedure on Eben Frost.³⁸⁴

The next day, a published account of the painless tooth extraction appeared in the *Boston Daily Journal*, presumably written by Tenney.³⁸⁵ The day after that, October 2, the *Boston Transcript*, perhaps not to be outdone, reported an account of "A New and Valuable Discovery," wherein the writer noted that "The discovery is destined to make a great revolution in the arts of surgery and surgical dentistry."³⁸⁶

These public notices made all the difference—as they often does in a culture driven by the media and poised for technologic advances—for they caught the eye of Dr. Henry J. Bigelow (1818-1890), a junior surgeon at the Massachusetts General Hospital who had the ear of the senior surgeon, Dr. John C. Warren. Bigelow also shared Warren's heartfelt desire to quell the horrid pains of surgery—and he shared Warren's faith that there must be chemicals that could achieve this in a controlled fashion. It was Bigelow who was instrumental in arranging for Morton to demonstrate his anesthetic in front of the medical eyes of America at the MGH.

An official letter written by Dr. Warren and signed by the Dr. C. E. Hayward, the House Surgeon at the Massachusetts General Hospital, gave Morton forty-eight hours to prepare that

³⁸⁴Fenster, *Ether Day*: 73. The extension of an invitation to a newspaper reporter was a bold move for Morton because he risked public and/or scientific exposure of the ingredients of his ether concoction before he could patent it and hence the loss of significant pecuniary rewards. Morton's second astute move, after inviting the press to Frost's painless extraction and perhaps to counter the potential disadvantage of the first astute move, was to hire a patent attorney, R. H. Eddy. Morton and Eddy first met on October 1, 1846—at the latest. *Ibid.*, 75.

³⁸⁵<http://www.general-anaesthesia.com/images/henry-bigelow.html> accessed June 9, 2008. Also see *ibid.*, 73-74. It is also possible that Morton wrote the article and transmitted it to Tenney for publication.

³⁸⁶*Ibid.*, 74.

“which you have invented to diminish the sensibility to pain.”³⁸⁷ Hence, despite the failure of Wells, Warren offered Morton the opportunity to anesthetize a surgical patient in the surgical amphitheater of the MGH in front of a very interested and somewhat disbelieving medical public.³⁸⁸ But there is more to the administration of anesthesia than the chemical itself. Morton had to perfect a device that would safely and effectively transfer the drug from the vessel to the lungs of the patient by means of inhalation. On this problem, which Morton had initially approached with an ether-soaked handkerchief over Frost’s nose and mouth, he worked diligently up to a few minutes of the surgery scheduled for 10 AM on October 16, 1846.

Fame

The results of this operation [on October 16, 1846] led to the repetition of the use of ether in other cases and in a few days its success was established, and its use resorted to in every considerable operation in the city of Boston and its vicinity.

-Dr. John C. Warren

Dr. Warren’s patient was Edward Gilbert Abbott, a slight, twenty-year-old Boston printer and editor. The elder surgeon scheduled Abbott to remove a vascular tumor from his neck.³⁸⁹ This was another instance of the important historical and medical connection between cancer,

³⁸⁷The House Surgeon’s name has been spelled variously as C. E. Haywood, Heywood, Hayward, and others. I chose this spelling for Hayward because it was the spelling used by Dr. Warren in his brief account of Ether Day and its immediate aftermath. John C. Warren, "Inhalation of Ethereal Vapor for the Prevention of Pain in Surgical Operations," *The Boston Medical and Surgical Journal* 35, no. 19 (1846): 376.

The quotation is from Nuland, *Anesthesia*: 68.

³⁸⁸Fenster, *Ether Day*: 5-6.

³⁸⁹Leroy D. Vandam and John Adams Abbott, "Edward Gilbert Abbott: Enigmatic Figure of the Ether Demonstration," *The New England Journal of Medicine* 311, no. 15 (1984): 991. Dr. Nuland and others wrote that Abbott was a painter. Nuland, *Anesthesia*: 68. This appears not to have been the case.

I highlight the fact that Abbott (also spelled Abbot by *ibid.*) was a thin man because his paucity of adipose tissue may have made it easier for Morton to anesthetize him. Less fat to take up the anesthetic leaves more to cross the blood-brain barrier and induce “insensibility” quicker and, depending upon the total dose and other factors (“area under the curve”), longer.

surgery, and anesthesia. It is interesting to note that Abbott's tumor and the tumors that afflicted Dr. Long's first anesthetized patient, James Venable, were both "neck tumors."³⁹⁰

Morton, having spent much time during the past two days tweaking his inhalation apparatus, was late to the operation by a few minutes.³⁹¹ In fact, Warren was poised to begin Abbott's operation in the traditional way, *sans* anesthesia, when Morton burst through the amphitheater's doors with his "preparation" and inhalation apparatus in hand.³⁹²

The cooperative young Abbott inhaled the volatile ether slowly and deliberately from Morton's stopcocked glass flask. Within three minutes, Abbott was stuporous.³⁹³ His arms fell to his side. Morton alerted Dr. John C. Warren that his patient was ready. As he had done for decades, Warren operated as quickly and efficiently as possible, always cognizant of the urgency of time and his patient's sensibility.³⁹⁴ As the operation proceeded, the senior surgeon noted that the patient began "to speak incoherently, and appeared to be in an agitated state."³⁹⁵ Nonetheless, Warren completed his surgery without difficulty.

Mr. Abbott fully awoke shortly thereafter. John C. Warren immediately questioned his patient: How bad was the pain? Nothing more than a scratch, answered Abbott. Were you

³⁹⁰It was interesting because such tumors were not high on the list of prevalent lesions at the time. Still, it must be remembered that at a stage in the history of medicine prior to the invention of internal imaging devices *in vivo* (as opposed to autopsy findings after death), it was much more likely that the first tumors to be operated upon under surgical anesthesia—or to be operated upon at all—would be "superficial" tumors such as those of the skin, breast, or cervix.

It is most likely that Abbott's tumor was a congenital vascular malformation—a benign swelling that may have been unsightly, but was not malignant. Vandam and Abbott, "Abbott," 992.

³⁹¹Nuland reproduced a photograph of Morton's first inhalation flask at Nuland, *Anesthesia*: opposite 68.

³⁹²"Preparation" was the term for Morton's anesthetic used by the *Boston Daily Journal* author in his notice of October 1, 1846. See *ibid.*, 67.

³⁹³Warren, "Inhalation," 376.

³⁹⁴A *post hoc* depiction of Warren's Ether Day operation on Abbott may be seen in a mural in the Ether Dome. http://upload.wikimedia.org/wikipedia/en/3/36/MGH_Ether_Dome_Mural_29Jan2008.jpg accessed July 6, 2008.

³⁹⁵Warren, "Inhalation," 376.

aware of what was happening? Yes, but there really was no pain.³⁹⁶ Warren was demonstrably impressed with Morton's anesthesia. The surgeon turned to the audience in the steep-vaulted amphitheater (known forever after as the "Ether Room") and, in an understatement hallowed in the halls of historical quotations, uttered the famous words: "Gentlemen, this is no humbug."³⁹⁷

What was that miracle vapor?

Despite this amazing sequence of events, no one—neither Warren, nor the amphitheater observers, nor the patient, nor anyone else but Morton (except maybe Jackson, who was not there)—knew the composition of the magic insensibility gas. The dentist had purposely kept his "ethereal vapor" a secret. Although the 1840s were distinguished by an entrepreneurial spirit perhaps exceeded only during the 1870s, 1920s, and 1990s, American medical ethics at the time decried the harboring of a "secret formula" that could benefit mankind. This was the creed of the Massachusetts Medical Society and would soon be that of the American Medical Association.³⁹⁸

Members of the medical establishment immediately pressed Morton for his secret formula, but Morton—always on the outlook for a rich nugget and sensing a gold mine—wanted to secure a patent for his "invention" prior to divulging its contents. Here was a clear ethical and moral dilemma. How could Morton reap the rewards of his discovery without divulging its oh-

³⁹⁶Ibid.

³⁹⁷There are many, many accounts of Dr. Warren's operation on Edward Gilbert Abbott. One of the most contemporaneous—before the hubbub of controversy set in—was written by Dr. Henry Jacob Bigelow, one of the observing surgeons in the amphitheater, and published in the *Boston Daily Journal* and the *Boston Post* the next day, October 17, 1846. Nuland, *Anesthesia*: 71.

³⁹⁸Fourteen founders established the Massachusetts Medical Society, "the oldest continuously operating medical society in the United States," in 1781. One of the founders was John Warren (1753-1815), father of Morton's senior surgeon, John C. Warren. Founder Warren wrote that one of the main purposes of the Society was "to promote medical and surgical knowledge"—a goal clearly contradicted by Morton's secrecy with respect to his surgery-altering vapor. http://www.massmed.org/Content/NavigationMenu/About/History/Our_History.htm accessed June 8, 2008.

The AMA was founded in May, 1847, a few months after Ether Day. Two of its founding principles were to raise ethical standards in medicine and to disseminate medical information more effectively among its members and the public. Morton would violate both and would later be censured by the AMA. Ibid., 99.

so-common active ingredient to those who pressed him in the name of suffering mankind? In the United States, rights of claim to monetary compensation for an invention were and are established through patent rights. Morton chose the strategy of putting a new name on an old chemical and then applied for a patent. He chose the name “Letheon,” after the river of Hades in Greek mythology, the waters of which, when drunk, produced forgetfulness of the past.³⁹⁹ As to the patent, he had already engaged a patent attorney, R. H. Eddy, on or before the date of his experiment with Eben Frost—and more than two weeks before his encounter with Abbott and Dr. Warren under what came to be called the “Ether Dome.”⁴⁰⁰

Word spread quickly that Morton had discovered a new nostrum that allowed patients to undergo surgery without pain. The next day, an article in the *Boston Daily Journal*, published with the aid of Dr. Bigelow, trumpeted “that the success of Dr. Morton’s experiment was complete,” and that the patient, “not manifest[ing] the slightest symptoms of suffering...appeared to be totally insensible to what was going on.”⁴⁰¹ Morton received all the credit. Morton was a hero—maybe, in the hyperbole of the day, the public considered him a demigod.

That, however, was hardly the end of the matter, for the stakes were too high, the times too competitive, and the number of contributors to the birth of surgical anesthesia in Morton’s circle too great for him to walk away with the prize of Discoverer—and all that potentially went with it—uncontested or unscathed. On October 23, 1846, merely a week after Morton’s first demonstration of etherization in the MGH amphitheater, Professor Jackson visited Morton to

³⁹⁹“Letheon” is not an apt name, for one can forget only those things once remembered. Ether, like most surgical anesthetics, forestalls the memory of happenings that occur under their influence.

⁴⁰⁰Fenster, *Ether Day*: 75.

⁴⁰¹Nuland, *Anesthesia*: 71.

claim his share of the prize money that both believed would surely follow from the rapidly-spreading utilization of Letheon in the medical world.⁴⁰² Despite a pitch of jealousy and anger that surely rankled the proud, haughty Jackson as he witnessed the accolades he wanted so much for himself instead showered upon the conniving “dentist,” the two reached an agreement under which he would be paid ten percent of the American (and later, global) sales of Letheon to Jackson in exchange for the relinquishment of any claim to his rights in the patent.

Patent? What Patent?

Still, so much of this pecuniary speculation rested upon patent attorney Eddy’s judgment on whether or not ether could be patented. On advice of counsel, Letters Patent No. 4,848 of “C. T. Jackson and Wm. T. G. Morton” were signed and witnessed October 27, 1846, and later combined with the full patent dated November 12, 1846.⁴⁰³ Unfortunately for Morton and Jackson, their patent, which was eventually voided years later, created more problems than profit.⁴⁰⁴ Indeed, the elusive affluence that never followed this patent had much to do with the destruction of both men, for it turned out to be as difficult to patent Letheon as it would have been to patent opium or nitrous oxide. Perhaps Morton would have lived a richer and happier life if he had patented the glass vessel used to administer the Letheon, or his method of administration, rather than its chemical ingredients.

Word of Morton’s ethereal vapor for painless surgery spread rapidly, aided not only by Morton—whose imaginary fortune seemed to increase with each additional use of Letheon,

⁴⁰²Ibid.

⁴⁰³Surgeon and historian of medicine Sherwin B. Nuland vigorously attempted to obtain a copy of the Patent, which could be helpful in discerning exactly what Morton claimed and his justifications for the patent. Unfortunately, owing to the response that “no copy of this document is on file in the Patent Office,” Dr. Nuland could not. Instead, he reproduced Jackson and Morton’s “Letter of Specification”—rather than Patent No. 4848—as his primary source text on the history of anesthesia. Ibid., opposite 72.

⁴⁰⁴Judge Shipman declared the patent void in January, 1862. Wolfe, *Tarnished idol : William Thomas Green Morton and the introduction of surgical anesthesia : a chronicle of the ether controversy*: 448.

whether administered by himself or anyone else⁴⁰⁵—and the local newspapers, but by a seminal article in *The Boston Medical and Surgical Journal*.⁴⁰⁶ That paper, based upon an abstract read on November 3, 1846, and an essay delivered before the Boston Society of Medical Improvement given on November 9, 1846, was by none other than junior surgeon Henry J. Bigelow. It was Bigelow who had been so instrumental in convincing Warren to invite Morton to administer Letheon to Edward Gilbert Abbott a few weeks earlier.

A Public Announcement to the Medical and Scientific Communities

What now promises to be one of the important discoveries of the age.
 -Henry J. Bigelow, November 1846⁴⁰⁷

Not content with merely a presentation to his peers, Bigelow immediately published a long and dramatic essay in the *Journal* entitled “Insensibility produced by Inhalation.” In contradistinction to Crawford Long’s unpublicized, personal use of ether beginning four and one half years earlier, Bigelow’s essay spread word of Morton’s Letheon and the discovery of surgical anesthesia to a wide audience. Bigelow garnered fame for Morton that Long might have attained for himself had he published his findings sooner.

The term “anesthesia” had not yet been adopted by Morton and his community, for Oliver Wendell Holmes, Sr.’s letter to Morton explaining Holmes’ preference for use of the word “anesthesia” (which Holmes defined as “insensibility, more particularly (as used by Linnaeus [sic]

⁴⁰⁵Morton probably realized from the beginning that it would be difficult to maintain the secret formula of his ethereal vapor for long. Therefore, he offered surgeons “a person fully competent to administer [Morton’s] compound to patients who are to have surgical operations.” Nuland, *Anesthesia*: 75. In addition, he could reap fees for the administration of the vapor as well as the vapor itself. In fact, for a fee he could teach students how to administer Letheon and, additionally, collect a royalty on its administration by his graduates. No wonder he fought so hard for so many years to secure his patent. Curiously, Morton might well have prospered more if he had patented the glass vessel used to administer the ether to patients or if he had become the world’s expert in its administration (like Colton with nitrous oxide; see Footnote 327).

⁴⁰⁶Henry Jacob Bigelow, “Insensibility During Surgical Operations Produced by Inhalation,” *The Boston Medical and Surgical Journal* 35, no. 16 (1846).

⁴⁰⁷*Ibid.*, 317.

and Cullen) to objects of touch”) was dated three days after the publication of Bigelow’s essay.⁴⁰⁸

Bigelow’s essay was a stirring yet measured trumpeting of Morton’s Letheon. However, it was not, as we have seen, “the first public announcement of the discovery of surgical anesthesia,” for the newspapers had carried this message from October, 1846 on.⁴⁰⁹

The *Journal* article began with the problem of ages—how “to devise some method of mitigating the pain of surgical operations.”⁴¹⁰ Rapidly, Bigelow shifted to the astounding events of October 16, which he labeled “remarkable phenomena.”⁴¹¹

Like others who witnessed first-hand the magic of Letheon, Bigelow then wrote that he had “experimented” upon his patients with sulphuric ether, believing it the most likely candidate for the active component of Morton’s preparation because of “the odor of which was readily recognized.”⁴¹² Nevertheless, he quickly dismissed ether as the major constituent of Letheon because “the exhilaration was so considerable that the subject became uncontrollable, and refused to inspire.”⁴¹³ In addition, he noted with prescience, “much caution...is required in

⁴⁰⁸Morton had requested that Holmes, a man of letters as well as a physician, suggest names to describe the state induced by Letheon. Holmes’ response, dated November 21, 1846, is the famous letter to which some mistakenly point as the birth of the term “anesthesia.” Holmes’ response to Morton’s query may be viewed at <http://www.general-anaesthesia.com/misc/index.html>, accessed June 26, 2008.

⁴⁰⁹Bigelow made this self-promoting claim for his article in a volume of his collected works, published in 1900. Henry Jacob Bigelow, *Surgical Anaesthesia: Addresses and Other Papers* (Little, Brown, and Company, 1900). 3. To Bigelow’s enduring credit, his article in *The Boston Medical and Surgical Journal* may have been the first professional announcement of surgical anesthesia.

⁴¹⁰“Insensibility,” 309.

⁴¹¹*Ibid.*

⁴¹²*Ibid.*, 310.

⁴¹³*Ibid.*

inhaling the vapor of ether, as the imprudent inspiration of it has produced lethargic and apoplectic symptoms.”⁴¹⁴

Certainly the older medical literature supported his low opinion of ether, for, because of its widespread recreational use, so many had written of its ill and unpredictable effects.⁴¹⁵ Yet Morton’s Letheon, whatever it might contain chemically, worked well more often than not. Bigelow, a careful and conscience physician, wondered what adverse effects had befallen the dentist’s “upwards of two hundred” patients—a very sensible question to ask about so powerful an agent.⁴¹⁶ Morton had noted some nausea and vomiting, particularly in children (because of this, “Dr. M” refused to administer Letheon to children⁴¹⁷), but adverse effects appeared minimal. Bigelow also wondered if Letheon—so useful for short operations—could be administered during more “severe” or longer operations—like those for the treatment of cancer.⁴¹⁸ He was soon to receive an answer in the affirmative, but in the month or so after October 16, 1846, what he surely knew was that Morton’s ethereal agent was revolutionary and a dream come true for the myriad patients who needed and would need surgery.

“The application of the process to the performance of surgical operations is...new,” Bigelow concluded.⁴¹⁹ Perhaps he sensed something of the contentiousness of discovery that was brewing between Morton and Jackson and even Wells, for he followed his support of

⁴¹⁴Ibid., 311.

⁴¹⁵Ibid., 310-12.

⁴¹⁶Ibid., 313.

⁴¹⁷Ibid.

⁴¹⁸Ibid., 309, 16.

⁴¹⁹Ibid., 316.

Morton (“a skillful dentist”⁴²⁰) as discoverer with a disclaimer that “If it can be shown to have been occasionally resorted to before, it was only an ignorance of its universal application and immense practical utility that prevented such isolated facts from being generalized.”⁴²¹ For Bigelow, regardless of who may have used similar agents before, it was clear that Morton, although perhaps with the assistance of “a distinguished chemist,”⁴²² (Jackson), was the discoverer of surgical anesthesia.

The word on the discovery of surgical anesthesia was out, and the word was clear. Bigelow had played an enormous role in publicizing “what now promises to be one of the important discoveries of the age.”⁴²³ Thanks to the widespread readership of the *Boston Medical & Surgical Journal*, Bigelow had reached the surgeons and other practitioners who most needed to know about Morton’s discovery and could use it for the benefit of their cancer and other patients.

Letheon’s True Nature Revealed

Within weeks, physicians all over the United States were using Letheon or its equivalent. This was especially true after the revelations of a letter to *The Boston Medical and Surgical Journal* by J. D. Mansfield dated November 10, 1846, and published on December 23. Mansfield discovered at “a social party” (i.e., Ether party) that a mixture of “sulph. ether, water and morphine, with a few drops of diluted sulphuric acid” produced effects “similar, if not identical, with those produced by the *vapor* now so much in vogue” (i.e., Letheon).⁴²⁴ Others

⁴²⁰Ibid.

⁴²¹Ibid.

⁴²²Ibid.

⁴²³Ibid., 317.

reproduced Mansfield's findings forthwith, reaching similar results. As the *Journal* had been the organ that disseminated knowledge of Letheon surgical anesthesia, so it became the means by which the proprietary status of Letheon was destroyed. The patent was effectively valueless.

Even the United States Army failed to respect Morton and Jackson's United States Government patent, using the anesthetic without acknowledgement or royalty payments during the Mexican War.⁴²⁵ Ironically, perhaps the only group not to use Letheon or its probable components in 1846 out of respect for Morton and Jackson's patent was the MGH group—led by Warren, Bigelow, and Hayward. They determined that “We were not justified in encouraging the further use of this new invention, until we were better satisfied” that it was legal to use it.⁴²⁶ Still, patients at Massachusetts General routinely received Letheon, administered by Morton, for the dentist was caught between the ethical standard of the Massachusetts Medical Society that a benefit to mankind could not be patented, and his own desire to propagate its use for profit.

Legally, the Army and multitudinous others technically used sulphuric ether—not Letheon—but what, in the final analysis, was the difference? Physicians and hospitals derided Morton for attempting to patent something ubiquitous and salutary at the same time, even as

⁴²⁴J. D. Mansfield, "The Inhalation of Ethereal Vapor, &c.," *The Boston Medical and Surgical Journal* 35, no. 21 (1846). cited by Fenster, *Ether Day*: 151.

Morton may have prefigured the exposure of his active agent, for soon after taking out the patent he sought to place exclusive agents in high-volume venues to administer Letheon and collect royalties. He even brazenly asked Horace Wells to be his agent in New York City, but Wells—still perplexed by his exclusion from recognition for his role in the discovery of surgical anesthesia and personally distraught—refused.

⁴²⁵The first known wartime use of surgical anesthesia occurred on March 29, 1847, when the American Edward H. Barton administered sulphuric ether during an amputation in Vera Cruz, Mexico. George A. Swanson et al., "Military Opposition and Religious Objections to Anesthetics, 1846-1848," *Anesthesiology* 101(2004). Thus, as with many medical discoveries intended to improve the quality of an individual's life in peacetime, anesthesia was quickly adopted for national wartime purposes.

⁴²⁶Warren, "Inhalation," 377.

Morton, who wanted Warren and everyone else to use Letheon—but perhaps not until his patent was solid—agreed “to supply assistance to administer the inhalation whenever called upon.” And, according to Warren, so he did. Ibid.

Morton administered it to thousands of dental and medical patients throughout the late 1840s, 1850s, and the Civil War.⁴²⁷

Surgical Anesthesia envelopes Europe and Beyond

The establishment of union by the first intention, the safe ligature of the great arteries, the substitution of lithotrity [*sic*], the rejection of pernicious ointments and plasters in the management of wounds, the constitutional treatment of local diseases, and the free external use of cold water, mark the present as a golden period of surgical science. The introduction of ether enabling us to perform operations, and apply remedies without pain, crowns all these improvements.

-John C. Warren, 1848⁴²⁸

Ether anesthesia rapidly gained a foothold in England and then Europe, thanks to a letter dated November 28, 1846, that included a copy of the *Journal* article mailed by Henry Bigelow's father, Jacob, to his friend Dr. Francis Boott in London.⁴²⁹ Boott, in turn, forwarded the historical announcement of "a new anodyne process" to *The Lancet*, which published it on January 2, 1847.⁴³⁰

In fact, at least two English practitioners had used ether anesthesia even before the publication of Bigelow's article in the British *Lancet*. Boott, on December 19, 1846 (a Saturday), had a dentist by the name of James Robinson extract a tooth in Boott's study from a patient under the influence of ether.⁴³¹ Two days later, on December 21, Robert Liston (1794-1847), then Professor of Clinical Surgery at University College, London, performed what was

⁴²⁷Morton served as a volunteer surgeon in the Army of the Potomac during the Civil War. He used ether at least two thousand times to facilitate surgery on wounded soldiers. <http://www.general-anaesthesia.com/images/william-morton.html> accessed June 16, 2008.

⁴²⁸Warren, *Etherization; with surgical remarks*: 87.

⁴²⁹Nuland, *Anesthesia*: 85.

⁴³⁰Francis Boott and Henry Jacob Bigelow, "Surgical Operations Performed During Insensibility, produced by the Inhalation of Sulphuric Ether," *The Lancet* 49, no. 1218 (1847).

⁴³¹Nuland, *Anesthesia*: 88.

widely acclaimed as the “first European operation under ether anesthesia.”⁴³² Liston, famous for his amazingly rapid surgeries in an age when surgeons routinely performed surgeries at a breakneck pace to minimize the duration and severity of pain, had gained knowledge of ether anesthesia only two days before.⁴³³ On the twenty-first, he performed an above-knee amputation on a butler, Frederick Churchill, that reportedly lasted a total of twenty-eight seconds—including closing the stump with sutures!⁴³⁴ Liston then used ether anesthesia in tearing off the nail on a patient’s great toe. This procedure was, in Liston’s own words, “one of the most painful operations in surgery”—without anesthesia.⁴³⁵ Liston, perhaps betraying his own skepticism for a surgeon whose entire life was devoted to the minimization of surgical pain through speed, announced to his crowd of expectant onlookers that “We are going to try a Yankee dodge today, gentlemen, for making men insensible.”⁴³⁶ The term “Yankee dodge,” immortalized by Liston, was surely meant by him to deride this cheap American-originated method to avoid the pain of surgery which would presumably be as ineffective and unscientific as hypnosis. But the results of the operation convinced him otherwise. Echoing Warren’s “No humbug” declaration of two months earlier, Liston then voiced his new-found belief in surgical anesthesia when he announced to his shocked audience, “This Yankee dodge, gentlemen, beats mesmerism hollow.”⁴³⁷ (As chance would have it, in the audience sat young Joseph Lister, then an

⁴³²Ibid., 85.

⁴³³Ibid.

⁴³⁴<http://www.general-anaesthesia.com/people/robert-liston.html> accessed June 28, 2008.

⁴³⁵Nuland, *Anesthesia*: 85.

⁴³⁶Ibid.

A picture of Liston’s amputation of Churchill’s leg, surrounded by bystanders, may be seen the page before *ibid.*, 88.

⁴³⁷Ibid., 85.

undergraduate student and later the “Father of Antisepsis.” As a result of this chance attendance, Lister was present at the European birth of both of the greatest advances in nineteenth-century medicine—anesthesia and antisepsis.)

In the ensuing weeks and months, surgeons in Germany and France, as well as Great Britain, began using this “anodyne.” One Englishman wrote that “No great improvement in the practice of medicine was probably ever established so readily as the inhalation of ether for the prevention of pain.”⁴³⁸ Dr. Hayward of the Massachusetts General Hospital declared succinctly that ether was, for “suffering humanity, the greatest boon it ever received from science.”⁴³⁹

Morton’s Travail

As Morton watched word of his discovery and the recognition that accompanied it encircle the globe, he began to realize that, despite efforts to obtain patents overseas, his dreams of riches would never be fulfilled. He spent years of bitterness in poverty attempting to defend his patents and seeking, with the aid of politically-connected Bostonians, a monetary reward of \$100,000 from Congress.⁴⁴⁰ Nonetheless, after years of wrangling and contention with Jackson and others, any hope for an official United States government award disappeared. In 1862, out of frustration, Morton brought suit against the New York Eye Infirmary for patent infringement, which, like so many other charitable institutions in the States, used ether anesthesia.⁴⁴¹ The

⁴³⁸John Snow, *On Chloroform and Other Anaesthetics: Their Action and Administration*, Special ed., The Classics of Medicine Library (London: John Churchill, 1858; repr., 1989). 19.

⁴³⁹Wangensteen and Wangenstein, *The Rise of Surgery*: 280. Dr. Nuland’s source book on *The Origins of Anesthesia* is filled with testimonials trumpeting the efficacy of ether anesthesia in the reduction/elimination of surgical pain. Nuland, *Anesthesia*.

⁴⁴⁰The House of Representatives approved appropriation bills to award Morton \$100,000 in 1852 and 1854, but both efforts failed in the Senate. He regularly appealed to Congress for monetary compensation and even met with President Pierce on the subject. Jackson played a significant role in thwarting Morton’s efforts to receive money from the United States government.

⁴⁴¹Amazingly, this was the first occasion, according to Julie Fenster, on which Morton used the courts to defend his patent. Fenster, *Ether Day*: 217.

judge annulled the patent—once and for all time.⁴⁴² Two years later, the American Medical Association censured Morton for acts against medicine.⁴⁴³ His multiyear quest to become wealthy on the wings of Letheon was at an end.

William T. G. Morton discovered a better mousetrap and promulgated its blessings to a thankful but unremunerating world. Neither he nor Wells nor Jackson ever reaped the riches they expected from their insights and efforts to lessen the pains of mankind. In fact, Morton surely received much less than he deserved, for even the partial recognition he garnered as the discoverer of surgical anesthesia was insufficient reward for the man who brought etherization to the attention of the world.

Even his death, rather than befitting a man who brought the promise of surcease from surgical pain, was ignominious and, perhaps, hastened by the frustration in which he spent the last two decades of his life competing with others for recognition and compensation. As Jackson reportedly lost his mind at the sight of Morton's panegyrical grave-monument, so did Morton after reading an article in the June, 1868 issue of the *Atlantic Monthly* that credited the discovery of surgical anesthesia to Jackson.⁴⁴⁴ Shortly thereafter, on a hot summer's day that July, in New York City's Central Park, Morton collapsed and died, probably from a stroke. He was 49 years old.⁴⁴⁵

⁴⁴²Ibid.

⁴⁴³On June 24, 1864, the AMA censured William T. G. Morton for "suits brought against charitable medical institutions for infringements of an alleged patent covering all anesthetic agents, not claiming sulfuric ether only, but the state of anesthesia, however produced, as his invention, has by this act put himself beyond the pale of an honorable profession and of true labors in the cause of science and humanity." Nuland, *Anesthesia*: 99.

⁴⁴⁴Anonymous, "The Discovery of Etherization," *Atlantic Monthly*, June 1868. The credit to Professor Jackson begins at the start of the article and follows throughout. The article portrays Morton as a conniving also-ran who was informed by Professor Jackson, on September 30, 1846, "of the anaesthetic power of ether vapor, where to get it, showed him exactly how to administer it, and assured him that it would make the patient completely insensible to pain." (720)

⁴⁴⁵<http://www.general-anaesthesia.com/images/william-morton.html> accessed June 16, 2008.

By the fall of 1880, all the major protagonists in the drama for recognition as the discoverer of surgical anesthesia—William T. G. Morton, Charles T. Jackson, Horace Wells, and Crawford Long—were dead. But ether as the agent of anesthesia, born in chemistry, competition, and controversy, lived on for decades thereafter, until it, too, was supplanted by better agents.

Ether and Cancer

To produce a narcotism of an hour's duration.

-Henry J. Bigelow, 1846 ⁴⁴⁶

The nexus between cancer and the origins of ether surgical anesthesia is a strong one, both medically and historically. Medically, the depth and duration of judiciously-administered ether anesthesia is much more conducive to the successful performance of cancer surgery (which, in the mid-nineteenth century, was often more complicated and of greater duration than other surgeries) than the safer—but shorter duration—nitrous oxide. Historically, ether anesthesia was quickly recognized as a godsend by practitioners and cancer patients the world over. This is clearly reflected in the historical record, as many of the first patients to undergo surgery under the influence of ether anesthesia were operated on for cancers and other tumors.

The first patient ever to receive ether anesthesia in public, Edward Gilbert Abbott, was operated upon by Dr. John C. Warren to excise tumors from his neck.⁴⁴⁷ Of the first four patients operated upon by Dr. Hayward, the House Surgeon at the MGH, under ether anesthesia (administered by Morton), all before December 7, 1846, three likely had tumors. As Hayward wrote,

⁴⁴⁶Bigelow, "Insensibility," 316.

⁴⁴⁷Vandam and Abbott, "Abbott."

The first case was the removal of a tumor from the arm of a woman; the second, the amputation of the limb of a girl, 20 years of age...; the third, the removal of the breast of a lady, in private practice; and the fourth was the same operation, which I did Saturday last, at the Hospital.⁴⁴⁸

Hayward performed the arm tumor excision under etherization on October 17, 1846, only a day after Warren's operation on Abbott—the day after Ether Day. Both Warren and Bigelow reported this case to a worldwide audience.⁴⁴⁹ The rapidity with which ether anesthesia spread throughout the civilizing world is both amazing—amazing for its speed of adoption and as an example of the notion that there are some great ideas whose time has come, for so many had searched for so long to find an anodyne for surgical pain.

A few days after Hayward's limb resection, Dr. J. Mason Warren (John C. Warren's youngest son) excised a tumor from the arm of another young woman under the influence of Letheon. John C. Warren, more the observer than chief operator at the surgery performed by his son, was stupefied by the effect of the ether. "So entirely tranquil was she," wrote the elder surgeon, "that I was not aware the operation had begun, until it was nearly completed."⁴⁵⁰ Nine days thereafter, the younger Warren removed a tumor "which covered nearly the half of the front of the right thigh" from yet another patient under ether anesthesia.⁴⁵¹ In short succession, the Warrens and their colleagues operated upon many more tumor cases with the aid of Letheon in Boston and environs.

⁴⁴⁸Nuland, *Anesthesia*: 10-11 in "Circular – Morton's Letheon" following text page 77.

I cannot verify the exact nature of the lesions that Hayward excised without pathological analysis of the tissue removed during these operations. However, operating on a breast in the age before antisepsis was not undertaken without good reason and careful forethought. One of the few good reasons to cut into the breast and accept the risk of dying from post-operative infection was because of the presumed presence of a tumor that threatened the life of the patient.

⁴⁴⁹Warren, "Inhalation," 376. and Bigelow, "Insensibility," 309.

⁴⁵⁰Warren, "Inhalation," 377. The date of the operation was November 12, 1846.

⁴⁵¹*Ibid.* The date of this operation was November 21, 1846.

It is important to note that Morton was not the sole beneficiary of surgical anesthesia. Reciprocity ruled. Certainly, any fame that Morton achieved during his lifetime could not have been earned without the advocacy and promotion of Letheon by the renowned surgeons at the Massachusetts General Hospital. And ether anesthesia, in turn, raised the hospital's stature in the world, as memorialized through the naming of Ether Day and the Ether Dome, both of which attract attention to the present.⁴⁵² Had Crawford Long performed the same operation on James Venable's neck at the Mass General, rather than in his village in rural Georgia, the world might never have heard of William T. G. Morton. The Boston dentist, cognizant of the contribution made by MGH's surgeons to his own reputation, dedicated his seminal 1847 work *On The Proper Mode of Administering Sulphuric Ether by Inhalation* "to the Surgeons of the Mass. Gen. Hospital, as an Evidence that Their Early and Continued Interest in the Administration of Sulphuric Ether is Gratefully Appreciated."⁴⁵³

As Morton needed Warren and colleagues to champion ether anesthesia, so the dynamic interdependence between the rise of ether anesthesia and the increase in the number of cancer surgeries was of critical importance to the history of cancer. At a time when only a few operations per week on all patients for all indications was the norm, this concentration of operations on tumor patients in the days and weeks following Morton's administration of Letheon to Abbott is remarkable. It is even more extraordinary when one remembers that physicians and patients considered surgery for cancer to be a last-ditch treatment when all else had failed.

⁴⁵²The Ether Dome at the Massachusetts General Hospital was designated a National Historic Landmark on January 12, 1965. <http://tps.cr.nps.gov/nhl/detail.cfm?ResourceId=249&ResourceType=Building> accessed July 6, 2008.

⁴⁵³Wm. T. G. Morton, *Remarks on the Proper Mode of Administering Sulphuric Ether by Inhalation* (Boston: Dutton and Wentworth, Printers, 1847).

Nevertheless, it was only the beginning, for in the days and weeks after what would come to be called Ether Day, surgeries on tumors were not the only operations performed under ether anesthesia either at the Massachusetts General Hospital, or even in and around Boston and elsewhere. Practitioners used ether for all types of surgical indications. The time for surgical anesthesia had been long in coming but, when it finally arrived, it was welcomed and accepted as a long-anticipated gift by all those who were well aware of what surgery and surgical pain had been like before. And ether, more than nitrous oxide or chloroform, gave birth to surgical anesthesia.

Paeon and Valediction

With Truth so elusive, with personalities so dominant, where does Verity lie? Historians may never learn the answer for sure, but my inclinations are to give credit to all, each with due respect and reward. To Humphry Davy, I confer the award for the intellectual conceptualization and chemical directive that led to surgical anesthesia. To Crawford Long, I bestow the title of “Discoverer,” for until a documented Leif Ericson comes to supplant Columbus, the affidavits are on Long’s side.⁴⁵⁴ To Horace Wells I grant the conceptual leap from entertainment gas to anesthesia, for he was the first to speak his mind—if not his retrospective pen—out loud. To Charles Jackson I bequeath the title of facilitator, for he opened the mind of Morton to the chemistry of ether, and possibly more. And to William Morton, I confer implementer, publicizer, and promoter, for without his amphitheatrical demonstration on that Friday morning in October, 1846, under the Bulfinch dome at the MGH, the trajectory of the treatment of cancer and surgical history in general may well have been very different.

⁴⁵⁴Congress seems to have agreed with this judgment for all the reasons given above. A statue of Crawford Long of Georgia resides in an honored place in National Statuary Hall in the United States Capital building. Long was also commemorated on a two-cent “Famous American Scientist” U. S. Postal Stamp of April 8, 1940 (Scott 875).

For what, when all is said and done, is the value of discovery (Long) if no one knows of it (Morton)? And can the pride of insight (Wells and maybe Jackson) find solace when the face of fame smiles on another (Morton)? Crawford Long blithely and stoically went about his practice, perhaps never quite appreciating just how revolutionary his use of anesthesia really was. Wells never found peace and suffered as his epiphany contributed to the relief of the pain of countless others. Jackson relinquished probity in search for acclaim, and Morton chased riches into an early grave. Certainly the history of the beginnings of anesthesia is not a “happy history,” but—perhaps for the mirth induced by nitrous oxide and ether—it is not often that the “happy” and “history” go together.

Chloroform

I have sung the praises of ether anesthesia in the history of medicine and the treatment of cancer, for it was the first major anesthetic known to surgery, but ether left much to be desired.⁴⁵⁵ Its smell drove grown men to distraction. It was relatively weak and required large quantities to induce sleep. Its inhalation irritated the bronchial tree, inducing coughing and sometimes a feeling of choking. It inflamed the stomach, leading to nausea and vomiting. It agitated the nervous system, causing dilated pupils, strange body movements, and the emission of eerie sounds from patients under its influence. In the word of the day, it “impassioned” the heart, leading to tachycardia (rapid pulse).⁴⁵⁶ Its onset of action was often slow, depending upon the patient’s size and age, requiring several difficult minutes to anesthetize the patient adequately.⁴⁵⁷ On the other hand, sometimes it worked too well, for some patients were difficult

⁴⁵⁵A compelling contemporaneous description of the adverse effects of ether and the patient precautions that must be observed upon consideration of its administration may be found in Eliakim Littell and Robert S. Littell, “Painless Operations in Surgery,” *Littell's Living Age*, 12 June 1847., especially on pages 491-492 as cited by Fenster, *Ether Day*: 257 Endnote “Negative aspects of ether.”.

⁴⁵⁶Bigelow, “Insensibility,” 310-12.

to return to their normal state of consciousness for quite some time after the conclusion of their procedure. It invited abuse.⁴⁵⁸ Chemically, it was a volatile gas that evaporated if left uncontained. And, to top it all off, it sometimes exploded in the operating suite.⁴⁵⁹

As a result of these problems with ether and the relatively short duration of action of nitrous oxide (which worked exquisitely well for quick tooth extractions, but not for more time- and labor-intensive cancer surgery), it was not long before physicians sought new and different chemicals to use for the induction of surgical anesthesia. In fact, the quest began almost immediately after public knowledge of the anesthetic effects of ether reached across the Atlantic.

Dr. James Young Simpson, Scottish Self-Experimenter

James Young Simpson (1811-1870), a Scot by birth, who blazed a path of achievement to become full Professor of Medicine and Midwifery at Edinburgh by the age of twenty-eight years, experimented with different chemical candidates for surgical anesthesia as early as January, 1847.⁴⁶⁰ Like so many others, he was an early adopter of ether anesthesia but, unlike others, he used it to alleviate the pains of childbirth rather than those of tooth extractions or general surgery.⁴⁶¹ Indeed, on January 19, 1847, James Y. Simpson became the first known physician to

⁴⁵⁷In general, consistent with known pharmacologic principles, the heavier and younger the patient, the slower the onset of anesthetic action.

⁴⁵⁸Unfortunately, nitrous oxide and chloroform, albeit to different degrees, could also be addictive.

⁴⁵⁹The inflammable nature of ether, well known to chemists even before its use as a surgical anesthetic, was particularly dangerous in the age of candlelight. When there was no choice but to operate by candlelight at night, as during the Civil War, surgeons avoided ether because of its explosiveness. See <http://fredericksburg.com/News/FLS/2006/092006/09022006/218099> accessed July 2, 2008.

⁴⁶⁰Simpson was not the first to look for alternatives to ether, but his work is best known because it led to the popularity of chloroform. Wells and Morton had individually experimented with chemicals other than nitrous oxide and sulphuric ether even before Ether Day. The articles in the Boston newspapers and, especially, Bigelow's essay in *The Boston Medical and Surgical Journal* on November 18, 1846, led to an outpouring of suggestions for the use of other agents to induce surgical anesthesia. Nuland, *Anesthesia*: Bibliographic Entry #11.

⁴⁶¹Simpson published a monograph on the subject, J. Y. Simpson, *Notes on the Employment of the Inhalation of Sulphuric Ether in the Practice of Midwifery* (Edinburgh 1847).

use ether anesthesia in obstetrics.⁴⁶² Nonetheless, he rapidly concluded that ether was not the ideal anesthetic for obstetrics. In addition to the general problems with ether noted above, Simpson was concerned that there were particular problems with the use of ether in childbirth—direct effects on the contracting uterus, for example—that made the use of ether during parturition even more problematic.

The difficulties with the use of anesthesia during childbirth went beyond the specific problems of ether and its womb effects to encompass the theological question as to whether or not maternal pain during childbirth should be alleviated.⁴⁶³ The Scriptures were clear—“I will greatly increase your pangs in childbearing;” said the Lord God to the woman in the Garden of Eden within sight of the apple-less branch on the Tree of the Knowledge of Good and Evil. As a result, continued the Lord God, “in pain you shall bring forth children.”⁴⁶⁴ Therefore, the pain of childbirth was not by chance. Rather, the imposition of maternal pain was purposeful and clear in intent and thus not treatable by the fruits of human discovery. Furthermore, to deny the Will of God—regardless of the salutary spirit of the action—was iniquitous.

Simpson’s motivation for the alleviation of such pain began similarly to that of Wells, Morton, and Warren for the relief of surgical pain in general. During the pre-anesthesia era, he also wrote of “that great principle of emotion which both impels us to feel sympathy at the sight of suffering in any fellow creature, and at the same time imparts to us delight and gratification in

⁴⁶²Rachel E. Collis, Felicity Plaat, and John Urquhart, *Textbook of Obstetric Anaesthesia*, 1 ed. (Greenwich Medical Media, 2002). 3.

⁴⁶³<http://www.general-anaesthesia.com/images/james-simpson.html> accessed July 17, 2008.

The literature on the religious controversy over the alleviation of parturition pain is vast. A good starting place, after *Genesis* (s.v.), would be Simpson’s *Answer to the Religious Arguments advanced against the Employment of Anaesthetic Agents in Midwifery and Surgery* (1847).

⁴⁶⁴Genesis 3:16.

the exercise of any power by which we can mitigate and alleviate that suffering.”⁴⁶⁵ For Simpson, the natural distress of parturition was additionally vexing, for giving birth was akin to neither disease nor disorder, but rather followed the natural order of things.

Although a pre-Darwinian romantic, he could not subscribe to the pontifications of clergy and laity (predominately men, who, obviously, never bore children) that the woman’s pain of childbirth was God-given and that the alleviation of such pain constituted a sin. In fact, he argued in return that God had also introduced the first “obstetrical” anesthetic, for “the Lord God caused a deep sleep to fall upon the man (Adam), and he slept; then he took one of his ribs and closed up its place with flesh. And the rib that the Lord God had taken from the man he made into a woman.”⁴⁶⁶ No, Simpson could not countenance the Bible-ordained punishment as a reason to accept without question the destructive pains of delivery that he witnessed daily. He cogently answered the objections of those opposed to anesthesia in a full-length pamphlet.⁴⁶⁷

If not Ether, What Then? Discovering Better Anesthetics

Unperturbed by Scripture, Dr. Simpson worked hard to discover a less objectionable anesthetic than ether. Every Thursday evening, he gathered a few of his colleagues around his dinner table and inhaled candidate chemicals he had chosen.⁴⁶⁸ His medical journal reveals that that these potential substitutes were variations on a theme; chemicals known to induce stupor,

⁴⁶⁵<http://www.general-anaesthesia.com/images/james-simpson.html> accessed July 17, 2008.

⁴⁶⁶Genesis 2:21-22.

⁴⁶⁷J. Y. Simpson, *Answer to the Religious Objections advanced against The Employment of Anaesthetic Agents in Midwifery and Surgery* (Edinburgh: Sutherland and Knox, 1847). reproduced in Nuland, *Anesthesia*: Bibliographic Entry #24.

Simpson’s quotation from *Genesis* is on page 21 of the *Answer to the Religious Objections*.

⁴⁶⁸Fenster, *Ether Day*: 165-66.

Nuland, *Anesthesia*: following page 109. reproduces a photograph of Simpson’s (in)famous dining room from No. 52 Queen Street, Edinburgh. Those were hard wooden chairs in which the participants thrashed about!

like volatile ether, but with the property of “a more fragrant or agreeable odor.”⁴⁶⁹ Tested prospects included “the chloride of hydrocarbon, acetone, nitrate of oxide of ethyle, benzin, the vapour of iodoform.”⁴⁷⁰

The obstetrician spent the better part of a year attempting to identify just the right anesthetic. He was helped and encouraged in this search by David Waldie (1813-1889), a Liverpool chemist with whom Simpson had matriculated. Waldie had a particular interest in chloroform, which had become a component of cough syrups, pain relievers, and the like,⁴⁷¹ for he had developed a method to synthesize a purer form of the chemical.⁴⁷² It was Waldie who suggested that Simpson try chloroform at one of his Thursday-evening soirees.⁴⁷³

Finally, on November 3, 1847, Simpson decided that he would follow Waldie’s suggestion and experiment with the clear, colorless, refractive liquid that was also highly volatile, sweet to the taste, and, importantly, non-flammable.⁴⁷⁴ The next day was a Thursday, so Simpson and friends congregated and sniffed the volatile chemical *de la semaine*. Within moments, he and his colleagues were transported to what seemed to be a dream-like state in

⁴⁶⁹Fenster, *Ether Day*: 166.

⁴⁷⁰*Ibid.*

It never ceases to amaze me that these astute, informed gentlemen-scientists routinely put their lives in jeopardy by sniffing, snorting, breathing, imbibing, injecting, or otherwise taking in all manner of potentially life-threatening compounds.

Simpson’s neighbor, Mr. James Miller (a surgeon), habitually visited the Simpson household the morning after these testing sessions to ascertain whether there were any casualties. Nuland, *Anesthesia*: 108. and Fenster, *Ether Day*: 166. I am not aware that he ever discovered any.

⁴⁷¹ <http://www.discoveriesinmedicine.com/Bar-Cod/Chloroform.html> accessed July 23, 2008.

⁴⁷² <http://www.whonamedit.com/doctor.cfm/2532.html> accessed July 23, 2008.

⁴⁷³Thomas Bryant, *A manual for the practice of surgery*, Second American from the Third Revised and Enlarged English ed. (Philadelphia: Henry C. Lea, 1879). 897. Available at http://books.google.com/books?id=926qQyzh4aIC&printsec=titlepage&source=gbs_summary_r&cad=0 accessed July 23, 2008.

⁴⁷⁴Fenster, *Ether Day*: 166-7. and <http://www.general-anaesthesia.com/images/chloroform.htm> accessed July 17, 2008. The website reference contains a photograph of chloroform in a thick-glass bottle that implies its volatility—there are not one, but two caps to prevent evaporation.

another place and time. Indeed, Simpson suddenly believed himself to be in a cotton mill with all its characteristic sounds and shapes.⁴⁷⁵ Upon regaining consciousness, however, he found himself not at a mill, but lying awkwardly under his dining room table! His two colleagues were no better positioned. “This is far stronger and better than ether,” he said to himself.⁴⁷⁶ It was not long before he began to affectionately call it “Chlory.”⁴⁷⁷

Unfortunately, the under-the-table experience was followed shortly by the weekend, for otherwise Simpson would surely have employed chloroform as a replacement for ether during his deliveries. Thus, he waited until Monday, November 8, 1847, poured just half a teaspoon of chloroform (much less than the amount of ether than would have been required to induce a comparable stupor in the average-sized patient) onto a handkerchief, and chloroformed his first obstetrical patient.⁴⁷⁸ The results were stellar. In honor of this painless miracle, the mother named her baby Anaesthesia.⁴⁷⁹

Before this November workweek concluded, Simpson had developed considerable expertise with chloroform and succeeded in publishing a pamphlet, *Account of a New Anaesthetic Agent*, on its virtues as an obstetrical anesthetic.⁴⁸⁰ By November 15th, merely a week after his first chloroform-aided delivery, he added a postscript to his November 12th *Account* that noted that he had, “up to this date, exhibited the Chloroform to about fifty

⁴⁷⁵Ibid., 167.

⁴⁷⁶H. Laing Gordon, *Sir James Young Simpson and Chloroform (1811-1870)*, Masters of medicine (New York: Longmans, Green & Co., 1898). as cited by Nuland, *Anesthesia*: 108-09.

⁴⁷⁷Fenster, *Ether Day*: 168.

⁴⁷⁸Nuland, *Anesthesia*: 109.

⁴⁷⁹<http://www.discoveriesinmedicine.com/Bar-Cod/Chloroform.html> accessed July 24, 2008.

⁴⁸⁰J. Y. Simpson, *Account of a New Anaesthetic Agent, as a Substitute for Sulphuric Ether in Surgery and Midwifery*, American ed. (New York: Rushton Clark, & Co., 1848). cited by and included in Nuland, *Anesthesia*: Bibliographic Entry #22.

individuals.”⁴⁸¹ Better still, “in not a single instance has the slightest bad result of any kind whatever occurred.”⁴⁸² Within months, Simpson published these and other cases and remarks in the United States, one-upping America with a new anesthetic, a British anaesthetic—new in degree, if not kind—in exchange for ether.⁴⁸³

Anti-Anesthesia, Anti-Chloroform

The use of chloroform as an obstetrical (i.e., woman’s) anesthetic engendered controversy far beyond that visited upon its predecessors. Nitrous oxide for dental extractions and ether for deeper surgical anesthesia were immediately recognized on both sides of the Atlantic as godsend. Chloroform anesthetic to assuage the pains of childbirth was a harder sell. In part, this reluctance on the part of physicians to employ chloroform during deliveries was religious, for Genesis left little doubt for observant Christians that the pain of childbirth was not to be circumvented. But the winds of secularism had swept sufficiently across the medical landscape to produce the likes of Dr. Simpson—practitioners who could accept the alleviation of such pain without themselves suffering overwhelming religious guilt.

Still, there were other arguments against chloroform and obstetrical anesthesia, especially in the United States. Dr. Charles Delucena Meigs (1792-1869), a man of high intellect, many interests, and great influence in the field of obstetrics, could not accept the use of anesthesia,

⁴⁸¹Simpson, *Account of a New Anaesthetic Agent, as a Substitute for Sulphuric Ether in Surgery and Midwifery*: 19-24, quotation on 24. as reproduced by Nuland, *Anesthesia*: Bibliographic entry #22.

⁴⁸²Simpson, *Account of a New Anaesthetic Agent, as a Substitute for Sulphuric Ether in Surgery and Midwifery*: 24. as reproduced by Nuland, *Anesthesia*: Bibliographic Entry #22.

⁴⁸³Simpson, *Account of a New Anaesthetic Agent, as a Substitute for Sulphuric Ether in Surgery and Midwifery; Remarks on the Superinduction of Anaesthesia in Natural and Morbid Parturition: with Cases Illustrative of the Use and Effects of Chloroform in Obstetric Practice* (Boston: William B. Little & Co., 1848).

The title page to Simpson’s *Account* includes a quotation attributed to Francis Bacon: “I esteem it the office of a physician, not only to restore health, but to mitigate pain and dolours.”

especially in childbirth.⁴⁸⁴ He doubted the “nature of any process that the physicians set up to contravene the operations of those natural and physiological forces that the Divinity has ordained us to enjoy or to suffer.”⁴⁸⁵ Certainly he embraced the Scriptural pronouncement, but his reasons went deeper—to the heart of what it means to think as a physician. Meigs, like Simpson, worried about the direct effect of chloroform anesthesia on the mother and child. The main force of delivery, in a pre-routine-Caesarian-section world, was engendered by the mother’s uterine contractions. Anesthesia might enfeeble those contractions, leading to great prolongation of parturition, severe dystocia (difficult labor), and even loss of life. Adverse effects of the anesthesia on the newborn’s developing brain were another source of concern, for who knew what lifetime damage might result from a few minutes of anesthesia-induced pain relief for the mother? For Simpson, these were potential problems to be considered, tested, and, hopefully, dismissed. For Meigs, they represented sufficient concerns to avoid the use of anesthesia altogether.

In addition, who could countenance the woozy, drunken state produced by chloroform and other anesthetics? Had they not, after all, had their origins in the superficial baseness of parties filled with frivolities and the induction of a state bordering on—if not flowing over into—inebriation? In the context of the 1840s, as temperance reforms and reformers raked across the

⁴⁸⁴Meigs, who was brought up and received his college education within miles of Crawford Long’s Jefferson, Georgia, practiced with great success in Augusta, GA, until, “owing to his wife’s aversion to slavery...he removed to Philadelphia.” In 1841, he became Professor of Obstetrics and Diseases of Women at the Jefferson Medical College in Philadelphia. <http://www.meigs.org/charles219.htm> accessed July 28, 2008.

In this prestigious post, from which he wrote one of the most popular obstetrical textbooks of the day, *Woman; Her Diseases and Remedies*, he influenced a generation of young physicians. Meigs’ Syndrome, a gynecologic condition comprised of the triad of benign ovarian tumor with ascites (fluid in the abdomen/peritoneum) and pleural effusion (fluid around the lungs) with disappearance of the fluid after tumor resection, is named for Charles Meigs.

⁴⁸⁵See <http://www.general-anaesthesia.com/people/charlesdelucenameigs.html> accessed January 26, 2009.

United States from the Burnt-Over district of New York, how could even a physician, accept, condone, and consciously prescribe yet another inebriant-soporific for the swaying masses?

Pain, on the other hand, was for Meigs the opposite of an inebriant. Pain focused. Pain chastened. Pain made one grateful for moments of painlessness. In short, pain was good. The pains of childbirth, wrote Meigs, are “a most desirable, salutary and conservative manifestation of the life force.”⁴⁸⁶ And what was childbirth if not the ultimate manifestation of “the life force”?

No, Meigs was not about to lend his advice and consent to the use of anesthesia during childbirth. Years after the advent of nitrous oxide, ether, and chloroform, Meigs continued to marginalize anesthesia in his widely-acclaimed textbook of obstetrics, *Woman: Her Diseases and Remedies*.⁴⁸⁷ In fact, there was no mention at all of the word “anesthesia.”⁴⁸⁸ Nitrous oxide rendered the brain “hyperneuristic” (hyper-stimulated nerves)—like champagne.⁴⁸⁹ Ether was mentioned only as something to be avoided—as a chemical that poisoned the brain. Life continued under etherization only by virtue of the fact that the respiratory center of the brain was the last to be affected by ether’s destructive effects.⁴⁹⁰ Meigs cautioned believers in anesthesia that “no man ought to arrogate to himself the right to plunge these organs [brain and spinal cord—LK] into the temporary annihilation of etherization.”⁴⁹¹ Further, he warned, “if the ether

⁴⁸⁶Nuland, *Anesthesia*: 116.

⁴⁸⁷Charles D. Meigs, *Woman; Her Diseases and Remedies. A series of letters to his class*, Second Edition Revised and Enlarged ed. (Philadelphia: Lea and Blanchard, 1851).

⁴⁸⁸Based upon a Google Books word search of Meigs’ text for “anesthesia,” “anesthetic,” “anesth*,” or “anaesth*,” performed July 28, 2008.

⁴⁸⁹Meigs, *Woman; Her Diseases and Remedies. A series of letters to his class*: 375.

⁴⁹⁰*Ibid.*

⁴⁹¹*Ibid.*, 490.

be given long enough, and in quantity sufficiently great...., the patient dies.”⁴⁹² Meigs was clear—ether killed. And chloroform? He did not even mention it.⁴⁹³

John Snow, M.D.—Anesthesia with Caution and Care

Despite Meigs’ strenuous efforts, chloroform became the most popular surgical and obstetrical anesthetic of the nineteenth century. In the face of such opposition, how could this be? The answer requires a return to Great Britain, where royal events decided the fate of chloroform for decades to come and sustained the medicinal control of surgical and obstetrical pain.

Dr. John Snow (1813-1858) was a physician whose inauspicious beginnings in poverty and as a colliery surgeon fade into insignificance in the face of his great contributions to medicine in its evolution from a natural philosophy to a science. Chronologically, his work in anesthesia precedes and surrounds that of the cholera epidemic of 1854 and the Broad Street Pump for which he is most famous (more in Chapter 8). But it was his careful attention to detail through the quantification and measured administration of anesthetics (with his inhaler), that played a major role in the acceptance of ether and chloroform as surgical and obstetrical anesthetics.

John Snow’s youthful intelligence and curiosity led him at the age of fourteen to become an apprentice to William Hardcastle, a surgeon-apothecary in Newcastle-Upon-Tyne. Like generations of other apprentices before him, apprenticeship severely restricted his personal life (no marriage, no alcohol), but gave him glimpses of sickness and suffering at the Newcastle Infirmary the memory of which lasted a lifetime. Not until nine years later, however, did Snow

⁴⁹²Ibid., 658.

⁴⁹³Based upon a Google books word search of Meigs’ text for chloroform, chlory, trichloromethylene, trichloromethane, methyl trichloride, CHCl₃, performed on July 28, 2008.

seek the official University education that made him a physician and bestowed the title “Doctor.”⁴⁹⁴

At the Hunterian School of Medicine in London, named for John Hunter’s older brother, William, Snow received a firm grounding in obstetrics as well as general medicine.⁴⁹⁵ Obstetrics had been one of William Hunter’s special interests, as manifested by his magnificently illustrated text, *The Anatomy of the Human Gravid Uterus*.⁴⁹⁶ By the second quarter of the nineteenth century, childbirth was being medicalized from the province of midwives to that of physicians, a transformation begun to no small extent by Hunter’s *Anatomy* and hastened later in the century by the advent of anesthesia, antiseptics, and other specialized aspects of scientific medicine that midwives were unable or unwilling to provide on a routine basis.⁴⁹⁷

⁴⁹⁴The medical titles, “Doctor” and “Mister,” depend greatly on the historical and/or geographical context of the physician. In England, barber-surgeons and apothecaries retained the title “Mister” well into the eighteenth century. “Doctor” was reserved for physicians who earned a University medical degree. With the elevation of the profession of surgery in the nineteenth century as a result of the history related in this chapter, and the establishment of the Royal College of Surgeons, the title of “Mister” became a badge of honor. Currently, in Great Britain, a University medical school graduate is entitled “Doctor” until s/he becomes a Fellow of the Royal College of Surgeons, at which time her/his title reverts to “Mrs.,” “Ms.,” “Miss,” or “Mister—a title of high distinction. In the United States, all physicians are titled “Doctor.”

For an excellent article on the early history of barber-surgeons, especially in England, see Charles E. Bagwell, “Respectful Image”: Revenge of the Barber Surgeon,” *Annals of Surgery* 241, no. 6 (2005).

⁴⁹⁵Michael A. E. Ramsay, “John Snow, MD: anaesthetist to the Queen of England and pioneer epidemiologist,” *Proceedings of Baylor University Medical Center* 19, no. 1 (2006).

⁴⁹⁶William Hunter, *Anatomia uteri humani gravidi tabulis illustrata The anatomy of the human gravid uterus*, The Classics of Medicine Library (Birmingham,: John Baskerville [etc.], 1774; repr., 1980).

⁴⁹⁷Judith Walzer Leavitt compellingly relates and analyzes the process of the medicalization of childbearing in America in “‘Science’ Enters the Birthing Room, The Impact of Physician Obstetrics,” Chapter 2 Judith Walzer Leavitt, *Brought to Bed: Childbearing in America 1750 to 1950* (New York: Oxford University Press, 1986). 36-63.

Another major contributing factor to the medicalization of pregnancy and childbirth in the nineteenth century was the ascendance of male (physician) supremacy and the weakening of women’s (midwives’) rights and powers in Victorian England and America.

Nevertheless, the effects of social class also figured into whether a pregnant woman would be delivered by a physician or midwife, for physicians generally charged more than midwives.

A later transformation of the process of childbirth, also propelled by scientific medicine, was the move to the hospital—not unlike the institutionalization of cancer related in Chapter 2 of this dissertation.

In Great Britain, James Simpson and John Snow were part and parcel of the medicalization of childbearing through their work in obstetrical anesthesia.⁴⁹⁸ Snow, like Simpson, was also consumed by the quest to quell the pain of parturition. A man of many talents, Snow had experimented with ether as early as 1843 (one year prior to receiving his M.D. degree) in an attempt to find an agent that *increased* respirations.⁴⁹⁹ By the time of Morton's promotion of the use of ether as an anesthetic three years later, Snow was already familiar with its many effects—both good and bad. As a result, he invented an apparatus in 1847 that carefully meted out a small dose of ether while monitoring its temperature at all times.⁵⁰⁰ With this device, he sought to avoid two of the major adverse effects of ether—overdose and explosion.

Unlike Morton and Jackson, Snow never sought to patent either an anesthetic or his inhalation apparatus. Nonetheless, he reaped great rewards—unlike the Americans—because, as a result of his scientific knowledge of the gas and his inhaler (diagrams of which he published for all to see and use), his colleagues quickly recognized him as “the most accomplished anaesthetist in the British Isles.”⁵⁰¹ Snow and his anesthesia were in such demand that, within a

⁴⁹⁸In recognition of his discovery and work on chloroform, James Young Simpson was knighted in 1866. He was the first person ever knighted for services to medicine. For the inscription on his coat of arms he chose *Victo Dolore*, pain conquered.

⁴⁹⁹Ramsay, "John Snow, MD: anaesthetist to the Queen of England and pioneer epidemiologist."

⁵⁰⁰An engraving of Snow's 1847 ether inhaler may be seen as Figure 3 at <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1325279> accessed August 2, 2008, and online version of *ibid.*

⁵⁰¹*Ibid.*

Snow fulfilled the ethic promulgated on both sides of the Atlantic that great medical discoveries were public goods. Morton and Jackson, living in a less mature economic environment at a time of financial insecurity (hard on the days of the 1837-1843 depression in the United States) did not. Each had his medical, dental, and chemistry practices, respectively, to depend upon as a source of income, but Morton, especially, made the conscious decision to pursue fame and riches through patent protection whereas Snow achieved fame and riches through the renown of being the best known and accomplished in his field. Snow's approach, given the potential competition from Robert Liston, Simpson, and many others, made success more difficult, but Morton's was more problematic and, in the historical climate of his day, ultimately flawed.

few years, he administered anesthesia in over five thousand cases and received the emoluments that accompanied all those procedures.⁵⁰² Snow's renown was founded upon his expertise in the administration of anesthesia, and that was based upon his respect for the gases and knowledge of the evil they could do.

The Death of Hannah Greener

Dr. Snow's acquired experience with ether, derived from his diligent study of the anesthetic and his careful approach to its administration, easily translated to the use of chloroform after its introduction by Simpson in late 1847. One chloroform-related event in particular may have shaped Snow's approach to the anesthetic and, in the long run, gave him an advantage in its administration that accrued much to his benefit—and to the welfare of supporters of surgical and obstetrical anesthetics everywhere. That was the mysterious demise of young Hannah Greener, the first recorded death from chloroform anesthesia.

On January 28, 1848, fifteen-year-old Ms. Greener underwent surgery to remove a toenail.⁵⁰³ She had undergone a similar excision on her other great toenail under ether anesthesia in November, 1847 without complications. This time, however, according to her anesthetist, Dr. Meggison, she “appeared to dread the operation, and fretted a good deal.”⁵⁰⁴ Hannah's anxiety perplexed Meggison because of the recent successful operation on the other great toenail and the performance of the procedure in the familiar setting of her own home—the most common venue for surgeries on well-heeled patients at the time and a source of comfort for most patients.⁵⁰⁵

⁵⁰²Ibid.

⁵⁰³Most of my account of the Case of Hannah Greener is John Snow's summary with notes of an article that appeared in the *London Medical Gazette*, Volume xli, page 255 ff. as published in his monograph. Snow, *Chloroform*: 123-27.

⁵⁰⁴Ibid., 124.

The anesthetist poured a teaspoonful of chloroform on a handkerchief and held it over the fifteen-year-old's nose and mouth. About thirty seconds later, Meggison determined that Hannah was "insensible" and requested Mr. Lloyd, the surgeon, to begin the operation. Shortly thereafter, the patient "gave a kick or twitch," which led the anesthetist to assume that the patient was inadequately anesthetized and required more chloroform.⁵⁰⁶ "I was proceeding to apply more to the handkerchief, when her lips, which had been previously of a good colour, became suddenly blanched, and she spluttered at the mouth, as if in epilepsy."⁵⁰⁷ Ms. Greener was unresponsive. All attempts to revive the patient—cold water thrown on her face, brandy, and even the opening of her jugular vein—failed. She was dead. Meggison was appalled and alarmed. In his own words, "The whole process of inhalation, operation, venesection, and death, could not, I should say, have occupied more than two minutes."⁵⁰⁸

Open inspection of the deceased's organs the next day revealed that "both lungs...[were] in a very high state of congestion," but that the heart appeared "quite healthy."⁵⁰⁹ The examiners concluded that "chloroform caused death by producing congestion of the lungs."⁵¹⁰ Snow disagreed. Writing a few years later, he concluded that "From the lips becoming suddenly blanched...there is every reason to conclude that the heart was suddenly paralysed."⁵¹¹ Dozens

⁵⁰⁵The modern hospital, with its sterile, fluorescent-lit hallways and uniformed attendants, is a frightening place for many, compounded by the fear-provoking condition(s) that led to hospitalization in the first place. Movements throughout the twentieth and early twenty-first centuries to "domiciliate" the hospital environment have had mixed results.

⁵⁰⁶Snow, *Chloroform*: 124.

⁵⁰⁷*Ibid.*

⁵⁰⁸*Ibid.*

⁵⁰⁹*Ibid.*, 125.

⁵¹⁰*Ibid.*

⁵¹¹*Ibid.*, 126.

of other cases supported Snow's supposition.⁵¹² (More recent research, even at the cellular level, has justified Snow's contention that chloroform caused cardiotoxicity and could indeed provoke heart "paralysis."⁵¹³)

Slow, Steady, and Safe

By January of 1848, hardly two months after the discovery of the anesthetic properties of "chlory" by Simpson (and his two thrashing colleagues), chloroform had become the surgical anesthetic of choice. Its increased potency compared to ether and increased duration of action compared to nitrous oxide permitted a shorter induction period and greater durability of effect than its competitors. Surgeons could start the operation quicker and finish sooner, a very appealing advantage.

Nevertheless, Snow, a careful and cautious man by temperament, worried that faster was not better—or safer. Thus, he engineered a chloroform vaporizer apparatus that, like the ether apparatus, administered a small (no more than four or five percent chloroform mixed with air), steady dose to the patient—nothing that would overwhelm the heart (or any other organ).⁵¹⁴ Many anesthetists drenched their cloths in chloroform, nearly asphyxiated the patient with forceful application of the cloth to his/her face, and repeated the dose a second time if the patient showed any sign (even a false sign, as is probable in the case of Hannah Greener) of sensibility.

⁵¹²In his monograph, Snow reviewed and analyzed fifty "fatal cases of [chloroform] inhalation," of which Hannah Greener was the first. *Ibid.*, 120-200.

⁵¹³Studies of chloroform cardiotoxicity have clearly shown that chloroform poisoning of the heart is time-dependent, i.e., a bolus of chloroform may be lethal whereas a smaller concentration of the anesthetic administered over a long period of time with the same total dose, would not be. See, for example, N. S. el-Shenawy and M. S. Abdel-Rahman, "Evaluation of chloroform cardiotoxicity utilizing a modified isolated rat cardiac myocytes," *Toxicology Letters* 69, no. 3 (1993).

⁵¹⁴Snow previously took a similar calculated approach to the administration of ether. "THE point requiring most skill and care in the administration of the vapour of ether," wrote Snow in the opening line of his 1847 monograph on ether, "is, undoubtedly, to determine when it has been carried far enough." John Snow, *On the Inhalation of the Vapour of Ether in Surgical Operations: Containing a Description of the Various Stages of Etherization, and a Statement of the Result of Nearly Eighty Operations in which Ether Has Been Employed in St. George's and University College Hospitals* (London: J. Churchill, 1847). 1.

Snow, on the other hand, dispensed the chloroform-air mixture in small but frequent aliquots. Should the patient reveal any sign of arousal, Snow found it “generally desirable to let the patient have a few inspirations of air charged with chloroform vapour every half minute or so, whilst the operation continues, in order to keep up the insensibility.”⁵¹⁵ Further, he warned, “The first rule...in giving chloroform is to take care that the vapour is so far diluted that it cannot cause sudden death.”⁵¹⁶ This method of administering anesthetics in small but steady doses remains the standard of practice for most forms of general anesthesia to this day.

Royal Accoucheur

John Snow’s experimental knowledge, expertise, and enviable safety record with his measured approach to the administration of chloroform caught the attention of the Royal family as well as his colleagues.⁵¹⁷

In 1847, he updated his listing in the *London Medical Directory* to add “physician and *accoucheur*” (a man who assists women in childbirth) by virtue of his increasing professional focus on the administration of anesthesia during childbirth.⁵¹⁸ At about the same time, despite the theological controversy over the use of anesthesia during childbirth, Queen Victoria and, especially, her husband, Prince Albert, took an interest in chloroform anesthesia. This followed after the birth of the sixth of her nine children.⁵¹⁹ Even her seventh child, Arthur, Duke of Connaught (1850-1942), was delivered without anesthesia, despite its ready availability. Perhaps

⁵¹⁵*Chloroform*: 97.

⁵¹⁶*Ibid.*, 251.

⁵¹⁷Thomas E. Keys, "John Snow, M.D., Anesthetist," *Journal of the History of Medicine and Allied Sciences* 1, no. 4 (1946). noted with respect to Snow’s administration of chloroform “more than four thousand times with entire success.”

⁵¹⁸Peter Vinten-Johansen et al., *Cholera, Chloroform, and the Science of Medicine: A Life of John Snow* (Oxford: Oxford University Press, 2003). 104, Note 19.

⁵¹⁹<http://www.general-anaesthesia.com/images/queen-victoria.html> accessed August 5, 2008.

the pain of that childbirth was the final straw for Victoria's Albert, the Prince Consort, who found it difficult to watch the birthing tribulations of his beloved in light of his knowledge of the availability of anesthesia.⁵²⁰ Despite criticism from Sir James Clark, the Queen's Senior Physician, who adjudged anesthesia to be a panacea for none but the lower classes, Albert endeavored to take advantage of the new science of anesthesia to ease his wife's parturient pains—and perhaps fears.⁵²¹

Prince Leopold and Princess Beatrice

In early April, 1853, Prince Albert summoned Dr. John Snow, Great Britain's best-known, most-respected, and probably first specialist in anesthesia, to Buckingham Palace. The Prince Consort displayed considerable knowledge of anesthesia and was apparently well pleased with his interview of Dr. Snow.⁵²² On April 7, 1853, four days later, Victoria and Albert—despite the dubious physicians and ecclesiastic controversy that swirled around them—decided that Snow should administer chloroform for the birth of their eighth child.

Snow, for his part, was not about to overdose the Queen of England. He administered only small doses of the compound. Victoria was awake but woozy. For a woman who had experienced seven painful deliveries, chloroform was a miracle. "Doctor Snow," she wrote, "gave that blessed chloroform and the effect was soothing, quieting, and delightful beyond

⁵²⁰Albert had actually read some of Snow's monographs. Thomas Dormandy, *The Worst of Evils: The Fight Against Pain* (New Haven: Yale University Press, 2006). 274.

⁵²¹Princess Charlotte (1796-1817), the only child of George IV and higher in line to be Queen of England than Victoria, died after a fifty-hour (anesthesia-less!) stillborn labor. Sir Richard Croft, her obstetrician, was condemned (figuratively, not literally) for not using forceps. (Whether or not it would have made a difference to the delivery of a nine-pound, five-ounce stillborn son is questionable.) Three months after the death of Charlotte and her son, Sir Richard shot himself, leading to the so-called "triple obstetrical tragedy." Shingleton, "The Tumultuous Marriage of The Prince and The Princess of Wales," *ACOG Clinical Review* 11, no. 6 (2006).

⁵²²<http://www.general-anaesthesia.com/images/queen-victoria.html> accessed August 5, 2008.

measure.”⁵²³ For his part, the circumspect and judicious Dr. Snow remarked only that “Her Majesty is a model patient.”⁵²⁴

Following this successful birth of Prince Leopold (1853-1884), the Queen would never again entertain delivering without anesthesia. The Royal couple’s last child, Princess Beatrice (1857-1944), was born with the aid of chloroform four years later. Again, the Royal *accoucheur* took pains to administer minute, non-threatening doses—enough to ameliorate pain, but not enough to tarnish the reputation of “the greatest gift to suffering mankind” [and womankind—LK] in the first half of the nineteenth century. With the royal stamp of approval, medical and ecclesiastical opposition to surgical and obstetrical anesthesia slowly but surely diminished over time.⁵²⁵

Anesthesia Affirmed—With Caveats

From the death of Hannah Greener (1848) to the birth of Queen Victoria’s Beatrice (1857), surgical anesthesia in general and chloroform in particular underwent a remarkable acceptance, if not vindication. Administered with Dr. Snow’s eye for detail—in small, steady amounts mixed carefully with (diluting) air—the practice of surgery was transformed from a harrowing experience of hasty excision and amputation to a more measured, deliberate—even cerebral—experience with time as friend rather than enemy.

As W. W. Keen wrote two generations and many wars later, anesthesia transformed the practice of surgery from frantic celerity prompted by shrieking and moaning to “quiet and leisure

⁵²³<http://www.general-anaesthesia.com/images/queen-victoria.html> accessed August 5, 2008.

⁵²⁴Ibid.

⁵²⁵A direct correlation between Victoria’s acceptance of obstetrical anesthesia and the acquiescence of the medical and clerical communities on the use of anesthesia for surgery and delivery is impossible to prove. Of course, the occurrence of one event following another does not prove that the second event was caused by the first-in-time event (*post hoc ergo propter hoc*), but newspapers and magazines of the time seem to have made this connection, and there is a clear decline in anti-anesthesia literature in England after 1853.

which is essential to the performance of many, if not most, of our modern, elaborate, and prolonged surgical operations.”⁵²⁶ For both patient and operator, surgery became a time to care and a time to learn, rather than a race against the clock—and pain.

“The Greatest Gift” or Pandora’s Box?

The science of anaesthesia [in 1861] was in its infancy.

-Sir Rickman John Godlee (1924)⁵²⁷

Nevertheless, the hope placed in anesthesia sometimes outstripped its performance. No anesthetic is perfect. Anesthesia, to this day, remains a work in progress.⁵²⁸ Dosage, mode of administration (inhalation, later intravenously, intrathecally—injection into the spinal canal, etc.), duration of administration, and the treatment of adverse effects—let alone the risks specific to a given patient—were and are question marks in the use of “the greatest gift to mankind.”⁵²⁹

One reason for the reluctance to administer anesthetics was fear of their potential ill effects. Religious issues aside, the Committee on Surgery of the American Medical Association, as early as 1848, asked whether “the risks and evils attendant upon the use of these agents in

⁵²⁶Keen, *Addresses*: 254.

⁵²⁷Godlee, *Lister*, 205: 102.

⁵²⁸Hence the advent of the specialty of anesthesia as one of the first medical/surgical specialties. Also note that the specialty of anesthesia arose soon (one-two years) after the discovery of the first surgical anesthetics, rather than being co-opted by the general surgeon or languishing in medical-surgical purgatory for many years. Other specialties originated generations, centuries, or even millennia after the discovery of their underlying diseases (cancer), methodological approaches (surgery, medicine), organs (cardiology, gastroenterology), or mechanisms (hypertension). Of course, many factors were involved—enough to fill many books on the history of anesthesiology.

And note that I title those who administer anesthetics as anesthetists rather than anesthesiologists. (The latter designation has more to do with those who study the science of anesthesia than those who administer it, although in practice those who hold the M.D. degree are usually designated anesthesiologists, and non-M.D.s are called anesthetists.) Nonetheless, the complexities and risks of anesthesia particularly lent themselves to early specialization decades before the rise in the late nineteenth and twentieth centuries of the great organ-dedicated specialties.

⁵²⁹The routine visit by the anesthetist (or her/his representative) prior to surgery today is (at least in part) a reflection of the complexity of mixing and matching anesthetics to specific patients that was evident to Morton, Simpson, Snow, and others over one hundred fifty years ago. Of course, today’s selection algorithm is more complex, given the great increase in the number of available anesthetics, the ability to administer several anesthetics concurrently, and the growth of knowledge in patient-drug interactions and adverse effects.

surgery, counterbalance the advantages afforded by exemption from pain, and to what extent and under what circumstances is it proper to use them?"⁵³⁰ There was no easy answer, and there was no single agent to which the question alluded. As noted, the use of each anesthetic had advantages and disadvantages, thus requiring the surgeon and/or anesthetist to tailor the anesthetic to the situation and the patient at hand.⁵³¹

Chloroform, albeit the last of the major nineteenth-century anesthetics to be synthesized, had significant adverse effects. Although more concentrated in effect, possessed of a more pleasing smell, and less explosive than ether, chloroform could cause sudden death. Even worse (if there is worse), death from chloroform was idiosyncratic (due to individual susceptibility) and therefore unpredictable. Some called it "paralysis of the heart."⁵³² The incidence (number of events in a cohort) was believed to be as frequent as 1:3,000—a frighteningly high level.⁵³³ (By contrast, the surgical mortality rate from ether administration was about 1:20,000⁵³⁴ and 1:1,370,000 for nitrous oxide.⁵³⁵) The sudden death of Hannah Greener was likely a consequence of what was later determined to be chloroform's arrhythmogenic (heartbeat

⁵³⁰Quoted by Pernick, *A calculus of suffering : pain, professionalism, and anesthesia in nineteenth-century America*: 94.

⁵³¹The reader must be aware not only that not every surgical patient after 1846 received anesthesia but also that not every surgery or delivery after 1847 was attended by an anesthetist. Some surgeons used anesthesia all of the time; many some of the time; others, like Meigs, rarely if ever. For a detailed analysis of this issue, see *ibid.*

Although historical change may occur on the margins of society or, in this case, of medicine, the great mass of the people in the mid-nineteenth century (and beyond) in the United States and Britain had neither the power nor the purse to demand anesthesia or anesthetists. Although Americans and Englishmen today cannot conceive of surgery or even the delivery of a child without anesthesia (unless intentionally refused), this is not true in many less-developed (i.e., poorer) parts of the world.

⁵³²<http://www.discoveriesinmedicine.com/Bar-Cod/Chloroform.html> accessed August 12, 2008.

⁵³³Wawersik, "History of chloroform anesthesia."

⁵³⁴*Ibid.*

⁵³⁵Adrian Padfield, "A brief history of British 'chair' dental anaesthesia," *International Congress Series* 1242(2002).

irregularity) effect.⁵³⁶ Such was certainly Henry Bigelow's conclusion, for he called it "death by 'shock'."⁵³⁷

Thus, none of the three major nineteenth-century anesthetics was faultless. If the practitioner decided that the patient was a candidate for anesthesia (given the patient's overall health, the disease state, and the proclivities of the physician), how was he to decide which agent to use? For the most part, nitrous oxide remained confined to the realm of short-lived medical and dental procedures, due to its relatively brief duration of effect. Longer procedures, from amputations to many cancer excisions, presented a dilemma, for, although ether and chloroform both had a longer duration of action than nitrous oxide, each had its own problems. Often the choice was a lesser of evils. Certainly the anesthetic selected was predicated on what the operator judged was best for his patient, but there appear to have been additional overarching considerations.

Who Used What, When?

Unfortunately, the decision tree for selecting the best anesthetic for a longer-duration procedure was not always patient-centered. To a not insignificant extent, it was—consonant with the times—nationalistic! Physicians in the United Kingdom and Germany tended to favor chloroform. Those in the United States, in similar operative circumstances, utilized ether much more. Of course, Simpson and Snow (with the noted contributions of Queen Victoria and Prince Albert) developed chloroform in the U.K.—and the Royal House of Hanover of Great Britain

⁵³⁶Not until 1911-1912 was it determined, by Dr. A. G. Levy, that "[L]ow concentrations of chloroform produce marked cardiac irregularity (idiopathic ventricular contractions) in cats." This finding was later reproduced in other animals and man. Torald Hermann M.D. Sollmann, *A Manual of Pharmacology and its applications to Therapeutics and Toxicology* (Philadelphia and London: W. B. Saunders Company, 1917). 569.

⁵³⁷Bigelow, *Surgical Anaesthesia: Addresses and Other Papers*: 110.

had significant kinship ties with the German rulers.⁵³⁸ And Long and Morton had developed ether in the United States.

But the decision on anesthetic selection went deeper than origins and personalities, for surgeons on both sides of the Atlantic were aware of the advantages and disadvantages of each.⁵³⁹ Usage numbers are straightforward. By the late nineteenth century, upwards of 95% of operations in the United Kingdom and Germany that utilized anesthesia involved chloroform.⁵⁴⁰ In part, this extreme inclination to prefer chloroform over ether anesthesia followed the Report of Chloroform Committee of Royal Medical and Chirurgical Society.⁵⁴¹ In the United States, the comparable figure was only about 50%.⁵⁴²

General Anesthesia for Cancer Surgery

In his 1858 valedictory *On Chloroform and other Anaesthetics*, including ether, John Snow wrote of his administration of anesthesia during specific cancer operations.⁵⁴³ Not surprisingly, given his background and expertise, he favored chloroform for such procedures. To support chloroform as his anesthetic of choice, he cited its more rapid onset of action, decreased

⁵³⁸Of course, the Royal House of Hanover was German by origin and only assumed the British throne after George I succeeded Queen Anne, the last of the Stuarts, in 1714. The Hanoverians ruled Great Britain until Victoria's death in 1901.

⁵³⁹Henry Bigelow in the United States and John Snow in Britain were only two of countless physicians who wrote on the adverse effects of anesthetics. For their contributions to the process of anesthetic selection and risks involved, see, among other works, Bigelow, *Ether and chloroform*. and Snow, *Chloroform*.

⁵⁴⁰Wawersik, "History of chloroform anesthesia."

⁵⁴¹<http://www.general-anaesthesia.com/images/chloroform.htm> accessed August 19, 2008.

⁵⁴²Edward E. Squibb, *New York Medical Journal* 13(1871). cited by <http://www.general-anaesthesia.com/images/chloroform.htm> accessed August 12, 2008.

Chloroform was used commonly during the American Civil War because of the fear of ether-induced explosions during nighttime operations, but declined in usage thereafter. Chloroform fell into disuse in Great Britain after the First World War, as did ether in the United States after the Second World War as new agents with improved properties (increased safety and efficacy) replaced them. Long after the period covered by this dissertation, chloroform was found to be carcinogenic. As such, its use was outlawed in the United States in 1976—an ignominious demise for a drug discovered with such high hopes and so rich in history.

⁵⁴³Snow, *Chloroform*: 280-89, 91, 94, 308-10.

volatility, and a lesser frequency of nausea, vomiting, and other adverse effects compared to ether. He also minimized the mortality risk of chloroform, believing (partially incorrectly) that cautious administration of the gas would forestall disaster.⁵⁴⁴ (He did, however, correctly note that ether was less lethal than chloroform, for “ether is altogether incapable of causing the sudden death by paralysis of the heart, which has caused the accidents which have happened during the administration of chloroform.”⁵⁴⁵)

It is important to emphasize that the types of cancer operations common to Snow’s time during the era of traditional cancer surgery were more superficial in location than they are today. In the early twenty-first century, operations on “deep” cancers such as lung, stomach, liver, colon, and prostate are common. During the mid-nineteenth century, operations on internal organs were quite unusual because of their high mortality rates—from infection, not anesthesia. Instead, cancer operations on “superficial” parts of the body, like the breast, face, skin, penis, and vagina, were common. Rare surgical attempts to remove ovarian cysts and other “internal tumors” typically ended badly. Of the ten cases of ovarian tumor surgeries recorded by Snow during which he administered chloroform, at least five died in the immediate post-operative period.⁵⁴⁶

Operations on breast tumors were especially common in mid-century after the advent of anesthesia. Snow noted two hundred and twenty-six breast surgeries during which he administered chloroform over approximately a ten-year span (1848-1858), of which two hundred

⁵⁴⁴As noted (page 114), chloroform cardiotoxicity is idiosyncratic, meaning that it is peculiar to the makeup of the individual and therefore rarely predictable. On the other hand, there may be some element of dose-dependence (the higher the dose the greater the lethality), in which case Snow’s sub-therapeutic dosing would have reduced the incidence of death by chloroform.

⁵⁴⁵Snow, *Chloroform*: 362.

⁵⁴⁶*Ibid.*, 308-10. These deaths were typically from peritonitis, a “localized” form of sepsis in the region of the surgery—not from anesthesia. The next section of this chapter will delve into the history of antisepsis.

twenty-two were women.⁵⁴⁷ Many of these procedures were of long duration and involved considerable loss of blood, thus, in the minds of many, favoring chloroform anesthesia over ether.⁵⁴⁸

Although Snow believed that the duration of the ideal operation for the use of chloroform anesthesia was two to three minutes,⁵⁴⁹ cautious administration of additional anesthetic with his restrictive inhaler could provide adequate levels of narcotism for much longer periods of time. Thus, tumors of the jaw, breasts, bones, ovary, and vagina, which required longer operating times than the excision of more superficial lesions, could potentially be operated upon successfully with chloroform and a careful operator.⁵⁵⁰

One additional development respecting the intersection of cancer, surgery, and anesthesia bears mentioning, and that is the use of an operating table versus an operating chair. Although this distinction appears trivial, it actually led to profound alterations in the accessibility of different organs to surgeons over the course of the nineteenth and twentieth centuries.

Head and neck surgery is a case in point. Nineteenth-century drawings and photographs from the early days of anesthesia (such as the “re-enactment” of the first Warren-Morton operation on Edward Gilbert Abbott on October 16, 1846 under the Ether Dome) often depict the

⁵⁴⁷Ibid., 285-87. This was an enormous number of surgeries to be attended by one individual in one decade during the pre-antisepsis era.

Interestingly, the four cases in men were all malignant, while many of the operations on women’s’ tumors were re-operations for benign as well as malignant recurrences. Ibid., 287, 85.

⁵⁴⁸Years later, investigators determined that large doses of chloroform—certainly larger than the conservative Snow would ever use—could damage the liver, thereby reducing the synthesis of factors essential for clotting (like fibrinogen), and lead to significant hemorrhage. G. H. Whipple and S. H. Hurwitz, "Fibrinogen of the Blood as Influenced by the Liver Necrosis of Chloroform Poisoning," *The Journal of Experimental Medicine* 13, no. 1 (1911).

⁵⁴⁹Snow, *Chloroform*: 294.

⁵⁵⁰However, the same risk of death from infection (bone, osteomyelitis; breast, mastitis; ovary, peritonitis; vagina, vaginitis) with these deeper versus superficial cancer surgeries remained.

patient in an operating chair with his head in a raised position.⁵⁵¹ Anesthetization created a difficulty, for the unconscious patient would lose muscle tone and have to be held by several attendants to prevent his/her sliding off the chair!⁵⁵² In addition, the inhalation of anesthetic gases through the operative area with the patient in the upright position created problems for both the anesthetist and the surgeon, for the operative field was small and the respective needs of both for visualization of the same area was great.⁵⁵³ By lowering the patient into the recumbent (horizontal) position—for example, as onto an operating table rather than in a chair—the head was thrust back and the neck exposed. Thus, the anesthetist gained access to the airways to administer gas through a narrow tube while the operator enjoyed a more open view of the jaw or neck for the purpose of exploration, dissection, and/or resection.⁵⁵⁴ The advent of anesthesia may thus be one of the reasons why operations today are commonly performed on a table rather than in a chair.⁵⁵⁵

Other Anesthetics for the Surgery of Cancer

The ideal anæsthetic has not yet been obtained. No one who reads the journal from week to week, and sees the sad headings “Death from Anæsthetics,” and especially

⁵⁵¹One of many such pictures can be found at <http://www.choosegha.com/images/History/Morton.jpg> accessed August 16, 2008.

⁵⁵²Perhaps this is one reason that many pictures from the early days of anesthesia depict the patient surrounded by many, many attendants, several with their hands supporting the patient in the operating chair. Ibid. and Snow, *Chloroform*: 294.

⁵⁵³Antiseptic requirements later in the nineteenth century added the additional problem of attempting to maintain a “clean” operative site—despite the patient’s “unclean” mouth and nose full of microbes.

⁵⁵⁴Abbott’s neck tumor admitted itself to such open positioning, but operations inside the mouth, such as Grover Cleveland’s, remained problematic until the advent of routine endotracheal anesthesia in the twentieth century. Louis J. Acierno, *The History of Cardiology: men, Ideas and Contributions* (Informa Health Care, 1994). 619-20.

⁵⁵⁵Brain and some other head and neck surgeries are still often performed with the patient in an upright position, but these are today the exception to recumbent positioning for surgery, rather than the rule.

In addition to the surgical procedures noted above, there are other operations, including colonoscopy, spinal column, and gynecologic operations, performed with the patient on an operating table, but not flat on his/her back.

“Death from Chloroform,” can fail to see that both ether and chloroform, and also a few others which occasionally replace them, have very real dangers.

-W. W. Keen, 1897⁵⁵⁶

Nitrous oxide, ether, and chloroform produce general anesthesia—a state of complete unconsciousness. General anesthesia is often best suited for the surgical treatment of cancer when the operation is of long duration or deep within the body. But what if the lesion is localized, for example, on the neck, in the mouth, or on a leg? Is general anesthesia really necessary? Do the risks attendant to loss of consciousness and the individual agents outweigh the potential reward? As surgeons and anesthetists gained more experience with the general anesthetics and, particularly, their shortcomings, during the second and third quarters of the nineteenth century, they began to wonder if a more restricted form of anesthesia that acted solely on the local area or region around the tumor might allow surgery with fewer adverse consequences. Restraining a possible drive toward more local anesthesia in the early years of the second half of the century, however, was the prevalent notion during the era of traditional cancer of constitutionalism. This made the use of local or regional anesthesia problematic and counter-intuitive. But time teaches and utilitarianism seeks the less painful or less dangerous path in life. Why remove a lip cancer if the cancer will subsequently reappear in short order on the neck, torso, or leg?

Thus, in addition to the pain of surgery in the pre-anesthetic era and the risk of post-operative infection, belief in the constitutional nature of cancer dissuaded practitioners in the era of traditional cancer from excising localized cancers or from removing cancers locally. Local anesthesia in the era of traditional cancer was available and may have reduced the pain of

⁵⁵⁶“Semicentennial Address in Surgery,” delivered at the Semicentennial Meeting of the American Medical Association at Philadelphia, Pa., June 3, 1897. Keen, *Addresses*: 255.

surgery in a circumscribed area, but it neither disabused operators of the theoretical underpinnings of cancer constitutionalism nor removed the risk of death after surgery.

Two localized methods of producing numbness in the part of the body in question—pressure (arterial compression, nerve compression)⁵⁵⁷ and freezing⁵⁵⁸—were known to the Ancients and commonly used well into the nineteenth century.⁵⁵⁹ They reduced or eliminated sensation distal (away from the center of the body) to the site in question, but did not counter potentially deadly post-operative risks such as infection. Therefore, local and regional anesthetics were of little force in the surgical treatment of cancer until the onus of constitutionalism and the risk of post-operative infection were minimized. The conceptual leap to a localistic model of cancer formation in the late nineteenth century provided theoretical support for the practice of local or regional anesthesia, as the invention of antisepsis reduced a much-feared post-surgical hazard.

Local and Regional Anesthesias Defined

In case the heart is diseased, and the patient far advanced in years, it [local anesthesia] may be of the greatest value.

-Daniel Lewis, 1892 (commenting on the advantage of local anesthesia for the surgical treatment of breast cancer)⁵⁶⁰

⁵⁵⁷Sufficient pressure on the carotid sinus (part of the internal carotid artery) in the neck, for example, causes syncope (loss of consciousness). The etymology of “carotid” reveals that the Ancient Greeks were well aware of this pressure-induced phenomenon, for the word means “to plunge into deep sleep.” *Oxford English Dictionary* online, Second Edition (1989) accessed August 22, 2008.

⁵⁵⁸Numbness to pain by freezing or, more commonly, as a result of frostbite, was a battlefield observation. It was recognized by Thomas Bartholinus in the sixteenth century, well known to Severinus in the seventeenth, re-publicized by John Hunter during his animal experiments in the eighteenth, and used to advantage by Napoleon’s (and Fanny Burney’s) Larrey during the French Wars of the late eighteenth and early nineteenth centuries. Allen, *Local and Regional Anesthesia*: 19. The Polish Campaigns of Napoleon, in particular, provided a “natural laboratory” for Larrey’s discovery, as he wrote in his *Mémoires de Chirurgie Militaire et Campagnes*, D. J. Larrey, *Memoirs of Military Surgery, And Campaigns of The French Armies*, trans. Richard Willmott Hall, 2 vols., vol. 2 (Baltimore: Joseph Cushing, 1814; repr., 1987). 142, 58.

⁵⁵⁹The application of pressure to induce loss of sensation had an additional advantage during amputations, for pressure also constricted the circulation of blood to the limb, thereby lessening operative hemorrhage from the site and decreasing the risk of death by exsanguination (extreme loss of blood).

⁵⁶⁰Lewis, *Cancer*: 104.

Local anesthesia is the induction of anesthesia in a small part of the body, such as part of the mouth (commonly used today for dental procedures) or skin (such as to remove a pre-malignant mole), usually as the result of an injection of an anesthetic into that area. Regional anesthesia, a term that is frequently used synonymously with local anesthesia, should apply only to anesthesia achieved in a part of the body, such as an arm or leg.⁵⁶¹ (Conduction anesthesia, a term that encompasses both local and regional anesthesia, is achieved by injecting a local anesthetic that diffuses through the tissues into a nerve that “carries” or “conducts” the anesthetic to produce a loss of sensation throughout the distribution of that nerve.) General anesthesia induced by the inhalation of nitrous oxide, ether, or chloroform follows the distribution of the inspired gas from the airways into the bloodstream and then to the brain, heart, lungs, kidneys, and other organs throughout the body. The desired result of general anesthesia is loss of sensibility usually as a result of the loss of cerebral consciousness, but the effect on the other organs of the body could be deleterious. On the other hand, local and regional anesthetics are usually injected through the skin into a particular site to anesthetize either the local operative field (local anesthesia) or the entire distribution of an anatomical complex such as nerves, veins, or arteries that supply the area of the operation (regional anesthesia).⁵⁶² There should be no loss of consciousness with local or regional anesthesia, thus reducing the risk that the patient would not “wake up” post-operatively.⁵⁶³

⁵⁶¹For the sake of simplicity, I will also use the term “local anesthesia” to encompass both local and regional—unless otherwise noted.

⁵⁶²Exceptions to injection include the application of ethyl chloride (chloroethane), which can be sprayed on the painful skin by baseball trainers, mothers, and others to achieve a very superficial numbness. Unfortunately, ethyl chloride, like ether, is flammable, a scientific and historical fact that is still forgotten. For an unfortunate twenty-first-century example of the flammability of ethyl chloride, see <http://www.ismp.org/Newsletters/acutecare/articles/20040826.asp> accessed August 23, 2008.

⁵⁶³Although the preservation of consciousness and loss of sensibility in the area of concern are the laudable goals of local and regional anesthesia, it should be noted that patients to whom such anesthesia is administered often

Injections to achieve Local Anesthesia

Although neither the application of pressure or cold to induce local anesthesia required an injection, the use of chemicals to make an area insensible usually did.⁵⁶⁴ Thus, the invention of methods by which anesthetics could bypass the barrier of the skin to effect their insensibility in or through the tissues underneath the skin was critical to the evolution of local and regional anesthesia.

Injecting chemicals into the body is probably older than knowledge of human anatomy, but the dissections of human and other animal corpses by Galen, Vesalius, and others, when added to the closed-system, ubiquitous distribution of the circulatory system discovered by Harvey, provided a roadmap for practitioners to inject anesthetics under the skin (subcutaneously), into the underlying muscles (intramuscularly), or into the network of veins (intravenously) or arteries (intra-arterially) that help form the human corpus. In 1659, the famed English architect and polymath, Christopher Wren (1632-1723) proposed to Robert Boyle (1627-1691) that the latter might be able to induce interesting effects in a dog if chemicals were administered directly into its vein with “slender Syringes or Quills, fastened to Bladders.”⁵⁶⁵ Only eight years later, in 1667, Johann Major of Kiel, in northern Germany, achieved the first successful administration of an intravenous drug for the purpose of inducing anesthesia in a man.

The idea of intravenous administration of anesthetics, however, seems to have been abandoned

receive sedatives to assuage the anxiety that normally accompanies such procedures. The patient is “drugged” but arousable. This is called “conscious sedation” and is often employed for “minimally invasive” surgeries like colonoscopy and gastroscopy.

⁵⁶⁴Again, ethyl chloride spray and its congeners are exceptions to the necessity to inject the agent to achieve its local anesthetic effect. Interestingly, ethyl chloride was discovered not long after chloroform and was initially inhaled, like chloroform. Only later was its ability to produce local anesthesia by freezing discovered. Dr. B. W. Richardson (1828-1896) of Glasgow, Scotland, began the use of ether spray for the freezing of tissues in 1866. George A. H. Barton relates the early history of ethyl chloride in George Alexander Heaton Barton, *A Guide to the Administration of Ethyl Chloride* (London: H. K. Lewis, 1907). 10-12.

⁵⁶⁵Wangensteen and Wangenstein, *The Rise of Surgery*: 286. Boyle followed Wren’s suggestion and injected opium through a quill directly into the dog’s vein. The dog promptly fell asleep.

and rendered less necessary with the advent of the inhalation anesthetics until the last decades of the nineteenth century.⁵⁶⁶

Local Anesthesia in the Nineteenth Century

Despite an apparent two-century hiatus, the intravenous technology of Wren, Boyle, and Major was the forerunner of the invention of the hypodermic (literally, “under the skin”) in the nineteenth century. The hypodermic syringe is a needle-based system constructed from a beveled, hollow needle (to easily penetrate the skin) plus a reservoir to hold the agent to be administered and a plunger to push the agent through the needle past the skin barrier into veins, arteries, nerves, and other underlying tissues.

It was probably invented by Francis Rynd (1801-1861), an Irish physician working in Edinburgh, in May, 1844.⁵⁶⁷ The contributions of Rynd and those after him showed not only that medicines could be given through the skin, but that this route of administration could be used to administer a host of medications in addition to anesthetics while causing minimal pain.⁵⁶⁸

⁵⁶⁶Ibid., 287.

With the advent of barbiturate anesthetics (derivatives of barbituric acid, first synthesized around 1864 by Adolph von Baeyer, who won the Nobel Prize in Chemistry in 1905—but is not of Bayer aspirin fame) by Emil Fischer (1852-1919) (whose Doctoral Advisor was Adolph von Baeyer) and Josef von Mering (1849-1908) in 1903, and particularly after the discovery of improved barbiturates like Phenobarbital (1912) and sodium pentothal (1929), the use of intravenous anesthesia was secured and became a staple of anesthetic administration that continues in full force to this day.

⁵⁶⁷Allen gives the date as 1845, but Rynd claimed in the March 12, 1845 issue of the *Dublin Medical Press* that he developed the subcutaneous needle in May, 1844. See <http://www.our-ireland.com/irish-inventors-fr.html> accessed August 23, 2008 and Allen, *Local and Regional Anesthesia: 20*. Others ascribe the invention of the hypodermic syringe to Charles Gabriel Pravaz (1791-1853) in 1853, and Alexander Wood (1817-1884) shortly thereafter in 1853. See <http://www.discoveriesinmedicine.com/A-An/Anesthetics.html> accessed August 23, 2008.

Of note is the fact that the 1840s and 1850s, as we have seen again and again, were decades of great technologic innovation as a result of the industrial revolution and its scientific underpinnings.

⁵⁶⁸Even today, local and regional anesthetics constitute only a small proportion of medicinals administered intravenously, intramuscularly, and so forth. In general, physicians, diabetics, drug addicts, and others utilize the “parenteral” [outside the oral pill route of the digestive tract (the “enteron”)] route of administration to gain a faster onset of action (such as intravenously during a medical emergency [e.g., a diuretic to a patient in acute heart failure] or to achieve a rapid “high” (heroin)] or to bypass the medicine-digesting enzymes and acid of the stomach (insulin).

All that was needed was a local anesthetic agent that was effective, safe, and readily available. Morphine and tincture of opium may well have been the first injected agents given to ease the pain of surgery and induce a state of calm. Unfortunately, neither was a very good local anesthetic. Their main effects probably derived from that portion of each agent that reached the central nervous system from the site of injection and acted like other general anesthetics.⁵⁶⁹ Ether was formulated as a freezing spray, but its efficacy was limited.⁵⁷⁰ Chloroform was injected locally in an attempt to create a field of anesthesia. It worked, but the skin toxicity it caused made it unusable for this purpose. Chloroform was rapidly abandoned as a local anesthetic, but continued to be inhaled as a general anesthetic well into the twentieth century.⁵⁷¹

Cocaine

The chemical that secured a permanent place for local anesthesia in the armamentarium of the cancer practitioner and others was cocaine. Many of the properties of the coca leaf and, later, its extract, cocaine—endurance without hunger, loss of feeling, gastrointestinal quiescence—were well known to the peoples of the Andes, especially in the regions of modern-day Peru and Bolivia.⁵⁷²

The coca leaf was imported from South America into Europe by von Scherzer around 1850 and its active agent, cocaine, was chemically isolated from the plant by Gaedicke in

⁵⁶⁹Allen, *Local and Regional Anesthesia*: 20.

⁵⁷⁰Arthur D. Hirschfelder and Raymond N. Bieter, "Local Anesthetics," *Physiological Reviews* 12, no. 2 (1932): 190.

⁵⁷¹Allen, *Local and Regional Anesthesia*: 20. Note that many agents are toxic by some routes but not others. In the case of chloroform, for example, bronchial toxicity (by inhalation) is much more tolerable than skin toxicity (by injection).

⁵⁷²In the early twentieth century, Parke-Davis, a major pharmaceutical company, advertised that cocaine "could make the coward brave, the silent eloquent, and render the sufferer insensitive to pain." <http://www.a1b2c3.com/drugs/coc03.htm> accessed September 2, 2008.

Germany in 1855.⁵⁷³ German and Austrian scientists, then near the height of their global dominance in science and chemistry, played a major role in determining the chemical and, later, the anesthetic properties of cocaine. In 1860, Albert Niemann, a doctoral student at the University of Göttingen, synthesized cocaine and gave it its present name.⁵⁷⁴ His dissertation advisor, Friedrich Wöhler, Professor of Chemistry, had earlier noted that cocaine numbed the tongue, as did Karl Ritter von Schroff, a Vienna pharmacologist, who reported the same fact independently two years later.⁵⁷⁵ Parallel to the invisibility of ether's potential as an anesthetic, despite decades of ether frolics, cocaine's power to induce local anesthesia went unrecognized for many years thereafter. In 1879, Vassili von Anrep found that the skin just above a site injected with cocaine became insensitive to a pin prick. He even remarked that the agent could be used as a local anesthetic, but his discovery went unheralded and von Anrep did not pursue the idea further.⁵⁷⁶

The *annus mirabilis* for the discovery of the local anesthetic properties of cocaine occurred in 1884, when Sigmund Freud (1856-1939) (the year after his initial evaluation of "Anna O.," but before his concentration on psychoanalysis⁵⁷⁷), then a young physician at the Vienna General Hospital, and Karl Koller (1857-1944), a younger house officer at the same hospital, began a systematic search of alkaloids in an attempt to find a local anesthetic that could

⁵⁷³Haagensen and Lloyd, *A Hundred Years of Medicine*: 233-34.

⁵⁷⁴Gaedicke called the active alkaloid erythroxylin, after the scientific name for the coca plant, *Erythroxylinum coca*. Niemann's work on the isolation of cocaine is chronicled in *On a New Organic Base*, which earned him his doctorate. <http://www.knowledgerush.com/kr/encyclopedia/Cocaine/> accessed September 2, 2008.

⁵⁷⁵Hirschfelder and Bieter, "Local Anesthetics," 190. and Haagensen and Lloyd, *A Hundred Years of Medicine*: 234.

⁵⁷⁶Hirschfelder and Bieter, "Local Anesthetics," 190.

⁵⁷⁷Freud first met Bertha Pappenheim, alias Anna O., in 1880, the year before he received his Doctor of Medicine degree. http://www.freudfile.org/chronology_1.html accessed September 2, 2008.

serve as a viable substitute for the less-effective-than-thought-yet-addictive morphine.⁵⁷⁸ Freud noted that cocaine rendered mucous membranes (the tissues lining the inside of body cavities like the mouth and anus) insensitive to pain. Koller, in one of the many serendipitous events of medical history, unintentionally got some of the cocaine solution into his eye. He immediately noted that his eye was insensitive to touch or pain.⁵⁷⁹ Koller made the leap to the possibility of using cocaine as a local anesthetic—as had Horace Wells forty years earlier to the potential use of nitrous oxide as an anesthetic.⁵⁸⁰ Koller followed up his discovery with experiments. Like many medical and other scientists of the time, he conducted these investigations on himself as well as animals. He rapidly found that his enthusiasm for this new agent was justified. In particular, he found that even a very dilute two percent solution of cocaine rendered a frog's eye impervious to pain.

Koller then extended the use of cocaine as a local anesthetic to eye surgery. His discovery was remarkably important, for the reflex closure (blinking) of the human eye to any stimulant made ophthalmologic surgery extremely frustrating and distressing for surgeon and patient alike. General anesthesia made eye surgery possible, but the risks of general anesthesia seemed so much greater than necessary. Further, most such surgeries are technically much easier to perform on the conscious patient. Cocaine seemed an ideal agent for eye surgery because it

⁵⁷⁸Hirschfelder and Bieter, "Local Anesthetics," 190.

Alkaloids are organic molecules that contain nitrogen and have a pharmacologic effect on humans. They are found in many plants and, like organic bases (as opposed to acids), have a very bitter taste. Morphine was the first "alkaloid" to be discovered. The year was 1817.

⁵⁷⁹Indeed, he rapidly concluded that both superficial layers of the eye, the conjunctiva and the cornea, were anesthetized. Ibid., 191.

⁵⁸⁰Reportedly, Coupard and Borderon noted the ophthalmological anesthetic properties of cocaine in 1880, but their finding seems not to have been promulgated. Allen, *Local and Regional Anesthesia*: 20. Again, note the seeming analogy to Crawford Long's unreported use of ether anesthesia in 1842 compared to William Morton's fanfare in 1846.

removed most of the morbidity and mortality attendant to the general anesthetics while conferring insensibility to the eye while in an awakened state.

In September 15, 1884, only a few months after their initial discovery of the anesthetic properties of cocaine, Koller and Freud reported their findings to the Ophthalmological Congress, held that year in Heidelberg, Germany.⁵⁸¹ Even before the Congress, Koller had suggested to one of his colleagues that cocaine could be used for laryngological surgery.⁵⁸² By the end of the Congress, surgical circles throughout the Continent were abuzz with news of this new, effective, and seemingly safe anesthetic that could be applied locally.

The excitement sparked by cocaine seems to have been akin to the reception of Morton's Letheon in Boston thirty-eight years earlier. Within two months of the announcement of Koller's findings, physicians on both sides of the Atlantic were using cocaine to anesthetize the mouth (including the gums), throat, larynx, and other mucous membranes—as well as the eye.⁵⁸³ As we have seen, beginning in the spring of 1885, Dr. Douglas liberally applied a four percent solution of cocaine to General Grant's cancer both for diagnosis (the biopsy) and treatment.⁵⁸⁴ When President Cleveland underwent cancer surgery on the Long Island Sound in 1893, Dr. Bryant injected cocaine anesthetic—also in a four percent formulation—directly along the

⁵⁸¹Hirschfelder and Bieter, "Local Anesthetics," 191.

Dr. Koller did not actually present his own work because he was too poor to pay for the trip from Vienna to Heidelberg. Instead, his friend, Dr. Josef Brettauer of Trieste, read Koller's seminal paper on the anesthetization of the eye with cocaine. Peter D. Olch, "William S. Halsted and Local Anesthesia: Contributions and Complications," *Anesthesiology* 42, no. 4 (1975): 480.

⁵⁸²Hirschfelder and Bieter, "Local Anesthetics," 191.

⁵⁸³One of the Americans present at the meeting, Dr. Henry D. Noyes of New York, publicized Koller's findings in the States with an open letter to *The Medical Record* that was published on October 11, 1884. Olch, "William S. Halsted and Local Anesthesia: Contributions and Complications," 480.

⁵⁸⁴Dissertation Chapter 3, page 97 and ff.

Note also that the seven-percent solution used by the fictional Sherlock Holmes suggested a large concentration of cocaine aimed to overcome tolerance and strongly indicative of addiction.

margin of the tissue to be excised.⁵⁸⁵ Drs. Bryant and Hasbrouck also used cocaine—in addition to the weak general anesthetic, nitrous oxide—to minimize the amount of potentially dangerous ether necessary to sufficiently anesthetize the patient.⁵⁸⁶ It worked. To no small extent, the success of Cleveland’s cancer surgery and benign post-operative course rested on the judicious timing and balance of the anesthetics he received.

Of course, every medicine has its downside, and cocaine proved to be no exception. Although Freud and Koller initially believed that cocaine could bestow its anesthetic and analgesic (painkilling) effects without causing addiction, patients and physicians rapidly learned that such was not the case. Within weeks of first receiving cocaine, General Grant found himself requiring larger and larger doses to achieve the same level of pain relief.⁵⁸⁷ He also became addicted, writing a few weeks before his death that he felt “the want of it very much.”⁵⁸⁸ (President Cleveland suffered no such tolerance or addiction because he received cocaine only briefly for the purposes of anesthesia rather than palliation.)

William Stewart Halsted

The Promise of Cocaine as a Local Anesthetic

The triumph and tragedy of cocaine can be witnessed in the professional and personal life of William S. Halsted, the innovative and often daring American surgeon famous many contributions to medicine, including radical breast cancer surgery. His investigations into the

⁵⁸⁵Dissertation Chapter 4, page 244.

⁵⁸⁶Dissertation Chapter 4, page 243.
The operators minimized the dose of ether to lessen the risk of ether further damaging Cleveland’s “nephritic” kidneys.

⁵⁸⁷Dissertation Chapter 3, page 130.

⁵⁸⁸Major General Ulysses S. Grant 3rd, “Grant’s Last Victory,” in *Ulysses S. Grant: Warrior and Statesman* (New York: William Morrow & Company, Inc., 1969), 447.

promising properties of cocaine as an anesthetic began within two months of the presentation of Koller's work at Heidelberg.⁵⁸⁹

In late 1884, Halsted was a young surgeon operating at several hospitals in New York City. This was only four years after his return from Germany where, as a post-graduate student, he had been steeped in the tenets of scientific medicine (as had his good friend, William Henry Welch⁵⁹⁰)—a methodology of theory and practice that he transferred to fertile American soil. Upon reading of Karl Koller's amazing discovery in mid-October,⁵⁹¹ and highly desirous of employing a safe and effective agent to induce local anesthesia in surgical patients, Halsted and some of his colleagues and students at the Roosevelt Hospital Outpatient Department in New York began to experiment with the new anesthetic.

Their investigations began by injecting cocaine solutions under the skin with hypodermic syringes. True to the times, their first experimental subjects were themselves. They soon discovered that they could anesthetize not only the skin overlying the site of the injection, but the entire distal distribution of the nerve that passed through that anatomical location.⁵⁹² In short, an injection of cocaine into the brachial plexus of the axilla (armpit) could anesthetize the entire

⁵⁸⁹Hirschfelder and Bieter, "Local Anesthetics," 191.

⁵⁹⁰Welch and Halsted paralleled each other in their collegiate and graduate educations, although Welch was two years senior to Halsted. Welch graduated from Yale College in 1870, Halsted in 1874. Both graduated from the College of Physicians and Surgeons in New York, Welch in 1875, Halsted in 1877. They both trained at worked at Bellevue Hospital (N.Y.C.) and did post-graduate studies on the Continent, especially in Germany. As is well known to historians of medicine, their most famous collaboration was as two of the "Big Four" on the faculty of the newly-formed Johns Hopkins University School of Medicine, where Welch served as Dean and Professor of Pathology and Halsted as Professor of Surgery. (The other two of the Big Four were William Osler (1849-1919), Professor of Medicine, and Howard Kelly (1858-1943), Professor of Obstetrics and Gynecology. The four were memorialized in John Singer Sargent's powerful "The Four Doctors" of 1905. For multiple views and the context of the painting, see http://jssgallery.org/Paintings/The_Four_Doctors.htm accessed September 6, 2008.)

⁵⁹¹Dr. Henry D. Noyes, a New Yorker who witnessed the presentation of Koller's paper in Heidelberg, publicized the discovery of cocaine anesthesia in a letter to *The Medical Record* dated October 11, 1884. Henry D. Noyes, "The Ophthalmological Congress in Heidelberg," *The Medical Record (New York)* 26(1884). cited by Olch, "William S. Halsted and Local Anesthesia: Contributions and Complications," 486FN4.

⁵⁹²"William S. Halsted and Local Anesthesia: Contributions and Complications," 481.

arm down to and including the fingertips. Today, this is called a nerve block and is the foundation of regional anesthesia—the kind of anesthesia that allows an orthopedist to operate on a hand or leg without putting the patient to sleep.

Halsted and his “body of gentlemen”—as George F. Shrady called them— thus began by performing nerve blocks on each other before executing them on patients.⁵⁹³ Their first publication, authored by Richard J. Hall, Halsted’s colleague at Roosevelt, appeared in the *New York Medical Journal* only a few weeks later, on November 26, 1884.⁵⁹⁴ Within two years, Halsted and colleagues had employed cocaine anesthesia in “nearly two thousand operations.”⁵⁹⁵ This was an extraordinary achievement for such a new agent. Suddenly, operations ranging from deep abscesses to penile amputations for cancer could be performed under the influence of the safer local anesthesia of cocaine rather the general anesthesia of ether or chloroform.⁵⁹⁶ In a larger sense, the advent of local anesthesia highlights the anti-Whiggish, circuitous nature of history—as Morton and Warren discovered almost forty years earlier—that a new discovery opens floodgates to new and unpredictable findings that motivate others to further discoveries and innovations in science and medicine.

The Perils of Cocaine Local Anesthesia

Unfortunately, Halsted and colleagues did not stop using cocaine on themselves when they started employing it on patients. In a short period of time, they became addicted. Initially,

⁵⁹³Ibid.

The reference to a “body of gentlemen” is from an editorial describing the group and its work on the “hypodermic effects of cocaine” by George F. Shrady, consultant to General Grant and Prince Friedrich, in *The Medical Record* of December, 1884. George F. Shrady, “The earlier employment of cocaine,” *Medical Record (NY)* 26(1884). cited by Olch, “William S. Halsted and Local Anesthesia: Contributions and Complications,” 486FN6.

⁵⁹⁴Richard J. Hall, “Hydrochlorate of cocaine,” *New York Medical Journal* 40(1884). cited by Olch, “William S. Halsted and Local Anesthesia: Contributions and Complications,” 486FN7.

⁵⁹⁵“William S. Halsted and Local Anesthesia: Contributions and Complications,” 481.

⁵⁹⁶I selected abscesses and penile amputation because they represented actual instances upon which Halsted operated with cocaine local anesthesia in the early years of 1884-1886. Ibid.

they believed—following Freud and Koller—that cocaine was non-addictive.⁵⁹⁷ Only later did they reach the alarming conclusion that the exhilarated high was followed by, as Halsted wrote, “late effects which to a delicately organized individual sometimes are truly horrible.”⁵⁹⁸ Halsted was hospitalized for his addiction in 1886 and 1887 for several months each time.⁵⁹⁹ He was one of the luckier members of “the body of gentlemen,” for many of his colleagues suffered ruined lives or died.⁶⁰⁰

Thereafter, Halsted lost interest in cocaine specifically and local anesthesia in general. Not even able to bear writing the word “cocaine,” he later reminisced “I was enthusiastic on the subject of local anesthesia for about two years but the novelty wore off, my colleagues did not become interested, I disliked then and still dislike to operate on a conscious patient, and I had seldom if ever had a death which I thought should be ascribed to the ether and so I relapse and used local anesthetic only for trifling operations.”⁶⁰¹ Halsted’s conscious dismissal of local anesthesia may have been a great setback for the development of the science of

⁵⁹⁷Freud persisted in his belief long after overwhelming evidence of cocaine addiction appeared in the literature. Freud was not alone. William A. Hammond (1828-1900), the influential former Surgeon General of the United States Army during the Civil War (1862-1864), shared Freud’s belief. *Ibid.*, 482. Given the vast influence of the two, acceptance of the habituating effects of cocaine was postponed for many years. Why didn’t Halsted and his “gentlemen” sound the alarm? Living in the very different world of Victorian America, Halsted and his fellow sufferers, despite their firsthand knowledge of the addictive properties of cocaine, sought to hide its habituating tendencies rather than promote them.

⁵⁹⁸William S. Halsted, “Cocaine Anesthesia by the Distention Method,” in *William S. Halsted Papers, Welch Medical Library, Johns Hopkins University* (Baltimore 1902). cited by Olch, “William S. Halsted and Local Anesthesia: Contributions and Complications,” 482.. Olch noted that this was the only admission he had ever seen that Halsted wrote about his cocaine habit. *Ibid.*

⁵⁹⁹In May, 1886, Halsted was admitted to Butler Hospital in Providence, Rhode Island, for “treatment.” In an attempt to attain anonymity after his admission to Butler Hospital for cocaine addiction, Halsted gave his name only as “William Stewart.” “William S. Halsted and Local Anesthesia: Contributions and Complications,” 484. This was no oversight. He was discharged November, 1886. *Ibid.*, 481. The second admission was from April 5, 1887-December 31, 1887. *Ibid.*, 484.

⁶⁰⁰*Ibid.*, 482-83.

⁶⁰¹Halsted, “Cocaine Anesthesia by the Distention Method.” cited by Olch, “William S. Halsted and Local Anesthesia: Contributions and Complications,” 482.

anesthesiology.⁶⁰² His prestige as Professor of Surgery at the influential Johns Hopkins University School of Medicine could have promoted local over general anesthesia and saved many lives lost unnecessarily to general anesthesia.⁶⁰³

Halsted never recovered from his addiction. Outwardly, his mien changed from adventuresome, bold and extroverted to plodding, meticulous, and reclusive.⁶⁰⁴ After his hospitalizations, he preferred the research laboratory over his beloved operating suite. Inwardly, he battled demons that drove him from cocaine to morphine and alcohol.⁶⁰⁵ Most of his colleagues thought that he underwent this change in behavior as a sort of payment for his triumph over addiction. Only a few knew the truth—that the transformation in his outward demeanor was an attempt to compensate for the ravages of continued addiction. Many of his colleagues were fooled, but not those close to him.⁶⁰⁶ Those with whom he operated knew the truth. So did his Hopkins colleagues, William Welch and William Osler.⁶⁰⁷ Despite the tragedy of his addiction, Halsted's productivity in the laboratory and in the operating room is a great tribute to him and had a profound effect on the science of medicine and cancer through his work

⁶⁰²The word “an(a)esthesiology” was not used until the twentieth century (1914), according to the *OED*, but the thought, as we have seen, was evident before the second half of the nineteenth century.

⁶⁰³The Flexner Report of 1910 cited Johns Hopkins as a model for other medical schools to follow. Abraham Flexner, *Medical Education in the United States and Canada: A Report to the Carnegie Foundation for the Advancement of Teaching - Bulletin #4*, The Classics of Medicine Library (Boston: The Merrymount Press, 1910; repr., 1990). Given the post-doctoral training of Welch and Halsted, it is not surprising that the educational model followed by Johns Hopkins in medical studies was that of the mid-nineteenth-century German university.

⁶⁰⁴Olch, "William S. Halsted and Local Anesthesia: Contributions and Complications," 480, 85.

⁶⁰⁵*Ibid.*, 483.

⁶⁰⁶*Ibid.*, 479.

⁶⁰⁷Whereas Welch, Osler, and Kelly were invited to Johns Hopkins to assume professorships or to head departments, Welch brought Halsted to Baltimore, in Olch's words, “to work in his laboratory as a form of occupational therapy.” *Ibid.*, 483. Osler's disclosure of Halsted's continued addiction to “morphia,” perhaps by the 1890s even unsuspected by Welch, came in the pages of a manuscript that was not published until long after their deaths. W. Osler, "The Inner History of the Johns Hopkins Hospital, edited, annotated, and introduced by D. G. Bates and E. H. Bensley," *Johns Hopkins Medical Journal* 125(1969).

on the surgery of breast cancer (“radical mastectomy”), hemostasis (control of bleeding), minimizing tissue trauma during surgery, surgery on the thyroid and hernias, and his introduction and promotion of the idea that sterile gloves should be worn by operators during surgical procedures—all related in one way or another to the careful, methodical approach he developed to surgery after the onset of his addiction.

Local Anesthesia after Halsted

The quest for safer, local anesthetics rather than the consciousness-depriving general anesthetics certainly did not end with Halsted or his personal tragedy. True, his reluctance to use local anesthetics after his cocaine addiction may have dissuaded others in his circle—including some of his students who went on to direct surgical departments all over the United States in the early twentieth century—from using local anesthetics, but others continued the search within the realm of local anesthesia for what W. W. Keen termed the “ideal anaesthetic.”⁶⁰⁸

The development of modern organic chemistry, a direct evolution from the innovations in chemistry in the early nineteenth century, set the foundation for the discovery of more effective and less risky local anesthetics to replace cocaine. Cocaine, however, continued (and continues) to be used, especially since its synthesis in pure form in 1891.⁶⁰⁹ In 1913, a Pharmacology Manual dedicated fifty of its more than two hundred pages to the uses of cocaine.⁶¹⁰ In addition, many of the local anesthetics familiar to readers today—novocaine, benzocaine, lidocaine—take their suffix from co-caine.⁶¹¹

⁶⁰⁸Keen, *Addresses*: 255.

⁶⁰⁹Y. A. Ruetsch, T. Boni, and A. Borgeat, "From cocaine to ropivacaine: the history of local anesthetic drugs," *Curr Top Med Chem* 1, no. 3 (2001).

⁶¹⁰<http://www.cocamuseum.com/htm/historycocaine.htm> accessed September 11, 2008.

⁶¹¹Alfred Einhorn, a German chemist, first synthesized novocaine in 1896. During the First World War, it was renamed procaine in the United States to invalidate German patents. Wangensteen and Wangensteen, *The Rise*

The Geography of Local Anesthesia

Local anesthesia is as much geographic as it is pharmacologic. That is, where you inject is as important as what you inject. As Halsted infiltrated the brachial plexus of the arm to induce insensibility throughout the distribution of the nerves of the entire arm, so others injected different sites to induce varied distributions of local and regional anesthesia.

In 1885, not long after Freud and Koller's discovery of cocaine, James Leonard Corning (1855-1923), a New York neurologist, accidentally pierced the dura mater (the fibrous sheath) covering the spinal cord of a dog with a needle and then injected cocaine. The dog appeared to loss sensation in the lower half of its body. Corning then injected the local anesthetic around the spine of a patient, who rapidly developed insensibility in the lower half of his body.⁶¹² This was the clinical beginning of spinal anesthesia. Corning's method for the induction of spinal anesthesia, however, did not become widespread until 1899, when August Bier (1861-1949) of Germany rediscovered it and extended the technique for use in abdominal surgery.⁶¹³ In the twentieth century, anesthesiologists in wealthier nations have to a large extent replaced spinal anesthesia with epidural anesthesia. Poorer countries, however, continue to utilize spinal anesthesia because of its low cost, relative ease of administration, and a duration that can last for two hours—enough to encompass most surgeries.

Cancer surgery highlighted one of the earliest problems with local anesthesia, for sometimes the local anesthetic "wore off" (lost potency) before the completion of the operation.

How to prevent rapid loss of the anesthesia effect from the site of injection and operation (by

of Surgery: 662 Footnote 56. Today, the generic name for Einhorn's synthetic anesthetic is still procaine, but the trade name is Novocain. Thus, today's reader is more likely to be familiar with the name Novocain than the original novocaine—another unintended consequence of war.

⁶¹²Rudolph Matas, "Local and regional anesthesia: A retrospect and prospect," *American Journal of Surgery* 25, no. 2 (1934): 366.

⁶¹³*Ibid.*, 369.

means of the blood and lymphatic drainage) was of major concern, for the cost of cocaine when first used as a local anesthetic was enormous.⁶¹⁴ The neurologist J. Leonard Corning is often credited with the discovery that the effect of the anesthetic could be prolonged by constricting the circulation to and from the area anesthetized. (Constriction reduced outflow of the anesthetic from the site of injection and prolonged contact between the anesthetic and the tissues in question for an increased length of time compared to no constriction.) There is evidence, however, that Halsted, not Corning, should be credited with this important, practical discovery, for it is quite possible—if not likely—that Corning learned the technique from Halsted.⁶¹⁵

Before the end of the nineteenth century, medical scientists discovered a chemical that obviated the need for the physical constriction of an arm or leg to sequester the local anesthetic in the operative site for a longer period of time. That chemical was adrenaline, otherwise known as epinephrine—the “fight or flight” hormone.⁶¹⁶ It was first isolated by Napoleon Cybulski (1854-1919), a Polish physiologist, in 1895 and by William Bates (1860-1931), a New York ophthalmologist, in 1894, although not publicized until 1896.⁶¹⁷ First synthesized by Friedrich Stolz (1860-1936), a German chemist, in 1904, adrenaline was found to cause blood vessel constriction. Not only did vasoconstriction prevent escape of the anesthetic from the surgical site, but it also reduced the total blood lost as a result of surgical incisions (less total blood at the

⁶¹⁴By November, 1884, the price of one gram of cocaine increased to US\$7.50—a 200% increase from two months earlier. Olch, "William S. Halsted and Local Anesthesia: Contributions and Complications," 480. This was a considerable sum at a time when \$1 per day wages represented a decent income. Unfortunately, the high cost of cocaine led to much adulteration in its preparation and many patients suffered in consequence.

⁶¹⁵*Ibid.*, 481.

⁶¹⁶In the United States today, Adrenalin (without the “e”) is the trade name of epinephrine. Epinephrine and adrenaline also point by etymology in different languages to the site of origin of this powerful and multi-faceted hormone. Epi-nephine means “upon the kidney” in Greek, while ad-renal-ine can be interpreted as “next to kidney” in Latin. Supra-renal might have been a better Latin derivative, for the hormone is made by the glands atop the kidneys.

⁶¹⁷<http://www.vision-training.com/Bates/Biography.htm> accessed September 13, 2008.

operative site) and prolonged the nerve block and loss of sensation that followed its course.

Thus, by the early twentieth century, many of the problems associated with local anesthesia had been resolved.

Would/Could/Should Local Anesthesia replace General Anesthesia?

By the turn of the twentieth century, it appeared that almost all operations could be performed under local anesthesia. The German surgeon and anesthesia researcher, Carl Ludwig Schleich (1859-1922), said as much in 1898.⁶¹⁸ So did many of his colleagues.⁶¹⁹ Rudolph Matas, like other Americans steeped in the advantages of local over general anesthesia, claimed that by 1900 he “had gradually reduced the indications for the general anesthetics to at least 50 or 60 per cent of the cases that in previous years I would have had to resort to ether or chloroform.”⁶²⁰ The heyday of local anesthesia had arrived.

As with many exciting, new discoveries that capture the imagination of physicians and the public and are at first utilized for a host of different indications only to find a more restricted use in the therapeutic armamentarium with more experience (cortisone in the 1950s and medical lasers in the 1990s come to mind), the first bloom of local anesthesia began to fade in the early twentieth century. Certainly there are operations today for which few circumstances would require anything but local anesthesia. (Ironically, these include many of the dental procedures that served Horace Wells and William T. G. Morton as the foundational indications for the birth of general anesthesia.) On the other hand, there are operations, including the excision of cancers

⁶¹⁸Matas, "Local and regional anesthesia: A retrospect and prospect," 368.

⁶¹⁹Ibid.

⁶²⁰Ibid.

deep within the body (lung, pancreas, liver, stomach), where the use of any anesthesia other than general would have been unlikely.⁶²¹

Combination Anesthesia

By the early twentieth century, one of the most common modes of anesthesia administration was a combination of local/regional and general anesthesia. This may appear to reduce or even eliminate the advantages of local versus general anesthesia, but practice has shown that this is not so. Surgeons began using local anesthesia in conjunction with general anesthesia to gain the best of both worlds while actually reducing the risks attendant to general anesthesia alone.

One such risk was the acute onset of circulatory collapse during a major operation under general anesthesia, such as a brain or pancreatic cancer excision, due to a shock-like syndrome.

⁶²¹In the ever-changing world of medical information and technology, dogmatic statements are often rendered silly with the passage of time. My comments on the relative usage of general and local anesthesia are likely to fall into this category.

The routine endoscopic procedures of today, colonoscopy and esophagogastroduodenoscopy (visualization of the esophagus, stomach, and first part of the small intestine), replaced the large-incision, long-recovery-time, general anesthesia abdominal operations of the early-to-mid-twentieth century. Conscious sedation (injected tranquilizer and painkiller) replaced general anesthesia. Outpatient procedures replaced multi-week post-operative hospital stays. Morbidity and mortality fell dramatically.

Laparoscopic surgery, wherein instruments are inserted into the abdomen and elsewhere through small incisions under local anesthesia to perform surgical operations that would have required much larger incisions and general anesthesia only a few years ago, is a growing replacement for the older "open" operations that required much longer recovery times in the past. The two-week stay in the hospital after open cholecystectomy (gallbladder removal, such as for gallstones) under general anesthesia as recently as the 1970s (or even 1980s in some locations) is now an overnight stay after regional anesthesia *and* has resulted in lower morbidity and mortality. Laparoscopic operators administer valium-like tranquilizers and regional (spinal) anesthesia during such procedures. Linda M. Collins and Himat Vaghadia, "Regional Anesthesia for Laparoscopy," *Anesthesiology Clinics of North America* 19, no. 1 (2001). Although the anti-anxiety agents are not strictly anesthetics, they do serve to significantly relax the patient and may well put him to sleep.

In endoscopic surgery, a field in which I have hands-on experience, the development and acceptance of NOTES (Natural Orifice Transluminal Endoscopic Surgery) may render many open operations obsolete. In NOTES, an endoscope (tube with a light on the end that can project a real-time image from the tip of the scope to a viewing monitor) is passed through a "natural orifice" (mouth, anus) along the inside of the bowel (like a routine colonoscopy or endoscopy) to the abdominal or peritoneal (behind the abdomen) site in question (appendix, gallbladder, liver, spleen, stomach) and the procedure is performed through the wall of the intestine. Although in 2008 this is more the stuff of science fiction than everyday medicine, NOTES has been performed successfully on many animals and a few humans. (For a brief summary of NOTES, see <http://www.medscape.com/viewarticle/553471> accessed September 10, 2008.) The promise is great because it combines the safety of incision-less endoscopy with internal laparoscopy to markedly reduce anesthesia requirements (local/regional versus general), long post-operative recovery times, and other risks of open surgery.

Surgeons George Crile (1864-1943), a founder of the Cleveland Clinic, and Harvey Cushing (1869-1939), famed neurosurgeon who trained with William Halsted at Hopkins (Cushing was Halsted's surgical resident), surmised that "painful" (albeit unconscious) impulses conducted from the site of the operation to the central nervous system occurred during operations under general anesthesia. To counter the fall in blood pressure, rise in pulse, and general shock-like effects that occurred occasionally, they advocated a combination of local/regional and general anesthesia in addition to the measurement of the patient's pulse, blood pressure, respirations, and temperature. Indeed, the first of twenty-four texts written by Crile during his lengthy career was *An Experimental Research into Surgical Shock*, a monograph that grew out of his research at the College of Physicians and Surgeons (Columbia University) as well as his post-doctorate studies abroad with Billroth in Vienna, and Victor Horsley (1857-1916) and a physiologist with a great interest in the shock syndrome, Charles Sherrington (1857-1952), in London.⁶²² Administration of a local or, more prevalently, regional anesthetic (with adrenaline/epinephrine) in combination with general anesthesia and the monitoring of vital signs, reduced the development of shock, as Crile and Cushing discovered around 1900.⁶²³

Pain, Anesthesia, and the Treatment of Cancer

The fierce extremity of suffering has been steeped in the water of oblivion, and the deepest furrow in the knotted brow of agony has been smoothed away forever.

-Oliver Wendell Holmes, Sr.⁶²⁴

By the dawn of the twenty-first century, few areas of the body had escaped the needle of the anesthetist. From tiny scalp injections of local anesthetics to remove a precancerous nevus (mole) to continuous-flow intrathecal (injections within a sheath that surrounds the spinal cord)

⁶²²George Washington Crile, *An experimental research into surgical shock : an essay awarded the Cartwright prize for 1897* (Philadelphia: Lippincott, 1899).

⁶²³Walton, Beeson, and Scott, *Oxford Companion to Medicine*, 49.

⁶²⁴Quotation from Keen, *Addresses*: 255.

catheters that administer a small but constant dose of an anesthetic to achieve intra-operative spinal anesthesia or post-operative pain relief to the use of multiple anesthetics during the course of a single operation administered by inhalation, subcutaneous, intravenous, or other routes to provide continuous general and/or local anesthesia, the small beginnings of Koller and Halsted mushroomed into the very vibrant and popular specialty of Anesthesiology.

Today, the science of anesthesia has progressed to the point that a patient expects no pain during an operation.⁶²⁵ It matters little whether the operation is the extraction of a tooth or the excision of a large colorectal (large intestinal) cancer. Even after the operation, when the normal catabolic (breaking down) processes of the body have metabolized the anesthetics so that they no longer have their effect, the expectation is that additional medications, usually in the form of analgesics, can be given to ameliorate or eliminate post-operative pain and discomfort. So many agents with so many different effects are used today that it is sometimes more a matter of semantics than physiology as to whether an anesthetic should be labeled local, regional, conduction, or even general.

The measurement and monitoring of vital signs (blood pressure, pulse, temperature, respiratory rate, oxygen saturation, urine output, etc.) during and after operations, combined with increasing knowledge of the pharmacokinetics (the movement of the drug through the tissues of the body) and pharmacodynamics (the action of the drug on the tissues of the body) of old and new anesthetic agents, have created a science of anesthesia—*anesthesiology*—with the ability to control the pain of injury or surgery far beyond the wildest dreams of Long, Wells, Jackson, Morton, Koller, Halsted, or any of the other nineteenth-century pioneers. Thus, pain, one of the greatest banes of human existence and a major reason for the aversion to surgery that

⁶²⁵The most prevalent patient desire is to “sleep” during an operation; i.e., to have no memory of its beginning or ending.

characterized the treatment of traditional cancer has been controlled to the point where it no longer prevents cancer patients from undergoing surgery to remove malignancies.

The Legacy of Anesthesia

A great change has been brought about in the practice of operative surgery by the introduction of *Anæsthetics*; patients will now submit to operations which formerly they would rather have died than endure, and thus many operations which without anæsthesia would have been absolutely impracticable, are now perfectly feasible and are frequently employed. In this way the range of operative surgery has been greatly extended.

-John Ashhurst, Jr., 1871⁶²⁶

Anesthesia was America's greatest contribution to medicine in the nineteenth century. Further, it was a necessary (but not sufficient) element in the development of modern cancer surgery.⁶²⁷ If one of the characteristics of the treatment of traditional cancer was pain (especially, but not exclusively related to surgery), then one of the hallmarks of modern cancer treatment is painlessness through anesthesia (also especially, but not exclusively related to surgery).

Anesthetics converted the screams of pain-racked cancer patients during treatment into the soft, rhythmic sounds (from respiratory machines to radio music) of the modern operating suite.⁶²⁸ Anesthetics transformed fear of the cancer operation into fear of the prognosis. Anesthetics made essential cancer surgeries possible for operators to perform and even acceptable for patients.⁶²⁹

⁶²⁶John Ashhurst, Jr., *The Principles and Practice of Surgery* (Philadelphia: Henry C. Lea, 1871). 72.

⁶²⁷Other necessary but not sufficient contributions to the development of the treatment of modern cancer by surgery included localism and antisepsis.

⁶²⁸For a clear, concise history of the "Operating Theater," see Abdullah Al-Othman, Naif Al-Awad, and Shyam K. Parashar, "Surgeons and the Operating Theater: Past, Present and Future," *Annals of Saudi Medicine* 18, no. 1 (1998).

⁶²⁹Essential surgeries are those performed when the patient is in imminent danger of significant morbidity or mortality. They differ from elective surgeries, where the urgency is less.

In medical research, anesthetics enabled experimentation. It made animal experimentation palatable to the operator and non-anti-vivisectionist, for the animal's inability to produce a scream does not preclude the pain experienced by the animal subjected to cutting or dissection from having a marked effect on the vicariously-suffering human observer.⁶³⁰

And, perhaps most important of all for culture and society in the long run, anesthesia showed a pain-ridden world that physical suffering—at least in the short term—could be obviated; that man did not have to live with the pain of injury or surgery.⁶³¹ The intellectual power of life without pain to a species riddled with pain from the beginning of time cannot be overestimated—both medically and culturally.⁶³² Almost overnight (at least in evolutionary terms), feats of physicality, previously undreamed of, became possible for those who realized that anesthesia offered a cessation of pain not only for those who suffered pain through no fault of their own (injury, surgery), but also for those who dared to defy the limitations of the human form.

A Blessing and a Great Turning Point in the Treatment of Cancer

⁶³⁰Vivisection, etymologically the cutting or dissection of a living organism, is a subject in late-nineteenth-century medical history in and of itself. The American Anti-Vivisection Society, for example, was founded in 1883 in Philadelphia (where the American Anti-Slavery Society was founded exactly fifty years earlier and the first anti-slavery Quakers, Benjamin Lay and John Woolman, condemned lifelong bondage a century before that)—just before the advent of local anesthetics. Its mission goes beyond the humane treatment of animals during experimentation (for example, using anesthetics during experiments) “to ending experimentation on animals in research, testing, and education.” See <http://www.aavs.org/history.html> accessed September 16, 2008.

⁶³¹The continued difficulty with the treatment of chronic pain makes the control of all types of pain (acute, intermittent, and chronic) an unrealized goal.

⁶³²The use of cocaine was not restricted to medicinal products. The “soft drink,” Coca-Cola, was not always so soft (although, technically, a soft drink is soft because it does not contain alcohol), for it contained cocaine (up to nine milligrams per glass) from its debut in 1886 (the company was founded shortly after its invention in 1885 in the State of Georgia as a patent medicine in deference to local prohibition laws) until coca leaves were no longer used in its production beginning in 1903. (<http://www.casapalmera.com/articles/the-history-of-cocaine/>) accessed October 4, 2008. More true than they could have known, Coca-Cola's original slogan was “Exhilarating. Invigorating.” It is not by chance alone that both the drink and the drug are known to this day as C/coke.

For surgeons, patients, and others involved in the treatment of cancer in the late nineteenth century, anesthesia was a blessing. It also represented a major watershed in the treatment of cancer.⁶³³

The blessing of anesthesia for cancer was its salutary effect on the treatment of the disease. Anesthesia changed the mood and atmosphere of cancer surgery from frantic fear to measured hope. The ability to operate without pain relieved the practitioner of an enormous distraction and allowed him to concentrate on the task at hand. Anesthesia gave the operator time—time to work, time to think, time to consider the best method to achieve the desired end with the least adverse consequences. In the process, the physician who treated cancer by surgery became less of a manual laborer and more of an artisan—a skilled worker who had the wherewithal to add the value of deliberation to his work. As a result, the probability of a successful outcome for the patient on the operating table as well as those who would follow increased.

In essence, anesthesia transformed the operator scarcely removed from being a barber into a surgeon. Given that the primary goal of the treatment of cancer was cure, anesthesia made the attainment of that goal more realistic by making surgery more appealing to patient and surgeon alike. In the process, surgery became a more palatable and even desirable pursuit for young (and some older) physicians, thus attracting some of the best and the brightest talent into the field. For surgeons, in essence, anesthesia was a godsend.

For patients, anesthesia reordered the relative desirability of surgery among the panoply of treatments to which they would submit. Patients with cancer and other diseases amenable to surgical treatment who would never have considered an operation before the advent of anesthesia

⁶³³My choice of the word “blessing” for the anodyne of anesthesia is not by chance. The original meaning of blessing was probably “to make ‘sacred’ or ‘holy’ with blood.” (*OED*, “bless” as verb) The parallels between blessing in this sense and surgery are strong, with or without a religious component.

because of pain became convinced that surgery might be preferable to the less proven and less definitive treatments available in the second half of the nineteenth century for the treatment of cancer. The speed with which operators adopted anesthesia supports the contention that—despite the religious and fearful naysayers—practitioners rapidly recognized the gift of anesthesia as a boon to patients with cancer and other surgically-amenable diseases. Statistics support the rapid and widespread adoption of anesthesia over the course of the nineteenth century. In 1845, the year before Morton's Letheon demonstration, surgeons at the Massachusetts General Hospital performed a total of thirty-seven operations.⁶³⁴ In 1898, the number of operations performed at the same hospital was 3,700.⁶³⁵

Two factors determine the history of the hospital; society on one side, medicine on the other.

-Henry Sigerist⁶³⁶

Anesthesia thus benefited patients, surgeons, and also hospitals. By the end of the nineteenth century, patients of all socioeconomic strata began to find hospitals as more acceptable—even preferable—sites at which to receive medical care. Patients began to believe that only in the hospital—with its specialists, specialty care, and scientific instruments—could they receive the best that medicine had to offer. This was especially true of potentially life-threatening diseases like cancer.

In consequence, the number of hospitals increased as did the number of beds per hospital.⁶³⁷ Paul Starr cited an 1873 government survey that there were about two hundred

⁶³⁴Degenshein, "Golden Age of Surgery," 933.

⁶³⁵Ibid. Of course, other factors served to increase the number of surgeries performed in-hospital, but it is unlikely that significantly more operations would have been performed without anesthesia.

⁶³⁶Henry E. Sigerist, "An Outline of the Development of the Hospital," *Bulletin of the Institute of the History of Medicine* 4(1936): 576.

⁶³⁷Rosner, *A once charitable enterprise*: 3.

hospitals in the entire United States at the time.⁶³⁸ By the end of the century, there were thousands.⁶³⁹ Anesthesia was one of the major elements that helped transform the pre-modern xenodochia (guest house) and early-nineteenth-century charitable almshouses— called hospitals (as places of “hospitality”)—into citadels of science by the end of the century. In short, the advent of anesthesia contributed to the transformation of the hospital from an area to avoid to the site of choice for those in need of substantial medical and, especially, surgical care.⁶⁴⁰

Necessary But Not Sufficient

By itself, however, anesthesia did not bring about the birth of the modern treatment of cancer by surgery. It may have been a necessary component in the genesis of modern surgery, but it acted in concert with other forces to foster the cultural ideology and technical know-how that undergirded the positive societal and medical attitudes that developed toward the surgical treatment of cancer in the late nineteenth century.

Cast yourself into the mind of a physician-surgeon in the 1850s, 1860s, or even 1870s. Yes, anesthesia reduced or eliminated the pain engendered by surgical procedures. Yes, the adverse effects of anesthetics might be minimized or even overcome by the judicious use and greater knowledge of the pharmacology of the various agents. And yes, surgeons down the block and across the globe had developed a certain facility with these agents as experience spread. Nevertheless, practitioners were well aware of the fact that there were problems related to surgery that anesthesia did not solve.

⁶³⁸Paul Starr, *The Social Transformation of American Medicine: The rise of a sovereign profession and the making of a vast industry* (New York: Basic Books, Inc., 1982). 73 Footnote 50.

⁶³⁹Ibid.

⁶⁴⁰Rosner, *A once charitable enterprise*, 4.

Anesthesia was a means to an end, not an end in itself. It did not select those patients who might be most fit to undergo a cancer operation. It did not inform the operator as to the best approach, safest method, and finest instruments to use to remove the cancer. It did not, by itself, generate new knowledge of cancer. It did not, by itself, spur on cancer research.

The use of anesthesia enabled more invasive and longer-duration surgeries than ever before, but there were still other considerations that stayed the hand of even the most aggressive operators. These included a need for new surgical techniques (that allowed the operator to take advantage of the extra time and passivity of the patient) and, above all, the need to reduce or eliminate wound infections. For anesthesia did not remove the second major bane of traditional cancer surgery—post-operative infections, including and especially sepsis.

ANTISEPSIS

Without anæsthesia and antiseptis modern surgery would be an impossibility.
-W. W. Keen, 1897⁶⁴¹

Once having subdued the problem of pain, surgeons and other cancer-treating physicians faced the even more formidable task of eradicating infection.⁶⁴² Certainly surgeons had operated on patients for thousands of years without adequate painkillers, but before the blessings of anesthesia could be applied to increasing numbers of surgical candidates for the treatment of cancer and other diseases, the scourge of sepsis and other life-compromising infections had to be overcome. W. W. Keen, writing in the last years of the nineteenth century after the development

⁶⁴¹Keen, *Addresses*: 257.

⁶⁴²I consider infection a more difficult problem to attack than pain, because, although both pain and infection are internal responses to external stimuli, the “stimulus” to infection—as we shall see in this section—was much less obvious than the cause of pain. And although knowledge of causation is neither necessary nor sufficient to finding a solution to medical problems in general and the problem of infection specifically, in this case, knowledge of the cause of infection contributed enormously toward its eradication.

of effective antiseptic techniques, noted that while anesthesia reduced the agonizing pain of surgery, antiseptics reduced the “after-suffering.”⁶⁴³

The concept of antiseptics must be distinguished from the more ancient idea of anti-putrefaction. Surely the most primitive of men noted that food and flesh rot—the basis of the state of being putrid. But the notion of sepsis and antiseptics are more recent concepts that require a knowledge of the process or method by which things putrefy. Even in English language, putrid and putrefaction are the older terms, probably originating with early Modern English in the fifteenth century.⁶⁴⁴ The first use of the term antiseptics, however, is usually credited to Sir John Pringle who, in 1750, wrote in his chapter on “Jail or Hospital-fever,” that “were putrefaction the only change made in the body by contagion, it might be easy to cure such fevers by the use of acids only, or other antiseptics.”⁶⁴⁵

Further, it seems that in no medical endeavor are theory and practice so closely interwoven as in the treatment of infections during the nineteenth century and beyond. My goal in this section, however, is to focus on action rather than thought—what was done to reduce the risk of surgical infection and, if such an infection did develop, the actions taken by those who treated it to quash its progression. In the next chapter, I will take up the question of theories of infection as I explore the issue of cancer causation through the lens of investigations into the nature of the disease.

Cancer and Infection

⁶⁴³Keen, “Progress of Surgery,” 328.

⁶⁴⁴The *OED* notes that “putrefaction” was first used in approximately 1400 CE.

⁶⁴⁵John Pringle, *Observations on the diseases of the army in camp and garrison. In three parts. With an appendix, ...* By John Pringle, Special ed., The Classics of Medicine Library (Philadelphia: Edward Earle, 1810). 355. Pringle also devoted Paper I. of the Appendix to experiments with “several powerful antiseptics.” *Ibid.*, 366-74.

In no department, perhaps, has the introduction of antiseptics...after the antiseptic method brought about a greater improvement than in operations for tumors.

-W. W. Keen, 1901⁶⁴⁶

Infection is a frequent complication of cancer as well as its treatments. The relationship between infection and cancer is special and important on many levels. In the epigraph immediately above, William Keen referenced the greater likelihood that a cancer patient would survive surgery after the advent of antiseptics than before. But the connections are much deeper and thus lent greater urgency and value to the application of antiseptic techniques to the cancer patient than others with different diseases. As was identified in the late nineteenth century, cancer patients are more susceptible to infections in general than non-cancer patients. Cancer patients are also more likely to develop post-operative infections than surgical patients without cancer. Indeed, in the middle decades of the nineteenth century, physicians and surgeons recognized infection as a frequent cause of morbidity and mortality in cancer patients—with or without surgery. And by the end of the century, as will be the focus of the next chapter, many cancer researchers believed that infection itself caused cancer.

These are weighty claims, and although the pathophysiological interfaces between cancer, infection, and the immune system (the body's main bulwark against infection) were largely unknown in the late nineteenth century,⁶⁴⁷ medical science has since discovered interactions between cancer and the immune system that both contribute to the development of

⁶⁴⁶Keen, "Progress of Surgery," 347.

⁶⁴⁷Paul Ehrlich and Ilya Mechnikov received the 1908 Nobel Prize in Physiology or Medicine for their pioneering contributions to immunology—the study of the immune system. In the waning years of the 1890s, Ehrlich applied his deep knowledge of chemistry to describe the “side-chain theory” of antibody formation while the Nobel Committee cited Mechnikov for his 1882 discovery of phagocytes—cells that “devour” invading (usually non-self) cells such as bacteria. Both findings are relevant to cancer medicine.

cancer as well as reduce the resistance of the cancer patient to infection.⁶⁴⁸ As has often been the case, scientific experimentation eventually elucidated clinical observation.

That cancer patients were more susceptible to infection—and more likely to suffer a severe infection such as sepsis—was well recognized clinically both in and out of the surgical suite. The many patients with ulcerated cancers exposed to the external environment (for example, skin, lip, breast, cervix) suffered especially high rates of infections. Necrotic (dead) tissue is a hallmark of cancers that have outgrown their blood supplies and is therefore more susceptible to infection since the compromised tissue lacks many of the immunologic defense mechanisms (often in the form of white blood cells and chemical signaling messengers called chemokines) conveyed by the bloodstream to normal tissue. It is likely, although unprovable, that General Grant's waxing and waning course during the first half of 1885 followed the vagaries of infections in and around his necrotic throat cancer tissue, as well as his known localized hemorrhages. More certain are mortality statistics compiled by the Woman's Hospital of the State of New York, which showed in the early 1870s that the most common cause of death in their cancer patients was septicemia.⁶⁴⁹

In the mid-nineteenth century, cancer patients were also believed to be more susceptible to the development of post-operative infections than non-cancer surgical patients. The debilitated state of the cancer patient at the time of late-stage traditional surgery contributed to

⁶⁴⁸Cancer immunology is too vast a subject and too multifaceted to reduce to a few citations. Entire textbooks (R. Adrian Robins and Robert C. Rees, *Cancer Immunology* (Dordrecht: Kluwer Academic, 2001)), medical academies (Academy of Cancer Immunology), and clinical-research departments (e.g., the Department of Cancer Immunology & AIDS at the Dana-Farber Cancer Institute affiliated with Harvard Medical School) are devoted to the discipline.

⁶⁴⁹Memorial Hospital Archives, "Record Group 500, Box 2, Folder 35 "Cancer therapy, Early treatment, 1847-1930," in *Hayes Martin Collection* (New York 1950).

the increased incidence of post-operative infections as did what is now known to be impaired functioning of the immune system in such patients.⁶⁵⁰

The cancer patient therefore had many risk factors that portended a relative increased incidence of infection—the underlying effects of the disease on the ability to withstand infection in non-surgical situations; the risks of the procedure to which all surgical patients were susceptible; and the potent combination in the cancer surgery patient of the compromised immune system with the insult of surgery. Indeed, the importance of infection to the cancer patient cannot be overestimated. Any reduction in the incidence of infection in such patients therefore would have a multiplier effect on their health and well-being.

Many historians attribute substantive achievements in the realm of antisepsis primarily to the last third of the nineteenth century. I agree. Nonetheless, there is a deep history of physicians, surgeons, and others who attempted to prevent and treat infections in cancer patients and others—surgically related or not—long before the last tertile of that century. Their contributions significantly affected later developments, including those of the late nineteenth century. Thus, the “discovery” of antisepsis was more evolution than revolution. A brief examination of those efforts, starting with a clarifying definition of antisepsis, will provide a contextual framework for a discussion of Joseph Lister and the rise of modern antisepsis in the late nineteenth century.⁶⁵¹

To Tame the Scourge of Infection

⁶⁵⁰Different degrees of immune system malfunction attend various cancers. AIDS, with its high incidence of unusual (“opportunistic”) infections and cancers (e.g., Kaposi’s sarcoma) due to viral invasion of CD4+ T-lymphocytes (often called Helper T-cells), and certain types of leukemia, are among those most prone to infection because of their direct destructive and dysfunctional effects on key cells in the immune system.

⁶⁵¹Joseph Lister is often termed the “Father of Antisepsis.” Like many other “Fathers” in history, curiously, he had no children. Whether this is a statistically significant observation, or even cause and effect, one can only conjecture.

Je le pansai, Dieu le guérit.⁶⁵²

—Ambroise Paré (c. 1510-1590)

The acute pain of the operation was abolished [by anesthesia], but the after-suffering [sepsis]...was something dreadful to see.

—W. W. Keen⁶⁵³

Antisepsis is the prevention or treatment of infection or sepsis (putrefaction) by action against its causative agent(s).⁶⁵⁴ Since the first extant writings on the subject in ancient times—both the Edwin Smith (17th century BCE) Papyrus and the Ebers (c.1552 BCE) Papyrus contain descriptions and treatments of infections—healers sought to forestall the onset or progression of infections in trauma and operative patients alike. Some of the methods chosen by these Ancients—cleansing, burning, disinfecting—are discussed above in conjunction with the explication of the Four Horsemen of Death.

In broad perspective, the prevention and treatment of wound infections before the nineteenth century assumed that the agent of injury [spear/arrow/bullet/knife (surgical or otherwise)] was the source of infection. Logically, it followed that treatment involved another agent or agents to counteract the forces of infection initiated by the weapon. That additional agent was often hot, painful, and even gooey—like boiling oil, plant derivatives, and treacle.

In the fourth century BCE, for example, Hippocrates applied pitch in a cerate formulation to compound fractures in an attempt to reduce post-traumatic suppuration.⁶⁵⁵ About 77 CE, Pliny the Elder taught in his *Naturalis Historia*, that the resin of the terebinth tree (a native of the

⁶⁵²“I dressed him, God healed him.”

⁶⁵³Keen, "Progress of Surgery," 328.

⁶⁵⁴Disinfection, by contrast, is the destruction of the agent(s) of sepsis/infection by direct exposure to physical or chemical agents—today called disinfectants. Disinfection, therefore, is subsumed within the more general term antisepsis.

⁶⁵⁵Wangensteen and Wangenstein, *The Rise of Surgery*: 302.

Cerate is a stiff, waxy ointment that includes other ingredients—in this case, pitch. (*OED*) Pitch is a residue obtained from the distillation of turpentine or wood tar.

Mediterranean region and a source of turpentine⁶⁵⁶) when mixed with olive oil and put on a wound lessened the development of pus in that wound.⁶⁵⁷ During the Middle Ages, medical luminaries such as Guy de Chauliac (c. 1300-1368) and Hieronymus Brunschwig (1450 - c. 1512) used turpentine itself as the treatment of choice for wound infections.⁶⁵⁸ As late as 1800, William and Robert Crowther reported that they had treated twenty-eight consecutive compound fractures conservatively with only a hot “wood tar” dressing to prevent infection. Amazingly, they had no fatalities, but the burning tar must have been torturous.⁶⁵⁹

By the 16th century, the military surgeon Ambroise Paré, having witnessed his full measure of war and suffering from the wounds of battle as well as medical treatments (and only twenty-six years of age!), sought to reduce his personal contribution to the baleful cries of the injured by his abandonment of the routine use of scalding hot oil—the standard of care at the time—to prevent and treat infections that occurred following gunshot wounds. As Paré noted, the established cure for the gunshot wounds (the “poison” of which was believed to cause infection/putrefaction), was to “burne or cauterize them with oyle of Elders scalding hot.”⁶⁶⁰ Instead, in 1536 he offered a more “natural” and definitely less painful application, “that I might

⁶⁵⁶According to the *Oxford English Dictionary*, the word turpentine evolved directly from Terebinth resin through an intermediate, “terebentyne.”

⁶⁵⁷Wangensteen and Wangenstein, *The Rise of Surgery*: 302 and 664 Footnote 6.

⁶⁵⁸*Ibid.*, 302.

De Chauliac was a noted 14th-century surgeon who ministered to at least three Popes during his career—surely the pinnacle of medical stardom at that time. His *magnum opus* was *Chirurgia magna*, published in 1363.

Brunschwig used distillery chemistry and a vast knowledge of plants with presumed medicinal qualities to formulate a compendium of herbal remedies for many ailments, including wound infections. Brunschwig published his surgical text, *Buch Der Chirurgia*, in 1497.

⁶⁵⁹*Med. & Phys. J.*, London (1802); 7: 307-310 cited by *ibid.*, 666 Footnote 30.

⁶⁶⁰Ambroise Pare, *The Apologie and Treatise of Ambroise Pare containing the Voyages made into Divers Places with many of his writings upon Surgery*, The Classics of Medicine Library (Birmingham: The Classics of Medicine Library, 1984). 137.

not leave them undrest, to apply a digestive made of the yolke of an egge, oyle of Roses, and Turpentine.”⁶⁶¹ This radical approach to such wounds, however, rattled him. He became fearful that he had deviated too far from the path of accepted wisdom by using something other than boiling oil to treat these wounds, and that, as a consequence, God might not be there to heal his patients. Hence Paré “rose early in the morning...and beyound expectation, I found such as I had dressed with a digestive onely, free from vehemencie of paine to have had good rest, and that their wounds were not inflamed, nor tumified.”⁶⁶² Others adopted Paré’s less painful mixture, in various forms, for the treatment of wounds well into the nineteenth century. It may not have been as sadistic as boiling oil, but, unfortunately, its efficacy was limited. Paré sought other anti-infectives.

In his search for even better wound treatments, Paré utilized *aqua vitae*, the “water of life,” another ancient antidote for infection.⁶⁶³ Alcohol, the active ingredient of *aqua vitae* (and a popular anodyne long before the anesthetics revolution of the mid-nineteenth century), found favor as an antiseptic through the ages. During the second century, Galen of Pergamum—the Aristotle of medicine—dressed wounds in bandages soaked in wine to dry out the wound (alcohol readily evaporates) and reduce the risk of infection.⁶⁶⁴ During the Middle Ages, new distillation techniques advanced the ability to produce concentrated alcohol solutions like *aqua vitae*.⁶⁶⁵ By the eighteenth century, such alcohols became the treatment of choice for the

⁶⁶¹Ibid., 138.

⁶⁶²Ibid. “Tumified” means swollen.

⁶⁶³Ibid., 69.

⁶⁶⁴Wangensteen and Wangenstein, *The Rise of Surgery*: 312.

⁶⁶⁵Ibid.

Other concentrated/distilled alcohol solutions include whiskey, brandy, tequila, and vodka, all of which have an alcohol concentration greater than thirty percent. Beer and wine, on the other hand, have a maximal alcohol

prevention and treatment of infections. Surgeon Theodor Kappenhagen, for example, opined in 1745 that brandy (his choice of *aqua vitae*), was the best therapy for putrid ulcers.⁶⁶⁶ In 1763, the Hôpital des Invalides believed concentrated spirits so useful to the treatment of patients that each day the administrators of the hospital distributed an aliquot to its surgeons. Any alcohol remaining at the end of the day had to be returned to the pharmacist, who duly placed the remainder under lock and key for use the next day.⁶⁶⁷ As a result, higher-proof alcohols became more available to physicians and others for wound care and, given the potent antiseptic properties of concentrated alcohols, quickly gained widespread use for their relative efficacy in the prevention and treatment of wound infections.⁶⁶⁸

The Chemistry of Antisepsis—Early Nineteenth Century

The rise of modern chemistry in the first half of the nineteenth century imparted new meaning and direction to the prevention and treatment of infections. Fanciful descriptive terms like *oyle of Roses* and *aqua vitae* faded from use and were replaced by chemical names such as benzene and ethanol, familiar to practitioners today. Various forms of silver (e.g., silver nitrate), creosote (an oily liquid derived from coal tar) and related phenols (a vast class of compounds that have in common a six-carbon benzene ring with a hydroxyl group) took center stage in the

concentration of about fifteen percent. This is because fermentation by yeast generally ceases above an alcohol concentration of fifteen percent. Thus, whiskey is fermented and distilled while beer and wine are fermented but not distilled.

⁶⁶⁶Ibid., 313.

⁶⁶⁷Ibid.

⁶⁶⁸Interestingly, the concept of alcoholic proof, a measure of the alcohol content of a given beverage, was curiously intertwined with the nature of gunpowder. In the eighteenth century, British sailors received rations of rum. Distributors often watered down the rum. Sailors “proved” that the rum had been diluted by adding gunpowder and then igniting the mixture to see if it would burn. If it did not burn, it was “under proof” (less than 57% alcohol by volume, or ABV). The modern notion of alcoholic proof—twice the percentage of alcohol by volume (e.g., 37.5% ABV is 75 proof)—derived from the idea of “proved by gunpowder.”

treatment of wound and other infections. Over the course of the century, these new chemicals and their applications to medicine led directly to the birth of modern antisepsis.⁶⁶⁹

Silver as Antiseptic

Silver is a most unusual candidate for antisepsis, for its popular image was and is that of a precious metal used as a store of wealth rather than as a restorer of health. Nevertheless, its use for the prevention and treatment of wound infections spans millennia—perhaps longer than any chemical other than alcohol.

The Ancient Greeks applied silver to wounds to enhance healing. Hippocrates noted that superficial wounds like ulcers could be treated with “the flowers of silver alone, in the finest powder.”⁶⁷⁰ In the first century, Pliny the Elder wrote that silver “has healing properties...being extremely effective in causing wounds to close over.”⁶⁷¹

During the Middle Ages and Renaissance, silver came of age for use in a host of different diseases in addition to infections.⁶⁷² Its medicinal (as well as its pecuniary) value was so great that anyone who could afford to eat with silver utensils and drink from silver cups did so. The

⁶⁶⁹Without delving too deeply into the medicinal chemistry of the nineteenth century, my goals are to show that (1) Joseph Lister’s antisepsis was clearly derived from the work of many before him, and (2) several of the agents used by Lister and others for antisepsis were closely related in their chemical properties.

⁶⁷⁰Eric J. Rentz, "Historic Perspectives on Clinical Use and Efficacy of Silver," <http://lifesilver.com/history.htm>. accessed 12/26//2008.

⁶⁷¹Pliny, *The History of the World, Commonly called The Natural History of C. Plinius Secundus*, ed. Paul Turner, trans. Philemon Holland (1601) (New York: McGraw-Hill, 1962; repr., 1964). Book XXXIII, Section CV “Some medical uses of metals”.

⁶⁷²In addition to the known anti-infective properties of silver since the days of the Ancient Greeks and Romans, part of the allure of silver for medical usage during the Middle Ages may have been its increasing use in Church ceremonies. Discoveries of silver ore in various parts of Europe over the centuries, as well as foreign trade, increased the supply of silver. Combined with the imprimatur of the Church and belief in the cause and effect relatedness of sin and disease, the increased availability of silver served to make it an attractive candidate for the prevention and treatment of diseases. The discovery of large quantities of silver ore in the New World furthered its usage.

metal of treasure became a precious commodity for health, well known to reduce the risk of infection.⁶⁷³

The employment of silver compounds for medicinal purposes increased further during the eighteenth and nineteenth centuries. In 1707, Antoine Maître-Jan used a common form of silver, silver nitrate [also known as “lunar caustic” due its similarity to the color of the moon (lunar) as well as its burning effect on skin (caustic)], to treat tumors of the eyelids.⁶⁷⁴ Beyond silver therapies, prophylactic uses of silver increased, for the element seemed to prevent putrefaction as well as to treat it. During the first years of the nineteenth century, for example, the Russian soldiers of Czar Alexander I who fought against Napoleon drank from silver-lined casks in order to purify drinking water obtained from passing streams and rivers.⁶⁷⁵ Settlers in the American West plopped silver dollars into bottles of milk to reduce spoilage—long before the advent of pasteurization and refrigeration.⁶⁷⁶ Proud parents gave their children silver teething rings, not only to reduce the pain of new dental eruptions, but to lower the risk of infection—a practice that continues to this day.

By the third decade of the nineteenth century, physicians utilized specific silver compounds to reduce the risk of infection in traumatic situations, including dreaded compound

⁶⁷³The chronic use of silver tableware has a downside, for elemental silver, which leaches from the goblets and spoons (forks came last to the dinner table), may cause the skin to take on a bluish hue, the most striking symptom of argyria (excessive silver in the body). The term “blue blood” may have derived from the finding that some aristocrats, the social echelon most likely to own and use silver tableware, developed argyria. Wikipedia provides a photograph of a man with argyria at <http://en.wikipedia.org/wiki/File:Argyria.jpg> accessed 12/26/08.

⁶⁷⁴Charles de Saint-Yves used the same application, apparently independently, in 1722. Wangenstein and Wangenstein, *The Rise of Surgery*: 318. Nevertheless, the insights of Maître-Jan and Saint-Yves went unheralded until late in the nineteenth century (see Crede, 1884 below).

⁶⁷⁵The Russian army continued this practice through the First and Second World Wars. Rentz, "Historic Perspectives on Clinical Use and Efficacy of Silver" 1-2. And, yes, silver significantly reduces the risk of bacterial infection from contaminated water.

⁶⁷⁶*Ibid.*, 1.

fractures, with their exorbitantly high mortality rates from sepsis. In 1826, John Higginbottom (1788-1876) advocated the application of silver nitrate to wounds caused by skin-penetrating fractures. By 1829, he published the second edition of his monograph on the use of silver nitrate to “cure” inflammation, wounds, and ulcers—including those caused by compound fractures.⁶⁷⁷ There, he noted that “It appears scarcely necessary to describe the immediate and well known effects of the application of the nitrate of silver to the surface of a wound or ulcer.”⁶⁷⁸ Further, he asked, “May not [it] be employed to exclude the atmospheric air, to close the external wound, and so to reduce the dangerous circumstances of a compound fracture to that comparative simple and innocuous case of a simple fracture.”⁶⁷⁹ In essence, Higginbottom maintained that the use of silver nitrate could reduce the great risk of death from an infection linked to a bone fracture that broke through the protective barrier of the skin from a high probability to a small likelihood typically found with simple fractures (that do not penetrate the skin). Thus, Higginbottom anticipated many of the concerns of later generations of surgeons (atmospheric effects, open wounds, high post-traumatic infection rates) and discovered an effective anti-infective for the prevention and treatment of wound infections decades before the birth of modern antisepsis.⁶⁸⁰

Nonetheless, credit for the discovery of antisepsis went not only to those who empirically employed various chemicals to achieve antisepsis—for, as we have noted, many such compounds had been used over the millennia—but to their method of application and, as in the

⁶⁷⁷John Higginbottom, *An Essay on the Use of the Nitrate of Silver, in the Cure of Inflammation, Wounds, and Ulcers*, Second ed. (London: R. B. Seeley and W. Burnside, 1829). This more extensive volume was an extension of his 1826 essay on the application of “The Lunar Caustic” to wounds.

⁶⁷⁸*Ibid.*, 9.

⁶⁷⁹*Ibid.*, xi.

⁶⁸⁰Even Higginbottom’s late work, “A Practical Essay on the Use of The Nitrate of Silver,” which contains the quotation on “the dangerous circumstances of a compound fracture,” was published in 1865—two years before Lister’s seminal article on the subject.

case of anesthesia, to the degree to which they were publicized.⁶⁸¹ As it is, less credit for the use of silver nitrate as an antiseptic is bestowed upon Higginbottom than on Carl S. F. Crede, a German obstetrician. In 1884, Crede, who had noted an association between mothers with venereal disease and the development of blindness in their infants, treated newborns with a dilute (1%) solution of silver nitrate to prevent such ophthalmia neonatorum.⁶⁸² It was (and is) very effective. Dr. Albert C. Barnes of Philadelphia made his fortune (today displayed in his phenomenal art collection displayed in the new Barnes Foundation complex) in the early twentieth century through sales of Argyrol, a silver-based antiseptic.

Silver's application is widespread to the present day, although the use of silver as an anti-infective by Crede and Barnes came years after the birth of modern antisepsis. Indeed, silver is such a good antiseptic that were it not for the advent of antibiotics in the twentieth century, it is likely that silver compounds would be a mainstay for the prevention and treatment of infections to this day.⁶⁸³

Washing as Antiseptic

Every now and then a man's mind is stretched by a new idea or sensation, and never shrinks back to its former dimensions.

-Oliver Wendell Holmes, Sr., *The Autocrat of the Breakfast Table* (1858)

⁶⁸¹On the issue of Higginbottom and his failure to receive credit for the discovery of antisepsis, see also Wangensteen and Wangensteen, *The Rise of Surgery*: 317, 22, 25.

⁶⁸²The application of a dilute solution of silver nitrate to the eyes of all newborns delivered vaginally (as distinguished from a sterile Caesarean delivery) continues in many countries around the world to this day—often required by law, although in some countries erythromycin ointment is used because it causes less irritation around the eyes.

⁶⁸³Scientific research on the properties of silver in era of modern antisepsis may have begun with Raulin, who in 1869 showed that *Aspergillus* (a common fungus) could not grow in the presence of silver nitrate. G. Sims Woodhead and Arthur W. Hare, *Pathological Mycology* (Edinburgh: Young J. Pentland, 1885). 17. Subsequent research revealed that silver is bactericidal (i.e., kills bacteria, as opposed to bacteriostatic—whereby bacteria are inhibited from growth but not killed), augments the regeneration of diseased tissues, and rarely if ever induces bacterial resistance (an enormous problem with antibiotics in the twenty-first century). As such, silver compounds have a broad spectrum of antimicrobial activity and have been undergoing a rebirth of their own as agents of antisepsis—e.g., as burn treatments and silver-lined catheters to prevent catheter-related infections.

Although burning oil, alcohol, and a precious metal captured the imagination of those who would prevent and treat infections related to surgical wounds, in order to make surgery safer, still others looked at the problem differently. In the process, they created alternative solutions that demanded unconventional interpretations. Two of the most recognized outside-the-box thinkers were Oliver Wendell Holmes Sr. (1809-1894) and Ignaz Semmelweis (1818-1865). Others were undeservedly less heralded, but nevertheless made significant contributions to the concept that infection is spread by contagion. These led to a relatively simple method of prevention, and, in the process, the birth of modern antisepsis.⁶⁸⁴

Alexander Gordon—The Personal Consequences of Contagion

Alexander Gordon (1752-1799) was a Scotsman educated at Edinburgh and Leiden, two of the best medical schools of the late eighteenth century. Thereafter, he received specific instruction in midwifery in London, undoubtedly making him one of the best-trained accoucheurs (obstetricians) of his time.⁶⁸⁵ As luck would have it, an epidemic of puerperal fever—an obstetrical disease—raged in Aberdeen, his home town, between 1789 and 1792.⁶⁸⁶

Puerperal fever, otherwise known as puerperal sepsis and childbed fever, is a clinical syndrome that usually begins in mothers a few days after childbirth. It is characterized by elevated body temperature, abdominal pain in the lower abdomen, and other signs of inflammation of the gynecologic tract and peritoneum (the membrane lining the abdominal

⁶⁸⁴Contagion embodies the idea—etymologically derived—of “touching together.” Thus, a contagious illness is, properly, a disease spread from one person to another through direct contact. (The word “contact” comes from the same Latin root, “tangere”—to touch.)

⁶⁸⁵George W. Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," *Medical History* 37, no. 4 (1993): 401.

⁶⁸⁶The 1789-92 epidemic was hardly the only such epidemic of puerperal fever during the latter half of the eighteenth century. Nonetheless, it was the epidemic on which Dr. Gordon trained his skills of observation, recording, and epidemiologic analysis.

cavity and its organs).⁶⁸⁷ In both symptoms and signs, it mimics other infections like erysipelas⁶⁸⁸ and wound infections and may be described as a womb infection.⁶⁸⁹ If unchecked, the infection can spread throughout the body, like other wound infections, to cause sepsis, circulatory collapse, and death. Although accurate statistics for the eighteenth and early nineteenth centuries are infrequent, it is likely that between one out of two and one out of three women who contracted the disease died from it.⁶⁹⁰ Mary Wollstonecraft Godwin (1759-1797), a pioneer for women's rights and author of *A Vindication of the Rights of Woman* (1792), died of puerperal fever days after delivering her daughter, Mary.⁶⁹¹ It was more dread than cancer, for it struck down more women than cancer and at an earlier age.

Although birth-related maternal fevers were well known in Hippocratic times, the term “puerperal fever” did not appear until the eighteenth century.⁶⁹² The relatively recent naming of the ancient syndrome may have been because puerperal fever was, to a large extent, an urban disease dependent upon clusters of parturient women. Its incidence soared to epidemic

⁶⁸⁷The word “puerperal” is derived from “parous” (bearing, producing) and “puerile” (child), thus creating the sense of bearing children. A woman with puerperal fever is thus a woman who developed a fever after childbirth.

⁶⁸⁸Puerperal fever, erysipelas, and wound infections may all be caused by Group A Streptococcus. This commonality of causation, although unknown to the physicians of the late eighteenth and early nineteenth centuries, may explain retroactively many of the similarities among the diseases.

⁶⁸⁹It is reasonable to consider puerperal fever to be a wound infection in and around the tissues of the uterus in its early stages until, like other wound infections, it becomes systemic (total body involvement).

⁶⁹⁰Christine Hallett, “The Attempt to Understand Puerperal Fever in the Eighteenth and Early Nineteenth Centuries: The Influence of Inflammation Theory,” *Medical History* 49, no. 1 (2005): Footnotes 14, 15.

⁶⁹¹Mary Wollstonecraft Godwin (1797-1851) went on to marry Percy Bysshe Shelley (1792-1822) to become Mary Shelley, author of one of the greatest criticisms of modern science and industry—*Frankenstein* (1818).

⁶⁹²Hallett, “The Attempt to Understand Puerperal Fever in the Eighteenth and Early Nineteenth Centuries: The Influence of Inflammation Theory,” 1. Hallett, op. cit., footnote 10, found that William Campbell, *A treatise on the epidemic puerperal fever*, (Edinburgh: Bell and Bradfute: 1822), 8, 12-13, credited Edward Strother, *Criticon febrium*, with the first use of the term in 1716.

Dr. Hallett's article may be found online at <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1088248> – accessed January 17, 2009.

proportions in the decades following the founding of Lying-in hospitals in major cities,⁶⁹³ beginning around the mid-eighteenth century,⁶⁹⁴ as midwives and then physicians delivered one pregnant woman after another in close proximity.⁶⁹⁵ Puerperal fever was less common before the advent of lying-in facilities as well as in rural areas and in private residential settings, where midwives and physicians assisted at the births of fewer infants (fewer vaginal examinations), transported fewer fomites (bed linen, towels) from one woman to another, rarely used the same instrument (forceps) on different women, and had longer intervals between deliveries during which they were more likely to wash or bathe.⁶⁹⁶

Perhaps as the best-trained accoucheur in the town at the time, Dr. Gordon found himself at the center of the epidemic. Throughout, he kept meticulous notes on his patients—what could be called Case Studies. He recorded symptoms of the disease, its course over time, how it was treated, and, most importantly for our purposes, what was done by practitioners to prevent its onset.⁶⁹⁷ Three years later, in 1795, he published his findings in *A Treatise on the Epidemic Puerperal Fever of Aberdeen*.⁶⁹⁸

⁶⁹³Lying-in is a synonym for childbed, which implies both a space (the bed) and time (from contractions and confinement through childbirth and the immediate period thereafter).

⁶⁹⁴The first recorded epidemic of puerperal fever was in 1646 at the Hôtel Dieu in Paris, but the majority of known epidemics occurred during the eighteenth and nineteenth centuries. Caroline M. De Costa, "The Contagiousness of Childbed Fever: a Short History of Puerperal Sepsis and Its Treatment," *The Medical Journal of Australia* 177, no. 11 (2002). available online at http://www.mja.com.au/public/issues/177_11_021202/dec10354_fm.html#i1067496 accessed January 31, 2009.

⁶⁹⁵E. Y. Bridson, "Iatrogenic epidemics of puerperal fever in the 18th and 19th centuries," *British Journal of Biomedical Sciences* 53, no. 2 (1996).

⁶⁹⁶Fomites are inanimate objects contaminated with viable disease-causing infectious organisms.

⁶⁹⁷Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," 401 Footnote 12.

⁶⁹⁸Alexander Gordon, *A treatise on the epidemic puerperal fever of Aberdeen* (London: G. G. and J. Robinson, 1795).

At the time, other childbirth attendants believed the cause of the pestilence to be the “Weed,”⁶⁹⁹ noxious air (miasma), or an “epidemic constitution.”⁷⁰⁰ Gordon did not claim to know the exact nature of the infectious agent that caused puerperal fever, but his studies revealed how that agent was spread. After the compilation of much evidence and repeated testing of his hypothesis, he concluded that the disease was spread by those who delivered the newborns, including himself. “By observation, I plainly perceived the channel by which it is propagated; and I arrived at the certainty...that I could venture to foretell what women would be affected with the disease, upon hearing by what midwife they were to be delivered or by what nurse they were to be attended during their lying-in; and almost in every instance my prediction was verified.”⁷⁰¹ He then acknowledged that “I myself was the means of carrying the infection to a great number of women”⁷⁰² Gordon’s ability to predict which patients would be infected was miraculous for its time and revealed a deep understanding of the contagious nature of the disease. Unfortunately, knowledge of the method of transmission did not lead to its cure, although it certainly may have contributed to its prevention.

⁶⁹⁹Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," 404.

⁷⁰⁰Sherwin B. Nuland, *The Doctors' Plague: Germs, Childbed Fever and the Strange Story of Ignac Semmelweis* (New York: W. W. Norton & Company, 2004). 45-46.

Please note again the prevalence of the concept of “constitution”—the physical nature of the body considered as a whole. The idea of the body constitution lasted well into the nineteenth century and hampered the development of the concept of localism that proved so important for the development of surgery as a treatment—or, at times, the treatment—for cancer.

⁷⁰¹Gordon, *A treatise on the epidemic puerperal fever of Aberdeen*. cited by Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," 406. Also cited by Oliver Wendell Holmes, *Medical Essays 1842-1882*, Special ed., The Classics of Medicine Library (Boston: Houghton, Mifflin and Company, 1883; repr., 1987). 103.

Some of Gordon’s findings that led to his conclusion on the transmission of puerperal fever are shown in two tables given by Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," 402 and 03.

⁷⁰²Cited by Nuland, *The Doctors' Plague: Germs, Childbed Fever and the Strange Story of Ignac Semmelweis*: 47.

In his 1795 monograph, Gordon named the names of those attendants who spread the disease: Mrs. Blake, Mrs. Elgin, Mrs. Smith, Mrs. Coutts, et. al.—seventeen in all.⁷⁰³ Even the inclusion of his own name on the list did not forestall his vilification by the midwife community of Aberdeen. Compounding the midwives' revulsion against Gordon was his treatment of the fever—voluminous bleeding early in its course with purgation (use of strong laxatives) throughout.⁷⁰⁴ These were treatments the midwives found repulsive, but they were perfectly consonant with then current medical dogma among the community of heroic physicians on both sides of the Atlantic.⁷⁰⁵ The syllogism was clear: if blood was the seat of fever, then removal of blood led to less fever and thus, improvement in the patient's condition.⁷⁰⁶ Few heroic physicians, including Gordon in Aberdeen and Benjamin Rush in Philadelphia, doubted that the blood was the focus of disease. Further, Gordon suggested preventive methods that, although they appear reasonable today, were extreme in the late eighteenth century. "The patient's apparel and bedclothes," wrote Gordon, "ought either to be burnt or thoroughly purified; and the nurses and physicians who have attended patients affected with puerperal fever ought carefully to wash themselves, and to get their apparel properly fumigated before it be put on again."⁷⁰⁷

⁷⁰³Ibid.

⁷⁰⁴Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," 407-8.

⁷⁰⁵For a clear exposition on the connection between inflammatory conditions and bloodletting, see Hallett, "The Attempt to Understand Puerperal Fever in the Eighteenth and Early Nineteenth Centuries: The Influence of Inflammation Theory." Hallett emphasized the eighteenth-century distinction between inflammatory (excitation of the blood) and putrid (pus, decay) conditions and concluded that Gordon's acceptance of the inflammatory model to explain the nature of puerperal fever led to his treatment of the disease by bloodletting.

⁷⁰⁶In the United States, as we have seen, Benjamin Rush was a major proponent of this thinking and treatment. Rush especially utilized bloodletting for the treatment of Yellow Fever during the epidemic (in Philadelphia and elsewhere) of 1793.

If the disease *was* its symptoms, as many then believed, lowering body temperature would ameliorate the disease.

Purgatives added to the idea of "cleansing" the body of evil humors by causing evacuation of stool and its (presumably) noxious contents.

⁷⁰⁷Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," 410.

Washing, burning, and otherwise purifying childbirth attendants and their clothing were preventive measures not easily adopted by Gordon's colleagues. They could neither sanction Gordon's reasoning nor accept their own complicity in the transmission of the disease.

The publication of Gordon's findings on the infectious nature of puerperal fever, which he called "the fatal secret,"⁷⁰⁸ was his undoing. The midwives, physicians, and other attendants on the pregnant women of Aberdeen found his accusations (for that is what they considered his list of names) reprehensible.⁷⁰⁹ Not long after the publication of his *Treatise*, Gordon relinquished all connections with obstetrics and went again to sea, as he had in his youth. By 1799, four years after the publication of *A Treatise*, he was dead of tuberculosis.⁷¹⁰

Gordon applied the methodology of careful observation, case study, and inductive reasoning (that would become so prevalent by the end of the nineteenth century) to the Aberdeen epidemic of puerperal fever in the waning years of the eighteenth century. As such, he developed an explanation of who became diseased and how. In addition, he offered solutions to

⁷⁰⁸Gordon, *A treatise on the epidemic puerperal fever of Aberdeen*. cited by Lewis, "Epidemiology of puerperal fever: the contribution of Alexander Gordon," 409.

⁷⁰⁹The enmity between Dr. Gordon and the Mrs. midwives in Aberdeen (for they were all listed as "Mrs.") went beyond either a gender conflict or a turf war. Certainly, male physicians—especially surgeons—had made inroads into the practice of midwifery. Female midwives resented this, not only because these men were stealing their business, but because the male physicians claimed technical superiority to the female midwives. Thus, it is my interpretation of the literature that gender and economic issues contributed to Gordon's ostracism from the Aberdeen midwifery community, but that these important issues might have been overcome had he not had the audacity to publish the names of the women midwives in what was clearly seen by them as an attack on their persons. (The *OED* lists the first use of the term "man-midwife" as 1607, but the dated supporting entries show that the noun was not used in its strictly obstetrical sense until the eighteenth century.)

Judith Walzer Leavitt addresses contentious issues between competing female midwives and male physicians in Leavitt, *Brought to Bed*: 4-5, ff. Laurel Thatcher Ulrich discusses these gender/economic issues in the context of Martha Ballard's changing medical world in Maine in the late eighteenth and early nineteenth centuries. Laurel Thatcher Ulrich, *A Midwife's Tale: The Life of Martha Ballard, Based on Her Diary, 1785-1812* (New York: Vintage, 1991). 254-58. Dr. Leavitt notes that as late as 1900, birthing in the United States was evenly split between midwife and physician attendants. Leavitt, *Brought to Bed*: 267. Note that by 1900, however, many physicians who delivered newborns were women. This may have reduced the animosity between the genders except, perhaps, to the extent that women physicians were paid less than male physicians.

⁷¹⁰Nuland, *The Doctors' Plague: Germs, Childbed Fever and the Strange Story of Ignac Semmelweis*: 48.

curtail the spread of disease that were so advanced for his time as to be unacceptable to the community at large. He suffered for his prescience (as well as for what might today be called his political incorrectness), but his efforts to pinpoint which women would develop puerperal fever represented one of the earliest rational methodologies to prevent infection.

Gordon's conclusions as to the prevention and treatment of at least this one infectious disease were abhorrent to many of those around him. Not surprisingly, few followed his teachings for years to come. Nevertheless, his findings were rediscovered and revived by future generations who bravely sought to reduce the incidence of infections in and out of birthing and surgical suites.

Gordon's Intellectual Heirs

It is likely that at least some physicians after Gordon's death adopted his notion that puerperal fever was a contagious disease and that the idea of contagion led to appropriate measures to prevent it. Unfortunately, even fewer put it in writing. I have drawn this inference because those who did explicitly follow Gordon's teachings treat them as almost matter-of-fact.⁷¹¹ Although the historical record on the contagiousness of puerperal fever is relatively sparse before the middle of the nineteenth century, the tone of the few writings on this frequently mortal illness supports the idea that many physicians believed that puerperal fever was contagious and that "cleanliness" was critical to the prevention of the disease.⁷¹²

Thomas Watson & the Causation of Wound Infections—"Innocent no longer"

⁷¹¹Lacunae in the historical record should not dissuade from this premise—although absence makes any hypothesis tentative—for there is a significant difference between the absence of proof and proof of absence.

⁷¹²The idea of "cleanliness," especially through frequent bathing, was relatively unknown in the United States until the 1830s. The health and cleanliness movement led by Sylvester Graham and others at that time may well have contributed to the notion adopted by physicians that specific forms of cleanliness—like hand washing—could prevent particular diseases, including puerperal fever. Thoughts connecting disease and uncleanness, though ancient in its origin, may well have been heightened by Graham's movement. For more details on Sylvester Graham and the idea of cleanliness in antebellum America, see Hoy, *Chasing Dirt*: 23ff.

One instance of explicit recognition of Gordon's findings and course of remedy occurs in the medical textbook of Dr. Thomas Watson (1792-1882), an English physician at the Middlesex Hospital (1827-1843) and professor at King's College in London (1835-1840).⁷¹³ Watson based *Principles and Practice* upon lectures he delivered annually at King's College during the late 1830s.⁷¹⁴ In Lecture LXV he wrote about diseases of the abdomen, including peritonitis (inflammation of the lining of the abdomen and its organs) and one of its most common causes, puerperal fever.⁷¹⁵

Watson had no doubt as to the cause and prevention of the life-threatening illness known as childbed fever:

The contamination may arise in the way of *contagion*: this horrible malady may be communicated from one lying-in woman to another by the intervention of a *third person*; and doubtless it is so carried and propagated, in many instances, by midwives and accoucheurs. Now this source of the disorder may be obviated; and therefore it is of the utmost importance that it should be clearly recognized, in order that it may be carefully provided against.⁷¹⁶

The cause was contagion—spread by a transmitter from one victim of the disease to another.

Primary prevention was, firstly, recognition of the cause.

Watson did not expect his auditors and readers to accept his causation statement on faith. He cited proof—statistical proof. Of thirty (30) patients attended by a midwife who had just been exposed to a case of puerperal fever, sixteen (16) contracted the disease. Of 380 patients

⁷¹³Thomas Watson and David Francis Condie, *Lectures on the Principles and Practice of Physic; Delivered at King's College, London*, Third American, From the Last London ed. (Philadelphia: Blanchard and Lea, 1855). Recognition of Gordon is located on page 732.

⁷¹⁴*Ibid.* The edition I accessed was the third American edition derived from the most recent London edition. Watson published the first edition in the early 1840s. He based all editions on the King's College lectures he delivered from 1836-1841.

⁷¹⁵*Ibid.*, 731-34.

⁷¹⁶*Ibid.*, 732. Italics in the original.

cared for by other midwives at the same institution, none (0) developed puerperal fever.⁷¹⁷ The positive and negative forms of proof offered by Watson to support the idea of contagion were compelling, to no small extent because no other explanation could even approximate the disparity noted by his findings.

In addition to the numerical method that supported his epidemiological proof, Watson offered a pathophysiological explanation for the development of this “loathsome and fatal disease.” The mechanism of infection, he proposed, was “direct inoculation” into a vulnerable endometrium. “Recollect,” Watson reminded his readers, “how minute a quantity of an animal poison may be sufficient to corrupt the whole mass of blood, and fill the whole body.”⁷¹⁸ Inject only a small amount of “animal poison” into a vulnerable tissue of the body and infection induced by the poison would surely take hold and spread. The immediate post-partum uterus was just such a fertile ground for infection. It was, in fact, just like an open wound. “The interior of the uterus form[ed] a large wound, and present[ed],...an exact analogy to the surface of a stump after amputation.”⁷¹⁹ What a historically significant analogy—the post-partum womb and the post-amputation stump—for Lister would adopt the stump as his site of experimentation against infection a generation hence! Both fetal delivery and surgical amputation exposed the “interior” of the body to contagion from the outside. Both occurred after an “insult” (the tissue-ripping process of birth and the cutting through skin and bone, respectively) exposed the normally protected tissues to external agents. Both had a similarly

⁷¹⁷Ibid., 733. Watson did not specify how many of the attendees of the uninfected 380 women had been exposed to a patient with puerperal fever before attending them. Nevertheless, these results are *too* good—like Gregor Mendel and his pea-plant genetic results. The 16:30 ratio for the “contaminated” midwife is credible, but 0:380 for all other midwives is not.

⁷¹⁸Ibid.

⁷¹⁹Ibid.

high rate of morbidity—and mortality. Had Lister been an accoucheur, his antiseptic experimentations might have focused upon puerperal fever rather than compound fractures that led to surgical amputations!

Nonetheless, knowledge of the proximate cause of a disease may be insufficient to prescribe a prevention, especially if there is an intermediary involved in the transmission of the disease. If the intermediary is necessary for the spread of the disease from one host to another, the illness may be prevented by blocking the transmitter.⁷²⁰ But how illogical—even unbelievable—was Watson’s idea in a pre-bacteriology world that the very hand that aided and even saved the new mother was itself the hand of death. Dr. Thomas Watson was a logician. To him—as to the Dr. Watson of literature who associated with a certain Holmes created by Arthur Conan Doyle, M. D. years later—if all other causes are excluded, the remaining cause (no matter how unlikely or seemingly impossible) must be the cause.⁷²¹ After reviewing his statistical findings, Watson knew the culprit and his/her responsibility in the prevention of personal tragedy:

Reflecting upon these facts, you will see too much likelihood in the dreadful suspicion, that the hand which is relied upon for succour in the painful and perilous hour of child-birth, and which is intended to secure the safety of both mother and child, but especially of the mother, may literally become the innocent cause of her destruction; innocent no longer, however, if, after warning and knowledge of the risk, suitable means are not used to avert a catastrophe so shocking.⁷²²

⁷²⁰Diseases such as yellow fever and malaria are spread by mosquito vectors (transmitters), but they are caused by microorganisms harbored within these vectors. The mosquito injects these infectious microorganisms into the victim’s blood as it feeds naturally. Prevention is aimed at killing the vectors rather than the pathogenic virus and protozoan that actually cause the diseases.

⁷²¹Is it possible that Sir Arthur Conan Doyle (1859-1930), who studied medicine at the University of Edinburgh (1876-1881) during the ebullient first flowerings of antiseptics and bacteriology, was not somehow influenced in the naming of his prime fictional characters—Sherlock Holmes and Dr. John H. Watson—by Drs. Thomas Watson and the physician-writer (like himself) Dr. Oliver Wendell Holmes—both of antiseptics fame?

⁷²²Watson and Condie, *Lectures on the Principles and Practice of Physic; Delivered at King's College, London*: 733.

Thomas Watson and the Prevention of Wound Infections—“To avert a catastrophe so shocking”

Once convinced of the contributory role of the midwife and the physician-accoucheur in the transmission of puerperal fever, Watson harbored no sympathy for those responsible for the spread of the disease. S/He who caused death through the transmission of disease after learning of the contagious nature of puerperal fever was no less culpable than a murderer who wittingly killed with an axe.

What specific measures could be applied to prevent the transmission of childbed fever? Gordon had advocated “purification” of exposed clothing by fire and fumigation as well as washing of the persons involved. Watson carried Gordon’s suggestions a step farther, for, lecturing well after the advent of the chemistry revolution in the early nineteenth century, he advocated specific chemicals to rid the third-party transmitter of contagion:

Whenever puerperal fever is rife, or when a practitioner has attended any one instance of it, he should use most diligent ablution; he should even wash his hands with some disinfecting fluid, a weak solution of chlorine for instance: he should avoid going in the same dress to any other of his midwifery patients: in short, he should take all those precautions which, when the danger is understood, common sense will suggest, against his clothes or his body becoming a vehicle of contagion and death between one patient and another.⁷²³

Watson made clear that these were not idle suggestions. Rather, he asserted, “This is a duty so solemn and binding.”⁷²⁴ Semmelweis later became famous for his advocacy of chloride-based hand washing, but Watson made it a part of his prevention regimen well before him.⁷²⁵

⁷²³Ibid.

⁷²⁴Ibid.

⁷²⁵When Watson delivered his lectures in the late 1830s, Holmes, who quoted from a physician’s letter advocating chloride hand washing in his monograph on puerperal fever and contagion, was away from Boston on the faculty of the Dartmouth Medical School (1838-1840) and Semmelweis had just begun medical school (1838). The University of Vienna awarded Ignaz Semmelweis his medical degree in 1844.

The fertile mind of Thomas Watson, inspired by the new-found manufacturing processes of the Industrial Revolution, conceived of another idea that might serve to destroy the ability of the hand to convey infection—cover the possibly contagious hand with a disposable glove.

Halsted is often credited with the invention of the surgical glove around 1889,⁷²⁶ but it is clear that Dr. Watson had the same idea more than half a century earlier:

In these days of ready invention, a glove...might be devised, which should be impervious to fluids, and yet so thin and pliant as not to interfere materially with the delicate sense of touch required in these manipulations. One such glove, if such shall ever be fabricated and adopted, might well be sacrificed to the safety of the mother, in every labour.⁷²⁷

The protective, preventing glove, however, remained nothing more than a construct of Watson's imagination. He was fully cognizant of the opposition to his idea of contagion that blaming the savior would generate among his colleagues. Nevertheless, Watson went further in his desire to prevent the wound infection of puerperal fever. Should the washings, cleanings, and chemicals fail in the attempt to prevent contagion, he suggested one final step for the no-longer-innocent professional—avoidance. "Should these precautions all prove insufficient, the practitioner is bound, in honour and conscience, to abandon, for a season, his vocation."⁷²⁸

Like the preventive measures against contagion advocated by Alexander Gordon before him, it is not clear to what degree Dr. Watson's measures influenced practitioners of his age.

⁷²⁶Haagensen and Lloyd, *A Hundred Years of Medicine*: 246-47. Furthermore, Halsted invented his rubber gloves to keep the harsh chemicals of the operating suite off the delicate hands of his nurse (and future wife), while Watson conceptualized the obstetrical glove to prevent contagion. It should be noted that Halsted's gloves, invented after the advent of the bacteriological revolution, were sterile. Watson had no such conception, but reasoned that as long as his gloves had not been exposed to the contagion of a previous patient with puerperal fever, they would not transmit disease to the next woman in labor. Surgical gloves are still used for the protection of the patient as well as the obstetricians and surgeons today, but I would assert without hesitation that Watson's goal of patient protection is far more important.

⁷²⁷Watson and Condie, *Lectures on the Principles and Practice of Physic; Delivered at King's College, London*: 733.

⁷²⁸*Ibid.*

Certainly he met with more success than Gordon, for Watson's text of compiled lectures was called "a universal favorite" by at least one of his followers.⁷²⁹ The author of that quotation, who recognized Gordon's monumental contribution to the health and welfare of pregnant women everywhere as well as Watson's compelling additions, was a young physician on the other side of the Atlantic, in Boston—Oliver Wendell Holmes.

Oliver Wendell Holmes and "The Contagiousness of Puerperal Fever"

["The Contagiousness of Puerperal fever"] is an article which will long keep [Holmes'] memory green in our ranks.

-William Osler (1909)⁷³⁰

We have met the eminent Dr. Holmes many times in our travels through the history of nineteenth-century American medicine, for his prominent Boston Brahmin family provided the young, witty raconteur with many experience-expanding opportunities.⁷³¹ He took full advantage of them. Early in his medical career, Holmes had the advantage of studying in France. His Continental sojourn during the 1830s exposed him to the most modern European techniques (for example, medical microscopy), which he applied to the education and training of physicians in his native United States. His erudition and ability to express himself in winsome prose lent him a role in the history of anesthesia. It was not by chance that William T. G. Morton approached Holmes with regard to the naming of Morton's anodyne, for the Harvard graduate

⁷²⁹Holmes, *Medical Essays*: 116.

⁷³⁰William Osler, *An Alabama Student, and Other Biographical Essays* (New York: Oxford University Press American Branch, 1909). 60.

⁷³¹Even the term "Brahmin," as applied to certain Boston families, is probably an Oliver Wendell Holmes Sr. creation. He first used it in Sr. Oliver Wendell Holmes, "The Professor's Story," *The Atlantic Monthly*, January 1860, 91. The *OED* lists the origin of the term as Holmes' *Elsie Venner*, which was originally serialized in *The Atlantic Monthly* as "The Professor's Story" beginning in December, 1859, and then published as a novel in 1861. (The *OED* gives the 1859 date.)

Holmes helped to increase the fame and distribution of *The Atlantic Monthly* with his literary contributions, beginning with the *Atlantic Monthly*'s serialization of his *The Autocrat of the Breakfast Table* (1857-1858)—arguably his most popular writing.

and soon-to-be Harvard professor⁷³² was, by the late 1840s, an acknowledged medical savant whose interests grew to include literature, poetry,⁷³³ and even new technologies.⁷³⁴

Holmes' medical studies in Parisian hospitals during the early 1830s gave him the opportunity to learn the profession as a student of Pierre-Charles-Alexandre Louis (1787-1872). Louis' seminal work on the "numerical method" (medical statistics), noted above, was one of the earliest efforts at what is today considered "outcomes research."⁷³⁵ Holmes adopted many of the Frenchman's ideas, including Louis' statistical reckonings of different treatment results as well as his propensity to see the physician as an aide to Nature rather than as its manipulator.⁷³⁶ Thus, Holmes approached the practice of medicine with measured steps, reasoned advances, and independent, counterintuitive thinking. As he wrote in letters from Paris in 1833-34,

⁷³²Holmes taught at Harvard Medical School, from which he received his medical degree in 1836, from 1847 until 1882.

⁷³³Through his mother, Holmes was a descendant of Anne Bradstreet (c. 1612-1672), the first published woman poet in what would become the United States of America.

⁷³⁴Holmes played a role in the development of the Stereoscope, a nineteenth-century viewfinder that re-created the appearance of three-dimensional images such as monuments and other tourist attractions from two-dimensional photographs by means of a *trompe l'oeil* effect.

⁷³⁵Outcomes research, as defined by the (Federal) Agency for Healthcare Research "seeks to understand the end results of particular health care practices and interventions." See <http://www.ahrq.gov/clinic/outfact.htm> accessed February 9, 2009. As Louis evaluated the effect of the treatment of bloodletting on patients to assess how their diseases responded (or did not respond), so outcomes research attempts to measure the results of other treatments today.

⁷³⁶P.-C.-A. Louis' *méthode expectante* was an antecedent of William Osler's therapeutic nihilism. Both countered a much-too-prevalent notion of medical therapeutics during the nineteenth century that some treatment—no matter how potentially harmful—was better than no treatment at all. Osler eyed unproven therapies with skepticism and, in the process, urged others to give evidence that a treatment worked. Louis had provided a methodology for testing the worth of a therapy sixty years before Osler when the Frenchman demonstrated, for example, that blood-letting was more harmful than beneficial.

Holmes adopted these scientific ideas. In 1842, he criticized homeopathy—the use of substances (in diluted aliquots) that reproduce the symptoms of the patient—on the basis of the failure of its proponents to use scientific methods or applications to prove its effectiveness. See "Homeopathy and Its Kindred Delusions" in Holmes, *Medical Essays*: 1-102.

I have more fully learned at least three principles since I have been in Paris: not to take authority when I can have facts; not to guess when I can know; not to think a man must take physic because he is sick.⁷³⁷

My aim has been to qualify myself...not for a mere scholar, for a follower after other men's opinions, for a dependent on their authority,—but for the character of a man who has seen and therefore knows; who has thought and therefore has arrived at his own conclusions.⁷³⁸

Holmes' Concern with Contagion

One consequence of Holmes' iconoclastic approach to the received medical wisdom of his time (for memory-laden didacticism ruled the day in the 1830s) was an attack on one of the time-honored traditions of physicians in the pre-antisepsis era—the “hands-on” approach to patient care in the birthing arena (and elsewhere, such as the surgical suite).

Holmes was deeply troubled with the consequences of the mechanism of contagion as he conceived them and, by extension, with the inability to prevent wound infections. Many believed before Holmes that diseases like puerperal fever were contagious. Nevertheless, his investigations into the nature of puerperal fever became an example of adverse thinking—adverse to the customary practices of the powers that were—that has become so critical to the evolution of medical thinking and practice over time. His inquiries into the nature of the disease also became a cornerstone in the effort to reduce wound infections related to obstetrical procedures specifically and surgery in general. Holmes' closely reasoned arguments led others to view favorably the validity of his conclusions on the contagious nature of puerperal fever. As such, they set in motion a theory and practice of infection that eventuated in a great increase in

⁷³⁷John Torrey Morse, *Life and Letters of Oliver Wendell Holmes*, 2 vols., vol. 1 (Boston and New York: Houghton, Mifflin and Company, 1896). 109. The date of the letter was August 13, 1833. Accessed online at Google Books and <http://www.archive.org/stream/lifelettersofoli01mors> on January 23, 2009.

⁷³⁸*Ibid.*, 130. Holmes dated this letter April 30, 1834.

the number of surgeries performed during the late nineteenth century, including surgery for the treatment of cancer.

I cannot doubt that most readers will be satisfied and convinced, to loathing, long before they have finished the dark obituary calendar laid before them.

-Dr. Oliver Wendell Holmes⁷³⁹

Holmes was aghast at the morbidity and mortality caused by puerperal fever. He, like other physicians (and patients) on both sides of the Atlantic, viewed with rising horror the widespread and growing incidence of the disease and, to no small extent, the great crisis in confidence it created against the practitioners of health care. In the 1820s, a Scottish physician and midwife, John Mackintosh, commented on the pervasiveness of puerperal fever when he wrote that “there is not a corner in Britain where this formidable disease has not made many mourners.”⁷⁴⁰ The situation in the United States was no less dire. In recent years, Irvine Loudon estimated that “there were, in the eighteenth and nineteenth centuries, about 2-3 deaths and 6-9 cases in every 1,000 deliveries. In epidemics...there were far more.”⁷⁴¹ Loudon concluded that about 250,000-500,000 women died from puerperal fever during the eighteenth and nineteenth centuries in England and Wales alone.⁷⁴² Holmes set out to demolish the prevalent non-contagion etiologies of his time with regard to the means of acquisition and spread of puerperal fever. His aim was to suggest an effective solution to prevent the spread of the disease and, ultimately, to eradicate it.

⁷³⁹Holmes, *Medical Essays*: 105.

⁷⁴⁰John Mackintosh, *A treatise on the disease termed puerperal fever* (Edinburgh: W. Blackwood, 1822). 5. cited by Hallett, "The Attempt to Understand Puerperal Fever in the Eighteenth and Early Nineteenth Centuries: The Influence of Inflammation Theory," FN11.

⁷⁴¹Irvine Loudon, *The Tragedy of Childbed Fever* (New York: Oxford University Press, 2000). 6.

⁷⁴²*Ibid.*, 6 and Footnote 10.

Causation as Key to Prevention

Despite the work of Gordon, Watson, and others, the cause of this potentially mortal affliction was generally accepted to be unknown in the early 1840s, when Holmes researched puerperal fever. However, as is often the case when the cause or mechanism of a disease is uncertain, physicians and others postulated many theories to fill the knowledge gap.⁷⁴³

To Holmes, the careful observations of Alexander Gordon and others beginning in the late eighteenth century had yielded testable theories as to its mode of transmission. Gordon found the major causation theories of his time—miasmatic (air), water (environment), economic (class), and moral (saints and sinners)—inadequate. To him, the only variable that seemed to explain who would acquire the disease and who would not was whether or not the attendant had been recently in the company of a woman with puerperal fever. Holmes was aware of the findings of Drs. Gordon and Watson, among others.⁷⁴⁴

An Interest Borne of Tragedy and Sorrow

The disease known as Puerperal Fever is so far contagious as to be frequently carried from patient to patient by physicians and nurses.

-Dr. Oliver Wendell Holmes⁷⁴⁵

The curiosity of the young Dr. Holmes on the nature of puerperal fever was piqued by “a certain supposed cause of disease, about which something was known, a good deal suspected, and not a little feared.”⁷⁴⁶ Specifically, his awareness of the disease and its cause were heightened by a chance encounter with “a case...of a physician who made an examination of the

⁷⁴³Hallett, "The Attempt to Understand Puerperal Fever in the Eighteenth and Early Nineteenth Centuries: The Influence of Inflammation Theory." reviews the major causal theories of puerperal fever prevalent in the eighteenth and early nineteenth centuries.

⁷⁴⁴Holmes, *Medical Essays*: 103 and 16.

⁷⁴⁵*Ibid.*, 103.

⁷⁴⁶*Ibid.*, 104.

body of a patient who had died with puerperal fever, and who himself died in less than a week, apparently in consequence of a wound received at the examination, having attended several women in confinement in the mean time, all of whom, as it was alleged, were attacked with puerperal fever.”⁷⁴⁷

How horribly tragic—and eerie! A man with what appeared to be the equivalent of puerperal fever! A physician cut himself accidentally while attending the body of a patient whose cause of death was thought to be puerperal fever. Over the next few days, the physician, during the worsening of his own feverish condition, had contact with several women about to deliver babies. Then he died. Shortly thereafter, the puerperal women with whom the physician had had contact during his own illness contracted the same condition as the case with which the physician had had initial contact.

Contact is the literal and figurative core of contagion. What else but contagion through contact could cause this tragic chain of events? Could the vagaries of chance cause this unlikely confluence of cases? No, Holmes calculated, the probability of a series of occurrences like this would be one in “a million million million, millions.”⁷⁴⁸ Others agreed, but still others did not.⁷⁴⁹ The young professor was bewildered and at the same time intrigued.⁷⁵⁰ He decided to pursue the cause of puerperal fever by the same means as would a young physician today—via a thorough search of the literature (where he found the works of Gordon and Watson) and

⁷⁴⁷Ibid.

⁷⁴⁸Ibid., 114.

⁷⁴⁹“In collecting, enforcing, and adding to the evidence accumulated upon this most serious subject,” wrote Holmes at the beginning of his 1843 essay, “I would not be understood to imply that there exists a doubt in the mind of any well-informed member of the medical profession of the fact that puerperal fever is sometimes communicated from one person to another, both directly and indirectly.” Ibid., 128-29. Of course, as is evident from the length and breadth of Holmes’ monograph, there were many who were not so “well-informed.”

⁷⁵⁰Holmes, although not yet a Harvard professor, had been a faculty member at the Dartmouth Medical School from 1838-1840.

consultation with more experienced colleagues. The result was Holmes' "The Contagiousness of Puerperal Fever," first published in 1843—a lengthy argument filled with evidence supporting the title's claim.⁷⁵¹

Holmes' investigations convinced him that puerperal fever was contagious and that physicians and other attendants spread the disease by contact from patient to patient. He sought to disseminate the story of contagion far and wide so as to convince his colleagues to take reasoned measures to prevent spread of the disease. At first, however, he fared no better in his quest than had Gordon, for Holmes initially presented his findings before only a small group of physicians—the Boston Society for Medical Improvement⁷⁵²—and then published his monograph in a short-lived periodical of limited circulation.⁷⁵³ Thus, few were initially aware of the existence of his essay, let alone his conclusions and suggestions for prevention.

Unlike Gordon, however, Holmes received a second chance, earned—at least in part—by his longevity in the field of medicine. For whereas Gordon essentially disappeared from practice shortly after the debut of his essay in 1795, Holmes became a renowned professor at Harvard.⁷⁵⁴

⁷⁵¹The essay plus a valuable introduction by Holmes may be found in Holmes, *Medical Essays*: 103-72. There are several online sources of the essay, including <http://www.bartleby.com/38/5/1.html> and <http://chestofbooks.com/health/general/Oliver-Wendell-Holmes-Medical-Essays/The-Contagiousness-Of-Puerperal-Fever.html> accessed January 30, 2009.

⁷⁵²A twentieth-century recreation of Holmes presenting his paper to the Boston Society by Dean Cornwell (1892-1960), entitled "That Mothers Might Live," may be viewed at <http://wrair-www.army.mil/index.php?view=artOfWrair> accessed January 10, 2009.

Holmes became a member of the Society in 1836. A history of the small, close-knit Society (its members usually numbered no more than forty and had many characteristics in common) may be found at http://www.archive.org/stream/storyofbostonsoc00mumf/storyofbostonsoc00mumf_djvu.txt, a reprint of J. G. Mumford, "The Story of the Boston Society for Medical Improvement" in J. G. Mumford, "The Story of the Boston Society for Medical Improvement," *The Boston Medical and Surgical Journal* (1901).

⁷⁵³The publication was the *New England Quarterly Journal of Medicine and Surgery*. Holmes published "Contagion" in the April, 1843 issue.

⁷⁵⁴Holmes was a member of the Harvard Medical School faculty from 1847-1882. He ultimately became the Parkman Professor of Anatomy and Physiology. Richard Herndon and Edwin Monroe Bacon, *Boston of To-day: A glance at Its History and Characteristics. With Biographical Sketches and Portraits of Many of Its Professional*

Holmes and his theory of contagion became widely known. As such, they also became open to attack. However, as is sometimes the perverse consequence of public attacks, he and his ideas became all the more famous and, with the substantiation of his theory in time, even revered.⁷⁵⁵

Those Opposed to Holmes' Notion of Contagion

I prefer to attribute [deaths from puerperal fever] to accident, or Providence, of which I can form a conception, rather than to a contagion of which I cannot form any idea.

-Professor Charles Delucena Meigs, 1852⁷⁵⁶

The most vocal opponent of Holmes' theory of contagion was Dr. Charles D. Meigs, the well-known and well-respected Professor of Obstetrics at Jefferson Medical College in Philadelphia. His protests against administering anesthesia to women in the throes of childbirth have already been discussed in terms of—among other concerns—his preference for religious credos over a compassion for human suffering.⁷⁵⁷

Meigs would not and could not accept a theory of contagion.⁷⁵⁸ His position is actually quite understandable for the time, for although today the idea of disease transmitted by external agents like viruses and bacteria is well established, in 1843 there was little cognizance of germs and even less acceptance disease-causing potentiality. Hence, Meigs had no “idea” of contagion.

and Business Men (Boston: Post Publishing Company, 1892). 262. His predecessor in that Professorship was Dr. John C. Warren, who, as we have learned, helped introduce anesthesia to the world.

⁷⁵⁵Reverence followed the decline in the number of cases of puerperal fever after the implementation of Holmes' post-puerperal fever exposure directives and, more so, after the acceptance of antiseptic techniques and the germ theory of disease during the last decades of the nineteenth century. Holmes described the confirmatory elements of germ theory as “the little army of microbes [that] marched up to support my position.” Osler, *An Alabama Student, and Other Biographical Essays*: 66. Holmes was fortunate to live long enough to witness both antiseptics and the explanatory theory of germs. He died in 1894 at the age of 85.

⁷⁵⁶P. M. Dunn, “Professor Charles D Meigs (1792-1869) of Philadelphia and persistent fetal circulation,” *Archives of Disease in Childhood: Fetal & Neonatal* 70, no. 2 (1994): F155.

⁷⁵⁷See pages 106-107 above.

⁷⁵⁸Meigs wrote more than one essay against the contagiousness of puerperal fever. Letter VI of Charles D. Meigs, *On the Nature, Signs, and Treatment of Childbed Fevers: in a Series of Letters addressed to the Students of his Class* (Philadelphia 1854). is cited most frequently.

Still, his argument against Holmes' principle of contagion went deeper, for Meigs was a gentleman of the South—a cavalier whose sense of propriety and rectitude transmuted cultural subjectivity into scientific objectivity.⁷⁵⁹ He believed that physicians could not carry puerperal fever from one woman to another as vehicles of contagion because physicians were gentlemen, and “gentlemen’s hands are clean.”⁷⁶⁰

No doubt Meigs also agreed with his Philadelphia colleague, Professor Hugh L. Hodge, that the “value and dignity” of the medical profession prevented a physician from ever becoming “the minister of evil” who could “ever convey, in any possible manner, a horrible virus, so destructive in its effects, and so mysterious in its operations as that attributed to puerperal fever.”⁷⁶¹ Further, he “begged his students”—those who would deliver the pregnant women of the future—“to divest their minds of the dread that they could ever carry the horrible virus.”⁷⁶²

⁷⁵⁹Charles Delucena Meigs lived in Athens, Georgia, from 1801 (age 9) until his graduation in 1809 at the age of 17 from the University of Georgia (where his father was President). After graduation from the University of Pennsylvania with a degree in medicine in 1817, he returned to Augusta, Georgia, for two years before removing permanently (perhaps against his will—his wife would not live in Georgia) to Philadelphia. <http://www.meigs.org/charles219.htm> accessed February 22, 2009.

⁷⁶⁰Charles Delucena Meigs, *Obstetrics, the Science and the Art*, Third ed. (Philadelphia: Henry C. Lea, 1856).

In the appendix to his 1855 essay update, Holmes took advantage of an 1852 article written by Meigs. (Cited as Meigs, *Obstetrics Phil.* 1852: 368, 375) Therein, Meigs names (James Y.) Simpson an “eminent gentleman.” However, Simpson, after attending the autopsies of two cases of a colleague’s cases of puerperal fever during which Simpson “freely handled the diseased parts,” found that his next four pregnant patients “were affected with puerperal fever”—“the first time he [Simpson] had seen it in practice.” Holmes concluded that “As Dr. Simpson is a gentleman (Dr. Meigs, as above), and as “a gentleman’s hands are clean” (Dr. Meigs’ Sixth Letter), it follows that a gentleman with clean hands may carry the disease.” Holmes, *Medical Essays*: 171.

⁷⁶¹Hugh L. Hodge, M.D., *On the Non-Contagious Character of Puerperal Fever: An Introductory Lecture*, delivered October 11, 1852. Also see *Medical Essays*: 103, 09.

Please note that the term “virus,” which today connotes a microscopic particle of nucleoproteins enveloped by a protein coat, then referred to “any agent causing an infectious disease.” (*OED*, “virus,” definition 2.a., online Draft Revision, Mar. 2009) accessed March 23, 2009.

⁷⁶²Osler, *An Alabama Student, and Other Biographical Essays*: 63-64.

The criticisms of Meigs and Hodge represented no idle chatter. Philadelphia, professional home to both men,⁷⁶³ was the epicenter of the theory and practice of obstetrics at the time in the United States.⁷⁶⁴ Furthermore, Meigs and Hodge were, in the words of William Osler, “the most distinguished professors of obstetrics in America.”⁷⁶⁵ Even Holmes acknowledged that they were “the two leading professors of obstetrics in this country.”⁷⁶⁶ By contrast, Holmes was a fledgling in 1843. Who would adopt the radical ideas of an untested newcomer in the long-standing debate over the nature of puerperal fever rather than the time-honored precepts of the established luminaries in the field?⁷⁶⁷

If I am right, let doctrines which lead to professional homicide be no longer taught from the chairs of those two great Institutions [Jefferson and Penn—LK]. Indifference will not do here.

-Oliver Wendell Holmes Sr.⁷⁶⁸

Holmes had predicted earlier that radical theories, such as his later advocacy of the contagiousness of puerperal fever, would provoke adverse responses from old-line physicians like Meigs and Hodge. In his Boylston Prize-winning essay of 1837 on the “Utility and Improvement of Direct Exploration in Medical Practice,” Holmes suggested why the great advances of his medical forbears [for example, Leopold Auenbrugger (1722-1809) on percussion and René Laennec (1781-1826) on auscultation] were slow to be adopted by their

⁷⁶³Charles D. Meigs was Professor of Obstetrics at Jefferson Medical College. Hodge was Professor of Obstetrics at the University of Pennsylvania. Ibid., 63.

⁷⁶⁴Ibid.

⁷⁶⁵Ibid.

⁷⁶⁶Ibid., 66.

⁷⁶⁷The path of least resistance for most is to accept the past unquestioned. Nonetheless, without radical or new ideas there would be little criticism of established conventions in medicine or society at large. Without critique there would be no change. Without change there would be no possibility of improvement. Without improvement, the present lives in slavery to the past.

⁷⁶⁸Holmes, *Medical Essays*: 128.

contemporaries. “It is perfectly natural that they [referring to the skeptical, older practitioners] should look with suspicion upon this introduction of medical machinery among the old, hard-working operatives;” he wrote, “that they should for a while smile at its pretensions, and when its use began to creep in among them, that they should observe and signalize all the errors and defects which happened in its practical application.”⁷⁶⁹

Hodge’s and Meigs’ criticisms of Holmes’ 1843 work on puerperal fever appeared in 1852 and 1854, respectively, for little notice was taken of “Contagiousness” until then. What was Holmes’ response? Did he cower in fear that his work would be judged wanting by his colleagues, a pitiful addition to the collection of medical knowledge on childbed fever and a step backwards in the overall fight against sepsis? No, quite the contrary. So sure was he of the validity of his etiology that he reprinted his 1843 essay in 1855 and added the trenchant comments of the Philadelphians to the frontispiece of his update—like trophies won in battle! In later years, Holmes remembered with “a savage pleasure” how he had attacked “those two professors—learned men both of them, skilful experts, but babies, as it seemed to me, in their capacity of reasoning and arguing.”⁷⁷⁰

Holmes had full confidence in the findings and conclusions he had reached in 1843. By 1855, he was even more confident that puerperal fever was contagious and in the deduced precautions necessary to prevent its spread. In the preface to the updated essay, he wrote, perhaps as a gibe against Hodge and Meigs, that “I do not know that I shall ever again have so good an opportunity of being useful.”⁷⁷¹ Pointing in the direction of Philadelphia, he added, “I

⁷⁶⁹Osler, *An Alabama Student, and Other Biographical Essays*: 59-60.

⁷⁷⁰Oliver Wendell Holmes Sr. wrote this to William Osler in a letter dated January 21, 1889. *Ibid.*, 65.

⁷⁷¹Holmes, *Medical Essays*: 105.

had rather rescue one mother from being poisoned by her attendant, than claim to have saved forty out of fifty patients to whom I had carried the disease.”⁷⁷²

Holmes’ Prescriptions for Prevention

It is not the man who first says a thing, but it is he who says it so long, so loudly, and so clearly that he compels men to hear him—it is to him that the credit belongs; and so far as this country is concerned, the credit of insisting upon the great practical truth of the contagiousness of puerperal fever belongs to Dr. Holmes.

-Sidney Smith⁷⁷³

What makes the Healing Art divine? The blazoned truth we hold so dear: To guard is better than to heal, The shield is nobler than the spear.

-Oliver Wendell Holmes Sr.⁷⁷⁴

I shrieked my warning louder and longer than any of them.

-Oliver Wendell Holmes⁷⁷⁵

Oliver Wendell Holmes was not the first to argue that the mode of dissemination of puerperal fever was contagion, but he was surely its most vocal proponent—for both mode of infection and consequent prevention. His writing on the contagiousness of puerperal fever stirred the thoughts and imaginations of generations of medical students and young physicians. Ironically, readers lost interest in Holmes’ essay years later only after the acceptance of germs as causative agents of disease made contagion the obvious method of transmission of puerperal fever.

Holmes was a man ahead of his time in both thought and action. Nevertheless, he was only one in a series of physicians which began before he was born who noted that the pattern of disease acquisition suggested that puerperal fever was contagious. Always fair-minded, he

⁷⁷²Ibid., 106.

⁷⁷³Osler, *An Alabama Student, and Other Biographical Essays*: 61.

⁷⁷⁴From an oration given at the 1860 meeting of the National Sanitary Association.
<http://www.library.musc.edu/resources/biomed/InfectCtrl/sld007.html> accessed September 21, 2009.

⁷⁷⁵Osler, *An Alabama Student, and Other Biographical Essays*: 66.

acknowledged those of the past and built upon their findings in terms preventive as well as epidemiologic.⁷⁷⁶

The goals of most of Holmes' essay were to convince the reader of the contagiousness of puerperal fever and that the very attendants who sought to help the mother through childbirth could be the cause of her demise. "My object," he wrote, "was...to show that women had often died in childbed, poisoned in some way by their medical attendants."⁷⁷⁷ Nonetheless, he would have been the first to acknowledge that his real purpose in writing the monograph was not to accuse (although he accomplished this compellingly), but rather to save the lives of at-risk women. Thus, having satisfied himself that he had convinced the reader of his etiologic objectives, he set out to put his findings to good use for primary prevention (i.e., to prevent the disease in the first place), for there was no cure for puerperal fever.

Prior to the publication of Holmes' essay, many proposals to reduce the spread of puerperal fever came from physicians directly involved in the throes of local and personal epidemics. Holmes collected their experiences and included them in his essay. One anonymous physician's letter dated January, 1843, for example, noted that the writer had had yet "another disastrous period" in the summer of 1835 during which several of his patients died of puerperal fever.⁷⁷⁸ The physician had tried everything he could think of to stanch the epidemic in his

⁷⁷⁶Holmes lists many of his intellectual forebears at Holmes, *Medical Essays*: 166., but their contributions to thoughts on the contagiousness of puerperal fever are scattered throughout the essay to support Holmes' own conclusions.

⁷⁷⁷*Ibid.*, 117.

⁷⁷⁸*Ibid.*, 150.

practice—changing his clothing, waiting between patient visits, traveling between patients—but nothing seemed to help.⁷⁷⁹

In desperation, the physician, while attending two women dying of puerperal fever, decided to put all his preventive efforts together and suggested one more. “I changed my clothes, and washed my hands in a solution of chloride of lime after each visit,” he added, with an emphasis on the hand washing.⁷⁸⁰ Thereafter, he “attended seven women in labor during this period, all of whom recovered without sickness.”⁷⁸¹ Needless to say, the physician was fully convinced that the results of his small, uncontrolled study (although it is doubtful that he thought of his personal experiment as such) supported the idea that the measures he adopted to reduce the plague of puerperal fever worked and that their ultimate import was that puerperal fever was contagious. “Until the year 1830 I had no suspicion that the disease could be communicated from one patient to another by a nurse or midwife; but I now think the foregoing facts strongly

⁷⁷⁹All three of these preventive measures—change of clothing, time, and distance—have a long-standing tradition in the history of the prevention of contagion. Thus, it was not strange that the physician would focus on these elements to reduce the possibility of disease dissemination.

Predictors (risk factors for) of developing a disease considered contagious in Holmes’ era also included the weather (hot and humid worse than dry and cold), the patient’s constitution or temperament (weak more susceptible than strong), the sex of the patient (female weaker than male), and whether or not the patient was in a hospital (very bad—see “hospitalism” above under “The Four Horsemen of Death”). On this last risk factor, Holmes wrote that “Within the walls of lying-in hospitals there is often generated a miasm, . . . tenacious so as in some cases almost to defy extirpation, deadly in some institutions as the plague; which has killed women in a private hospital of London so fast that they were buried two in one coffin to conceal its horrors.” *Ibid.*, 163.

Not surprisingly, many physicians considered lying-in pregnant woman the most susceptible of all to contagion.

⁷⁸⁰*Ibid.*, 151.

Note that this physician’s use of chloride of lime for prevention occurred more than a decade before Ignaz Semmelweis—whose work we shall soon examine—reported similar chloride of lime hand washings as preventing the spread of puerperal fever. Unfortunately, neither Holmes’ anonymous letter-writer nor Dr. Semmelweis received credit during their lifetimes for their enormously important prophylactic discoveries, perhaps, in part, because attendants had used chloride solutions for generations to reduce the spread of disease from “miasmas” in lying-in hospitals. As noted above, miasma was a common explanation for the spread of contagious diseases in Holmes’ time. See *ibid.*, 163.

⁷⁸¹*Ibid.*, 152.

favor that idea. I was so much convinced of this fact, that I adopted the plan before related.”⁷⁸²
 Experience is the ultimate teacher; success its strongest reinforcer.

What course are we to follow?

-Oliver Wendell Holmes Sr.⁷⁸³

Holmes provided sixty-five pages of evidence that puerperal fever was a contagious disease that could be disseminated from patient to patient by accoucheurs and other attendants of puerperal women. Only in the final two pages of the essay did he ask “What course are we to follow?”⁷⁸⁴ In response, he provided eight suggestions,⁷⁸⁵ all of which assume the contagiousness of puerperal fever. They are well worth analysis, for herein lies the seed of preventive medicine, at least with respect to the use of “precautions” for the prevention of infectious diseases.

1. A physician holding himself in readiness to attend cases of midwifery should never take any active part in the post-mortem examination of cases of puerperal fever.

Holmes was fully convinced that the contagion of puerperal fever did not die with its victim. Thus, the living must avoid post-mortems on those who died of the disease, not only to avoid catching it themselves, but also to prevent passing it to the next puerperal woman. Because few accoucheurs and midwives actually reported acquiring puerperal fever as such or in any of its variants (hand infection, erysipelas), Holmes must have imagined what is today called

⁷⁸²Ibid.

Note, à la Professor Hodge, that the physician references “a nurse or midwife” as contagious, but not himself.

⁷⁸³Ibid., 168.

⁷⁸⁴Ibid.

The 1855 version of Holmes’ monograph includes a supplement of three pages of “Additional References and Cases” after the conclusion of the original essay.

⁷⁸⁵Ibid., 168-69.

a “carrier state” wherein the accoucheur harbored the seeds of disease even though he himself did not exhibit signs of active infection.

Holmes’ goal with this first precept—as with those that follow—was to acknowledge the contagiousness of puerperal fever and avoid the spread of the disease from the dead to the living through an intermediary. Simply put, since puerperal fever was contagious, one infected patient must not serve as a source of contagion for another.

2. If a physician is present at such autopsies, he should use thorough ablution, change every article of dress, and allow twenty-four hours or more to elapse before attending to any case of midwifery. It may be well to extend the same caution to cases of simple peritonitis.

If a physician attends the autopsy of a woman who died of puerperal fever, he must reduce the probability that he will pass the contagion to others. (This instruction eventuated the adoption of “ablution” after all autopsies, for who could surely know whether or not the deceased was contagious?) To decrease the likelihood of disease transmission, Holmes suggested a trio of measures.

The first step, “thorough ablution,” required a careful and complete washing of the hands, arms, and face—an idea that was only beginning to catch on.⁷⁸⁶ Cleansing of other body parts now known to hide sources of infection—such as under the fingernails—developed only decades

⁷⁸⁶As Suellen Hoy makes abundantly clear in *Chasing Dirt*, “thorough ablution” was an alien concept to most Americans until the 1840s and, especially, after the Sanitary Movements of the Civil War and the acceptance of germ theories beginning in the 1880s. The avant-garde New York Hotel, for example, installed the first “private” (one to a room) bath in 1844, the year after the original appearance of Holmes’ essay. Before then, whatever ablution there was took place in shared baths and water closets or worse. Hoy, *Chasing Dirt*: 14.

later.⁷⁸⁷ Holmes does not specify the agent (presumably soap⁷⁸⁸) that should be used for washing—only that it should be “thorough.” Nonetheless, Holmes insistence on “thorough ablution” was relatively radical for his time.

Secondly, the change of “every article” of clothing was important, for clothing was well known to transmit disease via fomites. These are inanimate objects (like clothing, linen, and bed sheets) that could serve as intermediaries to carry contagious diseases from the stricken to the susceptible. (It is quite possible that the attendants who infected women during delivery with puerperal fever did so most frequently with their hands and secondly by means of their contagious clothing.)

The third measure, a waiting period of twenty-four hours, is particularly interesting for its specificity. Holmes offers no evidence to sustain this exact recommendation, but the daily rotation of the earth has served as a benchmark for change—and spiritual cleansing—from time immemorial. The most likely transformation that would have occurred in a twenty-four hour period during the 1840s would be a change of clothing rather than a “thorough ablution.”

“Simple peritonitis,” an inflammation of the membrane (peritoneum) that lines the abdominal cavity and its viscera (body organs like the liver), exhibited many of the symptoms and signs of puerperal fever. These included nausea, vomiting, fever, and abdominal pain. Holmes’ perspicacity recognized the similarities between these two morbid conditions and, invested as he was with a profound sense of care and caution, led him to suggest that those exposed to autopsies on cases of simple peritonitis should undertake the same safeguards as those exposed to autopsies on patients with puerperal fever. He later extended these preventive actions to other conditions that displayed similarities to puerperal fever, as in the next prescription.⁷⁸⁹

⁷⁸⁷Ann Davey and Colin S. Ince, eds., *Fundamentals of Operating Department Practice* (Cambridge: Cambridge University Press, 1999), 5.

⁷⁸⁸The ancient Babylonians were familiar with the cleansing properties of soap. Ancient Romans had soap factories, such as were discovered in the ruins of Pompeii. Although used more frequently today (“Employees must wash their hands!”), soap was well known in Holmes’ nineteenth-century America.

⁷⁸⁹All three conditions—puerperal fever, peritonitis, and erysipelas—are now known to be caused by similar—if not identical—bacteria.

3. Similar precautions should be taken after the autopsy or surgical treatment of cases of erysipelas, if the physician is obliged to unite such offices with his obstetrical duties, which is in the highest degree inexpedient.

Erysipelas was and is an infection of the skin. Puerperal fever was and is an infection of the gynecological tract. Holmes, who had noted the clinical similarities between puerperal fever and simple peritonitis, also recognized a kinship between the symptoms and signs of puerperal fever and erysipelas.⁷⁹⁰ Logically, therefore, erysipelas should not only require the same precautions suggested after contact with puerperal fever, but should also trigger an alarm to avoid cross-infection between patients with either disease. As a result, exposure of a physician to a patient with erysipelas should elicit the same precautions as if the erysipelas patient had had puerperal fever.

Note also that Holmes treated the physician exposed to an erysipelas patient at autopsy with the same concern as a physician involved in a surgical operation on a patient with the same disease. In an era before surgical technique mandated sterile practices before, during, and after surgery, this was a keen insight.

Holmes went a step further than suggesting inter-patient precautions by “obliging” a physician not to attend medical patients with erysipelas at the same time that he cared for women during childbirth. He urged this separation especially if there was a recent history of puerperal fever in the practitioner’s practice. As Holmes wrote in his delicious Victorian prose, “to unite

⁷⁹⁰Holmes did not know the underlying cause of the similarity in the clinical manifestations of erysipelas and puerperal fever, but within his lifetime physicians and scientists would discover the nexus. In 1874, Theodor Billroth, the German-born Austrian surgeon, demonstrated that the *Streptococcus* bacillus was present in both erysipelas and surgical wound infections (to which simple peritonitis may be causally connected). A decade later, in 1884, Pasteur found the same organism, soon to be called *Streptococcus pyogenes* by Ottomar Rosenbach (1851-1907), in puerperal fever. Thus, by the end of the nineteenth century, bacteriologists knew that puerperal fever, erysipelas, and simple peritonitis could be caused by the same pathologic bacterium, *S. pyogenes*, which is now classified as a Group A Streptococcus. For a brief history of the organism (from the human perspective), see <http://www.bbc.co.uk/dna/h2g2/A907481> accessed 12 April 2009.

such offices...is in the highest degree inexpedient,” for it may well lead to tragedy for both obstetrical and medical patients.

There is also an implicit scientific principle at work in Holmes’ prescriptions. The least number of variables in a problem, in general, is usually best in terms of pinpointing the components of that problem and then offering viable solutions to that problem. This is as true in medicine as it is in mathematics, physics, chemistry, and biological fields in addition to medicine. An increase in the number and types of patients (obstetrical, medical) and diseases (puerperal fever, erysipelas) that could lead to infection invites confusion through complexity. By reducing the probability of cross-contamination by not attending both obstetrical and medical patients, the astute physician—following Holmes’ precautions—minimized the risk of cross-infection and thus the chance of a disastrous outcome for his patients.

4. On the occurrence of a single case of puerperal fever in his practice, the physician is bound to consider the next female he attends in labor, unless some weeks at least have elapsed, as in danger of being infected by him, and it is his duty to take every precaution to diminish her risk of disease and death.

[The physician] is bound to stay away from his patients so soon as he finds himself singled out to be tracked by the disease.

-Oliver Wendell Holmes Sr.⁷⁹¹

What is a physician to do if one of his patients develops puerperal fever? First, he must weigh the consequences for his next patient at least as much as he considers his options for the stricken propositus (the infected woman or index case).⁷⁹² Next, he must follow the precautions

⁷⁹¹Holmes, *Medical Essays*: 115.

⁷⁹²I offer the comparator “at least as much” because, in an era before medical science could offer the puerperal fever patient much salutary treatment, let alone cure, prevention was (or should have been) the foundation of therapy. I have no doubt that Dr. Holmes shared this view.

set out in earlier propositions. In essence, this means that he should abstain from the care of women in labor and relinquish his obstetrical duties to another—an untainted physician.

In this fourth pronouncement, Holmes suggested an interval of “some weeks” following exposure to a case of puerperal fever before attending another patient in labor. In the second proposition, he had advised a minimum waiting period of only twenty-four hours after exposure to an autopsy patient who died of the disease before attending a delivery. Holmes offered no reason for this inconsistency, but it is possible that he considered the contagiousness of the living patient more virulent than that of the deceased. This hierarchizing of the potency of the “virus” (a general term in the early nineteenth century for an infective substance⁷⁹³) in living versus dead patients is consistent with pre-Pasteurian theories of vitalism. Not until the bacteriological revolution later in the century did Pasteur and others overturn such distinctions. Today, precautions followed with respect to the contagious and the dead are similar, implying conceptually comparable degrees of infectivity.

5. If within a short period two cases of puerperal fever happen close to each other, in the practice of the same physician, the disease not existing or prevailing in the neighborhood, he would do wisely to relinquish his obstetrical practice for at least one month, and

⁷⁹³See also Footnote 756 for the meaning of “virus” in the first half of the nineteenth century.

Although Dmitri Alexievich Ivanowski (or Ivanovski) (1864-1920) demonstrated that filterable particles caused disease (later characterized as the Tobacco Mosaic Virus) in 1892 (published 1894), and Peyton Rous (1879-1970) in 1911 published his work on the Chicken Sarcoma Virus (although he used terms such as “cell-free tumor extracts” and never called the agent a virus) that would (much) later lead him to be awarded the Nobel Prize (in 1966!), it was not until Richard Shope (1901-1966) published his work on the Rabbit Papilloma Virus in 1933 that the concept of the virus was given structural three-dimensionality, thanks to the high magnifying power of the recently-invented electron microscope.

Of interest is that John B. Buist actually visualized the first virus in 1887 with the light microscope, but neither he nor his colleagues had any idea that it was a virus. The particle was later discovered to be Vaccinia, a close relative of the Cowpox and Smallpox viruses and the basis of the vaccine that made devastating smallpox the rare disease it is today. Mervyn Gordon, “John Buist and the Elementary Bodies of Vaccinia,” *Nature* 139, no. 3517 (1937).

endeavor to free himself by every available means from any noxious influence he may carry about with him.

What if a physician discovers that not one, but two of his recent cases developed puerperal fever and yet other than himself there is no plausible explanation for the outbreak? For Holmes, the answer was beyond debate. First, the physician must stop attending pregnant women “for at least a month.” (Consistent with proposition 3, he should also take a leave of absence from those at risk for erysipelas. Identification of these high-risk patients in Holmes’ day, however, was difficult if not impossible.) Second, he must follow Holmes’ earlier suggestions for decontamination—cleansing the skin and changing clothing to rid himself of “any noxious influence,” i.e., any source of contagion.

Again, the indefiniteness of time enters the discussion. What is “a short period” between the instances of disease? Is it a day? A few days? A week? More? The clinical manifestations of puerperal fever are today known to occur most frequently twenty-four to seventy-two hours after exposure.⁷⁹⁴ Holmes’ investigations taught him as much, but he sought to relay the widest variability of onset so as to capture the greatest number of contagious physicians within his net of incrimination. Why a cessation of puerperal activity for at least a month rather than “twenty-four hours or more” (proposition 2) or “some weeks” (proposition 4)? Holmes did not offer a direct answer, but the clinical experience of the time did and reveals that Holmes was once again expanding the circle of time to force as many physician-offenders as possible into a period of abstinence from obstetrics for the sake of the patients. Holmes’ well-cited evidence established that most cases of suspected contagion appeared within days of exposure to the initial patient.

⁷⁹⁴Many studies have confirmed this incubation period. See, for example, Gibbon FitzGibbon and Joseph W. Bigger, “A Clinical and Bacteriological Investigation of Puerperal Fever in the Rotunda Hospital, Dublin,” *BJOG: An International Journal of Obstetrics & Gynaecology* 32, no. 2 (1925).

Few, if any, began more than a week later and, in those instances, the accurate identification of the index case had to be questioned. Thus, a month was time enough and more, based upon the clinical histories Holmes compiled, for the accoucheur to rid himself of the source of contagion. The young Brahmin, as was his wont, decided to err on the side of caution in a situation when a physician's too-early return to practice could be disastrous for his patients.

Nevertheless, two cases "close to each other" is only a suggestion that the physician is the cause of contagion. More evidence may be necessary. Hence proposition 6.

6. The occurrence of three or more closely connected cases, in the practice of one individual, no others existing in the neighborhood, and no other sufficient cause being alleged for the coincidence, is *primâ facie* evidence that he is the vehicle of contagion.

Three proximate cases of puerperal fever in a single physician's practice provide more evidence than two that the physician is the "vehicle of contagion." This finding is especially compelling if there were no alternative explanations such as a local endemicity (a disease regularly present in a community) or a regional epidemicity. To Holmes, the connection of three cases to the same physician was sufficient unto itself, "*prima facie*," that the physician was the cause. (Yet, three cases do not make a proof in medicine, for proof in medicine is highly elusive due, at least in part, to the large number of known and unknown variables regularly involved.)

A logician could bundle two living patients with puerperal fever and an autopsy on a woman who died of the disease (or one living and two autopsies; or three autopsies) to make "three...closely connected cases," but Holmes did not feel the need to take these alternative possibilities into account. As noted above, he might also have believed in an inequality of

virulence between the disease of the living and that of the dead, so that dead sources of contagion were deemed not as dangerous as those from the living.

Holmes' mandate is that a physician who finds himself at the nexus of three cases of puerperal fever should without question remove himself from practice and follow the precautions previously listed. Nevertheless, Holmes was not so explicit. Instead, in this sixth proposition, he believed that the finger of blame as the "vehicle of contagion" was sufficient to make his point. Two proximate cases could be coincidence; three were condemnatory.

7. It is the duty of the physician to take every precaution that the disease shall not be introduced by nurses or other assistants, by making proper inquiries concerning them, and giving timely warning of every suspected source of danger.

The physician's responsibility to his patients transcends his own actions. He is also answerable for other attendants—"nurses and other assistants"—under his authority. But how is he to know of their possible complicity in transmitting puerperal fever from one woman to another? Holmes suggests two methods. First, the physician should "mak[e] proper inquiries" by asking his attendants if any have been exposed to a woman with puerperal fever. Second, he should prospectively institute a system of disclosure whereby any exposure ("every suspected source of danger") would be immediately noted ("timely warning") so that proper precautions could be followed.⁷⁹⁵

⁷⁹⁵In the early twenty-first century, early warning systems are very much the norm. Both the CDC (Centers for Disease Control and Prevention) and the FDA (Food and Drug Administration) have "Event Reporting Systems" that cover health and disease issues ranging from food poisoning to drug reactions. In return, physicians and other health care providers can receive this collected and reviewed information almost instantaneously via email and such internet sites as the Health Care Notification Network (www.hcnn.net).

Holmes emphasized the safety of patients, not who might or might not have hands clean or dirty enough to carry the disease. The contrast between Meigs' and Hodges' physician-centered approach to puerperal fever and Holmes' emphasis on patient outcomes could not be clearer.

8. Whatever indulgence may be granted to those who have heretofore been the ignorant causes of so much misery, the time has come when the existence of a *private pestilence* in the sphere of a single physician should be looked upon, not as a misfortune, but a crime; and in the knowledge of such occurrences the duties of the practitioner to his profession should give way to his paramount obligations to society.

There is no tone deep enough for regret, and no voice loud enough for warning.
-Oliver Wendell Holmes⁷⁹⁶

The pestilence-carrier of the lying-in chamber must look to God for pardon, for man will never forgive him.
-Oliver Wendell Holmes⁷⁹⁷

Enough is enough. To those physicians who still did not believe in the contagiousness of puerperal fever, Holmes gave no quarter. No longer could ignorance of the contagiousness of puerperal fever serve to exonerate the guilty physician from his role in contributing to the morbidity and mortality of his patient. The days of blissful blamelessness embedded in a belief in "the slings and arrows of outrageous fortune" ended with the widespread distribution of Holmes' essay.⁷⁹⁸ Contagion was no longer a question; it became a statement. Puerperal fever

⁷⁹⁶Holmes, *Medical Essays*: 167.

⁷⁹⁷*Ibid.*, 128.

⁷⁹⁸Quotation from Shakespeare, *Hamlet, Prince of Denmark*, Act III, Scene 1. I chose these words from Hamlet's soliloquy because they well fit Oliver Wendell Holmes' struggle to bring the charge of "vehicle of contagion" against the entrenched interests of his time. As I read Holmes' original 1843 monograph, I imagined him thinking to himself: "To be, or not to be: that is the question:/Whether 'tis nobler in the mind to suffer/The

was contagious and physicians and their attendants were sources of that contagion. Thus, he who disseminated this “private pestilence” with his soiled (or gentlemanly “clean”!) hands was as much a criminal as the murderer who held the killing knife in his hands. The greater good was that of the patient and society, not the physician. In the final analysis, the physician was obligated to his patient and to society to still the hands that spread disease.⁷⁹⁹

Holmes in Context

During the 1840s and 1850s, the physician-centered old guard of the heroic age gave way to a more patient-centered medical model. States eased licensing requirements to open the medical profession to the less-stringently trained in an effort to be more “democratic.” New approaches to the treatment of disease like homeopathy (Samuel Hahnemann’s (1755-1843) *The Homeopathic Medical Doctrine, OR, Organon of the Healing Art*, for example, initially published in German, was first translated into English in 1833) and other water-based (rather than blood-based) therapies—what today might be termed alternative and complementary medicine treatments—offered a more patient-friendly approach to treatment.

In politics, the expansion of the electorate in many States during these decades and the outlawing of slavery in Northern States reduced emphasis on the elite and increased the role of the common man. Republicanism yielded to Democracy. In religion, the revivalism that swept across the United States from the Burned-over Districts of upper New York State to Joseph

slings and arrows of outrageous fortune./Or to take arms against a sea of troubles./And by opposing end them?” With an army of evidence much greater than Hamlet could muster, Holmes chose “to take arms.”

⁷⁹⁹Responsibility in society has a history. Today, for example, the mantle of responsibility for the consequences of an individual’s health-related behavior has spread beyond physician- and hospital-centered medical malpractice to include individuals who knew – or should have known – that they were vehicles of contagion. A recent Canadian court conviction of an HIV-positive man for spreading AIDS long after he knew he was contagious is just one of the more recent examples. See http://news.yahoo.com/s/afp/20090405/wl_canada_afp/canadajusticesociety_20090406001419 accessed April 6, 2009.

Smith's westward search for safety and security, and even Emerson's Transcendentalism, elevated the role and potentialities of the Everyman in society.

Oliver Wendell Holmes achieved the same for the Common Woman as he struggled successfully, with the power of his pen and the sharpness of his wit, to bring the contagiousness of puerperal fever to public knowledge. Holmes wrote of contagion and child-bed fever, but in a broader context his *mentalité*, as Emerson said, was "part or particle" of the greater democratizing influences around him.⁸⁰⁰ He was a medical "transparent eye-ball" in a sea-storm of historical change.⁸⁰¹

Holmes' contributions transcended the etiology of puerperal fever, for his emphasis on epidemiologic surveillance was a forerunner of investigative systems used today to identify and quell potential epidemics. Modern versions of Holmes' early warning system ("making proper inquiries" and "giving timely warning") are critical elements in the timely detection of biological weapons of mass destruction, influenza epidemics, and outbreaks of infectious diseases of all kinds.⁸⁰²

Oliver Wendell Holmes is justly lauded for his contributions to American medicine. He christened Letheon as a type of "anesthesia," deduced methods for the investigation of endemic and epidemic diseases, and promulgated convincing evidence that puerperal fever—the bane of young motherhood—was a contagious disease. In this last capacity, his insights yielded

⁸⁰⁰Ralph Waldo Emerson, "Nature" (1836). Available online at <http://www.vcu.edu/engweb/transcendentalism/authors/emerson/nature.html> accessed April 20, 2009.

⁸⁰¹Ibid.

⁸⁰²The New York City Medical Reserve Corps, of which I have been a proud member since shortly after 9/11 (2001), is a government-sponsored effort to mobilize healthcare professionals in the event of a possible or real WMD attack. See <http://www.medicalreservecorps.gov/detail.asp?id=253> accessed April 24, 2009. The Centers for Disease Control and Prevention uses means similar to Google Flu Trends and a cadre of on-the-ground investigators (specially-trained personnel and physicians) to monitor the dissemination of influenza and other infectious diseases throughout the United States. See <http://www.google.org/flutrends/> and <http://www.cdc.gov/mmwr/> accessed April 24, 2009.

preventive measures that contributed to the development of antiseptic techniques. Although well recognized for these accomplishments, another physician, thousands of miles away and a few years later, is more celebrated than Holmes for his work on childbed fever, including antiseptic methods to prevent this scourge of womankind and their infants. That man, a Hungarian physician, was Ignác Fülöp Semmelweis.⁸⁰³

The Progress and the Promise of the Tormented Genius who was Ignaz Semmelweis

Oliver Wendell Holmes argued that puerperal fever was contagious and that physicians and others could convey that contagion to pregnant women. Beyond these critical contributions to the history of antiseptics, however, lay numerous unanswered questions concerning the precise mode of spread of the disease and, by extension, how to prevent it (other than Holmes' advocacy of abstention from all contact between physician and patient).

As the idea evolved during the nineteenth century that infections could be averted (for this was not obvious until disease became generally conceived as a legitimate focus of scientific investigation rather than as the wages of sin), it became clear to surgeons and other practitioners that answers to additional queries about the transmission of disease were necessary before physicians would be able to formulate rational, generalizable programs of antiseptics. Only then could patients with cancer and other diseases undergo surgical treatment with little fear of post-operative sepsis and its dreadful and often deadly consequences.

In the realm of puerperal fever, physicians asked: What is the source of contagion? How does contagion occur? What in the constitution of the infected woman (the "host" in today's medical parlance) made her susceptible to the pathologic powers of contagion? What could be

⁸⁰³Translation of non-English names into universally-accepted English characters has never been straightforward. Although Dr. Semmelweis' name as transliterated in this sentence is close to how I believe he would have written it, for purposes of easy recognizability I will spell his name as Ignaz (Phillip) Semmelweis.

done to prevent contagion? Was it possible to devise antiseptic techniques that could be tested, verified, and applied to real-world situations in which sepsis would likely occur? Ignaz Semmelweis dealt with these questions and more.

The Man and his Mission

For much of his life, Semmelweis functioned as a man apart from his medical colleagues—intellectually and psychologically. He was born in a district of Buda, Hungary – a municipality metaphorically in need of union itself – decades before it became part of Budapest.⁸⁰⁴ Family wealth afforded him the opportunity to study in Vienna, a few hundred kilometers up the Danube River, where he began schooling in the law in 1837. It was not long before he found himself more enamored of medicine than law, however, so he transferred to the University of Vienna’s medical school and received his doctorate in 1844.

One of the earliest of many great disappointments in his life came when he sought employment after graduation. His first choice was a position in pathology which, as we have seen, was the premier, avant-garde medical specialty of the era. He was turned down. He then petitioned for work in a general medicine clinic, but here, too, his efforts went for naught. One of his medical school professors, the renowned Karl von Rokitansky (1804-1878), who made significant contributions to the development of pathological anatomy and modern medicine,⁸⁰⁵

⁸⁰⁴It was not until On November 17, 1873, more than eight years after Semmelweis’ death, that Buda and Óbuda from the West bank of the Danube unified with Pest from the East bank.

⁸⁰⁵Baron Karl von Rokitansky was one of the leaders of the pathological anatomy movement that helped transform medicine from a didactic exercise predicated upon past writings to the dynamic scientific study of the nature of the human body that dominates medicine to this day.

During his career, Rokitansky performed more than thirty thousand (30,000) autopsies and supervised more than twice as many. See <http://www.medicinenet.com/autopsy/page5.htm> accessed June 12, 2009. As far as I can determine, this experience with gross anatomic dissection is unparalleled in the history of medicine.

Unfortunately, Rokitansky, as we have discovered to be true of many others in his time, refused to add microscopy to his repertoire and came to many false clinico-pathological correlations that his use of the microscope might otherwise have avoided. Nonetheless, his name lives on eponymously in its association with several pathological abnormalities: Rokitansky-Aschoff sinuses (in the gall bladder); Rokitansky nodules (in teratomas);

finally granted him permission to dissect female cadavers. Rokitansky's thought may well have been that Semmelweis would assume the relatively lowly position of attending women during pregnancy and childbirth.

Despite the *éclat* of pathological anatomy during the 1840s, neither the dissection of female cadavers nor delivering pregnant women was considered glamorous or rewarding by the medical establishment, which was, not surprisingly, almost exclusively male. The cadavers of prostitutes and indigent women made up the bulk of the corpses Semmelweis dissected in the androcentric Viennese society of the mid-nineteenth century. In addition, as exemplified by John Snow's England, assisting at childbirth was then still primarily the province of women *qua* midwives.⁸⁰⁶ As a result, the position of accoucheur or male-midwife was, especially for a young, unknown doctor, hardly a position of prestige that would normally attract intelligent, driven physicians like Semmelweis.

Nonetheless, on July 1, 1846, Semmelweis—discouraged but unbowed—took up his position as Assistant to Dr. Johann Klein in the First Obstetrical Clinic at the Lying-In section of the Allgemeines Krankenhaus Wien (Vienna General Hospital).⁸⁰⁷ There were yet more reasons why the appointment was inauspicious. Despite Semmelweis' expectation that he would learn as much as he would teach in this post-graduate program, Professor Klein was not inclined to tutor

and even Von Rokitansky's syndrome (today more commonly called the Budd-Chiari syndrome—veno-occlusive disease of the liver).

⁸⁰⁶Indeed, John Snow's anesthesia-assisted delivery of Queen Victoria's Prince Leopold in 1853 contributed much to the transformation from women-dominated midwifery to man/physician-dominated obstetrics.

The etymology of the word "obstetrics" serves to illustrate that shift in gender. The earlier term "obstetrix," clearly signifying a female midwife ("-trix"), fell out of favor during the second half of the nineteenth century to be replaced by the gender-neutral but historically-meaningful "obstetrics." (*Oxford English Dictionary* online, Draft revisions Mar. 2004 and Dec. 2007)

⁸⁰⁷Ignác Fülöp Semmelweis, *The etiology, concept, and prophylaxis of childbed fever*, trans. Kay Codell Carter (Madison: University of Wisconsin Press, 1983). 61.

fledgling obstetricians under his wing.⁸⁰⁸ Worse, Semmelweis' two-year appointment initially lasted only about sixteen (16) weeks, for the previous Clinic Assistant, Franz Breit, displaced Semmelweis when he returned to the Clinic after obtaining a two-year extension to his previous appointment. (Breit had priority over the newly-appointed Semmelweis.) Despite these setbacks, Semmelweis eventually served in the First Clinic for more than two years and three months—split into two periods of service—and it was during these years that he made his seminal contributions to the development of antisepsis.⁸⁰⁹

The First Obstetrical Clinic

One wonders why he wanted to work in the First Clinic at all. It had a frightful reputation among the hospital staff and the general population. Patient suffering and death—especially from puerperal fever—were rampant. Pregnant women begged, yelled, and screamed not to be admitted to the First Clinic, hoping instead for admission to the Second Obstetrical Clinic, which boasted a much better safety record.⁸¹⁰ Destitute and abandoned women, knowledgeable of the deadly reputation of the First Clinic and not wanting to risk admission there, purposely went through the ordeal of delivering their babies on the by-roads and streets of Vienna—so-called “street births”—before bringing their infants to the Krankenhaus for care and placement. None of these real-life actions for self-preservation was lost on Semmelweis. He

⁸⁰⁸Ibid., 61, Footnote 1.

⁸⁰⁹Fortunately for Semmelweis, Dr. Breit received a professorial appointment to the medical school in Tübingen five months into his second two-year stint in Vienna. Semmelweis was re-appointed on March 20, 1847 and then served two years in addition to his initial July-Oct 20, 1846 appointment. Ibid., 61.

⁸¹⁰For a dramatic presentation of these events and Semmelweis' approximately two-year tenure in the First Obstetrical Clinic at the Allgemeines Krankenhaus, see Jim Berry's dark and brooding excellent short film, *Semmelweis*, available online at <http://scienceandfilm.org/films.php?film> (viewed May 1, 2009). *That Mothers Might Live*, which won the Academy Award for the Best One-Reel Short film (ten minutes long) in 1939, although considerably dated, also treats Semmelweis as protagonist in the struggle against childbed fever.

observed, upon witnessing for himself the excessive mortality of the First Clinic, that it “made me so miserable that life seemed worthless.”⁸¹¹

The Young have the Revolutionary Ideas – The Elders have the Power

Rather than giving in (to the “that’s the way it is” resigned medical attitude of his day) or giving up (to the “God’s Will” explanation for the causality of disease and death), Semmelweis made it his mission to explain the devastatingly high rates of morbidity and mortality from childbed fever that occurred in the First Clinic. To achieve this goal he asked questions such as: What is the true incidence of childbed fever in the First Clinic? How does it differ from that in the Second? Why is there a difference? What can be done about it? The new numerical method, applied and promoted by P.-C.-A. Louis only a few years earlier, served as Semmelweis’ investigative tool—his *modus operandi*.

When Semmelweis began to quantify the outcomes in the First Clinic in 1846, he discovered that the mortality rate in that Division was more than two and a half times that of the Second Division.⁸¹² From 1841-1846, there were recorded 20,042 births in the First Division, following which 1,989 mothers died in the puerperal period, for a mortality rate of 9.92%.⁸¹³ Numbers compiled for the Second Division during the same time frame showed 17,791 births accompanied by 691 maternal deaths, yielding a 3.88% mortality rate.⁸¹⁴ The difference

⁸¹¹Semmelweis, *The etiology, concept, and prophylaxis of childbed fever*: 86.

⁸¹²*The Etiology, the Concept and the Prophylaxis of Childbed Fever*, trans. M.D. Frank P. Murphy, Edited with Commentary and Translation of the Semmelweis "Open Letters" by Sherwin B. Nuland, M.D., and Ferenc A. and Gyorgyey, Special ed., The Classics of Medicine Library (Birmingham, AL: Gryphon Editions, 1861; repr., 1981). 356.

⁸¹³Ibid., 356, Table I.

⁸¹⁴Ibid. The mortality rate calculated in Semmelweis’ text is 3.38%. From the numbers given (691/17,791), the correct rate should be 3.88%. This is probably a misprint rather than a miscalculation.

Semmelweis took note of the discrepancy in the total number of births. He explained that the smaller number of births reflected the fact that the Second Division admitted patients during less total hours per week than

between the mortality rates of the First and Second Divisions was greater than the numbers related, for sick and dying patients—of whom there were many more in the former than the latter Clinic—were transferred to the General Hospital, where their deaths were not included among the mortalities for the First Division.⁸¹⁵ Even mothers of “street births” appeared to have a lower maternal mortality rate than those admitted to the First Clinic to give birth.⁸¹⁶

Why was the mortality rate of the First Clinic so much higher than that of the Second? Puerperal fever. But why was there so much more puerperal fever in the First division? Explanations abounded, but none rang true to Semmelweis. The most prevalent theory of the day, that puerperal fever was the result of an epidemic induced by “atmospheric-cosmic-telluric influences,” made no sense to the Hungarian physician.⁸¹⁷ (Theories like this would become, decades after the proto-medical-scientific era during which Semmelweis did his greatest work, unscientific, since they could neither be verified, falsified, nor used to make predictions about future events. They were interpreted more as metaphysical descriptions than scientific explanations of events.)

Semmelweis used logical reasoning to dispel the theory of causation offered by those who believed that environmental influences caused puerperal fever. He argued for several pages in his classic text that the atmosphere in the First Division, the Second, or even inside the Lying-In Hospital was essentially the same as that outside these patient areas and should make no

the First (despite patient outcry), causing the First Division to have fifty-two (52) more total admission days per year than the Second Division. *Ibid.*, 356.

⁸¹⁵The General Hospital included these transfer deaths in their numbers. *Ibid.*, 356-7.

⁸¹⁶This statement clearly represented more supposition than evidence-based fact, but such was the prevalent belief. Semmelweis comments on this indirectly in *ibid.*, 358-9.

⁸¹⁷Semmelweis termed his disbelief in the prevalent atmospheric theory his “unshakeable anti-epidemic conviction.” *Ibid.*, 358.

difference in disease onset, incidence, or mortality.⁸¹⁸ Adverse patient selection (whereby the sicker patients somehow had an increased probability of being admitted to the First Clinic) was not the answer, for admission to the First or Second Divisions depended solely on chance—the day and time that the patient entered the hospital.⁸¹⁹ Were there differences in age, weight, comorbid illnesses (non-puerperal diseases that weakened the patient’s overall health and made her more susceptible to puerperal fever), or other possible explanatory conditions? No, the two Divisions admitted patients with similar underlying characteristics (i.e., demographics).⁸²⁰ After much investigation, Semmelweis could not find an external or epidemic cause for childbed fever.⁸²¹ Thus, the cause had to be endemic—within the community. “On the whole,” wrote Semmelweis, “the unfortunate confusion of the concepts of an epidemic and of an endemic is the reason why the true cause of childbed fever was so long in being discovered.”⁸²²

As has occurred in medicine repeatedly throughout the centuries, simple observation by a mind primed for new thoughts offered the investigator (in this case Semmelweis) an idea that, through hard work and cogent analysis, revealed a critical distinction (between the First and Second Clinics) that led to a great insight. What Semmelweis discovered explained the higher

⁸¹⁸Ibid., 357-61.

⁸¹⁹Adverse patient selection could have played a role in the disparate mortality rates if prospective patients knew the hospital admission schedule to the two clinics and healthier and more informed patients appeared only during admission times to the Second Clinic. (It is less likely that sicker women would rationally seek admission to the more dangerous First Clinic.) I have seen no evidence that pregnant women knew the clinic admission schedules and Semmelweis noted no tendency to appear only during admission times to the Second Clinic. Ibid., 355-57.

⁸²⁰Ibid., 355-56.

⁸²¹Ibid., 360-61. An epidemic cause is a cause not generally found in a susceptible community. The introduction of smallpox by Christopher Columbus’ crewmen to Caribbean natives who had never been exposed to the pox before is an example of an epidemic. Once the infection gains a foothold in the community—always present in small numbers with occasional flare-ups to sicken new susceptibles (such as those never vaccinated against the disease)—it becomes endemic.

⁸²²Ibid., 389.

infection and mortality rates in the First division and, in the process, yielded a practical methodology to reduce the incidence of puerperal fever and sepsis in the future.

Medical Students and Midwives

Semmelweis found that although the patients and the atmospheres of the two divisions were similar, the daily routines of those who attended them were not. The major difference in the habits between the two groups was that medical students from the First Clinic routinely attended autopsies while the midwives of the Second Clinic did not. The medical students were obligated to observe and sometimes participate in autopsies as part of their education. The midwives were not.

This turned out to be a critical distinction between the two groups, but why this difference was so important was far from obvious. A personal tragedy provided the answer, for Semmelweis came to his theory of contagion not as a result of a patient's autopsy—whether assisted by medical students or not—but as a consequence of the horrendous death of his friend and colleague, Dr. Jakob Kolletschka (1803-1847).

Learning from Tragedy: The Death of Professor Kolletschka

Dr. Kolletschka, Professor of Forensic Pathology at the Vienna General Hospital and someone whom Semmelweis greatly respected, routinely performed autopsies for legal purposes as part of his specialty.⁸²³ Medical students frequently assisted at these necropsies. During one such examination, in March, 1847, a student “stuck” Kolletschka’s finger with the same knife used to perform the autopsy.⁸²⁴ Kolletschka subsequently developed an infection that spread

⁸²³A forensic pathologist is a pathologist who determines the cause of death, often for legal or criminal reasons, by conducting an autopsy on the deceased. The word “forensic” derives from the Latin “forum,” which was the place where ancient Romans held judicial and other public proceedings. The sense of the term is that the pathologist conducts his business (the examination of the deceased) in an open or public forum.

⁸²⁴Semmelweis, *Childbed Fever*: 391.

rapidly from the traumatized finger, up the forearm and the upper arm, and then into the axilla (armpit).⁸²⁵ Once past the axilla, the infection consumed the entire body. With no effective means to halt its spread (too late for amputation and decades prior to the advent of antibiotics), Professor Kolletschka died from overwhelming sepsis in a few short days.⁸²⁶

Something about the course of Professor Kolletschka's fatal disease triggered something in Semmelweis' thinking. He had seen this before. In a moment of acute awareness, he realized that the path to Kolletschka's death was akin to that of the course of so many women whose deaths from puerperal fever he had witnessed. "Day and night this picture of Kolletschka's disease pursued me, and with ever increasing determination, I was obliged to acknowledge the identity of the disease, from which Kolletschka died, with that disease of which I saw so many puerperae die."⁸²⁷

Once having recognized the similarity between Kolletschka's disease and that of the puerperae, it further occurred to Semmelweis that this process of infection involved not only Professor Kolletschka and women with mortal childbed fever, but also many of the newborns of those infected mothers who died shortly after birth from sepsis.⁸²⁸ In each case, something appeared to have been transmitted from one to the other (woman who died from puerperal fever to Kolletschka; mother to her infant). In the parlance of the day, the "exciting cause" of a woman's puerperal fever or a newborn's septicemia was unknown, but the "immediate cause" of

⁸²⁵In medical terms, Kolletschka developed lymphangitis and phlebitis of the upper extremity. Ibid.

⁸²⁶In Semmelweis' words, the systemic infection caused "bilateral pleuritis, pericarditis, peritonitis, and meningitis, and some days before his death a metastasis formed in one eye." Ibid.

⁸²⁷Ibid.

⁸²⁸Ibid., 392.

Professor Kolletschka's infection was known.⁸²⁹ It was the knife-stick from the blade that had cut the diseased corpse and then the Professor. Semmelweis was certain that it was not the wound, the atmosphere, or the knife itself.⁸³⁰ No, it was something that the knife conveyed from the woman who had died from childbed fever to the Professor that had infected Kolletschka.

Semmelweis mused that perhaps this critical clue from Professor Kolletschka's tragic demise could explain the great unknown: How did puerperal women contract childbed fever? In all cases with which Semmelweis was familiar, there seemed to be something about the corpse itself that linked to the patient's contraction of puerperal fever.⁸³¹ This was a startling insight, for it meant that seemingly disparate diseases like wound infections, childbed fever, and newborn sepsis could all have identical causes. In an era when disease was highly individualized—when, for example, one person's consumption⁸³² was considered by physicians to be unique to that individual—Semmelweis became convinced that disease was more connected and intertwined between and among individuals than conceived by his contemporaries. In the cases of Professor Kolletschka, mothers with childbed fever, and their septic newborns, he called that unifying connection “cadaverous particles.”⁸³³

⁸²⁹The exciting cause of a disease is its immediate cause, as opposed to its predisposing or underlying cause. One may die from a heart attack (myocardial infarction) upon witnessing a horrific scene (the exciting cause), but the individual may have been predisposed to a heart attack from years of increased plaque formation in the coronary arteries due to hereditary (familial hyperlipidemias) and/or environmental (excess cholesterol intake) predisposing factors.

⁸³⁰Semmelweis, *Childbed Fever*: 392.

⁸³¹*Ibid.*

⁸³²Consumption was a general term for a wasting process, such as a disease, that led to extreme weight loss. By the nineteenth century, consumption was the term commonly applied to what is today called tuberculosis. The tuberculous bacillus (bacterium), so-called because the disease it caused was characterized by tubercles (round nodules or swellings), however, was not discovered until 1882, by Robert Koch, so the word tuberculosis properly should not be applied until 1882 and thereafter.

⁸³³Semmelweis, *Childbed Fever*: 393.

“I answer in the affirmative”

The mere presence of cadaverous particles by themselves, however, was insufficient to cause puerperal fever. Had Kolletschka’s knife, laden with these deadly invisible corpuscles, not broken the protective barrier of his skin, no infection would have resulted. The particles were necessary but not sufficient in disease causation. Somehow, reasoned Semmelweis, they had to get into the body; specifically, into the bloodstream. “I must ask myself the question: Did the cadaveric particles make their way into the vascular systems of the individuals, whom I had seen die of an identical disease? This question I answer in the affirmative.”⁸³⁴

First, there had to be cadaverous particles. Next, those particles had to gain access to the individual’s vascular system. Then, disease could follow. To Semmelweis, these steps were necessary and sufficient.⁸³⁵

The Answer and the Solution

Herein lay the answer and the solution to the problem of Childbed Fever. The answer was that there were deadly particles separate from the individuals who harbored them, and that these particles had to be introduced into the bloodstreams of their victims to initiate what physicians called puerperal fever. That was how the hosts became infected. The solution was to stymie the process at its source—prevent the carriage of cadaverous particles from the autopsy room to the living patients, even if the two were in close proximity. Prevention, however, was no easy task, for several factors thwarted its implementation in the corridors of Semmelweis’ Viennese hospital.

⁸³⁴Ibid., 392.

⁸³⁵Semmelweis knew that there were other factors involved in disease causation, such as the response of the host (patient). He also was cognizant of the fact that not all women in the First Clinic developed puerperal fever, so some women probably had something that prevented them or protected them from contracting the disease. Today, we know, for example, that not all individuals exposed to HIV contract the virus (“elite controllers”). Host (the exposed individual) genetics and immunity play a major role in disease causation—and protection therefrom.

One, ironically, was the fascination with pathological anatomy in the 1840s. Physician and student attendance at autopsies, the principal venue for the teaching and learning of pathological anatomy, was all the rage. The interdiction of traffic from autopsy room to ward was all but impossible.⁸³⁶ Others factors that made restrictions difficult to enforce included the resistance of physicians to be being coerced to perform actions without compelling proof. (And Semmelweis had, at best, only circumstantial evidence for cadaverous particles.⁸³⁷) Another impediment was the cost in terms of time and money necessary to follow Semmelweis' directives. Semmelweis could not shut down the traffic from the autopsy room to the patient wards. Nor could he cajole his colleagues and other attendants into following his prohibitions. Instead, he sought to mitigate the effect of the cadaverous particles by minimizing their transfer from the infected to the susceptible.

To Prevent the Transfer of Cadaverous Particles

To achieve this, he believed, chemistry—whose applications to medicine were growing rapidly by mid-century—was the key. Semmelweis quickly saw that it was the transport of these presumed, invisible cadaverous particles from the autopsy room to the patients' wards on the hands and fingers of the conveyors that began the danger. Students and others then manually introduced them into their pregnant patients by through the avenues created by the traumas of natural childbirth by means of routine vaginal exams. To rid the fingers of the danger was the key.

⁸³⁶Semmelweis perceptively referred to this vogue as “the anatomic trend of the Vienna medical school.” Semmelweis, *Childbed Fever*: 392. The popularity of pathological anatomy, however, was hardly confined to Vienna. Neither was the unbounded movement of physicians and medical students from autopsy rooms to clinics and patient wards.

⁸³⁷Not until the germ theories of Pasteur and Koch gained credence in the 1870s and 1880s would “proof” substantiate Semmelweis' thoughts and actions.

If the hypothesis is correct, that the hand-borne cadaverous particles produce the same disease in puerperae, which the cadaverous particles clinging to the knife caused in Kolletschka, then, if by a chemical effect they may be completely destroyed on the hand, and thereby during examinations of gravidae, parturients, and puerperae,⁸³⁸ whose genitals may be brought directly in contact with the fingers and not with the cadaveric material, this disease can be prevented to the extent that it is dependent upon the effect of cadaverous particles carried by the examining finger.⁸³⁹

It did not seem to bother Semmelweis that he could neither see these cadaverous particles nor prove their existence through any direct analysis or measurement. Like many of his colleagues at the time, Semmelweis eschewed the use of the microscope. Had he been so bold as to believe that what he could have seen under the improved microscope of the mid-nineteenth century was a true vision of reality,⁸⁴⁰ he might have embraced the notion of germs—years before Pasteur or Koch. But Semmelweis did not.⁸⁴¹

Instead, Semmelweis assumed the presence of these invisible, deadly particles and sought to find a way to impede their transmission from one host to another. However, just as the carriage of particles from the autopsy room to the puerpera could not easily be prevented, so the examining finger could not easily be cleaned. Physicians washed with soap, probably more to eliminate the “cadaveric odor” from their hands than to achieve cleanliness.⁸⁴² But the very persistence of that odor after hand washing with soap meant, to Semmelweis, that some particulate matter remained. Semmelweis reasoned that he needed something stronger to remove all traces of the odor—and the dangerous particulate matter the persistent smell connoted. In the

⁸³⁸Gravidae (from the Latin) are pregnant women. A parturient is a woman in labor. A puerpera, as we have noted, is a woman who has just given birth. The last word derives from the Latin for “child” (puer) combined with “to bring forth” (pario). Puerperae is the plural.

⁸³⁹Semmelweis, *Childbed Fever*: 393.

⁸⁴⁰My apologies to Immanuel Kant and those who followed (and follow) him for my undissociated vision of man’s perception of reality (the “phenomenological”) from reality itself (“das Ding an sich”).

⁸⁴¹Nuland, *The Doctors’ Plague: Germs, Childbed Fever and the Strange Story of Ignac Semmelweis*: 116.

⁸⁴²The quoted words come from Semmelweis, *Childbed Fever*: 392.

process, he hoped, all cadaverous particles could be eradicated from the attendants' hands and puerperal fever could be prevented.

On some day during the middle of May, 1847, Semmelweis began to use “Chlorina liquida” to wash his hands and rid them of the cadaveric odor before examining pregnant women.⁸⁴³ He required medical students in the First Clinic to follow the same procedure.⁸⁴⁴ The dissolved chlorine gas solution, however, proved too expensive for routine use, so Semmelweis sought a cheaper alternative. He chose chlorinated lime—the hand washing solution for which he became famous.⁸⁴⁵

Chlorinated Lime

“I have...washed my hands in innocence. For all day long I have been plagued.”
-Psalm 73: 13-14

Hand washing by physicians was not a revolutionary nineteenth-century phenomenon. Rather, it is an ancient tradition. As long ago as the Judaic monarchic period a thousand years before the Common Era, Psalmists touted the physical and metaphorical benefits of hand washing to counter sin and disease for both patients and physicians.⁸⁴⁶ In the twelfth century, Maimonides (1135-1204), Jewish philosopher and physician, wrote a chapter in the *Mishneh Torah* devoted to hygiene. Therein he urged physicians to “Never forget to wash your hands

⁸⁴³Chlorina liquida, according to the *Companion to the latest edition of the British pharmacopoeia* (1877), was chlorine gas dissolved in about half its volume of water. Sir Peter Wyatt Squire, *Companion to the latest edition of the British pharmacopoeia* (J. & A. Churchill, 1877). 94.

⁸⁴⁴Semmelweis, *Childbed Fever*: 393.

⁸⁴⁵Chlorinated lime is a white powder that can be dissolved in water to make a solution. It is comprised of calcium hydroxide, chloride, and hypochlorite and used to this day to disinfect and bleach. Chlorinated lime is essentially bleaching powder.

⁸⁴⁶Michael David Coogan et al., eds., *The new Oxford annotated Bible with the Apocryphal/Deuterocanonical books*, Augmented 3rd ed. (Oxford ; New York: Oxford University Press, 2007), 838.

after having touched a sick person.”⁸⁴⁷ It is uncertain whether or not Maimonides’ contemporaries heeded his warning, for resistance to hand washing among physicians was, as noted, still prevalent in Holmes’ nineteenth-century America. To no small extent, this was because neither Maimonides nor Watson nor Holmes could offer a good, scientific explanation to support hand washing.

Semmelweis, however, did have a good argument in favor of hand washing, and that was to rid the hands of cadaverous particles. For him, the question was not whether to wash hands after attending a postmortem examination and then before examining a puerpera, but with what agent.

Soap was ineffective, for the noisome cadaveric odor remained on soap-washed hands. Chlorina liquida eliminated the smell, but it was simply too expensive to consider it for widespread, routine use. Chlorinated lime, on the other hand, was both effective and affordable.

Chlorinated lime, or chloride of lime, is a white powder comprised of calcium hydroxide, chloride, and hypochlorite.⁸⁴⁸ These chemicals are now known to destroy the cell walls of bacteria and other pathogens, thereby killing them. Thus, chlorinated lime is a potent disinfectant.⁸⁴⁹ In May, 1847, shortly after Semmelweis sought a less expensive alternative to chlorina liquida for hand washing, he found it in chloride of lime.

Mothers and Infants Saved

⁸⁴⁷<http://www.library.musc.edu/resources/biomed/InfectCtrl/sld002.html> accessed September 21, 2009.

⁸⁴⁸Today, chlorinated lime or chloride of lime is a powder is still used, most commonly in bleach.

⁸⁴⁹In general, chlorinated lime is safe for external use by humans, but, like many other chemicals, may be deadly when ingested. Its bleach-like effect on the inner lining of the gastrointestinal tract causes a sloughing of the mucosa, or inner lining of the digestive system, that may be fatal. The antidote is water (for dilution) or milk (to neutralize the acidic combinations with chloride, like hydrochloric acid. See <http://www.drugs.com/enc/chlorinated-lime-poisoning.html> accessed September 24, 2009.

The decrease in the number of cases of puerperal fever in the First Clinic within a month of the institution of Semmelweis' hand washing with chlorinated lime for himself and his medical students was nothing short of amazing. The incidence of puerperal fever in the First Clinic dropped from 12.24% to 2.38%.⁸⁵⁰ Astonishingly, this new rate of incidence of childbed fever was actually below that of the Second Clinic.⁸⁵¹ Semmelweis' careful compilation of morbidity and mortality statistics from the First Clinic, as shown in the chart below, documented the enormous month-to-month reduction in the incidence of puerperal fever.⁸⁵²

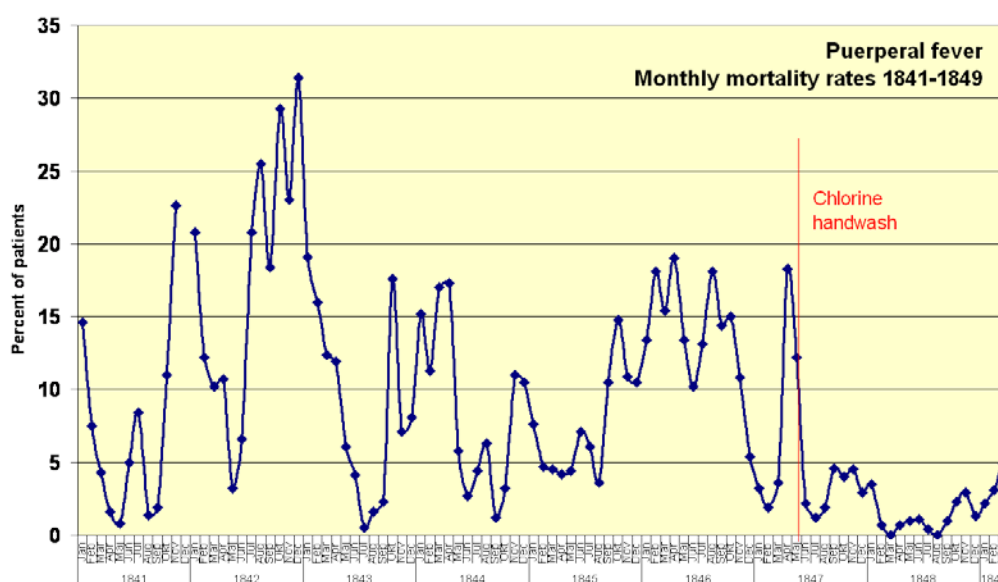


Figure 6. Puerperal Fever. (Monthly Mortality Rates 1841-1849) Percent of patients who developed Puerperal Fever before and after introduction of Chlorine hand wash⁸⁵³

⁸⁵⁰Semmelweis, *Childbed Fever*: 393 Table XV (cont'd).

⁸⁵¹Richard Gordon, *Great Medical Disasters* (New York: Stein and Day, 1983; repr., 1986). 89.

⁸⁵²Semmelweis' *Etiology* is replete with statistical tables. The most dramatic reduction in the incidence of puerperal fever is shown in Tables XV and XVI, out of more than sixty-five tables in the text. Modern mathematicians have analyzed Semmelweis' tables and found them to be sound statistical analyses that support his hypothesis. See, for example, Lyle D. Broemeling, "Studies in the history of probability and statistics: Semmelweis and childbed fever. A statistical analysis 147 years later," (Houston: Department of Biostatistics and Applied Mathematics, The University of Texas M D Anderson Cancer Center, 1994).

⁸⁵³ From http://upload.wikimedia.org/wikipedia/commons/0/07/Monthly_mortality_rates_1841-1849.png accessed September 24, 2009.

Cassandra Incarnate

In questions of science, the authority of a thousand is not worth the humble reasoning of a single individual.

-Galileo Galilei (1564-1642)

Within weeks of his adoption of washing hands in chlorinated lime water prior to the examination of puerperal women, Semmelweis became convinced of the enormous value of his discovery for reducing the incidence of childbed fever. From April to July, 1847, he noted, the number of cases of puerperal fever in the First Clinic dropped by over 90 percent.⁸⁵⁴ By March, 1848, less than a year after the adoption of his hand washing regimen, the incidence of puerperal fever in the Clinic actually dropped to zero!⁸⁵⁵ In addition, unlike so many before him, Semmelweis had an explanation as to why hand washing prevented puerperal fever; viz., it barred the transmission of the cadaverous particles.

Further, prophylaxis was so simple. Hand washing required neither expensive equipment, nor a steep learning curve, nor a long time commitment. In addition, the fact that Semmelweis practiced at one of the most prominent medical institutions in one of the most medically-respected cities in all Europe would lead one to think that word of his discovery would travel rapidly far and wide. Certainly, knowledge of Morton's Letheon, only a few months earlier (and from the remote wilds of America, no less!), speedily traversed the globe. Surely, Semmelweis' breakthrough would be hailed with similar eagerness as that of another genius in an age of medical miracles. But it was not.

⁸⁵⁴Semmelweis recorded the incidence of childbed fever in April, 1847 as 18.27% and, after the adoption of chlorinated lime hand washing, in July, 1847, as 1.20%. Thus, the decline was over 93%. See Semmelweis, *Childbed Fever*: Table XV, 389 and Table, 93, respectively.

⁸⁵⁵See Wikipedia's "Monthly Mortality Chart" above. From http://upload.wikimedia.org/wikipedia/commons/0/07/Monthly_mortality_rates_1841-1849.png accessed September 24, 2009.

Like Cassandra, Semmelweis spoke truth, but few believed him.⁸⁵⁶ This was nothing new when compared to his predecessors, for neither Gordon nor Watson nor Holmes enjoyed much immediate success in convincing their colleagues to follow their suggestions for prophylaxis. Understandably, Gordon was reviled by those he castigated, but Watson was respected and Holmes congenial—and still few listened. More like Gordon than Watson or Holmes, Semmelweis was often hated and reviled. Thus, given the propensity to pass judgment on the man rather than the message, few believed him no matter how compelling his medical-scientific arguments. Instead, his message of hand washing and its prophylactic effects were lost in the maelstrom that followed him. The message was, in short, subsumed in an *argumentum ad hominem*.

The Man Behind the Message

Many reasons explain why Semmelweis' message was neglected at best and damned at worst. Some physicians complained that washing in chlorinated lime water chapped their hands. Most explanations, however, revolved around Semmelweis himself. He was often difficult to work with. He was an Hungarian in an Austrian hospital. He sympathized with the revolutionaries of 1848. Indeed, some of his brothers were known to have participated in the Hungarian Revolution of that year.⁸⁵⁷ All these factors served to alienate Semmelweis from many of his superiors and colleagues, for they were often conservatives whose prosperous lives would be threatened by the success of such revolutions.

⁸⁵⁶According to Greek mythology, Cassandra, daughter of King Priam of Troy, was granted the gift of prophecy by Apollo for her great beauty. When she rejected his advances, however, Apollo bedeviled the gift he had given her with the proviso that no one would believe her prophecies.

⁸⁵⁷The Revolutions of 1848 were the subliminal context in which Semmelweis' theories were examined and judged by his superiors and peers—thus, not solely on the basis of their scientific merit, but in the context of old versus young, conservative versus radical, connected versus deracinated.

Another not insignificant reason for Semmelweis' difficulty in spreading knowledge of his discovery was that he did not publish his findings – at least not right away. Morton's findings were published within hours of his demonstration of the anesthetic effects of ether. Semmelweis did not produce a comprehensive compendium of his findings for over a decade after his discovery. Hence, dissemination of his breakthrough was initially by the relatively slow route of word of mouth. And word of mouth is too personal – too close to the author's persona – to allow a proper distance for disinterested objectivity to make a distinction between the man and the message.

In the case of Semmelweis, his intended audience conflated man and message because, too often, a gadfly will not be heeded, no matter how compelling his message. On the other hand, had Semmelweis used the published word sooner than he did, it is likely that the detachment between the man and the message would have been sufficient to give the idea of prophylactic hand washing in chlorinated lime its due and allow observers to confirm or reject his findings based on the validity of the message alone.

But, no, Semmelweis did not publish his findings until more than a decade after his discovery of the prophylactic effects of hand washing in the spring of 1847, and then only with reluctance. In between, he coaxed students to follow his example and argued with colleagues who did not. He insisted that his way was *the* way to prevent puerperal fever and that those who did not follow his way were apostates at best and murderers at worst. His inflammatory letters to some of the leading European obstetricians of his day, often published for the interested and the curious, served to diminish the popularity of his prophylaxis and postpone the day of its acceptance for many years. In the meantime, the lives of thousands of women that might have been saved were lost.

There was little subtlety in his judgment of his colleagues' refusal to follow his teaching.

In one of his more well-known castigations, he wrote to a Professor of Obstetrics:

I declare before God and the world that you are a murderer and the "History of Childbed Fever" would not be unjust to you if it memorialized you as a medical Nero, in payment for having been the first to set himself against my life-saving doctrine.

-Open Letter to Hofrath Dr. F. W. Scanzoni,
Professor of Obstetrics at Würzburg, from Dr. I. Ph. Semmelweis, 1861⁸⁵⁸

One example does not constitute proof of Semmelweis' persona (nor the sharpness of his pen), but even those who accepted the value of his prophylaxis must have been aghast after reading a diatribe such as this. Perhaps, one can understand why a man so convinced of the truth of his message, continuing to witness the loss of lives that could have been saved by that message, would become belligerent in the face of skepticism, denial, and polemical (rather than scientific) criticism from others. Perhaps, one may chart a path from this medical incredulity to the fragility of Semmelweis' psyche and his ultimate mental disintegration. Or, perhaps, one has little to do with the other. Facts must sometimes stand alone without bridges virtualized between them, despite our propensity to link them with fine lines drawn from our personal worldly experiences but which cannot be verified in a court of science. Such was the history of Ignaz Semmelweis – a modern medical Cassandra.

Semmelweis' Ideas and Actions

When finally published in 1861, Ignaz Semmelweis' major work, *The Etiology, the Concept and the Prophylaxis of Childbed Fever*,⁸⁵⁹ argued that puerperal fever was an infectious

⁸⁵⁸Semmelweis, *Childbed Fever*: 794.

⁸⁵⁹*The etiology, concept, and prophylaxis of childbed fever; Childbed Fever*. Portions of Carter's translation are available online at http://books.google.com/books?id=hnezngRghTgC&printsec=frontcover&source=gbs_summary_r&cad=0 accessed June 1, 2009.

but not a contagious disease.⁸⁶⁰ To him, this meant that although it appeared that one person spread the disease to another by direct contact (contagion), the true mode of dissemination was via intermediary infectious particles that could spread disease even without direct person-to-person contact. He wrote that these pathogens—the “cadaveric particles”—originated from the corpses of women who died from puerperal fever.⁸⁶¹ Physicians, other attendants, and even instruments and bedpans—anything (not just anyone) having contact with the deceased—could spread the agents of infection to cause others to develop not only puerperal fever, but also closely-related conditions like erysipelas and other diseases. In all regards, the key to antisepsis, to the Hungarian in Vienna, was cleanliness of approach.

Semmelweis also argued that although patients with puerperal fever had slight (and, sometimes, significant) variations of symptoms from each other, there was one cause—not many. This oneness of diagnosis despite symptom variability was quite different from the “unique” nature of each different patient (even with similar symptoms) thought to be the case at that time. Thus, if many physicians at the time believed that the disease of each patient with the same diagnosis (e.g., tuberculosis) was different from that of every other patient with the same diagnosis, Semmelweis held that all patients with the same diagnosis (e.g., puerperal fever) held commonalities that allowed one prophylaxis or treatment to apply to all. This cognitive breakthrough was part and parcel of the foundation of modern therapeutics, wherein the diagnosis—rather than the person—determines treatment.

The Burden of Being Right and Alone

⁸⁶⁰*Childbed Fever*: 387, 433.

⁸⁶¹*Ibid.*, 393.

Semmelweis defended the principle of hand washing throughout the remainder of his tragedy-shortened life of forty-seven years. Some, including his students and some British physicians—followers of Alexander Gordon, Thomas Watson, and Holmes—shared his enthusiasm for the use of chlorinated lime; most did not. Following the termination of his First Clinic contract in March of 1848, no one in Vienna would hire him. In 1850, he finally gave up on trying to find meaningful employment in the Austrian capital, “unable to endure further frustrations in dealing with the Viennese medical establishment.”⁸⁶² In essence, Semmelweis had been blackballed by the Austrian physicians. He returned to Pest-Buda, where he accepted a small, honorary, unpaid position as head physician on the obstetrics ward at St. Rochus Hospital—the equivalent of a non-teaching hospital.⁸⁶³ Here, he immediately achieved a significant reduction in the rate of death from puerperal fever.⁸⁶⁴ By early 1855, following his methodology, he reduced the death rate from puerperal fever to 0.85%.⁸⁶⁵ During those same years, the mortality rate in Vienna due to puerperal fever was still ten to fifteen percent.⁸⁶⁶

⁸⁶²*The etiology, concept, and prophylaxis of childbed fever: 67.*

⁸⁶³*Ibid.*, 106. Note that although St. Rochus was not a teaching hospital, and therefore did not have medical students who could cross-contaminate corpses to puerperae, the obstetrics ward was run by a head of surgery who effectively served the same function. This was because the surgeon was also a “juridical anatomist” who routinely went from childbed fever corpse to delivering woman “with contaminated hands.” *Ibid.*

⁸⁶⁴At St. Rochus, Semmelweis reduced the death rate from puerperal fever in part by severing the dual responsibilities of the head surgeon to oversee the surgical and obstetrical wards—which occurred as a result of Semmelweis’s assumption of the latter position with his obstetrical appointment on May 20, 1851—as well as through hand washing. He himself believed that hand washing prophylaxis became less necessary after the dissolution of the link between the surgical and obstetrical wards because the head surgeon, whom Semmelweis thought was the chief source of contamination, no longer attended the maternity ward. *Ibid.*, 107.

⁸⁶⁵Eight of 933 births died of puerperal fever in 1855-1856. By this time in his career, Semmelweis was able to pinpoint the source of the contagion in some cases. For example, he wrote that one of the eight victims died shortly after a surgeon “had performed an autopsy on a man who died of a gangrenous leg.” *Ibid.*, 108. Again, Semmelweis sought to make clear his belief in a connection between the two diseases, gangrene and puerperal fever, previously thought to be completely independent.

⁸⁶⁶Semmelweis, Ignaz Philipp." *Encyclopædia Britannica. Encyclopædia Britannica Online.* Encyclopædia Britannica, 2010. Web. 20 Feb. 2010 <<http://search.eb.com/eb/article-9066723>>.

Semmelweis again butted heads with the establishment in Pest-Buda over his advocacy of hand washing as prophylaxis against childbed fever. Many Hungarian physicians in authority at the time, including Ede Flórián Birly, the Professor of Theoretical and Practical Obstetrics at the University of Pest at that time, believed that puerperal fever resulted from “unclean” bowels. Thus, Birly and others rejected hand washing prevention and instead treated patients with the disease with bowel purgatives (which only made the patients worse and may well have hastened their demise).

In July, 1855, Semmelweis received an appointment to succeed the recently-deceased Birly at the University of Pest.⁸⁶⁷ This was quite ironic, given Birly’s rejection of Semmelweis’ prophylaxis. Nonetheless, the reduction in the incidence of puerperal fever attributable to Semmelweis’ technique finally received notice by a few who had the power to cause its adoption. But only by a few.

For even at this time, several years after Semmelweis first demonstrated the success of his hand washing prophylaxis, the Hungarian continued to encounter opposition wherever he went. In later years, Semmelweis wrote “Open Letters,”⁸⁶⁸ which he sent to European obstetrical authorities and medical publishers in his attempt to offer incontrovertible statistics to convince the medical establishment of the virtues of hand washing. The task of converting entrenched interests, however, was Herculean and painstakingly slow. Semmelweis’ deep and unbearable frustration is starkly evident in the animus with which he wrote the Letters.

By 1857, however, some physicians and surgeons in positions of power began to recognize the value of Semmelweis’ antisepsis. In that year alone, he was offered a position as

⁸⁶⁷Semmelweis, *The etiology, concept, and prophylaxis of childbed fever*: 108.

⁸⁶⁸Semmelweis published the “Open Letters” in 1861 and 1862.

Professor of Obstetrics at the University of Zurich (which he declined), achieved sufficient social stature to marry the much-younger-than-himself daughter of a successful Pest merchant, and found his articles of prophylaxis disseminated by the government of Pest to all district authorities—with directives to implement his teachings.⁸⁶⁹ Still, the medical establishment in the prominent Austrian capital continued to reject his prophylactic technique. The editor of the respected *Wiener Medizinische Wochenschrift* [Vienna Medical Weekly—LK], for example, castigated him for his repeated arguments in support of chlorine-based hand washing.⁸⁷⁰

*Die Ätiologie, der Begriff und die Prophylaxis des Kindbettfiebers*⁸⁷¹

by Ignaz Semmelweis (1861)

Perhaps to stifle his critics—or to build on some of the positive reinforcement he was receiving at long last; or to reify his principles for posterity while he could—Semmelweis began to set down his ideas in writing. His first published work on puerperal fever, a monograph entitled “The Etiology of Childbed Fever,” was printed in Hungarian in 1858 and translated into German (perhaps for his Austrian foes to digest). In 1860, he published a second essay delineating his ideas on cadaverous particles versus other considered sources of contagion (e.g., miasmas). Finally, in 1861, he published *Die Ätiologie, der Begriff und die Prophylaxis des Kindbettfiebers* (*The Etiology, the Concept, and the Prevention of Childbed Fever*).⁸⁷² This was his *magnum opus*, the culmination of his thoughts, experiences, and clinical discoveries. It is not an easy read because, like many polemical works, it seeks to refute, sway, and convince—but not

⁸⁶⁹“Semmelweis, Ignaz Philipp.” *Encyclopædia Britannica*. *Encyclopædia Britannica Online*. Encyclopædia Britannica, 2010. Web. 20 Feb. 2010 <<http://search.eb.com/eb/article-9066723>>.

⁸⁷⁰“Semmelweis, Ignaz Philipp.” *Encyclopædia Britannica*. *Encyclopædia Britannica Online*. Encyclopædia Britannica, 2010. Web. 20 Feb. 2010 <<http://search.eb.com/eb/article-9066723>>.

⁸⁷¹*The Etiology, the Concept, and the Prevention of Childbed Fever*

⁸⁷²Semmelweis, *Childbed Fever*.

always in the most logical sequence. Nonetheless, it is a *tour de force*, laden with close analysis and rejection of the dominant theories of his time on the causation of puerperal fever; his alarming history of the prevalence of childbed fever before 1847; his personal remembrances of how hand washing with chloride of lime came about; and pages and pages of statistics—descriptive and graphical—proving the validity of his antiseptic method.

Today, the value of Semmelweis' prophylactic hand washing is clear to health care providers who have direct contact with patients. Such acceptance, however, was hardly the immediate response to *Die Ätiologie*. Outside of Pest, *Die Ätiologie* was received with disdain. Professors of Obstetrics in the medical mecca of Vienna continued to reject his work. Other citadels of medical prominence in mid-nineteenth-century Europe—Berlin, Prague, Copenhagen—saw no value in Semmelweis' prophylactic practice of hand washing and sometimes instituted practices that directly contradicted everything Semmelweis stood for. In Berlin, for example, Professor of Obstetrics Joseph Hermann Schmidt allowed students during the quiet times of a long delivery or in between deliveries to visit the morgue, where he expected them to improve their skills in pathological anatomy by learning from those who had recently died from puerperal fever!⁸⁷³

Still, the single most damaging blow of all probably came from Rudolf Virchow. He had published his landmark *Die Cellularpathologie* only three years earlier but, unlike Semmelweis, received immediate international acclaim for his theory that the cell was the basis of disease. At a German medical conference, Virchow rejected Semmelweis' theory and practice. Had there been no others who rejected Semmelweis' teaching, this action by Virchow alone might have

⁸⁷³Gordon, *Great Medical Disasters*: 225-6.

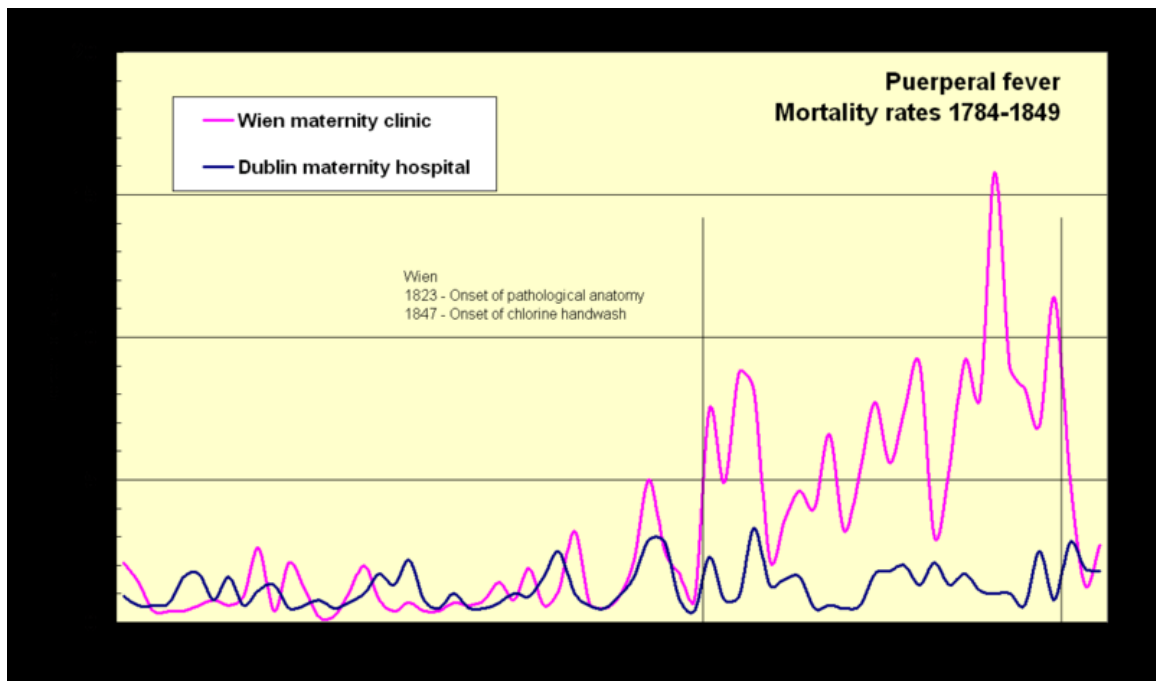
jettisoned prophylactic hand washing into the forgotten historical dustbin of rejected medical ideas.

Herein lies an important irony that should not be lost on even the most casual student of the history of antisepsis, for it was the very rise of pathological anatomy and its marked increase in traffic between the morgue and the clinic – between infected corpses and patients – that led to the marked increase in incidence of puerperal fever in the early nineteenth century.⁸⁷⁴

Decline, Dissolution, Death, and Disappearance

Thus, instead of kudos, compliments, and a fresh beginning, Semmelweis' publication of *Die Aetiologie* in 1861 marked the beginning of his end. Semmelweis' vituperative responses to his critics led to the publication of the "Open Letters" and further hastened his decline. As many have written, photographs and drawings of Semmelweis between 1857 and his death eight years later depict a man in rapid physiognomic and, by (questionably correlated) implication, mental

⁸⁷⁴Semmelweis knew this nexus and graphically exhibited the connection in a comparison of mortality rates between a hospital that emphasized pathological anatomy (in Vienna) and one that did not (in Dublin):



From http://en.wikipedia.org/wiki/File:Yearly_mortality_rates_1784-1849.png accessed April 3, 2010.

decline—as much as such pictures can reveal such a change.⁸⁷⁵ His behavior paralleled the decay in his appearance. He became more irascible, reportedly imbibed significant quantities of alcohol, and, in general, became anathema to his friends and family.

At the end of July, 1865, a colleague lured him to an insane asylum in Vienna.⁸⁷⁶ Semmelweis was sufficiently aware that he realized the ruse would lead to his incarceration, but he was unable to overcome the physical force of his jailers. Isolated, straitjacketed, and purged into submission, he grew weaker and weaker and died an ignominious death, alone except for the germ-infested surroundings that he had worked his entire professional career to prevent from infecting his patients. It has even been claimed that the immediate cause of Semmelweis' death was septicemia from the invasion of his bloodstream by “particles” that gained entry beyond his skin when he was cut and pummeled by the asylum attendants on his admission two weeks earlier; i.e., that he died from a process similar to that which led to the death of his friend, mentor, and inspiration, Professor Kolletschka. He died on August 13, 1865, at the age of forty-seven.

Like Karl Marx a few years later, few attended the funeral of Ignaz Semmelweis. Fewer still noted his passing. As required by his membership in the Hungarian Association of Physicians and Natural Scientists, Semmelweis was entitled to a memorial service after his death. None was ever given.⁸⁷⁷ His successor at the University of Pest refused to follow

⁸⁷⁵A good collection of pictures of Semmelweis and his world may be found at http://commons.wikimedia.org/wiki/Category:Ignaz_Semmelweis accessed March 31, 2010.

⁸⁷⁶The colleague was Ferdinand Ritter von Hebra, a renowned Viennese dermatologist.

⁸⁷⁷Semmelweis, *The etiology, concept, and prophylaxis of childbed fever*: 79.

Semmelweis' teachings. Mortality rates from childbed fever increased greatly.⁸⁷⁸ It was as though Semmelweis had disappeared—or never existed.

The Legacy of Ignaz Semmelweis

Within a few years after his death, the tragedy of Semmelweis' life transformed into a legacy of success. Had he survived into the late 1870s, and especially if he had lived into the 1880s, it is likely that his contemporaries would have treated him with respect and deference rather than contempt and ridicule. As was the case with his contemporary, Gregor Mendel (1822-1884), it remained for others to recognize and shed light on the importance of his work. In the case of Mendel, belated credit for the far-reaching consequences of his work on heredity in pea plants followed the early twentieth-century rediscovery and rebirth of his ideas on the particulate nature of inheritance. For Ignaz Semmelweis, posthumous acclaim followed the validation of his ideas on the particulate nature of infection, his use of statistical quantification to measure clinical outcomes, the notion that one disease had one cause,⁸⁷⁹ and, of course, that puerperal fever could be prevented with proper precautions, viz., by the operator washing his hands in chlorinated lime to effectively isolate both the infected patient and any particulate matter that had come in contact with the infected patient from one who was susceptible to the infection. The enormous importance of Semmelweis' work was especially recognized when it was discovered that it could be extended to less specific instances of communicability—such as in the surgical suite or the hospital ward—and helped explain the mechanism of the spread of infection.⁸⁸⁰

⁸⁷⁸http://en.wikipedia.org/wiki/Ignaz_Semmelweis accessed March 31, 2010.

⁸⁷⁹This is particularly (but not uniquely) true of infectious diseases and later codified by the Koch-Henle postulates.

⁸⁸⁰There is another legacy of Ignaz Semmelweis that I am reluctant to mention in the body of this chapter—the Semmelweis reflex or Semmelweis effect. This eponymous action is defined as the automatic or reflex-like

The refutation of spontaneous generation and the advent of germ theory by Louis Pasteur, as well as the innovative antiseptic practices of Joseph Lister, provided a mechanism by which his ideas could be understood and propelled Ignaz Semmelweis to become a medical hero of the first order. To Semmelweis is due thanks for the lives of countless women who would otherwise have died from puerperal fever during his lifetime and for generations thereafter. To Semmelweis is due thanks for a new way of thinking about contagion and infection – as particles of matter rather than as nondescript ethereal elements loosely correlated with air and/or climate and even sin. To Semmelweis is due thanks for laying the groundwork for the rise of surgery – and specifically surgery as the treatment of choice for patients with cancer – due to the decreased incidence of operative infections and postoperative sepsis in the late nineteenth century and thereafter.⁸⁸¹

With parallels to a Greek tragedy, however, in which the truth of the message is accepted only after the demise of the messenger, the hand washing prophylaxis of Semmelweis did not become a standard part of surgery until after another physician—of a vastly different personality—added his quieter but declarative voice to those who sought to prevent the

rejection of a new idea because it is believed to contradict deeply ingrained ways of thinking. I mention this legacy in a footnote because, as we have seen, this “reflex” or “effect” could have been named after a number of protagonists in the history of cancer.

⁸⁸¹Posthumous tributes to Semmelweis abound. Among them are Semmelweis University in what is now Budapest, Hungary; the Semmelweis Klinik for women; and a recent (2008) 50-Euro gold coin, which portrays Semmelweis’ 1860 visage on the obverse and the Vienna General Hospital on the reverse – the scene of Semmelweis’ great triumph and tragedy.



infections of surgery. That man, himself initially immersed in the inertial collective consciousness of his times, was Joseph Lister, whose contemporaries, decades hence, would dub him the Father of Antiseptic Surgery.

Pre-Listerian British Contagionism

English physicians initially accepted the concept of the contagiousness of certain diseases such as puerperal fever more than European physicians. Alexander Gordon and Thomas Watson encountered some resistance to the idea of contagiousness. Nevertheless, they convinced enough of the English-speaking world, including Oliver Wendell Holmes, that puerperal fever was a contagious disease so that it was hardly as novel a thought in mid-nineteenth-century England as it seemed to be at the same time in Semmelweis' Vienna.

James Young Simpson, whose chloroform anesthetic John Snow used to ameliorate the birth pangs of Queen Victoria, went so far as to criticize Semmelweis for, at best, adding nothing new toward an understanding of the cause of puerperal fever or, at worst, copying the work of others. Specifically, Simpson claimed that Semmelweis' theory of contagion merely parroted the work of Oliver Wendell Holmes, whose "Contagiousness of Puerperal Fever" had been first published only four years prior to Semmelweis' 1847 epiphany. Furthermore, Simpson invoked the legacy of Gordon and Watson when he wrote, soon after word spread about the Hungarian's insight, that "if Semmelweis were familiar with British medical literature he would know that the British had long regarded puerperal fever as contagious and preventable by precisely the methods that Semmelweis was claiming to have discovered."⁸⁸²

But Simpson and those of his countrymen who thought along these lines were wrong. Semmelweis had indeed added something new—something fundamentally and dramatically new.

⁸⁸²Semmelweis, *The etiology, concept, and prophylaxis of childbed fever*: 42.

Gordon, Watson, and, especially, Holmes had opined that the contagiousness of puerperal fever was the result of person to person contact; i.e., that the disease spread from one patient directly to another. Semmelweis, however, conceived of an intermediary—the cadaverous particles—that could spread the disease *even in the absence of the person from whom the contagion originated*. This was a critical insight because it entirely redirected the prevention of contagion. To Holmes, for example, prophylaxis meant separating the ill from the well. But to Semmelweis, separation of the infected from the susceptible was necessary but not sufficient. All objects—inanimate as well as animate—that were or had been in contact with the infected person could potentially spread the disease. Whole legions of contagious particles became potential agents of contagion, thereby making prophylaxis much more complicated than the considerably simpler isolation of infected patients and their caregivers. Prevention became much more difficult to achieve when not only the infected, but everything that had ever come in contact with the infected—bed sheets, towels, clothing, instruments, and so much more, including hands—had to be either rid of the invisible cadaverous particles or isolated from susceptible persons.⁸⁸³

Despite these important distinctions, the British concept of contagion was still closer to that of Semmelweis' than that proclaimed in the halls of the Vienna General Hospital. This similarity of thinking about the mode of contagion gave the English and the Scots an advantage over their Austrian and German counterparts when attempting to prevent the worst of the nosocomial contagious diseases, viz., the four horsemen of death—septicemia, hospital

⁸⁸³Had Semmelweis taken a more proactive course in promoting his concept of cadaverous particles through his own writings, it is possible that British critics like Simpson might have adopted the Semmelweis' perspective and helped him to convince others of the value of his teachings. Unfortunately for pregnant women and others exposed to infectious diseases everywhere, Semmelweis, as we have seen, did not advocate his ideas in writing until more than a decade after his initial conceptualization of contagious particles and hand washing in chlorinated lime. Promulgation of Semmelweis' ideas through second-hand accounts by students and visiting physicians in the late 1840s and early 1850s was insufficient to silence the denunciations of traditionalists against Semmelweis, his ideas, and his prophylaxis.

gangrene, erysipelas, and pyemia. As we have seen, these were the great fears of all those who underwent or undertook surgery and served to significantly reduce the number of potentially life-saving surgeries, including surgeries for the removal of cancers.

Into this diverse world of British contagionism entered a young English surgeon who was sorely troubled by the high mortality rate suffered by victims of a medical calamity that seemed worlds apart from childbed fever. These were infections that resulted from compound fractures of bone. And he was highly motivated to do something about it.

Joseph Lister, Surgeon

On August 12, 1865, the day before Ignaz Semmelweis died, a thirty-eight-year-old surgeon at the Glasgow Royal Infirmary instructed his house surgeon to lay “a piece of lint dipped in liquid carbolic acid upon the wound” of James Greenlees.⁸⁸⁴ James G. was an eleven-year-old boy who had suffered a compound fracture of the left lower leg when the wheel of an empty cart ran over him and crushed it. The surgeons knew that the boy’s life was at stake. They were not fearful of James’ mortality as a direct effect of his injury—from loss of blood or tissue damage—but rather as a result of a secondary infection beginning in his wound that often arose as a complication of that injury. In fact, experience with similar cases had taught the surgeons that perhaps half of those who had suffered similar fractures died as a result of overwhelming infection.

But James did not die. During the entire course of his multi-week hospitalization, he developed only a minimal amount of pus on the surface of the trauma site (“imperfect pus,” they called it). Nothing more. No spreading infection. No high fever. No sepsis. After his bones

⁸⁸⁴Joseph Baron Lister, *The Collected Papers of Joseph, Baron Lister*, 2 vols., vol. 2, The Classics of Medicine Library (Oxford: Clarendon Press, 1909; repr., 1979). 4.

knit firmly, the surgeon discharged young James in excellent condition. The surgeon, recording this patient's history, called the boy "Case I."⁸⁸⁵

Joseph Lister was one of those felicitous few who combined intelligence, a winning personality, and fortuitous timing to become a darling of history. For several years, this young surgeon in charge, had taken a personal interest in suppuration—i.e., the formation of pus that often was a harbinger of death from sepsis.⁸⁸⁶ Years after Lister's first Case I, an acquaintance recalled that as early as "1854 (or 1855)," the medical student who in 1865 would be James' surgeon had developed an interest in one of his professor's patients. The student looked at the patient's "clean" wound (i.e., free of infection) and proclaimed that "The main object of my life is to find out how to procure this result in all wounds."⁸⁸⁷ The goal of his life was surgery without fear of sepsis—antiseptic surgery.

Young Lister was not the first physician to take an interest in preventing wound infections. Hippocrates, more than two thousand years earlier, also had been fascinated with suppuration and had applied pitch to wounds in an attempt to suppress the oft-foreboding pus indicative of infection.⁸⁸⁸ In the sixteenth century, Ambroise Paré's use of *aqua vitae* sought the same goal but, like most attempts to achieve antisepsis before and for almost three centuries after his efforts, generated unpredictable results at best. Lister, however, had an advantage over

⁸⁸⁵Ibid., 4-5.

⁸⁸⁶Ibid., 3.

⁸⁸⁷Godlee, *Lister*, 205: 178. Sir John Batty Tuke's 1907 recollection of the twenty-seven-year-old student's intention may have been erroneous, but it is quite plausible. Lister's dedicated personality, focused mien, involvement of his wife in his quest, and the compulsiveness with which he followed his own directives, all portray a person highly devoted to a cause.

Nevertheless, it is important to recognize that Sir Rickman John Godlee, 1st Baronet (1849-1925) was Lister's nephew (Lister and Godlee's mother were brother and sister) and that the younger surgeon greatly admired – one might even say worshiped – his renowned uncle.

⁸⁸⁸Wangensteen and Wangenstein, *The Rise of Surgery*: 302.

Hippocrates, Paré, and many others over the centuries who sought to prevent the development of wound infections after trauma or surgery: Lister was familiar with the recent work of the French chemist Louis Pasteur on what would come to be called microbiology.⁸⁸⁹

The Insights of Louis Pasteur

During the third quarter of the nineteenth century, Louis Pasteur (1822-1895) described a rationale for understanding the causation and prevention of infectious diseases—germ theory.⁸⁹⁰ Neither he nor Lister nor anyone else knew or could have known the intricacies of the roles of microorganisms and their hosts (i.e., you and I) in the development of disease as we know those roles today (and, despite our knowledge, have so much more to learn than has been learned).⁸⁹¹ Nevertheless, Pasteur embarked on a series of chemical and biological explorations, beginning in the late 1850s, that gave Lister a framework and a foundation for his work of antisepsis.

This framework, to no small extent, was based upon attempts to answer a long-running controversy over the origin of life.⁸⁹² Did living organisms such as bacteria, flies, and worms

⁸⁸⁹The *Oxford English Dictionary* dates the first known use of both “microbiology” and “microbe” to 1880. http://dictionary.oed.com.ezproxy.cul.columbia.edu/cgi/entry/00308346?single=1&query_type=word&queryword=microbiology&first=1&max_to_show=10 and http://dictionary.oed.com.ezproxy.cul.columbia.edu/cgi/entry/00308334?single=1&query_type=word&queryword=microbe&first=1&max_to_show=10 accessed June 25, 2010.

⁸⁹⁰“Germ” in this context generally applies to a microorganism too small for the naked eye to visualize. There is often the added notion of a seed-like organism that “grows” by reproduction over time.

⁸⁹¹The modern disciplines of microbiology and infectious diseases are only two of many fields of knowledge that have developed from germ theory. Oncology, the medical specialty concerned with the study, diagnosis, and treatment of cancer, also owes much to germ theory.

⁸⁹²It is important at the outset of this discussion on spontaneous generation and its connection to the beginnings of antisepsis to make clear that by “origin” I am referring to the origin of your life and mine. The “other” origin of life, currently thought by scientists to be about 4.3 billion years ago, is a topic for biochemists, paleologists, and evolutionists not directly germane to my current discussion of antisepsis and its importance for the rise of cancer surgery.

Please note, however, that my use of the word “origin” in this context is intentional and, indeed, meant to be provocative rather than confusing, because the first origin of life billions of years ago always should have been a matter of concern to those who, like Virchow and Pasteur, disdained the idea of spontaneous generation. For unless one posits a universe that has had life throughout the entirety of its existence, there had to be a time before life and,

arise *de novo* from the inanimate matter surrounding them, or were they the offspring of an earlier generation of unicellular organisms, insects, and nematodes?⁸⁹³ Before the last half of the nineteenth century, the answer was very much under debate. Indeed, most laypersons observed that flies and worms came from rotten meat and dirt, not larvae and eggs, and no one was quite sure what generated Leeuwenhoek's "animalcules" and, indeed, the entire world of microorganisms.⁸⁹⁴

The competing conceptions of the origin of life were crucial to the prevention of wound infections and, by extension, the beginnings of modern antisepsis, because the means by which a wound infection developed made all the difference in terms of its prevention. Physicians knew long before the mid-nineteenth century that wounds became infected. What was unclear was how those infections became infected.

If a wound infection following a battle injury, compound fracture, or surgical procedure was caused by something that arose spontaneously, no preventive measures were likely to prevent its development once the wound occurred. Observers conceived such infections as arising from a host of possible causes—misfortune, chance, tainted air, punishment for sin, and more—depending upon his or her religious, social, or even political orientation. If, on the other

since life now exists in this universe, by logical extension, there had to be a time when life came from something other than life.

Scientific investigations into the origins of the first living organism continue unabated from before the highly touted work of Harold Urey and Stanley Miller in the early 1950s to the present day. See, for example, University of Montreal. "Origin of Life On Earth: Scientists Unlock Mystery Of Molecular Machine." ScienceDaily 1 March 2009. 26 June 2010 <<http://www.sciencedaily.com/releases/2009/02/090219105324.htm>>.

⁸⁹³There was no controversy about the origins of humans and other large animals. Offspring of these creatures clearly derived from their parents.

⁸⁹⁴Animalcules, which, from the Latin, mean "little animal," was Leeuwenhoek's expression for the motile forms he saw with his magnifying lenses. He especially used the term to describe what are now known to be spermatozoa. Of note is that Leeuwenhoek probably included some bacteria, which are today considered members of the plant kingdom, amongst his animalcules. Perhaps he should have called his microscopic forms "biocules" or "microbiocules." (I am glad he did not. —editor.)

hand, wound infections arose from something that entered the wound or from something that could be killed or eliminated even after it gained a foothold in the wound but before the infection actually began, then perhaps wound infections could be prevented. In the years just prior to James Greenlees' admission to the Glasgow Royal Infirmary for care of his fractured leg, Pasteur had shown that infections likely were caused by living microorganisms, and that such microorganisms did not arise *de novo*.

Spontaneous Generation – A Mode of Reproduction?

Spontaneous generation is the belief that living organisms can be produced from non-living matter—abiogenesis.⁸⁹⁵ Prior to the investigations of Pasteur, many scientists subscribed to the theory of spontaneous generation as an explanation for a host of medical and biological phenomena, including wound infections.

The Bible, when considered as a document in the history of medicine, is rife with visions of spontaneous generation and served as an early influence in its favor. God created the heavens and the earth from an amorphous emptiness (Genesis 1:2) and brought forth living plants and animals from those inanimate creations (Genesis 1:11). “And it was so” is the closest textual explanation for the process of creation.⁸⁹⁶ Sea creatures arose from the waters and land creatures sprouted from lifeless earth (Genesis 1:20 and 1:24, respectively). The creation of Man was special, of course, but certainly no evidence was put forth that Adam was created from a pre-

⁸⁹⁵“Abiogenesis” is the term often used today as a synonym for spontaneous generation. Abiogenesis means, as per its etymological roots, “created without life.”

Biogenesis is the holding that life can only be generated from pre-existing life.

⁸⁹⁶God is the Life Force. But if God was The Life Force for the creation of all the plants and animals of nature, was generation really spontaneous?

As is the case with the close examination of many controversial topics, precise definition of the matters in contention is critical. Of course, those definitions then become points of contention themselves. The meaning of the word “spontaneous” in spontaneous generation is more akin to the generation of life from lifeless matter than to its alternative sense of unplanned, ad-libbed, or all-of-a-sudden.

existing man or other living entity.⁸⁹⁷ God generated life spontaneously when He “formed a man of dust from the ground.”⁸⁹⁸

Observations over the centuries appeared to confirm the idea of spontaneous generation. New maggots appeared from lifeless meat.⁸⁹⁹ Mold grew from seemingly nothing on bread.⁹⁰⁰ Most believed that inorganic matter contained some vital life force—hence the term vitalism—that allowed lifeless meat and bread to give rise to life.

No less an authority than Aristotle had propounded the notion of spontaneous generation.⁹⁰¹ In Book V, Part I of his *History of Animals*, he wrote that, as with plants, “So with animals, some spring from parent animals according to their kind, whilst others grow spontaneously and not from kindred stock.”⁹⁰²

The Christian Church favored spontaneous generation. Saint Augustine, in his *City of God*, when explaining how all the creatures of the earth could fit into a vessel the size of Noah’s ark—approximately three stories high and one-and-one-half football fields long⁹⁰³—noted that

⁸⁹⁷The genesis of Man, in the name of Adam, conceals within itself its origins, for adam (אָדָם in Hebrew) is derived from adamah (אֲדָמָה)—meaning (red) earth.

⁸⁹⁸Coogan et al., *The new Oxford annotated Bible with the Apocryphal/Deuterocanonical books*, 2:7.

⁸⁹⁹Maggots are the vermiform (worm-like) larvae of certain insects, including many species of flies.

⁹⁰⁰Mold is the macroscopic manifestation of microscopic fungi. *Penicillium (notatum)*, from which Alexander Fleming derived penicillin, is a fungus that gave rise to mold on Fleming’s agar dishes in 1928.

⁹⁰¹This is not to say that life never arose from other life. Simple observation taught that only some life arose spontaneously.

⁹⁰²Aristotle, *The Works of Aristotle*, ed. Robert Maynard Hutchins, trans. D’Arcy Wentworth Thompson, Limited ed., 4 vols., vol. 4, Great Books of the Western World (Chicago: Encyclopedia Britannica, 1952; repr., Franklin Library, 1984). 333. Aristotle especially referenced the spontaneous generation of “a number of insects” from “putrefying earth.” Ibid.

⁹⁰³As related in *Genesis* 6:15, the actual dimensions were 30 cubits high, 300 cubits long, and 50 cubits wide. A cubit is a measure of length derived from the tip of the middle finger to the elbow – the forearm – approximately eighteen inches or 1.5 feet. (The word shares its etymology with terms like recumbent, presumably because one would recline or lie down on their forearms.)

when the Lord said that life in the ark “shall be male and female,” He excluded the myriad creatures that arose by spontaneous generation:

The words “they shall be male and female” [Genesis 6:19] are surely to be understood as referring to the need to renew the species, and so it was not necessary to have in the ark those creatures which can be produced without sexual intercourse from various substances, or from the decomposition of substances.⁹⁰⁴

Up to and including much of the nineteenth century, spontaneous generation had the strong support of the clergy. Only thereafter did the Church’s monopoly on the control of life’s vital milestones – like the origins of life and the causes of death – ebb away as natural philosophers *qua* scientists achieved a modicum of success in their investigations of the mysteries of life and death.

Francesco Redi – Controversy Engaged

Louis Pasteur was not the first to attack the notion of spontaneous generation. In 1668, Francesco Redi (1626-1697), an Italian physician, engineered one of the first scientific experiments [i.e., an experiment based upon the scientific method—hypothesis, experiment (including a control), results, conclusion, and consequent modification of the original hypothesis] to determine whether or not life could be generated spontaneously. Redi sought to test the hypothesis that maggots came from flies (biogenesis) rather than meat (abiogenesis).

In his most famous experiment, he took several jars and placed either a snake, some fish, eels, or meat (“milk-fed veal”) in each.⁹⁰⁵ Some of the flesh-filled jars he left open to the air.

Although the measure is not commonly used today, the original meaning of cubit – from elbow – lives on when a phlebotomist takes blood from the veins of the arm at the ante-cubital fossa, the depression on the inside of the elbow.

⁹⁰⁴Augustine and Henry Scowcroft Bettenson, *Concerning the city of God against the pagans* (Harmondsworth: Penguin Books, 1984). 647.

⁹⁰⁵Francesco Redi, Mab Bigelow, and Robert Payne Bigelow, *Experiments on the generation of insects* (Millwood, New York: Kraus Reprint Corp, 1969; repr., 1688, 1909). 33.

Other jars he covered with fine gauze that was impenetrable to flies (and their eggs). The remainder he sealed off from the air completely. After a few days, the open jars exhibited maggots; the gauze-covered jars revealed eggs and a few maggots on the gauze—but none on the meat itself; and the sealed jars disclosed no maggots. Redi concluded that lifeless meat did not give rise to living maggots. Rather, flies conceived offspring in the form of maggots (that developed into flies).⁹⁰⁶

Francesco Redi's findings led to the aphorism, *omne vivum ex ovo*.⁹⁰⁷ However persuasive his argument and experiments against abiogenesis may seem today, Redi was unable to convince his contemporaries to abandon the much-accepted belief in spontaneous generation.⁹⁰⁸

Microscopy's Confounding Influence

After Leeuwenhoek's discovery of "animalcules" with his personally-ground lenses in the late seventeenth century, the use of the microscope furthered, rather than dispelled, belief in spontaneous generation. The addition of a drop of water to a clump of hay led to a rapid observable increase in the number of animalcules in the water. The preponderance of opinion at the time favored the conclusion that the lifeless hay produced the new generations of living microscopic creatures.

The Nature of Nature

⁹⁰⁶Ibid., 33-34, 36-38.

⁹⁰⁷Literally, "all life from an egg." More figuratively, "all life comes from living things."

⁹⁰⁸Both Redi and his contemporary fellow investigator of natural phenomena, Galileo Galilei (1564-1642), a near-neighbor of Redi, offered attacks on accepted Church doctrines—Galileo on the place of the Earth in the known Universe, and Redi on the reality of spontaneous generation. Galileo was prosecuted and kept under house arrest by the Church for his condemned anti-Aristotelian "heresies," whereas Redi, who also espoused a strong anti-Aristotelian position only a few years later, was not. Thus, reasons other than Church dogma may have contributed to the conviction of Galileo and the lack of prosecution of Redi.

One of the reasons that natural philosophers of the early Enlightenment believed that non-living matter gave rise to life derived from their belief in the nature of matter. Unlike Henry Cavendish (1731-1810; the discoverer of hydrogen gas), Antoine Lavoisier (1743-1794; oxygen), Humphrey Davy (who, in addition to his seminal work on nitrous oxide noted above, contributed to the discovery of the elements chlorine and iodine), John Dalton (1766-1844; atomic theory) and many others of the late eighteenth century who gave birth to modern chemistry, philosophers in earlier times conceived of matter as relatively homogeneous and non-variegated. Thus, without a conception of dozens of different natural chemical elements and their complex interactions, animate and inanimate objects seemed closer in form and substance than we think of them today. Hay and animalcules, for example, might differ only by a few constituents and, therefore, appeared almost interchangeable. After all, foals ate hay and grew into enormous horses; human babies ate dead food and gained their weight in living tissues many times over. As such, it was easier for natural philosophers of the time to think that hay could generate animalcules than it became for a scientist of the nineteenth or twentieth centuries—with his knowledge of carbon, nitrogen, oxygen, and chemical reactions—to visualize such interconvertibility.⁹⁰⁹

Thus, the early eighteenth-century mentalité strongly supported the notion that at least the smallest living beings—visible (e.g., maggots) as well as microscopic (e.g., water-drop animalcules)—were generated spontaneously from non-living matter. When sharp-eyed natural philosophers viewed multiplying hay-fed microscopic creatures through their ground-glass lenses in the late seventeenth and eighteenth centuries, their explanation for the generation of

⁹⁰⁹The same argument applies to the decline in the popularity of alchemy with the rise of modern chemistry, for elemental chemistry predicted that the conversion of lead to gold, for example, would be no easy task.

living creatures reflected what they expected to see.⁹¹⁰ Belief in the spontaneous generation of life thrived.

John Needham: Spontaneous Generation Affirmed

One such example of the role of self-fulfilling prophecy in investigating the existence of spontaneous generation was that of John Needham (1713-1781), an English Catholic priest with an interest in the study of nature.

In the years between 1745 and 1748, Needham carried out a series of experiments designed to validate the theory of spontaneous generation, that built on the accepted notion that heat destroyed life.⁹¹¹ It was well known that chicken broth, left untended at room temperature, became spoiled. Microscopic examination revealed that spoiling was associated with a marked increase in the number of microorganisms in the broth. Heat destroyed these same microorganisms. Needham boiled the chicken broth, thus killing the microorganisms in it, put the boiled broth into a flask where the now-clear fluid could easily be examined, sealed the flask to ambient air, and waited. Within a few days, the boiled chicken broth became turbid and the microscope revealed teeming multitudes of microorganisms. Spontaneous generation, claimed Needham, was confirmed.

Spallanzani's Broth

Critics complained that Needham's experiments designed to affirm spontaneous generation were flawed. The Italian Lazzaro Spallanzani (1729-1799), also a Catholic priest and a naturalist, noted that there had been opportunities for microorganisms to enter Needham's

⁹¹⁰Fulfillment of expectations, when fallacious, represents a form of circular reasoning (and self-fulfilling prophecy). As such, it plays a recurrent role in the history of science. The expectation that microscopists believed they would see germs in cancer cells in the late nineteenth century led them to find germs in cancer cells and then to conclude that germs caused cancer.

⁹¹¹http://biology.clc.uc.edu/courses/bio114/protocols/spont_gen.pdf accessed May 22, 2010.

boiled chicken broth from the outside—either when it was poured into the flask (which was not sterile), or before the flask was covered. Between 1765 and 1767, he refined Needham’s technique to minimize the possibility of broth contamination.⁹¹² First, he repeated a variation of Needham’s main experiment by pouring chicken broth into a flask and then heating it. If the duration of boiling was only a few minutes, microorganisms rapidly repopulated in the broth. Then, he boiled the broth in the flask for an hour and immediately melted the mouth of the flask shut. He observed no growth of microorganisms in the long-boiled broth. In a third experiment, Spallanzani boiled chicken broth in an already-sealed flask. No microorganisms grew. Spallanzani concluded that if outside air could not gain entrance to the sufficiently-boiled chicken broth, life could not generate spontaneously.

Needham, well aware of Spallanzani’s experiments, countered that, rather than the Italian having proved that spontaneous generation did not exist, he merely showed that boiling killed the “life force” in the inanimate boiled broth that would have given rise to new microorganisms had it not been destroyed.⁹¹³ In addition, claimed Needham, sealing the flask prevented the life force in the ambient air from animating the broth in the flask.⁹¹⁴ Unable to test for—or refute the existence of—this invisible, indeterminate life force, Spallanzani’s experiments failed to

⁹¹²http://www.accessexcellence.org/RC/AB/BC/Spontaneous_Generation.php accessed May 22, 2010.

⁹¹³http://biology.clc.uc.edu/courses/bio114/protocols/spont_gen.pdf accessed May 22, 2010.

⁹¹⁴Needham’s arguments in favor of spontaneous generation are reminiscent of Johann Joachim Becher’s seventeenth-century contentions supporting phlogiston theory, viz., that combustible materials contained phlogiston—a colorless, odorless, massless substance, that was released when burned and gave rise to visible changes (like rusted metals) in the combusted material—as spontaneous generation gave rise to life in formerly lifeless materials. Abstract, constructed concepts like phlogiston and spontaneous generation (and the “ether” of the natural universe in the late nineteenth century—found to be unnecessary for the calculation of the speed of light by Einstein in 1905) are often used to explain the inexplicable. These retrospectively-determined-to-be fabrications serve a major function in science, however, for they create hypotheses that can be tested (like the existence of phlogiston, spontaneous generation, or ether) and that subsequently lead to new experiments, discoveries, and concepts.

convince natural philosophers of the eighteenth century that spontaneous generation was an illusion.

The battle for and against spontaneous generation raged for decades thereafter. Proof or denial of its existence gained greater urgency in the first half of the nineteenth century as the religiously-supported belief in spontaneous generation conflicted more and more with a growing body of scientific evidence that life was the result of chemical and biological processes rather than a life force. In essence, the disputation over spontaneous generation became a microcosm of the battle between vitalism and the new science—a thinly-veiled metaphor for the creation and meaning of life. If God did not generate life by breathing life into the lifeless, then how did life occur? Increasingly, the spontaneists' main argument, i.e., that there was no other reasonable explanation for the generation of life, crumbled before the accumulating scientific evidence of chemistry and knowledge of biological development. Scientific arguments were powerful because they could be tested and were increasingly discovered to successfully weather the trials of experimentation.

Virchow's Unoriginal Cells

In 1855, for example, the young patho-anatomist Rudolph Virchow (1821-1902) concurred with the non-spontaneists Redi and Spallanzani, based upon his research, in the formulation of his concept *omnis cellula e cellulae*—all cells are generated from previous cells.⁹¹⁵ In his monumental work on the cellular nature of disease, *Cellular Pathology*, first published in 1858, Virchow critiqued the general notion of spontaneous generation and expanded on his assertion that new living cells could only be conceived by older living cells:

⁹¹⁵<http://kentsimmons.uwinnipeg.ca/cm1504/celltheory.htm> accessed May 29, 2010. Virchow was thirty-three years old when he first published this conceptual gem derived from scientific deduction.

As long as living elements were conceived to be produced out of parts previously destitute of shape, such as formative fluids, or matters..., any...views could of course be entertained, but it is in this very particular that the revolution which the last few years have brought with them has been the most marked.⁹¹⁶ Even in pathology we can now go so far as to establish, as a general principle, *that no development of any kind begins de novo, and consequently as to reject the theory of equivocal [spontaneous] generation just as much in the history of the development of individual parts as we do in that of entire organisms...* Equally little are we disposed to concede either in physiological or pathological histology, that a new cell can build itself up out of any non-cellular substance. Where a cell arises, there a cell must have previously existed (*omnis cellula e cellula*), just as an animal can spring only from an animal, a plant only from a plant. In this manner...the principle is...established, that in the whole series of living things, whether they be entire plants or animal organisms, or essential constituents of the same, an eternal law of *continuous development* prevails. There is no discontinuity of development of such a kind that a new generation can of itself give rise to a new series of developmental forms. No developed tissues can be traced back either to any large or small simple element, unless it be unto a cell.⁹¹⁷

To Virchow, cells did not generate spontaneously and therefore, since he believed that the cell is the building block and fundamental unit of all life, life could not generate spontaneously. The German physician of growing influence clearly sided with the notion of biogenesis. Indeed, his apothegm *omnis cellula e cellula*, has become known as the “Biogenic Law.”⁹¹⁸

Pasteur’s Prize

Life is a germ and a germ is Life. Never will the doctrine of spontaneous generation recover from the mortal blow of this simple experiment.

—Louis Pasteur, April 7, 1864

The controversy reached fever pitch in the late 1850s. To address the issue (and put to rest what had become a very divisive dispute), the influential Academy of Sciences in Paris in

⁹¹⁶Virchow here referred to the growing ferment over spontaneous generation in mid-nineteenth-century Europe.

⁹¹⁷Rudolf Virchow, *Cellular Pathology as Based Upon Physiological and Pathological Histology: Twenty Lectures Delivered in the Pathological Institute of Berlin During the Months of February, March, and April, 1858*, trans. Frank Chance, 2nd ed., The Classics of Medicine Library (London: John Churchill, 1860; repr., 1980). 27-28. Italics and brackets in the original.

⁹¹⁸The Biogenic Law should not be confused with the Biogenetic Law, which is Ernst Haeckel’s (1834-1919) Recapitulation Theory that “ontogeny recapitulates phylogeny”; i.e., that the development and differentiation of an organism through its embryonic stages retraces the evolution of its species.

1859 offered the Alhumbert Prize of 2500 francs to anyone who devised an experiment or set of experiments that proved or disproved the validity of spontaneous generation.⁹¹⁹ Into the lucrative contest entered Louis Pasteur, whose experiments with microscopic living organisms (such as those that caused the fermentation of wine) gave him a distinct advantage in the quest to resolve the conflict one way or the another.

Pasteur, building upon the work of Redi and Spallanzani – and answering Needham’s objection to the exclusion of the “life force” from the broth – formulated a series of experiments that hypothesized the non-existence of spontaneous generation. Initially, he established a control by heating broth in an open-necked flask until the liquid turned clear and then observing the turbidity of the broth over time. Within a few days of heating the broth in the open-necked flask, the previously clear broth turned cloudy, teeming with microorganisms. [See Drawing (A)⁹²⁰]

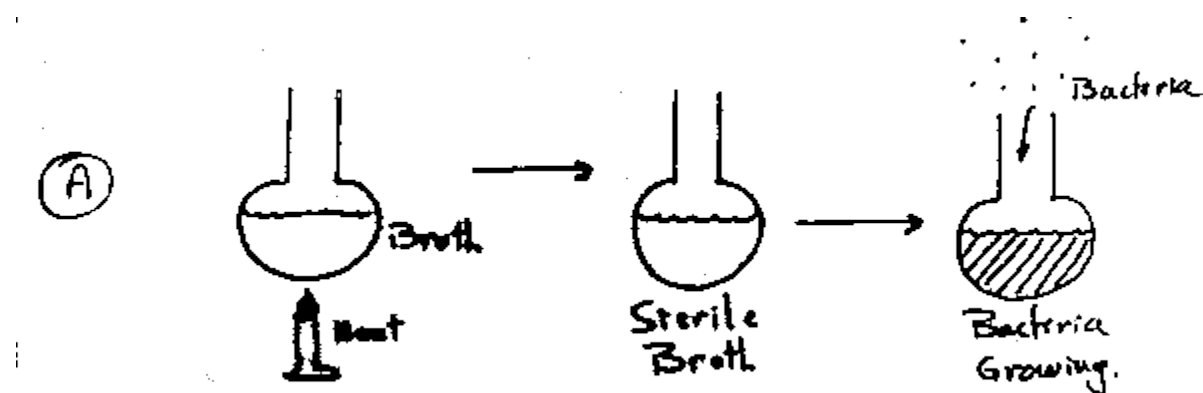


Figure 7. Pasteur Drawing (A)

The next experiment showcased his ingenuity and led to his victory in the race for the Alhumbert Prize. Whereas Redi had excluded fly larvae from the lifeless meat, and Spallanzani had stopped

⁹¹⁹<http://www.talkorigins.org/faqs/abioprob/spontaneous-generation.html> accessed June 22, 2010.

⁹²⁰Drawings from <http://kentsimmons.uwinnipeg.ca/cm1504/celltheory.htm> accessed June 22, 2010.

all air from entering the boiled broth, Pasteur sought to respond to Needham's objection to the shutting out of the hypothetical life force. He did this by leaving the next flask open to the air – but not quite! Before heating the broth in this flask, he melted the glass neck of the flask and bent it into a long S shape. As a result, a direct unobstructed path (albeit serpentine) from the external atmosphere to the broth persisted. The life force unquestionably had open entry to the broth. But the broth remained clear after heating. The life force could enter from the ambient air, but no life was generated!⁹²¹ Pasteur had reinforced the findings of Redi and Spallanzani while at the same time answering the objection of Needham. [See Diagram (B) top drawing]

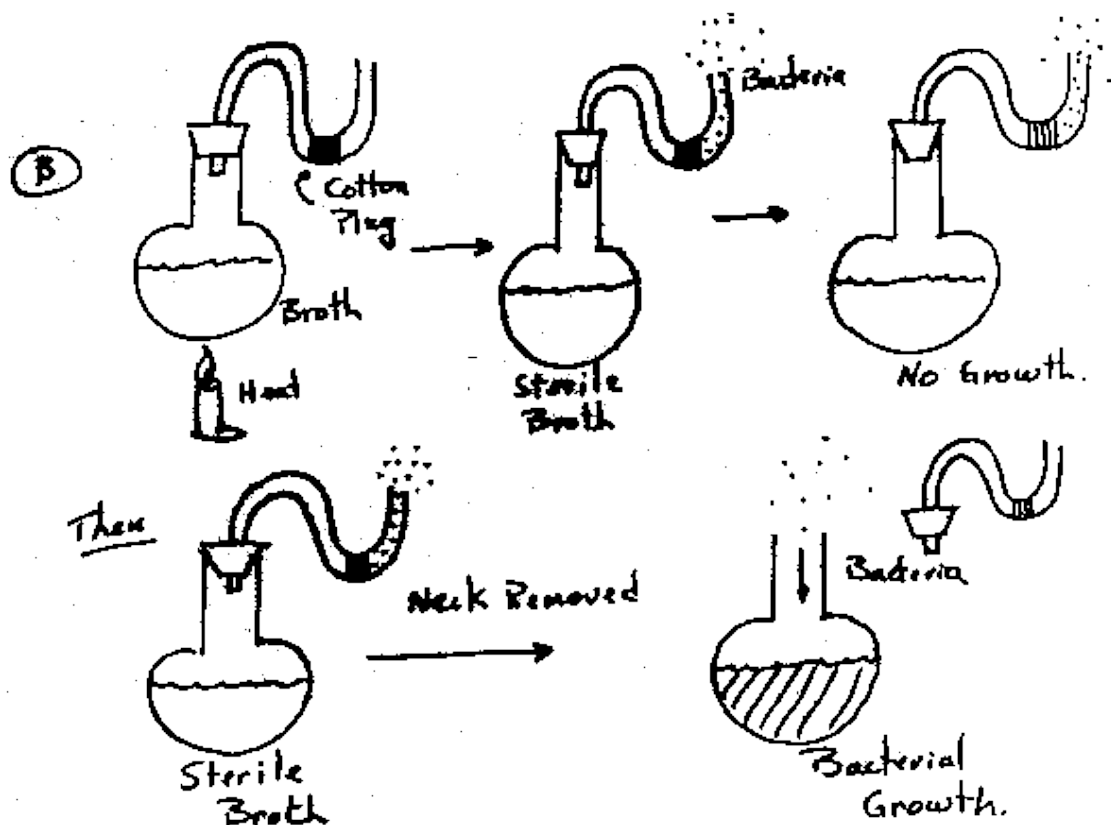


Figure 8. Pasteur Drawing (B)

⁹²¹“According to one freshman biology text, some of his original flasks, on display (in France), still are sterile.” http://biology.clc.uc.edu/courses/bio114/protocols/spont_gen.pdf page 3, accessed June 25, 2010.

Not satisfied with his having shown that the life force did not generate life in the heated flask with the S-shaped neck despite the open air passage to the broth, Pasteur carried out another set of experiments determine to show what would cause the clear, lifeless broth to turn cloudy with microorganisms. [See Diagram (B) bottom drawing] In essence, he sought to demonstrate that there was indeed a “life force” in the air, but that it was not the vitalistic principle the Spontaneists had conceived. First, he cut off the S-shaped neck of the flask with the clear broth and found that bacterial growth occurred in short order, as in the original control. This showed that the neck somehow had been instrumental in preventing bacterial growth in the flask. Then, he took another flask with an S-shaped neck that showed no evidence of turbidity after heating and tipped the flask so that the broth flowed to just make contact with the lowest point of the S-curve in the neck. He then immediately returned the flask to its original, upright position. Within days, the broth turned as turbid as had that in the open-necked flasks!

Pasteur had shown that life – in this case, heavier-than-air microorganisms – had sunk to the lowest point of the S-curved neck and could advance no further into the flask or broth against gravity. When the scientist tipped the flask, he brought the broth to the microorganisms rather than, as in the open-necked flasks, the microorganisms to the broth. Yes, there was a life force, but it was the invisible army of microscopic creatures floating in the air!

In his award speech before the Academy, Pasteur proclaimed that "*La génération spontanée est une chimère.*"⁹²² Exulting in triumph, Pasteur further predicted that “The theory of spontaneous generation will never recover from the mortal blow dealt it by this simple

⁹²²“Spontaneous generation is a chimera.”

Although many translate the word *chimère* as “dream” in this statement, I believe that Pasteur intended it to have a more negative connotation – something between a bad dream and the disorienting patchwork of animal parts connoted by the fire-breathing monster of Greek mythology from which the word derives. Or, perhaps, Pasteur used the term because he envisioned himself as Bellerophon, who slew the dangerous dragon. In support of this last contention, please see his prediction, following, wherein he states that he dealt spontaneous generation a “mortal blow.”

experiment.”⁹²³ Indirectly, he had shown also that Redi’s *omne vivum ex vivo* was valid. Thus Pasteur – at almost the same time that the publication of Darwin’s *Origin of Species* (1859) brought to the attention of the world that if there were an invisible hand guiding evolution, it could be time and circumstances rather than supernatural – affirmed that life came from life, not dead meat, dirt, or hay.⁹²⁴

Pasteur demonstrated that new life came from older life and that the world around us was full of invisible creatures that generated more of their kind – just like humans. The differences between the replication of microorganisms and humans were more a difference of degree (in size, generation time) than of kind (spontaneous generation versus sexual reproduction). As

⁹²³<http://www.talkorigins.org/faqs/abioprob/creationist.html> accessed June 26, 2010.

⁹²⁴In reality, Pasteur showed that life generated life. He neither disproved the possibility of spontaneous generation nor explained how life first originated, which, as stated earlier (Footnote 891) and sustained by experiments in the twentieth century, may well have originated from inanimate matter.

As to proving that all life comes from previous life, even this apothegm, when closely examined, is suspect. J. Craig Venter, famous for his race with Francis Collins of the Human Genome Project to decipher the human genetic makeup more than a decade ago, recently published an article on the first “Synthetic Cell.” Therein he showed that a computer-generated genome, when inserted into a bacterium, gave rise to a self-replicating organism. See Elizabeth Pennisi, “Synthetic Genome Brings New Life to Bacterium,” *Science* 328, No. 5981 (21 May 2010): 958-959 accessed 6/26/10 at <http://www.sciencemag.org.ezproxy.cul.columbia.edu/cgi/content/full/328/5981/958>. The original article by Venter’s group was published online May 20, 2010 at <http://www.sciencemag.org.ezproxy.cul.columbia.edu/cgi/content/abstract/science.1190719> and accessed 6/27/10.

The line between biogenesis and abiogenesis is much murkier today than it was in the years following Pasteur’s prize because the functionalities of ever-more-powerful non-living computers blur the distinction between animate and inanimate. Could one argue that the scientists at J. Craig Venter Institute (JCVI), who, as the title of their article proclaims, created “a bacterial cell controlled by a chemically synthesized genome,” have created life spontaneously? Venter, interviewed after the publication of the article, certainly thought so. But spontaneous generation – in the nineteenth-century meaning of the term – was heavily invested with the supernatural through vitalism. Inanimate matter became animate via the addition of some vital force.

The scientists at the JCVI certainly did not believe that they had created life from the lifeless by means of the addition of a supernatural or vital force. No, Venter and his group dissected and analyzed a particular component of a cell (in this case, the genetic material of a bacterium) and, with the help of computers, re-built a customized bacterial genome – they inserted their names, email addresses, and a few famous quotations into the genetic material – that, when introduced into a bacterium of another species, led to self-replication.

This is an amazing achievement that may well change the course of genomic research for years to come, but it was hardly spontaneous. It took fifteen (15) years and much trial and error to accomplish. Hence, there is an enormous difference between the notion of spontaneous generation that Pasteur fought against in the nineteenth century, and the artificial “designer genome” that Venter and colleagues “generated” in the twenty-first.

Pasteur discovered, microorganisms, with their rapid rates of replication, caused wine to ferment, meat to rot, and milk to sour.

Nisi Pasteur nil Lister?⁹²⁵

Joseph Lister, the young Glasgow surgeon, mindful of the work of Pasteur by the early 1860s, conceived an analogy between rotted meat and infected wounds. In the process, he determined that if the causative agent or agents of wound infections could be blocked from entering a clean, fresh wound, then an infection might be prevented. And, to his great honor and fame, he used the meat-wound analogy as a conceptual framework for devising methods by which he could accomplish this goal.

The proposition that external agents caused wound infections was not a common belief at the time. Most of Lister's contemporaries, either unaware of the work of Pasteur or rejecting it, believed that wound infections appeared *de novo* – as part of the intrinsic or constitutional nature of the individual's response to injury.⁹²⁶ Lister did not agree that such infections were built into the human makeup. On the contrary, he believed that something in the air – maybe the bad air of miasma, as he initially thought, or microorganisms, as he later came to accept – came in contact with the open wound and somehow caused infection.⁹²⁷

He did not come by this realization casually. Rather, it was the result of years of open-minded observation as a surgeon. Over these years, he had noted that simple fractures – those

⁹²⁵"But for Pasteur there would have been no Lister?" Courtesy of Professor Stefan Reif of Cambridge and Irwin Robins, Esq.

⁹²⁶Note the similarity to the genesis and progression of cancer as a constitutionally-driven phenomenon. Given the paucity of knowledge of population- or species-specific similarities at the time, it is perhaps not surprising that disease was so highly individualized. The rise of modern medicine in the last decades of the nineteenth century revealed that many dissimilarities between individuals were superficial rather than species-wide.

⁹²⁷Lister clearly believed in miasma theory until at least 1868, three years after his introduced his Antiseptic Principle for the prevention of wound infection. By 1871, he had adopted the idea that infective particles floating in the air could cause wound infection. See footnote 118 above. Note that in both cases – miasma and "floating ferments" – the source of infection was external to the wound, not intrinsic to the individual.

broken bones that do not break the skin and exposure the internal tissues to outside air – rarely led to infection, but that compound fractures – which do involve rupture of the skin and exposure to air – frequently became infected. If wound infections were intrinsic to the nature of the human body, then why would not both types of fractures lead to a similar incidence of wound infections? Surely the wound tissue itself was not sufficient to engender an infection within itself. Something else was necessary, and that something, he surmised, was extrinsic to the wound.⁹²⁸

This was Lister’s keen insight and the intellectual breakthrough that led to the development of antiseptic techniques followed by a marked increase in surgery in general and the use of surgery as the treatment of choice for cancer.

The Antiseptic Method

Given his hypothesis that the cause of a wound infection was extrinsic to the exposed tissue, Lister conceived of several possible avenues of prevention. Redi, Spallanzani, and Pasteur each had shown that boiling bacteria-laden broth prevented the appearance of microorganisms within the soup, but boiling wounded human flesh to prevent infection was not an acceptable option.⁹²⁹ Instead, Lister sought to discover a substance that would prevent infectious particles from coming into contact with the fresh wound and that were more tolerable to human tissue than “scalding oyle.”

Did Semmelweis inform the Antisepsis of Lister?

⁹²⁸Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 2.

⁹²⁹But note the military physicians’ use of “scalding hot” “oyle” in Ambroise Paré’s martial sixteenth century that differed so greatly from Lister’s century of Victorian sensibilities. See page 147 for the use of boiling oil and Paré’s personal reaction to it.

Is this not reminiscent of Semmelweis' objective? Did he not seek to accomplish the equivalent by preventing the "cadaverous particles" from coming into contact with the puerpera? What about his "antiseptic method"?

The shadow of Semmelweis looms large here. His disparaged prophylactic procedure, which preceded that of Lister by almost two decades, already had achieved antisepsis via hand washing by the time Lister undertook his own antiseptic experiments. Semmelweis thought that the method he initiated in 1847 either destroyed the infectious "cadaverous particles" already present on the operator's hands or prevented them from colonizing the hands before they could gain a foothold on the hands – and certainly before the particles could come into contact with the susceptible tissues of a pregnant woman. Semmelweis achieved both modes of antisepsis through the bacteriolytic effects of chloride of lime. He may not have known why the chlorinated lime was effective, but he knew that it was. His statistical compilations surely confirmed as much.

In the 1860s, Lister sought to achieve essentially the same antiseptic effect in wounds generated by compound fractures. The similarity between the puerperal uterus and a wound infection may not have been obvious to either Semmelweis or Lister at the time, but it should not go unmentioned. The uterus of a woman who has just given birth has many similarities to an open wound, for in both cases the first line of defense – the endometrial lining of the uterus and the skin, respectively – is breached, thus creating a portal for cadaverous or infectious particles to engender infection.

What did Lister know of the work of Semmelweis, and when did he know it? If Lister knew of Semmelweis' work, it would diminish his own contribution to antisepsis and make it difficult to entitle him its "Father."

It may never be known with certainty how much, if anything, Lister knew of the work of Semmelweis. No known works from the 1860s (or before) reveal a knowledge exchange between the two.⁹³⁰ Nonetheless, although their paths may not have crossed directly, they certainly had many colleagues in common. It is well documented, for example, that Lister resided in Vienna for about two weeks during his honeymoon in 1856, six years after Semmelweis left Vienna. There he met Rokitansky, the pathologist with whom Semmelweis had trained. There is no credible evidence that Lister and Rokitansky discussed Semmelweis' work. It is understandable that the great Rokitansky, who sought to marginalize Semmelweis during the latter's later years there,⁹³¹ would have spontaneously discussed the work of a physician who had left Vienna years before and whose work was, by that time, largely forgotten.⁹³² Nonetheless, other historians disagree.⁹³³

Thus, it is impossible to be certain whether or not Lister knew of the antisepsis of Semmelweis prior to his work on "Case I.— James G——." In the opening years of the twentieth century, years after the acceptance of the bacteriological principles that proved the

⁹³⁰O. H. Wangenstein has an extensive discussion of the Semmelweis-Lister antisepsis precedence controversy in Owen H. Wangenstein, "Nineteenth Century Wound Management of the Parturient and Compound Fracture: The Semmelweis-Lister Priority Controversy," *Bulletin of the New York Academy of Medicine* 46, no. 8 (1970). On page 586, Wangenstein concludes that "It is proper that Semmelweis be recognized as the discoverer of the role of antiseptics in preventing wound infection. It is fitting to honor Lister as the leader whose careful study of the influence of antiseptics on compound fractures lent meaning to the provocative work of Pasteur for surgery." Thus, the American surgeon Wangenstein gave precedence to Semmelweis, but others have disagreed, often – in my opinion – more for nationalistic than substantive reasons.

Nevertheless, I tend to take Lister at his word. Analysis of his body of work reveals Lister to be a medical scientist with much less of his ego invested in the acceptance of his findings and the adoption of his suggestions than was Semmelweis. As noted, he denied knowledge of Semmelweis' work prior to his first use of antisepsis to prevent wound infections in 1865. Today, on the other hand, denial of knowledge of the work of another in the same field would be improbable, unacceptable, and, frankly, unbelievable.

⁹³¹See page 181 of this chapter.

⁹³²Godlee, *Lister*, 205: 140.

⁹³³Wangenstein, "Nineteenth Century Wound Management of the Parturient and Compound Fracture: The Semmelweis-Lister Priority Controversy," 584-86.

worth of his hand washing prophylaxis, Semmelweis' work on antiseptics was heralded in his native Hungary. In 1904, "A teacher from Buda-Pesth"—as Lister's biographer and nephew, Sir Rickman Godlee, wrote – claimed that Lister had admitted that "Without Semmelweis my labour would have been in vain. Modern surgery owes most to the great son of Hungary."⁹³⁴ None could verify this statement, so those who sought precedence wrote to the aged Lister to confirm or refute it. In a letter dated September 15, 1906, Lister responded that "When in 1865 I first applied the antiseptic principle to wounds, I had not heard the name of Semmelweis and knew nothing of his work."⁹³⁵ Lister's intellectual inspiration, it appears, was Pasteur, not Semmelweis.⁹³⁶

What did Lister do?

Certainly infections cannot be attributed to the intervention of the devil but must be laid at the surgeon's door.

—Harvey Cushing, 1915⁹³⁷

Semmelweis sought to prevent infectious particles from coming into contact with the susceptible uterus by preventing such material from attaching to the hand that would transport it into the puerpera's "wound." Lister sought to prevent surgical infections by establishing a chemical barrier between the wound and the infective agent or agents, although he also

⁹³⁴Godlee, *Lister*, 205: 142.

⁹³⁵Ibid.

⁹³⁶If Lister was truthful – and his memory accurate – should he be criticized for his unfamiliarity with the work of Semmelweis which, after all, had been published in 1861 – only four years prior to Lister's initial work on his "antiseptic principle"? Perhaps, because medical research was and is built upon precedent, as is the law. Nonetheless, as we have discussed earlier, medical knowledge exchange at the time was in its infancy. In addition, those from whom Lister would have been most likely to obtain such trans-Continent information – his obstetrical colleagues – evinced no knowledge of the work of the then-denigrated Semmelweis. On this last point, see *ibid.*, 142-43. Others, however, believe that Lister's obstetrical associates must have known of the work of Semmelweis. See Wangenstein, "Nineteenth Century Wound Management of the Parturient and Compound Fracture: The Semmelweis-Lister Priority Controversy," 585-86.

⁹³⁷Harvey Cushing, "Concerning the results of operations for brain tumor," *Journal of the American Medical Association* 64(1915).

advocated hand washing – albeit with a chemical other than chlorinated lime. He did not know what these infectious agents might be until Pasteur’s early forays into bacteriology clarified their nature sometime after 1865, but he did know where they came from – outside the wound. Thus, Lister reasoned, if the wound could be “protected” from (“barricaded against” might be a more apt phrase) these external substances—whatever they may be—it could be kept free of infection.

This was the basis of Lister’s “Antiseptic Principle.” It was also an advance on Semmelweis’ hand washing prophylaxis because it was later appreciated that Lister’s prophylaxis was established physically closer to the ultimate site of infection—the wound. Thus, even if a puerpera’s physician had not washed his hands prior to examining her genital tract, Lister’s chemical impediment at the hand-vagina/cervix/uterus interface could forestall infection. Lister’s innovation – and the reason for his enduring fame – was his reasoning behind the use of a chemical barrier against infection as well as the barricade itself.

Carbolic Acid

When a seemingly revolutionary leap occurs in science, it proves, almost always, to be but a particularly long step by a particularly bold researcher, in a process for which the stage has been set by the work of others who came before.

—Sherwin Nuland⁹³⁸

Lister’s antiseptics was based upon carbolic acid, an inorganic compound composed of hydrogen, oxygen, and carbon whose chemical structure looks like an inverted kite on a string. (See chemical structures below.) He did not choose this compound lightly, at it is certain that his choice was not without precedent. Indeed, if the intellectual forefather of Lister’s Antiseptic Principle was Pasteur, those who preceded him in the quest for chemical antiseptics using similar compounds were many.

⁹³⁸Nuland, *Doctors*: 239. Dr. Nuland referenced Semmelweis with this quotation but it clearly applies to Lister and so many others in this history as well. To link this quotation to Lister is made easier by the title of Nuland’s chapter in which this quotation is found, “The Germ Theory before Germs” – a very apt description of Lister’s early work on antiseptics.

Creosol, Creosote, and early efforts to “Save the Flesh”

Carbolic acid, today more commonly known as phenol, is a derivative of creosol. Despite the venerable position of silver in the history of antiseptics, not silver, but creosol – another chemical compound used to prevent and treat infections prior to the advent of modern antiseptics in the late nineteenth century – played a more direct role in the foundation of modern antiseptics.⁹³⁹ This is because creosol, in contradistinction to silver, is a direct relation of the phenols and carbolic acid—chemicals that became the backbones of modern antiseptics.

Creosol is a component of creosote, a substance known for centuries as a wood preservative that contains a mixture of different chemical compounds derived from wood or coal tar. The etymology of creosol derives from the Greek “save the flesh,” because it was known in ancient times to delay the decomposition not only of wood, but also of fish, meat, and other organic materials.

The description and analysis of creosol was a nineteenth-century project – another result of the synergies that exploded into modern chemistry in the early decades of the century. Baron Dr. Karl von Reichenbach (1788-1869), a German chemist, discovered the phenolic compounds by distillation from wood-tar in 1832.⁹⁴⁰ The Baron’s work followed the pioneering physicochemical theories of John Dalton (1766-1844), as laid forth in the latter’s three-volume *New System of Chemical Philosophy*, published in 1808, 1810, and 1827.⁹⁴¹ In *Chemical Philosophy*, Dalton, who himself built on investigations into the structure of matter by the French

⁹³⁹Ironically, silver, which reached its denouement as an antiseptic with the rise of antibiotics in the second third of the twentieth century, is experiencing a rebirth as an antiseptic as bacteria become resistant to those same antibiotics and their derivatives. See, for example, <http://www.nytimes.com/2005/12/21/health/21iht-snsilver.html> accessed August 8, 2010.

⁹⁴⁰Baron Karl von Reichenbach is also known for his discovery of kerosene, a major energy source for cooking and heating throughout the nineteenth century.

⁹⁴¹John Dalton, *A New System of Chemical Philosophy*, 3 vols. (Manchester: George Wilson, 1827).

aristocrat Antoine Lavoisier (1743-1794),⁹⁴² hypothesized that molecules consisted of atoms combined in fixed proportions – a radical (but now well-accepted) theory at the time.⁹⁴³

Nevertheless, Dalton's use of Atomic Theory, revolutionary as it was in his time, had deeper roots that were both a revitalization and an extension of the philosophico-materialistic thinking of Ancient Greeks such as Leucippus (first half 5th Century BCE) and his student Democritus (c.460 BCE-c. 370 BCE).⁹⁴⁴ This reconceptualization of the nature of matter as elemental particles combined in fixed proportions captured the imagination of early nineteenth-century natural philosophers and, after years of experimentation, were validated and well accepted before the end of the century.⁹⁴⁵ In consequence, Dalton's work on Atomic Theory gave birth to modern chemistry and, not many years later, to many chemistry-derived advances in medicine such as anesthesia and antiseptis.

Creosote, which contains creosol, was thus long known as a preservative of wood and other organic tissues. Therefore, it is not surprising that physicians used its derivatives for anti-infective and anti-putrefactive purposes, because the decomposition of human tissue was viewed

⁹⁴²Lavoisier identified and named both oxygen (1778) and hydrogen (1783), among many other accomplishments in chemistry.

⁹⁴³For example, two atoms (not one, three, or four!) of hydrogen combined with one atom of oxygen to create water. Water was therefore 2 hydrogens:1 oxygen or what is today written H₂O.

⁹⁴⁴The atomic theory imagined a universe of fixed, unchanging particles. The contrary “flux” or “process” theory of Heraclitus (c. 535-475 BCE) and his intellectual descendants postulated an ever-changing universe where “Everything flows, nothing stands still.” Atomic theorists countered by explaining change as a rearrangement of immutable atoms.

⁹⁴⁵Interestingly, natural philosophers who investigated chemical phenomena adopted the idea of the atom much earlier than those who looked into the nature of the properties of forces and matter—later called physicists.

In the early twentieth century, those now-independent physicists discovered that the “indivisible” atom was indeed comprised of what are today called electrons, protons, neutrons – and a remarkable amount of (what is today thought to be) empty space. Since the early 1960s, those “elementary” particles have themselves thought to be composed of smaller particles called quarks (which combine to form hadrons like protons and neutrons). Thus, the atom, that corpuscle which was assumed uncuttable, has now been sliced into smaller and smaller particles seemingly limited in size only by the resolution of the physicist's instruments.

as a form of declension toward rottenness and decay.⁹⁴⁶ Creosote, like creosol, was used long before its chemical components were identified in the nineteenth century. Ancient Egyptians had little knowledge of the nature of chemical compounds as we know them today, but they surely had empirical knowledge of their properties. Retrospective analysis, for example, revealed that they used creosote as a preservative in their mummification process.⁹⁴⁷ Centuries later, the British Empiricist Bishop George Berkeley (1685-1753) celebrated the use of coal tar – especially in the form of “tar-water” – for its health benefits long before anyone knew its chemistry.⁹⁴⁸ In fact, Bishop Berkeley’s last two publications lauded the medicinal benefits of tar-water. In those writings he considered its attributes almost divine – including its antiseptic properties.⁹⁴⁹

Creosote and silver are just two of numerous examples that support the ideas that (1) physicians had anecdotal and experiential knowledge of medicinals, including antiseptics, long before the rise of scientific medicine in the nineteenth century and, closely related, (2) that many modern classes of drugs—including anesthetics and antiseptics—can trace their origins to the not-so-dark ages long before the advent of modern medicine.

⁹⁴⁶Coal-tar creosote is still used as a wood preservative, but its potential for carcinogenesis has curtailed its popularity.

It is interesting to note that smoke, a preservative known to Native Americans and before them for millennia, derives much of its power to preserve from creosote. Meats and fish, for example, are smoked—at least in part—to minimize their spoilage.

⁹⁴⁷Charles Milton Buchanan, *Antisepsis and antiseptics* (Newark: Terhune Company, 1895). 33-34.

⁹⁴⁸*Ibid.*, 27-28.

⁹⁴⁹The two works are *Siris: Philosophical reflexions and inquiries concerning the virtues of tar-water, and divers other subjects connected together and arising from one another* (1744) and *Further Thoughts on Tar-water* (1752). Berkeley’s belief in the properties of tar-water as a catholicon or panacea went far beyond antisepsis toward its use for almost any ailment. Interestingly, it was these last works of Berkeley’s life, not his philosophical tracts, that captured the attention of the public during his lifetime.

Further, what appeared to pre-modern scientists and physicians as natural therapies (used by natural philosophers) such as creosote, could be further refined with the new knowledge of nineteenth-century chemistry, into substances with purer properties than their parents. Within the field of antiseptics, creosol – derived from creosote – is an excellent example of a progenitor agent, for the chemical similarity between creosol and phenol turns out to be striking. (See chemical structures above.) The foundation of both molecules is a six-carbon (benzene) ring with an attached hydroxyl (-OH) group sticking off one of its six arms. The main difference is that creosol has a methyl (-CH₃) group attached to another arm of the molecule, whereas phenol does not. Certainly, a methyl group can make all the difference in the properties of a molecule, but the benzene ring is a fixture of many antiseptics, including the most famous historical antiseptic of all—carbolic acid.

Carbolic Acid and the Birth of Modern Antisepsis

Carbolic acid became Joseph Lister's preferred agent for the prevention of wound infections.⁹⁵⁰ Anyone who has visited a hospital is familiar with its odor, because carbolic acid/phenol gives the institution's corridors much of its "hospital smell" – a direct result of the antiseptic and disinfectant properties of the molecule popularized by Lister.

Lister may have happened upon carbolic acid by chance, but it was his powers of deduction combined with his knowledge of medicine that made carbolic acid the first great antiseptic of modern medicine. In 1864, months before he first used the antiseptic on James

⁹⁵⁰I will use the term carbolic acid rather than phenol from this point forward to maintain the spirit of Lister's times.

My preference for carbolic acid over phenol is consistent with the usage of the two terms over the past century and a half. Phenol, although the more frequently-used term in the twentieth century, was the term utilized much less often by Lister and his colleagues in the nineteenth century. In his revolutionizing *Lancet* article in 1867, for example, Lister first used the phrase "carbolic or phenic acid" in the beginning, but only carbolic acid thereafter). He never the term "phenol." Joseph Lister, "On the Antiseptic Principle in the Practice of Surgery," *The Lancet* II(1867): 353.

Greenlees' left leg, Lister read an article in a newspaper that struck a chord in his thinking about wound infections.⁹⁵¹ The piece mentioned that when the town of Carlisle, England⁹⁵² added very small amounts of carbolic acid to its sewage, not only was the smell of the cow pastures "irrigated" by the malodorous garbage reduced, but there also appeared to be a marked diminution in the number of diseased cows that grazed in those pastures.⁹⁵³

This realization was a seminal event in Lister's thinking, because it led him to link the smell of sewage – the similarity of which to a necrotic wound could not have gone unnoticed – to the parasitic "entozoa" that infested the cattle in the same area as the sewage.⁹⁵⁴ "My attention having for several years been much directed to the subject of suppuration, more especially in its relation to decomposition," wrote Lister in 1867, "I saw that such a powerful antiseptic was peculiarly adapted for experiments with a view to elucidating that subject, and while I was engaged in the investigation the applicability of carbolic acid for the treatment of compound fracture naturally occurred to me."⁹⁵⁵

There it was! The link between smell, sight, and sewage illuminated the solution to the problem of compound fracture wound infections. Combined with Pasteur's insights on the decomposition of organic compounds by microscopic organisms (e.g., the fermentation of sugar by yeast to produce alcohol and carbon dioxide), Lister realized that wound infections could be

⁹⁵¹Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 3.

⁹⁵²Carlisle is about three hundred miles north-northwest of London.

⁹⁵³Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 3. Lister used the word "irrigated" in this context.

Note that London also used carbolic acid as a deodorizer and disinfected during the cholera epidemic of 1866, a year after Lister began to use it as an antiseptic. Anton Sebastian, *A Dictionary of the History of Medicine* (New York: The Parthenon Publishing Group, 1999). 172.

⁹⁵⁴Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 3.

⁹⁵⁵*Ibid.*

caused by microorganisms from the air that “decomposed” human tissue (thereby causing putrefaction), that killing these microscopic organisms could prevent them from infecting the wound, and that carbolic acid might serve as the agent of prevention. Lister had followed the time-honored path to discovery, taking knowledge gleaned from one field – sanitation – and applying it (within the fertile context of considerable preparedness) to another – medicine.⁹⁵⁶ It was the epitome of an “Aha!” moment.

Nevertheless, Lister – like so many of the pioneers explored in this history – was a cautious, meticulous medical investigator. Armchair deduction might produce a testable hypothesis, but only experimentation could prove that the idea had utility in the real world. Lister, by his own testimony, first used carbolic acid to prevent a wound infection in a compound fracture not in James Greenlees, but on another patient in March, 1865. It failed miserably. Still, Lister would not be deterred and, after additional research into the forms and attributes of carbolic acid, he fixed upon “German creosote” – the liquid form of the acid – for use on James Greenlees and those who followed.

Was Lister the First to use Carbolic Acid as an Antiseptic?

Most questions of priority are vaguely settled on purely national and personal lines, and yet such an attitude is unjust and faulty in the extreme, for all history is but a record of the sequence of events, of acts and discoveries in which questions of priority of one sort or another continually arise, and if the contemporary historian is timid and does not set these things aright, how is he of later date, with less available information, to do justice to his task and utter the naked truth?

—Howard A. Kelly, M.D. (1901), writing on the Lister priority controversy⁹⁵⁷

During his lifetime, Lister received accolades and awards as well as fame and acclaim almost beyond measure. However, Lister was not the first to use carbolic acid as an antiseptic.

⁹⁵⁶The quotation “Good luck is preparedness meeting opportunity,” often attributed to the Roman Stoic philosopher Seneca (3 BCE-65 CE), cogently captures this idea.

⁹⁵⁷Howard A. Kelly, “Jules Lemaire - The first to Recognize the True Nature of Wound Infection and Inflammation, and the First to Use Carbolic Acid in Medicine,” *Journal of the American Medical Association* XXXVI, no. 16 (1901): 1083.

Nor was he the first to claim (in March, 1867) that the air surrounding the wound could contain particles that cause infection. Thus, it was not long after the publication of his seminal 1867 paper in *The Lancet* on “The Antiseptic System, On a *New* Method of Treating Compound Fracture, Abscess, Etc.” that a priority controversy erupted in the pages of the same journal.⁹⁵⁸

The question or controversy, depending upon your perspective, as to who deserves the credit for the origination of surgical antiseptics transcends the characters of its history. As such, it is directly relevant and important to the history of cancer because it informs the process by which investigators set in motion the methods that made surgery the treatment of choice for cancer by the end of the nineteenth century.

Simpson Vilifies Lister

If Mr. Lister had taken the slightest trouble to search English medical literature alone, he would easily have convinced himself of his own grave error.

—Sir James Y. Simpson, 1867⁹⁵⁹

Lister’s “own grave error,” claimed Sir James, was that Lister was neither the first to use carbolic acid as an antiseptic nor the first to describe its antiseptic properties. Dr. Simpson, who had found a better anesthetic than ether for obstetrics in the chemistry of chloroform and who had chastised Semmelweis for not acknowledging that the Hungarian had merely aped Holmes’ work on the prevention of puerperal fever, was again in the forefront of the controversy.

In late 1867, the portly Simpson was an aging but highly respected—if not revered—figure in Great Britain and beyond.⁹⁶⁰ In his November *Lancet* article of that year, he elaborated

⁹⁵⁸*The Lancet* serialized Lister’s original paper in March and April of 1867. Joseph Lister, “On the Antiseptic Principle in the Practice of Surgery,” *The Lancet* i(1867). The priority controversy may be found in *The Lancet* of November 2, 1867. Bart. Sir James Y. Simpson, “Carbolic Acid and Its Compounds in Surgery,” *The Lancet* ii(1867).

⁹⁵⁹“Carbolic Acid and Its Compounds in Surgery,” 548.

on a mountain of cited evidence to show that Jules Lemaire, a Parisian physician and “pharmaceutical chemist”—and not Lister – was the first to use carbolic acid as an antiseptic.⁹⁶¹ As Simpson explained, Lemaire, in 1863, had penned a three hundred page monograph on carbolic acid “devoted to its therapeutical effects and the theory of them.”⁹⁶² Two years later, Lemaire published an expanded seven hundred and fifty-four page book on the “disinfectant” carbolic acid that detailed the theoretical underpinnings for its use in medicine—“that the air does contain these alleged low vital organisms” and that, as these organisms multiply in a wound, they cause infection⁹⁶³—as well as the actual therapeutic uses to which it had been applied. These included compound fractures, abscesses, wounds in general, and even “cancerous discharges.”⁹⁶⁴ Simpson quoted articles and letters by several physicians in France and Germany that asserted that carbolic acid had been used for these purposes for several years.⁹⁶⁵ This all went to show, in Simpson’s words, that “the great thought and attention which Dr. Lemaire has

⁹⁶⁰Simpson was fifty-six years old in the Autumn of 1867. Even the Lister-loving Godlee, writing in the twentieth century, acknowledged that “Simpson had many followers who looked upon him as almost inspired.” Godlee, *Lister*, 205: 203.

Simpson died less than three years later. Respect for the physician at the time of his death was so great that a holiday in Scotland (his birthplace and ancestral home) was declared on the day of his funeral and a bust in his memory placed in the hallowed halls of Westminster Abbey in London. Upon the announcement of his death, the *New York Medical Journal* wrote “There was probably no one in the [medical] profession more widely known and esteemed than Sir James Simpson.” *New York Medical Journal*, “Miscellaneous and Scientific Notes,” *New York Medical Journal* 11, no. 4 (1870): 441.

⁹⁶¹Simpson, “Carbolic Acid and Its Compounds in Surgery.”

⁹⁶²*Ibid.*, 546.

⁹⁶³*Ibid.*, 547.

⁹⁶⁴Jules Lemaire, *De l'acide phénique: de son action sur les végétaux, les animaux, les ferments, les venins, les virus, les miasmes et de ses applications à l'industrie, à l'hygiène, aux sciences anatomiques et à la thérapeutique* (Paris: Librairie de Germer-Baillière, 1865). This expanded and revised second edition may be found in its entirety—in the original French—at <http://books.google.com> accessed August 29, 2010.

Simpson’s review of the second edition of Lemaire’s work may be found at Simpson, “Carbolic Acid and Its Compounds in Surgery,” 547-8.

⁹⁶⁵“Carbolic Acid and Its Compounds in Surgery,” 548.

bestowed on the therapeutical action and applications of carbolic acid; in that respect, as well as in originality, leav[es] Prof. Lister very far behind him.”⁹⁶⁶

For reasons that I will demonstrate, Simpson’s diatribe against Lister fell, for all intents and purposes, on deaf ears. Lister, then a relative newcomer to medical and scientific fame, went on to become one of the most lauded Englishmen of the late nineteenth century. Indeed, to this day, he is one of the most recognized and admired figures in British history.⁹⁶⁷ Nonetheless, a prominent American physician of the early twentieth century did not agree that Lister deserved the honors he received – and he explicated his opposition to Lister’s claim to fame (while Lister was still alive) in the most prominent United States medical journal, the *Journal of the American Medical Association (JAMA)*.

A Generation Later:

Kelly Promotes Lemaire over Lister

Henceforth the name of Lemaire will be duly invested with that respect and honor which are accorded to the few whom we reckon great benefactors of the race.
—Howard A. Kelly, *JAMA* (1901)⁹⁶⁸

Simpson’s attack on the praise given Lister for his use of carbolic acid—despite its personal as well as professional nature—was not without merit. Thirty-four years later, long after Simpson’s death and Lister’s wrinkling face sprouted the long, white mutton chops that

⁹⁶⁶Ibid.

Further, as Simpson had criticized Semmelweis for failing to review the medical literature before advancing his methodology to prevent puerperal fever, so Simpson castigates Lister: “if Mr. Lister had taken the slightest trouble to search English medical literature alone [let alone the European literature—LK], he would easily have convinced himself of his own grave error in this respect...most, if not all, the medical and therapeutic journals of England have alluded...to the subject during the last six or seven years.” Then Simpson lists eight references followed by “&c. &c.” Ibid.

It should be evident that Simpson felt personal acrimony toward Lister, as will be explained below.

⁹⁶⁷See, for example <http://www.britainunlimited.com/Biogs/Lister.htm> accessed September 23, 2010.

⁹⁶⁸Kelly, “Jules Lemaire,” 1084.

characterized his later years,⁹⁶⁹ Dr. Howard Kelly (1858-1943), a renowned gynecologist and one of the four lions of medicine at the early Johns Hopkins (with Welch, Osler, and Halsted), published an article in the *JAMA* that history was all wrong in crowning Lister the “Father of Antisepsis.”⁹⁷⁰ Jules Lemaire, shouted Kelly in the title to his first-page article, was “The First to Recognize the True Nature of Wound Infection and Inflammation, and the First to Use Carbolic Acid in Medicine.”⁹⁷¹

Kelly did not simply state that Lemaire deserved priority over Lister for the therapeutic use of carbolic acid in wound and other infections. No, the distinguished woman’s doctor wrote a detailed book review of Lemaire’s 1865 second-edition work for a wide American and international audience. The essay was filled with quotations repeatedly proving Lemaire’s ascendant priority over Lister. If Simpson’s blast of the claim that Lister deserved priority for his use of carbolic acid was pointed and specific, Kelly’s was blunt and universal. “If our ancestors could but read the historical writings of their posterity,” pontificated Kelly, “I feel sure that many a bitter cry of injustice would be raised.”⁹⁷² The recognition accorded Lister over the barely-remembered Lemaire was one such wicked iniquity.

Kelly analyzed Lemaire’s scholarly output on carbolic acid from 1860 to 1865 (two or more years before Lister’s first publication on antisepsis) from beginning to end. He showed that Lemaire had anticipated Lister’s theory of why sepsis occurs as well as the utility of carbolic acid in the prevention—and treatment—of numerous infectious conditions. Thus, years before Lister’s first articles on antisepsis—and long before Lister used Pasteur’s findings on

⁹⁶⁹http://www.google.com/images?hl=&q=joseph+lister&sourceid=navclient-ff&rllz=1B3GGGL_en_US232&ie=UTF-8&biw=1400&bih=868 accessed September 15, 2010.

⁹⁷⁰Kelly, "Jules Lemaire."

⁹⁷¹Ibid.

⁹⁷²Ibid., 1083.

fermentation to explain the etiology of wound infections and the foundational explanation for the success of his own Antiseptic Principle—Kelly reminded his readers that Lemaire had already written that “The ferments of the air are living beings” that caused infection. Further, Lemaire’s use of carbolic acid in the treatment of these infections inspired him to formulate “a new theory as to the formation of pus,” viz., that pus was related to, if not caused by, the airborne microbes that infected the wound.

Even more prescient, Lemaire determined that carbolic acid (saponified by the French physician-chemist from coal-tar) afforded him the ability to “arrest and to reproduce at will the formation of pus.”⁹⁷³ This was a most powerful realization, foreshadowing the Koch-Henle postulates – used to prove a causal relationship between a microorganism and a disease – by almost two decades. And, following Lemaire’s analysis of the chemical properties of carbolic acid and its many uses, he envisioned that his *L’Acide Phénique* was a great boon to surgery, for “I urged all the advantages surgery would enjoy from this preparation.”⁹⁷⁴ In Kelly’s opinion, Lemaire, not Lister, deserved the greatest thanks of Earth’s humanity for the ability to prevent surgical infections.

So Why is Lister the “Father of Antisepsis”?

I now perform an operation for the removal of a tumour...with a totally different feeling from what I used to have; in fact, surgery is becoming a different thing altogether.
—Joseph Lister, Letter to his father, Oct 20th, 1867⁹⁷⁵

Before the days of antisepsis and anæsthesia the field of operation was greatly restricted, and practically the removal of tumors, amputations, and a few other operations were all that were done.

—W. W. Keen, 1905⁹⁷⁶

⁹⁷³Ibid., 1085.

⁹⁷⁴Ibid.

⁹⁷⁵Godlee, *Lister*, 205: 196.

Lister, not Lemaire, made the practice of surgery “a different thing altogether.”⁹⁷⁷ But how can this be, given the incontrovertible evidence presented by Simpson and Kelly that Jules Lemaire – years before Lister – recognized the chemistry of carbolic acid, the nature of “ferments” (infectious particles), the application of carbolic acid as an antiseptic to medicine and surgery, and stoked its widespread use on the Continent during the early 1860s. What counter could Lister’s supporters possibly offer to show that he, not Lemaire, deserved the honors conferred upon him as the “Father of Antisepsis”? And, on the contrary, if Lister’s denigrators were correct, how could Lister’s contemporaries and generations of medical historians have been so wrong?

Lister’s contemporaries and historians since his time were not wrong. Lister was the progenitor of antisepsis and antiseptic surgery. He does indeed warrant the honors bestowed upon him for the revolution that antisepsis created in surgery. Lemaire was surely ahead of his time with his emphasis on the chemical properties of carbolic acid and his explanation for why it worked to suppress infection.⁹⁷⁸ These achievements alone should place Lemaire in the pantheon of medical giants. But they do not give him claim to “Father of Antisepsis.”

Process as Principle

A new principle necessitating fundamental changes in surgical practice.
—Rickman John Godlee⁹⁷⁹

It was the principle and method of its application that were new.
—Joseph Lister⁹⁸⁰

⁹⁷⁶Keen, *Addresses*: 340.

⁹⁷⁷Godlee, *Lister*, 205: 196.

⁹⁷⁸Indeed, Lister and others later concluded that Lemaire had become too enamored with the properties of carbolic acid. He claimed, for example, that carbolic acid “cures cancers...with a few touches with an *extremely* weak watery solution of the acid.” *Ibid.*, 205. Italics in the original.

⁹⁷⁹*Ibid.*, 197.

Lister deservedly received recognition over Lemaire for establishing the foundations of antiseptic surgery. This was due to the Englishman's methodology by which he achieved antiseptis and the revolution it engendered in the practice of surgery – not because of the antiseptic he used.

To some extent the conflicting claims between the Lemaireans and the Listerians must be adjudicated on the basis of the definition of “antiseptis.” If antiseptis is the application of a chemical disinfectant to prevent infection, then Lemaire's use of carbolic acid to attain antiseptis unquestionably preceded that of Lister. But, if antiseptis is a process – a series of steps that constitute a generally applicable method for the prevention of infection – then Lister's fame is justified. In the decades between the work of Lemaire and Lister in the 1860's and the early twenty-first century, antiseptis has been thought of as a process and thus rather more than the chemical antiseptic itself.

Lister invented a course of action intended to prevent surgical infections. He never asserted priority for the discovery of carbolic acid; nor to have been the first to use that chemical for antiseptic purposes; nor to have been the earliest to recognize that the air contained “floating particles” that could infect wounds. In a letter to *The Lancet* dated October 5, 1867, Lister clarified what he had and had not contributed to the practice of surgery:

I never claimed to have been the first to use carbolic acid in surgery. The success which has attended its employment here depends not so much on any specific virtue in it [carbolic acid—LK], as on the wonderful powers of recovery possessed by injured parts when efficiently protected against the pernicious influence of decomposition. I selected carbolic acid as the most powerful of known antiseptics; but I think it not unlikely that my object might have been gained by using, on the same principle, some familiar ‘disinfectant’ ...it is only by the light of sound pathology, and strict attention to practical details, that they [surgeons—LK] can hope to attain in their full measure the magnificent results which the antiseptic treatment is capable of affording.⁹⁸¹

⁹⁸⁰Letter from Joseph Lister to his father dated October 13, 1867, reproduced in *ibid.*, 203-05. The quotation is on page 204.

In fact, Lister did not even know of the work of Lemaire – nor even Lemaire himself – until he read the condemnatory writings of Simpson in *The Lancet* in late 1867.⁹⁸² But if or when Lister knew of Lemaire’s use of carbolic acid as an antiseptic before the Englishman’s implementation of the Antiseptic Principle is of no matter, because it is indisputable that Lemaire and the town of Carlisle used the chemical prior to Lister. But carbolic acid and antiseptics are not the same, and historians and physicians sometimes confound the two as one confuses the part for the whole. Carbolic acid was one of the first surgical antiseptics used in the modern era, but it was only one. Lister’s use of an interdisciplinary knowledge exchange was key. The principle of the process of antiseptics transcended the antiseptic.

Thus, carbolic acid was important, but it was the Antiseptic Principle, not the actual chemical used for antiseptics, that mattered most. (How different this was from anesthesia, at least in its early years, when Morton’s Letheon was thought to be both the chemical and the embodiment of anesthesia. Only over the ensuing decades following Morton’s initial use of ether did physicians realize that the process by which the anesthetic was administered was at least as important as the anesthetic itself.⁹⁸³) It is likely that other agents or, as Lister wrote, “some familiar ‘disinfectant’,” applied with Lister’s Anesthetic Principle in mind, would have performed with equal success.

Surgery Before Lister

1814

⁹⁸¹Letter from Lister to *The Lancet*, dated October 5, 1867, and reproduced in *ibid.*, 200-01.

⁹⁸²*Ibid.*, 200.

⁹⁸³Excellent insights into the evolution of anesthesia from ether to something much more may be found in Pernick, *A calculus of suffering : pain, professionalism, and anesthesia in nineteenth-century America*.

In order to understand the changes that Lister brought to surgical practice, it is imperative to visualize the actual practice of surgery before Lister.

The day is September 14, 1814. Dawn's early light had just broken over the ramparts of Fort McHenry, the guardian of Baltimore's vibrant harbor. The day and night before, the British invaders, fresh off their incendiary victory in nearby Washington, D. C., had bombarded the Fort relentlessly until about 4 AM. Inside, Major George Armistead tried to maintain order in the midst of chaos. Although the British had inflicted little overall damage on the Fort itself, enough cannonballs had scored direct hits to injure several of its occupants. One of those maimed was William Williams, a Maryland slave who had escaped from his master to join the United States Army. The twenty-one year old's leg was "blown off by a cannonball."⁹⁸⁴ The surgical practice of the time was to remove any loose tissue attached to (or hanging from) the injury with all deliberate speed and then bind up the open wound in rags using alcohol as an anesthetic and then prayer as much poultice to prevent a wound infection. The medic typically utilized these time-honored measures in an open space – such as on the battlefield or inner courtyard of a fort – or other non-sterile environment. Any instruments employed, such as a saw, would be used by the surgeon on one patient after another without washing or cleaning the saw – let alone sterilizing it.

Speed and the stanch of bleeding were the operative objectives of the day. The patient's pain and risk of infection were of less concern to the surgeon than the quickest repair of the acute trauma. Little or no thought was given to the prevention of wound infection because none of the interventions mentioned above (washing, poultices) succeeded with any reliability. Germs and

⁹⁸⁴<http://www.nps.gov/fomc/historyculture/william-williams.htm> accessed October 10, 2010.

floating ferments were in the minds of few at the time and, likely, no one in or around Fort McHenry had ever heard of them.⁹⁸⁵

Williams survived the acute trauma of the cannonball and was evacuated to the Baltimore Hospital. He died two months later, most likely from recurrent infections leading to sepsis.⁹⁸⁶

1840s

The 1840s witnessed the introduction of anesthesia – in the modern sense of the term (rather than alcohol and mandrake) – into theaters of war as well as civilian life. The first wartime use of anesthesia occurred during the Mexican War.⁹⁸⁷ Nevertheless, it was not until the American Civil War that surgical anesthesia became the norm rather than the exception – at least when a supply of chloroform or ether could be found on the battlefield.⁹⁸⁸

But surgical anesthesia, as we have seen, did not make surgery safe. Surviving a surgical operation may have won the battle, but only postoperative survival without infection won the war against the four horsemen of death. Warnings by Oliver Wendell Holmes and Ignaz Semmelweis that a physician take care for the cleanliness of his own hands and instruments when treating a woman in labor went unconnected and unapplied to men undergoing surgery on the battlefield.

⁹⁸⁵ Although the *Oxford English Dictionary* lists 1803 as the first known date for the use of the word “germ” as a “seed” of disease, I have rarely encountered the term with this meaning until the second half of the nineteenth century.

⁹⁸⁶ <http://www.nps.gov/fomc/historyculture/william-williams.htm> accessed October 10, 2010.

⁹⁸⁷ Douglas V. Meed, *Essential Histories: The Mexican War 1846-1848* (Oxford: Osprey Publishing Ltd., 2003; repr., 2005). 58.

⁹⁸⁸ <http://www.collectmedicalantiques.com/civilwar.html> accessed October 10, 2010. The explosiveness of ether often led to the use of ether by day and chloroform by night – to minimize the risk of igniting ether with the flame of the candle. The substitute for absent ether and chloroform was, literally, to bite the bullet. Ibid.

1862

In the autumn of 1862, Dr. William W. Keen had just received his medical degree from Jefferson Medical College. He then returned to the Civil War battlefield hospital outside Washington, D. C. where he had worked before he completed medical school.⁹⁸⁹ At that time, nearly twenty years after Holmes and Semmelweis advocated hand washing to prevent puerperal fever, the only reason for Keen or any other battlefield surgeon to wash his hands was to remove the encrusted blood, dirt, and grime after a long day of endless amputations. Surgeons also unknowingly increased the patient's risk of infection by inviting onlookers to "take a feel" inside the wound for teaching purposes.⁹⁹⁰ No wonder the mortality rate after amputation was greater than fifty percent and, when the amputation was higher up on the thigh, over ninety percent!⁹⁹¹

Thus operators, well into the second half of the nineteenth century, used instruments coated with the effluvia and excrement of previous surgical patients with nary a wipe of the sharp blade or handled saw. In fact, some surgeons sharpened their instruments on the soles of their muddied boots before reusing them.⁹⁹² Operators tied off bleeding vessels with silk threads wound around the buttons of the blood-stained coats they had recently worn for days and night on end. The operative area, such as it was, could be anything from the inside of a well-worn tent with mud floors covered with feces, urine, blood, pus, and expectorated phlegm to a slab of wood in the great outdoors used only moments before for a postmortem examination.⁹⁹³

⁹⁸⁹Keen, "Before Lister."

⁹⁹⁰<http://www.medscape.com/viewarticle/503947> accessed October 10, 2010.

⁹⁹¹Keen, "Before Lister," 851.

⁹⁹²James L. Stone, "America's Pioneer Neurological Surgeon," *Neurosurgery* 17, no. 6 (1985): 997.

⁹⁹³Ibid.



Figure 9. Civil War Surgery⁹⁹⁴

And then came Lister.

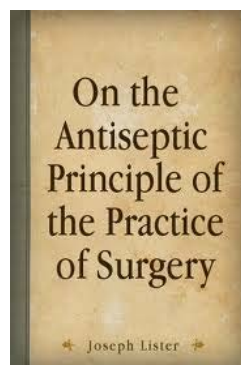


Figure 10. Book cover of Lister's *Antiseptic Principle*

⁹⁹⁴The photograph is from http://www.civil-war.net/cw_images/files/images/036.jpg accessed October 10, 2010.

The essential object is to guard against the introduction of living particles from without.

—Lister (1867)⁹⁹⁵

What, exactly, was Lister's antiseptic process? By what method did he significantly reduce the risk of developing wound infections as a consequence of surgery? Initially, Lister's technique was little more than that used by surgeons for centuries, viz., the application of a chemical to a bandage placed atop a wound. This was undoubtedly the procedure he used on James Greenlees, the eleven-year-old boy Lister named as Case I in his seminal 1867 paper. Lister instructed his assistant to lay "a piece of lint dipped in liquid carbolic acid upon the wound" for several days.⁹⁹⁶ That, however, was not the end of Lister's efforts to prevent post-operative infection in the boy, for he also had the foresight to otherwise close off James' wound to further exposure to ambient air. But the carbolic acid itself became a problem because its causticity irritated the boy's skin. As a result, Lister decreased the concentration of carbolic acid applied to the wound – a very important procedural change.⁹⁹⁷ The more dilute form of carbolic acid worked well. A good scar formed and the boy recovered without sepsis.⁹⁹⁸

Lister apparently realized shortly thereafter that Louis Pasteur's experimental findings had direct applicability to his own efforts to prevent wound infections. Most physicians and scientists prior to Pasteur's discoveries of the nature and consequences of the "floating particles"

⁹⁹⁵Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 32.

⁹⁹⁶*Ibid.*, 4.

⁹⁹⁷The concentration of the carbolic acid—or any antiseptic—is critical when applied to the living organism. Lister probably experimented more with the concentration of carbolic acid as an antiseptic than he did with different antiseptics.

Anyone who drinks alcohol, for example, rapidly learns that its effects are related to its concentration (designated as "proof") as well as the volume imbibed. These are basic principles of pharmacology that Lister early and importantly applied to his use of carbolic acid as an antiseptic. Although concentration and volume concerns were certainly not unique to Lister, they played an important role in his Antiseptic Principle.

⁹⁹⁸Lister's own description of this process may be found at Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 4-5.

believed that sepsis followed exposure to oxygen – a ubiquitous constituent of air.⁹⁹⁹ Attempts to exclude all air from a wound were not successful.¹⁰⁰⁰ Pasteur’s experiments pointed in another direction – that the cause of infection was microbes suspended in the air. As Lister wrote:

But when it had been shown by the researches of Pasteur that the septic property of the atmosphere depended, not on the oxygen or any gaseous constituent, but on minute organisms suspended in it...it occurred to me that decomposition in the injured part might be avoided without excluding the air, by applying as a dressing some material capable of destroying the life of the floating particles.¹⁰⁰¹

As a result, Lister immediately shifted his efforts from the exclusion of air from the wound to the killing of the infectious particles that had alit on the wound after floating in the air via chemical-soaked bandages. Lister carried this anti-sepsis further by seeking to rid the hands of the operators and attendants of these invisible threats. Note that the methods used by Oliver Wendell Holmes and Ignaz Semmelweis for the prevention of puerperal fever sought to achieve the same goal, but these physicians had much less understanding of why their methods worked and therefore had little ability to apply their prophylaxes generally. From early in his development of antiseptics, Lister knew why he sought to keep the wound “clean.”

Listerism

⁹⁹⁹Antoine Lavoisier, who is credited with the discovery of oxygen (1778), recognized that oxygen was a component of air. Shortly after his production of oxygen from mercuric oxide, he noted in his journal that “The feeling of it (pure oxygen—LK) to my lungs was not sensibly different from that of common air.” <http://oxygen.darkillusions.org/history2.htm> accessed December 6, 2010.

¹⁰⁰⁰It is best that such attempts to create an air-free zone around the wound were not successful. Had Lister or anyone else been successful in completely eliminating air from the wound, s/he may have created a wound environment that would have selected anaerobic bacteria – bacteria that thrive in an oxygen-free environment (like *Clostridium tetanii*, the cause of tetanus) – thereby leading to a different but potentially deadly wound infection.

¹⁰⁰¹Joseph Lister, “On the Antiseptic Principle in the Practice of Surgery,” A paper read before the British Medical Association in Dublin on August 9, 1867; published in the *British Medical Journal*, 1867, vol. ii, p. 246 and reproduced in Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 37-45. The quotation is on page 37.

Listerism is the “system” of antiseptic surgery developed by Joseph Lister. It is the term most frequently used to convey the techniques he employed before, during, and after surgery to achieve antiseptis. The first known use of the term is ascribed to MacCormac in 1880, but the process originated years earlier when Lister began to use an antiseptic spray during surgery in addition to his antiseptic-soaked wound bandages.¹⁰⁰²

Lister’s earliest insights into antiseptis came before his cognitive link between microbes and infections. Even after he gained this knowledge, courtesy of Pasteur, Lister could not see or otherwise easily observe the microbes he sought to bar from entering and infecting the wounds of his patients.¹⁰⁰³ Thus, his *modus operandi* became the application of carbolic acid to anything and everything that had or could have contact with the patient—operators, attendants, and more.

Lister required that the hands of all those who would touch the patient (surgeons and attendants) be washed in a 1:20 (5%) solution of carbolic acid (one part pure carbolic acid to twenty parts water). He insisted that all sutures, ligatures, and instruments also be immersed in a freshly-mixed carbolic acid solution for several minutes prior to use. In addition, the skin of the operative area and the wound were bathed in the same carbolic acid solution.¹⁰⁰⁴ Nurses wiped furniture stands and tables in the operative room with the same solution. Lister admonished all present to take care not to touch anything extraneous to the patient during the procedure, so as

¹⁰⁰²*Oxford English Dictionary* online, Second Edition, 1989, “Listerism.”

¹⁰⁰³Following the general adoption of germ theories of infection in the last years of the nineteenth century, a surgeon could have “seen” the microbes in a wound by “culturing” the wound (i.e., obtaining a sample of the wound by “swabbing” it with sterile cotton-wool on a small wooden stick—like a Q-tip—and then allowing microbes to grow into visible “colonies” to determine which organisms appear on growth-stimulating plates of nutrient agar). However, this is a labor-intensive process that requires about forty-eight (48) hours to learn which microbes are present. Thus, wound “cultures” were not a practical method to “see or otherwise easily observe” infectious microbes at the time of surgery.

¹⁰⁰⁴J. T. Maclachlan, “Lister’s Antiseptic Technique,” *British Medical Journal* ii, no. 4267 (1942): 466.

not to contaminate their previously-cleaned hands. If they did, they were required to wash thoroughly again “through three solutions” of carbolic acid.¹⁰⁰⁵

Lister’s Carbolic Acid Spray



Figure 11. Lister and his Carbolic Acid Spray¹⁰⁰⁶

In 1869, Lister added the use of a carbolic acid spray to his antiseptic system that already included the soaking of hands, sutures, and instruments in the diluted carbolic acid solution. As pictured above, Lister generated the spray by means of a flame that heated the liquid carbolic acid into a vapor. A hand-driven pump then dispersed the vapor all over the operative field.¹⁰⁰⁷

¹⁰⁰⁵Charles A. Webster, "Changing surgery," *Nova Scotia Medical Bulletin* 12, no. 5 (1933). as reported by Ian A. Cameron, *Canadian Family Physician* 2008 (Nov); 54 (11): 1579-1580.

¹⁰⁰⁶Image reproduced from <http://www.chemistryexplained.com/Kr-Ma/Lister-Joseph.html> accessed October 10, 2010.

¹⁰⁰⁷Lister determined that the concentration of the carbolic acid necessary for antiseptics against airborne particles could be half that of skin-applied carbolic acid, so he used a 1:40 solution to produce the vapor. This was likely Lister’s recognition that the concentration of airborne bacteria was much less than that of bacteria on the skin or wound. Thus, bacteria in the air could be killed with a less concentrated solution of the antiseptic. For Lister’s use of the 1:40 solution, see Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 206.

The spray was a direct attempt to kill airborne pathologic microbes before they could infect the surgical wound.

Lister called this an improvement “in the details of antiseptic surgery,” but it was, in the final analysis, an implicit recognition of Pasteur’s discovery that living “floating particles” could have a dreaded effect upon surgical wounds.

The Proof is in the Results -- Lister's Achievement

The effect of Lister’s antiseptic system on surgical outcomes was nothing short of stupendous. It is difficult to assess the exact contribution of the late-added spray to Lister’s armamentarium against wound infections, but the total onslaught was highly effective. Although Lister’s earliest papers on the prevention of wound infection were patient case studies that were more qualitative than quantitative (rather than cumulative quantitative results based upon his total cohort of amputees), he did present some numerical data in a study published in the *Lancet* in 1870.¹⁰⁰⁸

In the *Lancet* article, he compiled year-by-year comparisons of the number of his amputee patients who died or recovered from their surgeries both before and after the institution of his antiseptic system. In 1864, before his antiseptics, Lister recorded 17 amputations, of whom 10 recovered and 7 died, for a mortality rate of 41%.¹⁰⁰⁹ In 1866, the year before he began his system, there were 18 amputations, of whom 9 died, for a mortality rate of 50%.¹⁰¹⁰ Combining

¹⁰⁰⁸Joseph Lister, "On the Effects of the Antiseptic System of Treatment Upon the Salubrity of a Surgical Hospital," *Lancet* i, no. 2418 (1870). and *ibid.* This paper is also anthologized in *The Collected Papers of Joseph Lister*, pages 123-136, which I will use as my source hereafter.

¹⁰⁰⁹Lister, *The Collected Papers of Joseph, Baron Lister*, 2: 128.

¹⁰¹⁰*Ibid.* Lister noted that “the hospital rates are unfortunately imperfect” for 1866, thus explaining their absence from the paper. *Ibid.*

Although Lister included all amputations—from the shoulder to the ankle—he did realize that amputations of different limbs have different probabilities of causing death. *Ibid.*, 129. Upper limb amputations cause death from hemorrhage less frequently than lower limb amputations, so death related to upper limb amputation is more

the data from the two years before what he termed “the Antiseptic Period,” gives a total mortality rate of 46% (16/35). These percentages were typical of the pre-antiseptic era.

After the application of his antiseptic system in 1867, Lister noted mortality rates among his amputees of 0% for 1867, 18% for 1868, and 19% for 1869. The overall mortality rate for the first three years of the Antiseptic Period was 15% (6/40).¹⁰¹¹

Modern publications often noted that Lister reduced the post-amputation mortality rate by two-thirds, from 45% to 15%.¹⁰¹² These results may pale in comparison to Semmelweis’ reduction of deaths related to puerperal fever to less than 4%, but amputations, by the very nature of the fact that they expose subcutaneous tissues and their rich circulation, are more prone to wound infection than the “interior” cervix and uterus.¹⁰¹³ Given the two very different contexts, Lister’s reduction of the post-amputation surgical mortality rate bordered on the miraculous.

Against the Antiseptic System

Initially, Listerism was more condemned than revered. In practice, few surgeons could or would follow the disciplined, meticulous antiseptic program espoused by Lister. There were some who attempted to reproduce his results, but few succeeded. Those who failed blamed Lister for their failure rather than themselves. Interestingly, surgeons geographically closest to Lister tended to be his harshest and most vociferous critics. Most likely, this criticism stemmed

likely to be caused by pyemia/sepsis than that of lower limb amputation. My review of Lister’s data reveals that the number of amputations of upper versus lower limbs did not differ before and after the introduction of his antiseptic system, thus validating (albeit with small numbers) a comparison of the mortality rates of the two periods.

¹⁰¹¹Ibid. The absence of deaths in 1867 may well have been due to a tiny number of patients (7) receiving extraordinary attention, rather than an increase in the mortality rate over the first three years of Lister’s antiseptic program. Seventeen patients underwent amputations in 1868, and 16 in 1869.

¹⁰¹²Miller, Rahimi, and Lee, "History of infection control and its contributions to the development and success of brain tumor operations," 3.

¹⁰¹³See page 178 above for Semmelweis’ reduction in the mortality rate from puerperal fever.

from the threat Lister posed to their long-entrenched practices of surgery, but it is impossible to be certain.

Nonetheless, the reason most frequently offered by historians for other surgeons' inability to replicate Lister's striking reductions in wound infections was the failure of the surgeons to accept Lister's underlying conceptualization of the reason for the success of his antiseptic program; viz., germ theory. One eminent British professor of surgery quipped, "Where are these little beasts? Show them to us and we shall believe in them. Has anyone seen them yet?"¹⁰¹⁴ His skepticism was hardly unique. Many surgeons in Scotland, England, and, to a significantly lesser extent on the Continent, found Lister's reports of excellent outcomes not credible.

Focusing on the microbiota rather than the technique of the Antiseptic System, however, caused incredulous British and American surgeons to confuse cause with solution. During the late 1860s and early 1870s, physicians at the Massachusetts General Hospital (MGH), long a Harvard affiliate and, in the mid-to-late nineteenth century located immediately next to Harvard Medical School, warned the young J. Collins Warren (1842-1927) not to apply Lister's antiseptic technique to his surgeries because the "treatment had already been tried and discarded."¹⁰¹⁵ Further, as Ira Rutkow wrote, "The older generation would never fully accept Listerism."¹⁰¹⁶ Much to his credit, the young Warren did not heed the advice of his mentors.¹⁰¹⁷ For the

¹⁰¹⁴ <http://www.dynamicscience.com.au/tester/solutions/war/medicine/lister.htm> accessed February 10, 2011.

¹⁰¹⁵ Quoted by Ira Rutkow, *Seeking the Cure: A History of Medicine in America* (New York: Scribner, 2010). 70. from Edward D. Churchill, ed. *To Work in the Vineyard of Surgery: The Reminiscences of J. Collins Warren (1842-1927)* (Cambridge, MA: Harvard University Press, 1958), 138, 46.

¹⁰¹⁶ Rutkow, *Seeking the Cure*: 70.

¹⁰¹⁷ J. Collins Warren, who admired Lister greatly. John Collins Warren, "I Talked with Lister," in *To Work in the Vineyard of Surgery: The Reminiscences of J. Collins Warren (1842-1927)*, ed. Edward D. Churchill (Cambridge, MA: Harvard University Press, 1958), did not follow his elders' proscription and went on to successfully use Lister's techniques to the advantage of his many surgical patients. Also see an Editorial in the

majority of physicians on both sides of the Atlantic at this time, however, inability to accept the theory, practice, and reported results of Listerism forestalled the widespread acceptance of Lister's program.

On the other hand, there were some surgeons like the American Warren who did accept Lister's technique without an explanation of why it worked. Among them were William W. Keen (1837-1932) in Philadelphia and Ernst von Bergmann (1836-1907) in Germany, the same physician who attended Prince Friedrich with Morrell Mackenzie. But others required proof of the existence of infection-causing germs or some other biomechanistic explanation before they would adopt as radical a surgical program as Listerism. In the intervening years, mirroring the years of rejection of Semmelweis' life-saving hand washing, many patients needlessly died.

Asepsis

Surgeons who did not feel the need to have scientific proof that germs caused disease were often early adopters of Lister's empirically-derived Antiseptic System. Younger Germans physicians like von Bergmann, in particular, seemed to accept Listerism because it worked. Why it worked seemed less important. They soon found that their clinical results paralleled those of Lister.

Like the latticework crystal growing in a mineral medium or the development of a multi-limbed tree, it was not long before the idea of antiseptis founded on the principles of Lister's system spread to engender a myriad of new methods to prevent post-operative infections.

Some German physicians who were early adopters of Listerism took the prevention of surgical infections in the direction of a higher degree of antiseptis. They reasoned that if

Atlantic Monthly on "Science" [32 (1873): 760] and a further discussion of J. Collins Warren and (his admiration for) Listerism at Churchill, *J. Collins Warren*, 138 and 46ff.

The rejection or adoption of Listerism by old and young physicians, respectively, is, in general terms, a good example of inter-generational friction as a model for evolution in biological and medical thinking.

antisepsis – the elimination of pathogenic bacteria from infection-prone tissue surfaces – reduced the probability of post-operative infections, could not the elimination of all disease-causing organisms – asepsis – reduce the risk even more? In fact, could sterility – the total absence of all living organisms from a surgical field or instrument – totally eliminate the risk; i.e., reduce the probability of postoperative infection to zero?¹⁰¹⁸ But was the idea of sterility an impossible dream? Physicians and surgeons in the final years of the nineteenth century sought to find out.

It should be noted that although the roots of antisepsis and asepsis appear to grow from the last decades of the nineteenth century, the concepts of antisepsis and asepsis arose much earlier. In reality, Lister “merely” gave the concept of antisepsis (and its derivative, asepsis) renewed meaning. More than two millennia earlier, Hippocrates’ application of wine to wounds and their bandages can be interpreted as attempts to completely eliminate the causative agent(s) of suppuration, whether caused by internal humoral imbalances or some externality.¹⁰¹⁹ Similarly, Semmelweis’ handwashing sought to forestall post-delivery infection by totally eliminating its cause. Listerism was the prime mover for a paradigm shift in the prevention of wound infections and, in consequence, the performance of operations for cancer that could previously only be dreamed of in the mind of the operator. Indeed, Lister might have taken antisepsis toward asepsis himself had results from his antiseptic technique not been so excellent – and the accolades he received for his System years later not been so effusive.¹⁰²⁰

¹⁰¹⁸This was an intriguing question because the answer could point to the proof or disproof of the concept that germs were the sole cause of infection. (The answer, discovered many years later, was No – infection required host (e.g., human) susceptibility as well as inciting germs.)

¹⁰¹⁹I would argue that Hippocrates’ wine was more an attempt at antisepsis than asepsis, but treatises on asepsis include it in their chronologies. Typical is this sentence from “Infection, Asepsis, and Sterile Techniques”: “Hippocrates (460-377 BC), the great healer of his time irrigated wounds with wine or boiled water foreshadowing asepsis.” http://www.medtrng.com/blackboard/infection_asepsis.htm accessed October 10, 2011.

Lawson Tait – The Difficult but Scrupulously Clean Scot

Although German physicians may have implemented aseptic techniques not long after Lister began to promulgate his aerosolized and bandage-soaked approach to antisepsis, it was a Scottish surgeon, Lawson Tait (1845-1899), who deserves credit for the initial development of modern aseptic technique. Like J. Marion Sims before him, whose contributions to cancer medicine became overshadowed by his achievements in other areas of surgery, Tait is often remembered more for his contributions to what would today be considered gynecologic surgery than for his efforts to rid the operative field of microbial life.¹⁰²¹

The gynecologic focus of so many of our antimicrobial protagonists should not be surprising, because the gateway of the vagina leads too readily – and with too few obstacles – to the sterile, inner compartments of the body.¹⁰²² Thus, the female reproductive tract represents an apparent compromise between easy access of sperm to egg and too-easy access of pathogenic microbes to vulnerable, sterile internal tissues. The ever-present potential and high risk for gynecologic infection spotlighted the need for antimicrobial measures in reproductive organs to physicians like Holmes, Semmelweis, and Tait.¹⁰²³

¹⁰²⁰“Success breeds contentment,” although it is difficult to imagine that a personality filled with Lister’s intellectual vigor could ever reach full contentment!

¹⁰²¹Depending upon the source (especially the nationality of the writer), Sims and Tait have each been deemed “the father of gynecology.”

Tait is best known for initiating salpingectomy, starting around 1883, as the treatment of choice for an ectopic pregnancy; i.e., removing the Fallopian tube in which the extra-uterine pregnancy is growing before it bursts into the sterile space in the pelvis with potentially fatal consequences. But he was also so widely appreciated for his removal of diseased Fallopian tubes (such as for “P.I.D.,” short for Pelvic Inflammatory Disease) that the operation became known as “Tait’s operation.” Anna Greenwood, “Lawson Tait and Opposition to Germ Theory: Defining Science in Surgical Practice,” *Journal of the History of Medicine and Allied Sciences* 53(1998): 104 Note 18. In 1879, he also performed the third-recorded cholecystectomy (removal of the gall bladder), an example of the non-specialization (gynecologic versus abdominal surgery) of surgeons at the time.

¹⁰²²The reproductive organs – male and female – have numerous deterrents to infection from external microbial sources (chemical barriers like an acidic vaginal pH; physical barriers like the cervix; an immune system primed to attack foreign organisms), but relative to the barriers of other natural entries into the body (mouth, nose, ears, anus), these obstacles are weak and easily overcome by ill-placed fingers teeming with invisible bacteria.

Lawson Tait, however, believed in neither Listerism, nor Lister, nor his germ theory. His opposition to both is famous and has been reiterated numerous times by many authors.¹⁰²⁴ And, to those who did believe in germs and Listerism, he was not shy about making his beliefs known to multitudes of physicians in the British Isles as well as on the Continent. Tait, obstreperous in demeanor and adamant in his beliefs, published his anti-Listerism far and wide, “all the more so,” wrote Greenwood, “as it [germ theory] seemed to him absolutely preposterous.”¹⁰²⁵

Tait, despite his condemnation of germ theory, strongly – even fiercely – adhered to the idea of a clean surgical field. Whether his advocacy of cleanliness through sanitation and hygiene stemmed from a sense of Victorian order is not known for certain, but his goal was indisputable. In 1882, Tait wrote that “Medicine is powerless for the cure of zymotics,¹⁰²⁶ whilst hygiene is all powerful in their prevention, and the medicine of the future lies wholly in this direction. Drugs are impotent, but sanitary laws can and will banish all these diseases.”¹⁰²⁷ Despite this visionary postulation, Tait could not link hygiene and germs.¹⁰²⁸ Thus, he rejected Listerism and the idea that invisible “viruses” caused disease.¹⁰²⁹

¹⁰²³In this regard, Lister’s antiseptic take-off from compound fractures rather than infections of the female reproductive tract to antiseptic is something of an anomaly, but the enormous risks that the punctured skin of the compound fracture posed for post-amputation sepsis and death make his different starting point understandable.

¹⁰²⁴Excellent examples are John Scott Shepherd, *Lawson Tait: The Rebellious Surgeon (1845-1899)* (Lawrence, Kansas: Coronado Press, 1980). and a laudatory essay Greenwood, “Lawson Tait and Opposition to Germ Theory: Defining Science in Surgical Practice.”

¹⁰²⁵“Lawson Tait and Opposition to Germ Theory: Defining Science in Surgical Practice,” 106. Anna Greenwood wrote that Tait’s personal writings may have been destroyed after he died. *Ibid.* Nevertheless, Tait published frequently in the British medical literature of the day (especially *The Lancet* and the *British Medical Journal*) and broadcast his views through these widely-read and respected journals.

¹⁰²⁶Zymotics was a term commonly used in the nineteenth century to describe various infectious conditions that created the appearance of fermentation in the diseased. The term is derived from the Greek for “ferment.” Only through presentist eyeglasses would the historian view zymosis as the precursor of germ theory, but it is easy to see how this could occur.

¹⁰²⁷Lawson Tait, *Birmingham Philosophical Society Transactions* 3(1882). as quoted by Greenwood, “Lawson Tait and Opposition to Germ Theory: Defining Science in Surgical Practice,” 104.

In fact, cleanliness and germs were not clearly linked in general before the end of the nineteenth century, so it is not surprising that Tait could seek one without trying to eradicate the other. Rather, he sought cleanliness through a thorough analysis of all the different elements of the operating suite -- highly reminiscent of Semmelweis and Lister. One by one he mandated that they be “clean.” Surgeons, their garments, instruments, sponges, and dressings all had to be unsoiled through washing, scrubbing, and even boiling.¹⁰³⁰

Around 1880, Dr. Lawson Tait had turned away from Lister’s antiseptic method towards asepsis. Instead of application of Lister’s carbolic acid to the surface of the skin at the site of the operation, Tait replaced this with thorough cleansing of the site of the wound with soap and water; instead of Lister’s method of soaking the hands in carbolic acid, Tait paid attention to his own preparations - washing his hands with soap and hot water, and scrubbing his nails with a brush; instead of, as Lister had done, merely removing his jacket and pinning an unsterilized towel to his waistcoat, Tait wore a large, clean Mackintosh; instead of Lister’s method of a constant supply of carbolic-soaked towels and spraying carbolic acid around the operating theatre, the wounds and the surgical instrument, Tait used clean towels, and cleaned the area he was operating on, and used clean, washed instruments; instead of treating sponges with carbolic acid to mop up blood and fluids, Tait used a solution of washing soda; instead of using Lister’s carbolised catgut sutures, Tait used silk - which had been sterilized by boiling; instead of Lister’s carbolised dressings which were applied after the operation, Tait relied on clean, dry dressings.¹⁰³¹

Although far from sterile, Tait’s result was probably the closest approximation to a microbe-free operative environment achieved to that time. But Tait did not apply his cleanliness methodology to surgical procedures alone. He considered the entire hospital in need of a good scrubbing and admonished hospitals to apply his sanitary principles wherever sickness festered.

¹⁰²⁸To a large extent, Tait’s vision of sanitary nirvana as the height of disease prevention is more reactionary than forward-looking. Sanitation had ruled the halls of medicine (if not its hospitals) for decades. Germ theory was the newer concept at the time when he wrote those words in 1882.

¹⁰²⁹Before the actual visualization of viruses in the twentieth century, the term “virus” was truer to its Latin etymological roots as a poison or other noxious substance. Thus, “virus” could and often did imply a lifeless irritant or other substance.

¹⁰³⁰Anna Greenwood quotes Tait as rejecting the idea that he used boiled water, but others dispute this. See Greenwood, “Lawson Tait and Opposition to Germ Theory: Defining Science in Surgical Practice,” 104 FN16. and Shepherd, *Lawson Tait: The Rebellious Surgeon (1845-1899)*: 106ff.

¹⁰³¹*Lawson Tait: The Rebellious Surgeon (1845-1899)*: 106.

In an 1877 essay, he wrote that cleanliness inside the hospital was the key to reducing in-hospital mortality.¹⁰³²

The ability to prevent infection and sepsis, be it in the operating suite or inside the hospital in general, depended upon cleanliness. And cleanliness became dependent upon the washing and/or boiling of each element of the hospital room or the operative suite even before the patient was admitted to the ward or the surgeon made his first incision. This was the birth of modern asepsis.

Cleaner and Cleaner – Sterilization and Asepsis

How, precisely, could “cleanliness” to be achieved? As the notion that germs were unclean gradually gained acceptance, operators used heat sterilization, the process by which heat from a fire or other source killed all organisms on a surface, more and more. Such a technique was known to the Ancients, but it was not until the early nineteenth century that heat became an energy of choice to kill unwanted organisms. Food could be boiled, broiled, or, in general, cooked. This man had learned to do to reduce the risk of ill health through trial and error over millennia.¹⁰³³ But food was the exception. One could not heat or boil drapes, furniture, or the hands of a surgeon in the quest for sterility. Instead, “cleaning” methods other than fire (such as chemicals) had to be devised, and these would have to be specific to the properties of different materials.

¹⁰³²Lawson Tait, *An Essay on Hospital Mortality, Based upon the Statistics of the Hospitals of Great Britain for Fifteen Years* (London 1877), Tait *An Essay on Hospital Mortality, Based upon the Statistics of the Hospitals of Great Britain for Fifteen Years* (London: publisher unknown, 1877) as referenced by Greenwood, "Lawson Tait and Opposition to Germ Theory: Defining Science in Surgical Practice," 106 FN22.

¹⁰³³Around 1809, Nicolas Appert (1749-1841) was awarded a prize by the government of France for devising a method of preserving food by enclosing vegetables and fruits in glass jars and then heating the jars. This sterilization technique was invented decades before Louis Pasteur heated wine, milk, and other substances to increase their edible longevity (i.e., Pasteurization). Irini Soulatou, "A Short History of the Old Trip of Sterilization," Slide presentation, http://www.wfhs.com/html/educ/articles/educarticle_0012_en.pdf . .

Surgical instruments, prime targets for cleaning, prior to the last decades of the nineteenth century had not changed dramatically in shape, size, or composition from Ancient times (see photograph on page 686). Only some of these tools could be heated to achieve sterility. By the last three decades of the century, however, surgical instruments had become much more standardized and were routinely made of metal (e.g., steel) that could be heated without melting.¹⁰³⁴ Thus, by the 1870s and later, surgical instruments could be treated by fire – or, in more sophisticated settings, heat. Indeed, the treatment of surgical instruments was perhaps the first and best example of the transition from unclean to antiseptic to asepsis. Those who believed in germ theory knew the risks were high when operators inserted these tools directly inside the body where germs, viruses, or other organisms somehow caused potentially fatal infections.

Pressure Cooker Sterilizer – The Autoclave

Thus, in ancient times, fire achieved asepsis. In modern times, more controlled forms of heat in enclosed spaces served to sterilize surgical instruments and other potentially infected surfaces to achieve asepsis. In 1832, for example, William Henry (1774-1836), an English chemist, designed a dry heat sterilizer that purified the clothing of cholera victims to prevent contagion.¹⁰³⁵ Around 1879, Charles Chamberland (1851-1908), a Frenchman who was a

¹⁰³⁴Although steel was known to the Ancients, the Bessemer process, introduced by Henry Bessemer in 1858, commercialized steel by making the production of large quantities of steel much cheaper. The melting point of steel, relevant to the temperature used to sterilize instruments, depends upon the alloy used, but is at least 1130° C. The average candle, which achieves temperatures much hotter than the average autoclave (120°-190° C with the significant addition of pressure), reaches a temperature of about 1000° C. (Bunsen burners are ubiquitous in chemistry labs because their flames reach temperatures about 1400° C.) Few organisms can withstand such temperatures and pressures, with the possible exception of organisms living on the sea floor near hydrothermal vents.

¹⁰³⁵Dr. Henry did not seek to rid the cholera-infested clothing of germs. Rather, he held that cholera was spread by chemicals that could be neutralized or destroyed by heat. Paul Price, *Surgical Technology for the Surgical Technologist: A Positive Care Approach*, 2nd ed. (Clifton Park, NY: Thomson, 2003). 131. As in so many other

student of and then assistant to Pasteur, devised the first steam sterilizer that incorporated increased pressure in its design. It was called "Chamberland's autoclave."¹⁰³⁶

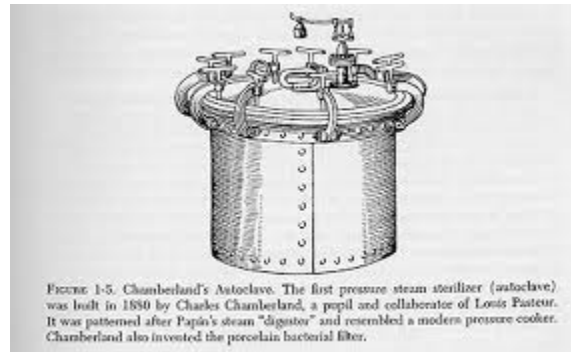


Figure 12. The Chamberland Autoclave¹⁰³⁷

By 1885, dry heat sterilizers, which looked like small versions of a modern pizza oven (and worked on the same principle), were being used in many hospitals.¹⁰³⁸

Ernst von Bergmann (1836-1907) introduced routine heat sterilization of medical instruments around 1891.¹⁰³⁹ Even Lister, who had maintained his use of dilute carbolic acid for years despite its many adverse effects (skin and lung irritation, among others) and the stinging criticisms of others, abandoned its use after von Bergmann and Koch showed that heat was a better disinfectant and sterilizer than carbolic acid.

The Appearance of Modernity

cases in medicine, it is better to achieve a good result for the wrong reasons than a bad result with right knowledge. Bad theory need be no impediment to good practice.

¹⁰³⁶Ibid. The term autoclave, still in use today for a pressurized sterilizer, derives from the Greek prefix auto-, meaning "self," and -clave, meaning "key." The autoclave was a self-locking sterilizer.

¹⁰³⁷Google images for "Autoclave," accessed March 6, 2012.

¹⁰³⁸My grandfather, William Koblenz MD, used a dry heat sterilizer for his surgical instruments from the time he began his medical practice in 1920 until his death in 1961.

¹⁰³⁹Soulatou, "A Short History of the Old Trip of Sterilization". Slide 19.

By the turn into the twentieth century the operating suite began to take on several aspects of the appearance of a modern operating room (OR). To no small extent, this was due to advances in antisepsis and then asepsis.



Figure 13. An Operating Suite in 1900¹⁰⁴⁰

Physicians and nurses, the mainstays of the turn-of-the-century operating room, wore special clothes for surgery. "Scrubs," as they would come to be called, were usually white, because germs and other unwanted OR invaders, it was thought, could be seen best against an all-white background. Nurses segregated instruments from the surgeons and other attendants, so as to maintain sterility – or, at the very least, cleanliness – as long as possible. The room was well lit for optimal visualization of the organ or organs in question, and sinks with water were ever-present to allow for easy hand washing should the occasion re-arise.

Other accoutrements added to the modern OR scene. Gustav Neuber introduced sterile surgical caps and gowns in 1881. William Halsted, the Columbia/Hopkins surgeon who popularized the radical mastectomy for breast cancer (among other innovative procedures),

¹⁰⁴⁰From <http://www.blatner.com/adam/consctransf/historyofmedicine/2-infection/lecture2.html> accessed April 11, 2012.

began the practice of using rubber surgical gloves around 1890, reportedly to prevent the hands of an OR nurse (whom he later married) from recurrent irritation. Mikulicz received credit for the first use of surgical masks around 1897.¹⁰⁴¹

As the above photograph of an operating suite in 1900 shows, not all these efforts to achieve sterility and prevent surgical wound infections were routine by the beginning of the twentieth century. Masks are not worn and only some of those present wear gloves. Nevertheless, with the increasing acceptance of germ theory as its driving force and the clinical success of antiseptics and then asepsis in reducing (if not quite eliminating) the incidence of wound infections, the practice of surgery by the last years of the nineteenth century was dramatically different from what it had been only a few years earlier – and unrecognizably different in so many ways from the centuries of relative changelessness from Ancient through pre-modern times.

But not completely – for the photograph also highlights some aspects of the operating room that had not changed over the course of the nineteenth century and, to a major extent, have still not changed. The OR was and is a very hierarchical workplace. There is a chief surgeon who is in command and control, a chief OR or scrub nurse who directly assists the surgeon, and (at the very least) a third individual who may not be "scrubbed" but is available to obtain needed materials or provide rapid message delivery to those for whom the OR flow is critical – scheduling, supplies, maintenance. Other physicians present include the assistant surgeon (probably the young, tall, white-clothed man on the left holding his gloved hands out to the side in order to prevent his touching someone or something or vice versa), several nurses contributing in different ways, an anesthesiologist at the patient's head with a dark probably rubber "mask" in his left hand (that fits over the patient's nose and mouth), and, depending upon the type of

¹⁰⁴¹ http://www.wfhss.com/html/educ/articles/educarticle_0012_en.pdf accessed April 11, 2012.

institution (teaching hospital, community hospital, etc.), a legion of medical students and other observers, some of whom are in the OR and others who may view the proceedings from above (an observation room) or, today, beyond (telemedicine).

Necessity dictates this hierarchy, based generally upon experience (and upon who is chiefly responsible for the patient's well-being). Education is another unchanging part of the operating room's way of life, for eager medical students and apprentice-like residents derive much of the skill set that they will bring to future patients from doing as well as reading. Doing is learning. The old mantra still holds: "See one, do one, teach one."

The Cancer Connection

Anesthesia and Antisepsis: The *Sine Qua Non* of Modern Cancer Surgery

By the end of the nineteenth century, the adoption of anesthesia, antiseptic techniques, and widespread standardization of instruments in the Western world had paved the way for surgery to become the treatment of choice for cancer. Nevertheless, this was only the beginning, for advances in these fields would continue to enhance the role of surgery in the treatment of cancer through the twentieth century to the present.¹⁰⁴²

Progress continued to proceed in the development of both anesthesia and analgesia as well as in antisepsis and asepsis. Surgeons and their assistants learned to administer anesthesia with more attention to the timing and the duration of the dose of administration. In the early years of anesthesia, too many patients had died from the prolonged administration of the anesthetic agent, or from the administration of an excessive dose that suppressed the patient's

¹⁰⁴²Advances in anesthesia, antisepsis, and instrumentation continue to this day. The agents of my own professional youth thirty years ago are hardly the agents of today. Until all perioperative pain is safely and efficaciously eliminated, progress in anesthesia and analgesia will continue. Until all risk of infection is safely and efficaciously eliminated, progress in antisepsis and asepsis will continue. Until no further instrumental or procedural innovations are necessary, progress in how and what surgery is performed will continue.

respiratory center to the point of asphyxia.¹⁰⁴³ The introduction of endotracheal anesthesia (administration of anesthesia by a tube inserted through the mouth directly into the lungs) by Samuel James Meltzer (1851-1920) and John Auer (1875-1948) in 1909, rather than the use of a chloroform-soaked gauze or gas-filled face mask, targeted the delivery of anesthetics to the blood-rich lungs (whose vessels carried the anesthetic to the brain and elsewhere) and improved outcomes.¹⁰⁴⁴ By the 1920s, anesthesia had become a specialty unto itself.¹⁰⁴⁵

Although the cocaine of William Halsted and Sigmund Freud was not the riskless panacea for local and regional surgical pain that physicians longed for, cocaine spurred the development of host of derivative compounds with somewhat different properties, like tropococaine (1891), stovaine (1904), and novocaine (1912).¹⁰⁴⁶ Similar but more arguably more profound advances in pain killers led to the production of morphine-like opioids that offered a diverse set of properties, including rapid onset of action for acute pain, prolonged duration of action for moderate-to-severe chronic pain, and a multitude of different routes of administration – oral, rectal (suppositories), subcutaneous, intramuscular, intravenous, buccal (inside the cheeks of the mouth) and topical (usually in the form of a skin patch).¹⁰⁴⁷ Few areas of the pained body have not had contact with analgesics.

¹⁰⁴³Asphyxia is the insufficient exchange of oxygen between the air and the lungs. Suffocation, for example, causes asphyxia.

For an excellent historical analysis of transformations in anesthesia over the course of the nineteenth century, see Pernick, *A calculus of suffering : pain, professionalism, and anesthesia in nineteenth-century America*.

¹⁰⁴⁴Sebastian, *A Dictionary of the History of Medicine*: 49.

¹⁰⁴⁵The forerunner of the American Society of Anesthesiologists was founded in 1905 as the Long Island Society of Anesthetists. England first recognized the practice of anesthesia as a separate intellectual and practical undertaking with the creation of a "Chair" (professorship) in anesthesia at Oxford in 1922.

¹⁰⁴⁶Sebastian, *A Dictionary of the History of Medicine*: 473.

¹⁰⁴⁷The great problem of addiction, however, has not been solved, although work continues. Contemporary attempts to reduce the addictive properties of opioids include imbedding or coating the analgesic with a chemical

As a result of these advances, the practice of surgery became less painful, safer and, because surgeons could now preference diligence over speed, more success in outcomes. Physicians and patients lauded these changes and acted accordingly. The number of surgeries performed overall increased rapidly, even as the number of procedures performed in patients' homes – unable to fulfill the requirements of antisepsis – dwindled. Surgeries at the Massachusetts General Hospital, for example, increased from 37 annually before anesthesia and antisepsis to 3,700 in 1898, after their implementation.¹⁰⁴⁸

Thus, surgeons performed more surgeries, and – as a result of the requirements of anesthesia and antisepsis – they performed an increasingly larger proportion of their surgeries in the hospital. The unclean, unsterilized, non-hospital environment – with all its customized patient comforts and friendly surroundings – no longer served as the dominant venue for surgery.¹⁰⁴⁹

Not only did the site of operations change, but the sites within the body amenable to surgical exploration and cancer excision also changed. Patients with skin cancer had had their cutaneous malignancies removed surgically long before modern anesthesia and antisepsis. In 1787, John Hunter operated upon a "cancerous fungous excrescence" – later confirmed to be a melanoma.¹⁰⁵⁰ But only a fool would venture to operate upon a cancer within the body. The

that antagonizes the euphoric properties of the analgesic when used improperly (such as when crushing the pill to snort or "shoot up").

¹⁰⁴⁸Degenshein, "Golden Age of Surgery," 933.

¹⁰⁴⁹As a result, and in an attempt to attract rich as well as poor patients to the inpatient setting, hospitals began to remodel patient rooms from wards filled with one or two dozen patients side by side to rooms with at most two patients at a time. The trend began with private rooms for private patients, but, with the increasing democratization of the formerly "aristocratic" and hierarchical hospital, began to include all patients, rich and poor (at least in non-profit, private hospitals). See especially Rosner, *A once charitable enterprise*.

¹⁰⁵⁰Confirmation of the diagnosis of melanoma, strongly suggested by Hunter's traditional description of the lesion as a fungus-like, out-growing cancer, occurred in 1968 as a result of the examination of Hunter's well-

patient's pain would be excruciating; the risk of postoperative death from sepsis unacceptably high. Such operations were performed, but surgeries on pathologic lesions within internal organs before the last decades of the nineteenth century were surgeries of last resort: patients were usually totally incapacitated or near death. Dr. Ephraim McDowell's historical ovariectomy (incision into or removal of an ovary) was just such an example. Mrs. Jan Crawford of Virginia, the patient, had an ovary that weighed more than twenty pounds – a remarkably weighty burden.¹⁰⁵¹ In 1809, two years before Fanny Burney's mastectomy, McDowell removed Mrs. Crawford's tumor within the pelvic cavity – without the aid of modern anesthesia or antisepsis. McDowell's effort was considered foolhardy by many of his fellow physicians because the mortality rate was known to exceed ninety percent, but, remarkably, the patient lived.¹⁰⁵² By the end of the century, however, former sacrosanct areas of the body, like the peritoneum (abdominal and pelvic cavities) and the brain, yielded to the surgeon's knife with relative impunity. W. W. Keen, an early adopter of Listerism in the United States, performed the first successful removal of an intracranial meningioma with the aid of anesthesia and antisepsis in 1887.¹⁰⁵³

Thus, anesthesia and antisepsis engendered revolutions in the surgical treatment of cancer, increasing the number of cancer operations, changing their venue, opening up previously

preserved specimens. <http://www.methodsofhealing.com/when-was-skin-cancer-first-discovered/> accessed May 28, 2012.

¹⁰⁵¹ A normal ovary weighs about an ounce.

¹⁰⁵² Indeed, we probably remember Dr. McDowell because the patient lived. And she lived for another thirty years thereafter. Indeed, McDowell's operation on Mrs. Jan Crawford of Virginia is often considered a turning point in the history of gynecologic surgery. "Ephraim McDowell," *Mayo Clinic Proceedings* 52(1977). *NEED NAME AND TITLE* If political history is written by the winners, medical history (at least until the 1970s) is/was written about successes. Since the 1970s, historians of medicine have taken a more balanced approach to the past, illuminating failures as well as successes.

¹⁰⁵³ A. E. Bennett, "The Secret Surgical Operation on President Cleveland," *the Pharos* 38, no. 4 (1975): 159. Lee gives the date as 1888. Lee, *Dates in Oncology*, 63. I believe the correct date is 1887.

off-limits portions of the human body, and instilling a feeling of hopefulness that had been sadly absent in the minds of patients and their physicians in the centuries before the advent of anesthesia and antisepsis.

THE KNIFE MOVES DEEP:

THE GOLDEN AGE OF SURGERY

Beyond Anesthesia and Antisepsis

The treatment of cancer was surely not the only disease therapy to benefit from improvements in surgical anesthesia, antisepsis, and instrumentation, but the surgical treatment of cancer was uniquely positioned to take advantage of those advances. Cancer surgery in the modern era became much less painful and much safer than had been the surgical treatment of cancer in the traditional age before the advent of the twin pillars of anesthesia and antisepsis. As a result, surgery quickly became the paradigmatic treatment for solid tumors in the final years of the nineteenth century.¹⁰⁵⁴

Critical as anesthesia and antisepsis were to foster surgery as the treatment of choice for cancer by the end of the nineteenth century, other forces also contributed to the development of cancer surgery.

Prevalence: More Cancer Patients

¹⁰⁵⁴My specific mention of "solid" tumors rather than all tumors is deliberate. Solid tumors are those in non-flowing organs like the breast, cervix, prostate, lung, and colon. They are relatively confined in space (and over short periods of time). On the other hand, liquid tumors are those that generally include large numbers of hematopoietic (blood cell-related) or lymphoid cells in a flowing medium such as blood or lymph. These include acute and chronic myelogenous (white blood cell-related) leukemias and acute and chronic lymphoid leukemias, the term "leukemia" having been coined by Virchow in 1845. Paul Ehrlich's stains, forty years after Virchow's naming, differentiated the types of leukemia based upon the underlying cell type (myelocyte, lymphocyte, etc.) and led Ehrlich, by logical extension, to chemical treatments for them – treatments he called "chemotherapy." Ehrlich may have begun the use of chemotherapy to treat cancer, but it was not until decades later (arguably the 1940s) that viable chemotherapeutic treatments became available for the treatment of cancer. Chemotherapies for infectious diseases like syphilis, however, started with Ehrlich's Salvarsan, Compound 606, which became available commercially in 1910.

The main point is that solid tumors became amenable to surgery. Liquid tumors were not.

One driving force often escaping consideration was the sheer increase in the number of cancer patients. As statistical compilations from such mid-nineteenth-century proto-statisticians as Domenico Rigoni-Stern (1810-1855) and Stanislas Tanchou began to reveal a rise in the number of deaths from cancer, physicians sought different and better modalities by which to treat or, ideally, cure their patients.¹⁰⁵⁵ In 1830, for example, Tanchou found that 668 persons died from cancer in the department of the Seine (Paris and surroundings). By 1840, the number he counted had swelled to 889, an increase of 33% in ten years!¹⁰⁵⁶ As more people developed cancer, the value of available non-surgical cancer therapies (e.g., pills and potions) came into sharper focus as failures. Surgery became a more desirable option.

Improved Communications: Printing and Traveling

Improvements in printing and transportation also hastened the adoption of surgery as the treatment of choice for cancer. Revolutions in printing following the advent of the steam-powered printing press by Friedrich Koenig (1774-1833) in the early nineteenth century – widely adopted by the 1840s for its economy and scalability – brought medical knowledge faster and at less cost to physicians in Europe and America.

Revolutions in transportation, from Robert Fulton's (1765-1815) commercially-successful steamboat (that allowed transportation upriver with relative ease) to the canals that sliced through Europe and America especially after the success of New York's Erie Canal (that

¹⁰⁵⁵On Rigoni-Stern and his "Nineteenth-Century Approach to Cancer Research" (the subtitle of their paper), see Joseph Scotto and John C. III Bailar, "Rigoni-Stern and Medical Statistics: A Nineteenth-Century Approach to Cancer Research," *Journal of the History of Medicine and Allied Sciences* 24, no. 1 (1969). Tanchou's seminal "Statistics of Cancer" may be found at Stanislas Tanchou, "Statistics of Cancer," *The Lancet* 40, no. 1040 (1843). Tanchou concluded that Europeans seemed especially susceptible to "cancerous degeneration" compared to other peoples. As we have shown, however, the diagnosis of cancer, which was less rigid and microscopically derived in 1840 than today, encompassed more conditions (e.g., inflammatory growths) than would be included today. It is likely, though, that the true prevalence of cancer did indeed rise as infectious diseases became less common and, as a result, people lived longer.

¹⁰⁵⁶"Statistics of Cancer." These numbers are liable to so many adjustments (e.g., net increase in the population of the district over the decade), but the basic point stands: Observers in France and England noted a sharp increase in the number of cancer patients starting in the mid-nineteenth century.

substantially reduced the cost of long-distance travel for goods and people from the Midwestern United States and Canada to the East coast) to the steam-powered railroads that crisscrossed Britain, America, and the Continent starting with the Middleton Railway (1812) in England and the Baltimore and Ohio in the United States (which opened to passengers in 1830 to allow Baltimore to compete with the success of New York's five-year-old Erie Canal) to the fine-coached railways emanating from Paris, Chicago, and elsewhere, allowed more people to travel longer distances safer and in more comfort than ever before.

As a result of these innovations in printing and travel, physicians read about cancer medical news faster and from wider world as well as attended more conferences and over a wider geographic area. And, as demand drives supply, the number of journals proliferated and more conferences were set up to accommodate the increasing numbers of those who wished to attend them.

Fruits of Progress: Good News Travels Fast

As a result of these radical changes in how physicians communicated and connected, new surgical ideas, techniques, and instruments for the treatment of cancer that worked (and some that did not) spread throughout the Western medical world faster than ever before. Indeed, the relative increase in the propagation of medical knowledge in general, including cancer knowledge, from the beginning to the end of the nineteenth century is perhaps rivaled only by the transition from the printed journal of the twentieth century to the web-based, speed-of-an-electron transmission of medical information today.¹⁰⁵⁷

¹⁰⁵⁷But is the knowledge that is disseminated so quickly true (i.e., evidence-based, reproducible, clinically validated) ? One of the problems with the lightning-fast transmission of medical information is that it may not be properly vetted and confirmed before it is made public. Many subsequent retractions have occurred, but few are as publicized as the initial "breakthroughs."

Hospital Renaissance: A New Direction for the Hospital

The move of big medicine to the hospital in general and then academically-affiliated hospitals in particular also made surgery a more attractive treatment for cancer. During the late nineteenth century, the hospital became a citadel for the sick rather than a charitable way station (or terminal station) for the poor. Both rich and poor moved their medical problems into the hospital. Gone were the days when surgeons like Napoleon's D. J. Larrey operated on flat countertops and tables using alcohol "anesthesia" in the homes of well-heeled patients like Fanny Burney. Over the course of the nineteenth century, the hospital, which, after all, closely circumscribed its original meaning of "shelter for the needy" from the thirteenth until well into the nineteenth centuries, became for rich and poor alike a hall of science replete with microscopes and surgical instruments unimaginable in such a venue only a few decades earlier.¹⁰⁵⁸

Anesthesia and antisepsis hastened the transformation of the hospital from charity hostel to *locus medicus*, for the increasing complexity of medical treatment intensified by these advances in surgical tolerability and safety favored an economy of space and time where everything necessary for medical treatments and surgical operations could be found in one place. And "everything" became a larger and larger set of specialized instruments, chemicals, medicines, uniforms, and people as the nineteenth century progressed. In consequence, the ill and diseased sought help and healing under a single roof, and many such roofs sprang up to accommodate them. Well-established hospitals like the Pennsylvania Hospital (1752), The New York Hospital (1771), and the Massachusetts General Hospital (1811) likewise expanded in size and scope. Not one given to understatement, William W. Keen wrote in an 1897 essay, "This

¹⁰⁵⁸ <http://www.etymonline.com/index.php?term=hospital> accessed June 13, 2012.

growth of hospitals has been within the last twenty years one of the striking features of our civilization."¹⁰⁵⁹

A Complementary Discipline: The Rise of Surgical Pathology

It is impossible to do intelligent surgery without a thorough understanding of the pathology of disease and it is equally impossible to make an intelligent interpretation of pathology without a clear understanding of its clinical implications.

—Stout's Dictum¹⁰⁶⁰

As surgeons moved into the hospital to take advantage of new instruments, machines, and the concentration of skilled personnel, patients followed. Nascent specialties that became central to the diagnosis and treatment of cancer patients either developed in the hospital or found a home in the hospital after its rebirth. Although anatomic pathologists could be found in schools of medicine from at least the time of Vesalius (Padua, mid-sixteenth century) and certainly from the era of Morgagni (also primarily Padua, mid-eighteenth century), an essentially new discipline of surgical pathology arose to meet the needs of more and more physicians performing surgery on increasing numbers of cancer patients.

The confluence of microscopy, cancer, and surgery occurred in surgical pathology.

Writing about the state of "pathological anatomy" in mid-nineteenth-century America, William

¹⁰⁵⁹Keen, "Semicentennial Address," 247. Keen delivered his "Semicentennial Address in Surgery," in Philadelphia on the occasion of the 50th anniversary of the American Medical Association.

Credit for the conception of the AMA is given to Dr. Nathan S. Davis, who proposed a national convention at the New York Medical Association in 1845 that led to the birth of the AMA. The actual founding of the AMA occurred at the Academy of Natural Sciences in Philadelphia on May 7, 1847. As with so many American institutions formed during the "Age of Reform," two of the AMA's initial endeavors were a Code of Ethics and the first nationwide standards for pre-medical and medical education – more than sixty years before the 1910 Flexner report. See <http://www.ama-assn.org/ama/pub/about-ama/our-history/the-founding-of-ama.page> accessed July 7, 2012.

¹⁰⁶⁰Howard D. Dorfman, "Book Review of Juan Rosai's *Guiding the Surgeon's Hand. The History of American Surgical Pathology*. Washington, D.C.: American Registry of Pathology, Armed Forces Institute of Pathology, 1997," *The Journal of Bone and Joint Surgery* 81(1999): 443.

Andrew Purdy Stout began his career at Columbia in 1914. In 1903, Columbia had established one of the first laboratories dedicated to surgical pathology in the United States. Stout played a significant role in the development of surgical pathology as a subspecialty of its own within pathology and trained several generations of surgical pathologists. See Mihai Merzianu, MD "A Brief But Rich Journey" online at <http://www.pdfio.com/k-21156.html> and accessed June 27, 2012.

W. Keen noted that "pathology and pathological anatomy were almost unknown sciences in 1847."¹⁰⁶¹ "The microscope, and especially microscopical methods of staining, section cutting, and the like were in their infancy, or may indeed be said scarcely to have existed."¹⁰⁶² By the end of the century, however, microscopical anatomy and surgical pathology had become fundamental to medical education and the practice of medicine and surgery. "What is now [in 1897] the heritage of every first year [medical] student," continued Keen, "was beyond the possibilities of the most advanced teacher of fifty years ago."¹⁰⁶³

The relationship between surgeons and surgical pathologists – i.e., anatomic (as opposed to clinical) pathologists who examine surgical specimens with the naked eye as well as with the microscope to discern the type of disease as well as its extent and severity – was and is very much reciprocal. In the early years of surgical pathology – the end of the nineteenth century and the beginning of the twentieth – many surgeons functioned as their own surgical pathologists. Over the course of the first decades of the twentieth century, however, surgical pathology became a specialty separate from surgery with its own specialists, a trend toward finer and finer specialization that has only continued in light of the rise of immunohistochemistry and a host of other specialties within specialties. The rapidly increasing numbers of biomarkers in the early twenty-first century, many of which are tested for in laboratories of surgical pathology, have enhanced the role of pathology laboratories in the quest for targeted cancer therapies and have further accelerated this trend.¹⁰⁶⁴ Nonetheless, whether today or a century ago, the cancer

¹⁰⁶¹Keen, "Semicentennial Address," 252.

¹⁰⁶²Ibid.

¹⁰⁶³Ibid., 252-3.

¹⁰⁶⁴A biomarker is a natural molecule produced by a specific cell type that facilitates the identification of that cell type and may allow specific "targeting" of that cell type by specific cancer therapies. Targeted therapies have the real or potential advantage of leaving non-target, presumably healthy, cells intact – great advance since the

surgeon needs the surgical pathologist and the surgical pathologist needs the cancer surgeon – and they generally come together in the hospital.¹⁰⁶⁵

Over the course of the late nineteenth and early twentieth centuries, as increasing numbers of physicians dedicated to surgery conducted more operations on increasing numbers of cancer patients, the new subspecialty of surgical pathology arose to confirm the diagnosis of cancer, differentiate one type of cancer from another (since patient treatments and outcomes often depend upon the specific type of cancer), evaluate whether or not the surgeon had removed all the cancer (by examining if the "margins" of the excised tissue are free of cancer cells under the microscope), and, ultimately, guide the surgeon's hand to remove the cancerous tissue (and, if possible, no normal tissue) to achieve the best outcome for the patient.

Since at least the early twentieth century in America, cancer surgery and cancer pathology have gone hand in hand. And the relationship between the two has continued to grow as new microscopes (e.g., the electron microscope) and chemistries (e.g., immunohistochemistry and its investigation of the molecular composition of cancers) diversified the field. The

era of chemotherapies that killed the patient as well as the cancer. The absence of a biomarker in cancerous tissue may be as important as its presence, for therapies (and their toxicities) not appropriate for the treatment of patients whose cells lack those biomarkers will be avoided. Hence biomarkers may tip the risk-reward calculation – or, in medicine, the efficacy-safety calculation – in favor of benefit.

¹⁰⁶⁵Over the past twenty years or so, this trend toward a greater concentration of services in the hospital has reverted to an increasing degree to the outpatient environment. Over the course of the twentieth century, many factors led the cost of hospital care to increase more rapidly than that of outpatient, "office" medical and surgical care. In an effort to cut overall healthcare costs, governments and other third-party payers (insurance companies that offer health insurance) have incentivized the performance of procedures on outpatients rather than in(-hospital)patients. Endoscopies, biopsies, cosmetic surgeries, and operations of all sorts that were previously exclusive to the hospital are now routinely performed on outpatients. As a result, many surgical pathologists have established independent, out-of-the-hospital laboratories or work for larger companies unaffiliated with hospitals (e.g., Quest, LabCorp) that receive, analyze, and report on outpatient biopsies and other test results.

However, having qualified the preponderance of in-hospital surgeons and surgical pathologists over their outpatient colleagues, surgeons still perform major cancer surgeries (e.g., lung removal for lung cancer, segmental colon resection for colorectal cancer) in the hospital and send the excised pathological specimens to in-house surgical pathologists.

interaction and interdependence between surgeons and surgical pathologists has never been closer. Long has been the shadow of Paul Ehrlich's multi-disciplinary, multi-colored fingers.

MEDICAL EDUCATION, THE UNIVERSITY HOSPITAL, AND THE EVOLUTION OF CANCER MEDICINE

The Academic Institution and the Treatment of Cancer

Not to be slighted in this analysis of the reasons for the changing treatment of cancer over the course of the nineteenth century is the seminal role of nascent modern academic medical institutions. Their facilitation of the transition of cancer surgery from home to hospital, from rare to commonplace, and from proprietary individualized therapies to widely-used treatments was critical.

The Flexner report of 1910 (a quintessential Progressive-era reform document, officially and understatedly titled *Medical Education in the United States and Canada*) defined what would become the requirements for an approved medical education for decades to come.¹⁰⁶⁶ One of the Flexner's most significant findings was that medical education must meld bedside instruction with book learning. Years earlier, several medical schools had taken this step to join education in the classroom with that in the clinic. Harvard Medical School moved physically and academically next to the Massachusetts General Hospital in 1847 in order to better integrate their functions. The Johns Hopkins University School of Medicine, immediately after its founding in 1893, began to concentrate talent as well as resources in the Johns Hopkins Hospital,

¹⁰⁶⁶Flexner, *Medical Education in the United States and Canada*.

The Flexner Report, otherwise known as Bulletin Number Four of the Carnegie Foundation for the Advancement of Teaching, was one of hundreds of publications with the goal of "improving teaching and learning." Abraham Flexner's 1910 report was hardly the last issued by the Carnegie Foundation on medical education. Bulletin Number Six, also authored by Flexner, examined *Medical Education in Europe* (1912) and Molly Cooke, David M. Irby, and Bridget C. O'Brien's *Educating Physicians: A Call for Reform of Medical School and Residency* (2010) attempts to reorient and transform graduate and post-graduate medical education in the twenty-first century as the Flexner Report did for medical education in the twentieth century. See http://www.carnegiefoundation.org/publications_archive accessed July 7, 2012.

which had opened four years earlier. Flexner pushed these collaborations further, because education without clinical experience, he believed, did not produce a competent practitioner. After Flexner, the days of studying rather than studying and training for the M.D. degree rapidly waned. Caring for actual patients became a requirement. And the hospital, not the medical school, was the obvious place to find (and "practice on") patients.

William Halsted's career highlights the increasingly common and dynamic integration of textbook and clinical education – school and hospital – that transformed medical training in general and the treatment of cancer specifically from the end of the nineteenth century into the twentieth. He was fortunate to attend a worthy medical school – Columbia's College of Physicians and Surgeons – which Abraham Flexner later commended as a model of graduate medical education (like Hopkins).¹⁰⁶⁷ Halsted made the journey from his years as a medical student (M.D., 1877) to the position of house officer at the New York Hospital (where he met William Welch, who later enticed him to come to Hopkins), to becoming the first chief of the Department of Surgery at the new Johns Hopkins Hospital (1889), to Professor of Surgery at the new Johns Hopkins University School of Medicine (1892-3). As such, his career wove together textbook education, clinical training, and teaching.

Although Halsted's seemingly seamless moves from book to bedside and from student to professor may have been the exception rather than the rule in his day, the integration exemplified by his career would become much more common over the course of the twentieth and twenty-first centuries – aided and propelled to no small extent by tenets explicit and implicit in Flexner's

¹⁰⁶⁷In his Report, Flexner especially praised Halsted's medical school, Columbia, for its teaching and research in anatomy, the basis of all surgery. "Anatomy," wrote Flexner on this department at Columbia's College of Physicians and Surgeons, "deserves to be especially mentioned, as perhaps the most elaborate plant of its kind in the country." *ibid.*, 268. Columbia, however, like most other medical schools that deserved merit in Flexner's opinion, fell short on using clinical materials (patients, cadavers, organs) to best advantage – even in anatomy. *Ibid.*, 278.

Medical Education. In the process, practicing surgeons *qua* professors like Halsted and others affiliated with institutions of medical education in his era brought to their students an abundance of hard-earned surgical knowledge and experience that altered the direction, practice, and utility of cancer surgery for generations to come. The near-century hegemony of Halsted's radical mastectomy as the treatment of choice for (invasive) breast cancer, for example, lasted as long as it did because of the power of Halsted's teaching and the teachings of his students to their students.¹⁰⁶⁸

The Art of Medicine

How often I have emphasized the science rather than the art of medicine! Such should not be a surprise in a history of nineteenth-century cancer medicine, because the single greatest cognitive advance in medicine over the course of the century was the application of scientific principles to the study and practice of medicine. One should not, however, believe that medical education and medical practice are all science and no art. The great transformation in medical education in the late nineteenth and early twentieth centuries – from pedagogy to patients – derived from the art of medicine as well as its science. The dual contributions of the art and science of cancer medicine are critical to an understanding of medical practice and are likely to

¹⁰⁶⁸Medical education, like many other graduate pursuits, is transgenerational. One generation teaches another. The second generation keeps some of the initial teaching, changes other parts, and adds new insights and discoveries to create its own unique understanding. And so on in the name of progress toward improved patient outcomes.

This implied medical inertia, however, sometimes leads to a delay in improved therapies, including surgical treatments. I chose the case of Halsted's large-tissue-removal (*en bloc*) radical mastectomy as an example because it was only as a result of thorough re-investigation of the basic science, clinical results, individual activism, and a public outcry that this disfiguring surgery was replaced by less "aggressive" procedures like lumpectomy and radiation. Yes, the radical mastectomy for invasive breast cancer was often successful, but it was not infrequently much more than was necessary. For an excellent analysis of the history of the radical mastectomy, see Barron H. Lerner, *The Breast Cancer Wars: Hope, Fear, and the Pursuit of a Cure in Twentieth-Century America* (Oxford: Oxford University Press, 2001).

remain so until the diagnosis and treatment of cancer are fully automated with little or no human input.¹⁰⁶⁹

Peruse the great writings of Sir William Osler – first Professor of Medicine at the oft-vaunted Johns Hopkins University School of Medicine and quintessential proponent of the application of science to medicine – to witness the importance of the art of medicine. In such collected writings as Osler's *Aequanimitas*¹⁰⁷⁰ and C. N. B. Camac's compilation of Osler's pithy sayings in *Counsels and Ideals*,¹⁰⁷¹ Osler repeatedly stressed the humanity of the physician as well as the contributions of science to what he entitled, in a series of lectures given at Yale later in life, "the evolution of modern medicine."¹⁰⁷² Flexner also emphasized the value of the social sciences and their humanitarian approach in illuminating a path to a more successful medical product; i.e., the modern physician.¹⁰⁷³ Art imbued the process of education with humanitarian

¹⁰⁶⁹One of the key debates in setting the criteria for admission to medical school to this day remains striking the "right balance" between a student's scientific knowledge and ability to learn versus the student's personality, non-academic achievements, and willingness to learn. As Professor David J. Rothman has repeatedly emphasized, "professionalism" is a key component of the successful practice of medicine. Years before the Physician Payment Sunshine Act of 2010 (to be implemented in 2013), David Rothman and Sheila Rothman, historians of social medicine at Columbia University, decried the decline of medical professionalism as a result of conflicts of interest (and other means) and offered suggestions for its revival. David J. Rothman, "Sounding Board: Medical Professionalism--Focusing on the Real Issues," *The New England Journal of Medicine* 342, no. 17 (2000). A professional attitude in a prospective medical practitioner begins long before medical school and has been, for some time, an implicit or explicit criterion for admission to medical school.

¹⁰⁷⁰William Osler, M.D., F.R.S., *Aequanimitas, With other Addresses to Medical Students, Nurses and Practitioners of Medicine*, Special ed., The Classics of Medicine Library (Philadelphia: P. Blakiston's Son & Co., 1904; repr., 1987).

¹⁰⁷¹William Osler and C. N. B. Camac, *Counsels and ideals from the writings of William Osler*, Special ed., The Classics of Medicine Library (Boston and New York: Houghton, Mifflin & Company, 1905; repr., 1985).

¹⁰⁷²Osler, *Modern Medicine*.

¹⁰⁷³There is no question that Flexner stressed the necessity to imbue medical education with science and learning from patient care rather than the humanity of the physician, but that is not surprising when one considers the unscientific medical education he fought against. However, he also gave recognition to the underlying humanistic qualities of the treating physician. The well-prepared physician, he wrote, "must rely for the requisite insight and sympathy on a varied and enlarging cultural experience." Flexner, *Medical Education in the United States and Canada*: 26. Even book and bedside learning, to the strongly opinionated Flexner, were insufficient by themselves to produce a complete physician.

values, for although the science may be the same regardless of the pupil, each student and patient was likely to be different in their wants and needs. As such, varied approaches would often be necessary to reach a desired outcome. And nothing was as variable as the student's background and the resultant humanity s/he brought to medicine.¹⁰⁷⁴

Who Rules? Who Benefits?

Gown vs Scrubs

Thus, medical education – its art and its science – ultimately came to be dependent upon this new and often tumultuous relationship between the medical school and its affiliated hospital(s) as school and hospital vied for educational and economic supremacy.¹⁰⁷⁵ Ultimately, regardless of whether the hospital or the university dominated their interactions and disputes, students and their patients were the beneficiaries of the University Hospital (the main hospital in a single or multiple-institutional consolidation most closely affiliated with the medical school) and its satellites as the form of medical education advocated by Flexner added a whole new realm of experience to the textbook learning of the physician.

From the perspective of the treatment of cancer, the amalgamation of institutions of higher medical learning and of patients at these institutions from whom students learned both art and science represented a watershed in the evolution of cancer knowledge and therapy.¹⁰⁷⁶ No longer would there be learning without doing. The basis of medical education and practice

¹⁰⁷⁴From the homogeneous (all-white male) medical classes of the pre-Civil Rights era to the global origins of today's American and Western European medical students, the dream of a graduating medical school class as heterogeneous as the patients they care for is a closer reality than ever – *Regents of the University of California v. Bakke* (1978) and other legal recidivisms aside.

¹⁰⁷⁵For more on this subject, see Rosemary Stevens, *In Sickness and In Wealth: American Hospitals in the Twentieth Century*, 1st ed. (New York: Basic Books, Inc., 1989).

¹⁰⁷⁶In the twentieth century, this synergy between medical schools and their hospitals continued beyond the boundaries of cancer surgery to include later forms of cancer therapy, such as radiation therapy, chemotherapy, and immunotherapy. Many advances discovered or invented in academic medical institutions translated into new therapies at the bedside.

shifted from the unsubstantiated hearsay and heroics of earlier eras to the ever-scrutinized foundations of modern diagnosis and treatment that came to be taught as accepted wisdom and common practice.¹⁰⁷⁷

The University Hospital centralized patients, doctors, drugs, and devices at one dedicated site. As a result, the Flexnerian format augmented medical education far beyond the economies of place and scale. Initially unforeseen synergies, today collected under terms like "interdisciplinary" and "team rounds," became the norm rather than the exception as the group comprised of specialists superseded the general practitioner.¹⁰⁷⁸

To What End?

In essence, the knowledge of cancer that grew exponentially beginning in the late nineteenth century adopted advances from real-world inventions in industry and technology to better both the education of the medical student and the likelihood of achieving the ultimate goal of medical practice: good health. Practicing physicians over the course of the nineteenth century took advantage of revolutions in printing, communications, and transportation to learn new techniques toward the amelioration of pain, the prevention or reduction of life-threatening infections, and the surgical treatment of the cancer patient. They did so by learning the successes (and failures) of their colleagues much quicker and with more evidence (for or against) than ever before – and then applied those new techniques to their own patients.

¹⁰⁷⁷Accepted wisdom, with all its faults and prejudices, stands firm as progress in the face of what went before it in the age of traditional cancer: a hodgepodge of cancer names, tenuous cancer diagnoses, and proprietary if not secretive untested treatments.

¹⁰⁷⁸The necessities of business (and sports) may have originated the team approach (beyond the family). And the practice of medicine may have been one of the last bastions of go-it-alone practice. But today it is rare that the "case" of a patient with an unusual cancer at a University Hospital or a common cancer at a smaller community hospital is not "presented" before the Tumor Board, a group of specialists representing the many disciplines necessary to lead to the best patient outcomes, including surgery, pathology, radiology, medical oncology, immunology, nursing, social services, and more.

Medical students and physicians in training (today known as residents and fellows) garnered the teachings of their forebears in the reborn hospital and through new specialties like surgical pathology to add layers of clinical skills upon the framework of age-old book learning toward the end of improving patient outcomes. The one-on-one apprenticeships of the early nineteenth century evolved into the clinical bedside rounds of the late nineteenth (and twentieth and twenty-first centuries) that sought to integrate teaching, experience, skills, and – to no small extent – the art of medicine into a more successful whole.¹⁰⁷⁹ Medical education was and is very much a "hands-on" affair. The marriage of the medical school and the hospital offered students a proximal source of patients on whom they could put their hands to use their senses, in addition to and in combination with their intellects, for the benefit of their patients.

Thus, the science-based hospitals that began to appear in the late nineteenth century – with their professors, practitioners, and students – provided form and content for the learning and practice that highlighted the failures of traditional cancer treatments at the same time that they spread knowledge and competency of the treatment of cancer that promised the most successful outcome – surgery.¹⁰⁸⁰

Undergirding this radical transformation in the treatment of cancer over the course of the nineteenth century – beyond the discoveries, the inventions, the new technologies, the new hospital, and the clinical educational techniques of modern medicine – was a powerful idea. And

¹⁰⁷⁹James Thomas Flexner, *Doctors on Horseback: Pioneers of American Medicine* (New York: Fordham University Press, 1937; repr., 1992). James Flexner's aptly-named study profiles seven American physicians in the eighteenth and nineteenth centuries, including Benjamin Rush, Ephraim McDowell, William Beaumont, and Crawford Long, who in many ways exemplified the apprenticeship and old methods of pre-Flexnerian medical education.

[James Flexner (1908-2003) was Abraham Flexner's nephew. James is known to many historians for his four-volume award-winning biography of George Washington published between 1965 and 1972.]

¹⁰⁸⁰The tenor of medical journal articles changed drastically from the mid- to late-nineteenth century as description-based articles about individual patients gave way to compilations of patient outcomes based upon the statistical analysis of surgical and other cancer treatment outcomes to determine their relative value to best advantage the cancer patient.

that critical concept – without which surgery would not have come to become the treatment of choice for cancer by the late nineteenth century – was that cancer began in one spot.

That One Spot, That One Cell:

Localism – The Foundation of the Golden Age of Cancer Surgery

Formerly cancer was very generally regarded as a constitutional affection, and therefore cure by operation alone was looked on as hopeless, and medicaments of all kinds were poured into the unfortunate patients so as to expel the black bile, or whatever else was supposed to be the cause of the disease. Operation was looked upon simply as a means of prolonging life for a short time, of relieving the patient's mental anxiety, and of getting rid of certain local troubles, and not as a means of permanently freeing the patient from the disease....

Of late, however, more especially since the microscope has revealed the character of the disease, the view of the local origin of cancer has been gaining ground, and surgeons for the most part now undertake these operations in the hope of curing the patient, and not merely of temporarily prolonging life.

-William Watson Cheyne (1896)¹⁰⁸¹

Revolutions find strength and sustenance in ideas. The revolution in the treatment of cancer in the late nineteenth century was no exception. A centuries-old debate is ongoing as to whether ideas or technologies drive innovation.¹⁰⁸² In essence, this is a debate between the relative values of rationalism and empiricism, a debate that has no unequivocal answer because they are two sides of the same coin. Technology without ideas is motion with no place to go. Ideas without technology are dreams with no possibility of fulfillment. Innovation requires both.

Thus, even revolutions in anesthesia, antisepsis, surgical techniques, communications, transportation, hospitals, and medical education may not have led surgery to become the treatment of choice for cancer in the late nineteenth century had there not been a foundational

¹⁰⁸¹W. Watson Cheyne, *The Objects and Limits of Operations For Cancer, with Special Reference to Cancer of the Breast, Mouth and Throat, and Intestinal Tract, Being the Lettsomian Lectures for 1896* (London: Bailliere, Tindall, and Cox, 1896). 14.

¹⁰⁸²One analysis of many in this regard is the work of Raymond Williams, who argues in his study of the television that ideas and culture drive technological change, not vice versa (the latter often being the position attributed to Marshall McLuhan). Raymond Williams, *Television: Technology and Cultural Form* (Hanover, N.H.: Wesleyan University Press, 1974; repr., 1992).

idea that proposed, propelled, and, to a greater extent than ever before, led to proof (if such can be said in medicine) that surgery achieved better outcomes in patients with cancer than other treatments. That foundational idea, the *sine qua non* of the golden age of cancer surgery, was localism – the idea that cancer began in a particular place.

Whatever may be considered to be the origin of cancer, the first manifestation of its presence to the microscope is the atypical cell-growth, confined to a particular locality, and spreading thus in a regular and progressive way to tissues in the immediate neighborhood.

-George F. Shrady (1887)¹⁰⁸³

For most of the nineteenth century, physicians and the population at large conceived of cancer as a body-wide disease indelibly inscribed within the individual's being, like an ontological assumption, and from which there was no more escape than a leopard from his spots. I have called this constitutionalism. Such a view is understandable given the *Weltanschauung* at the time. From time immemorial the common belief was that man had been created as an entirety of one—an indivisible self. The Bible taught this.¹⁰⁸⁴ Greek philosophy emphasized the rational whole. Roman law codified it. Certainly people knew that eyes differed from feet, but the entire being – functioning as a whole and set off from the inanimate world by a vital spirit – was the unit of life.

By the middle years of the nineteenth century, several transformations in culture and society had occurred to question and then attack this holistic, unitarian way of thinking about the human body. The division of labor (and the socioeconomy) wrought by nascent industrial capitalism, the secularization of religion in society, the rise of science as a potentially more powerful methodology for dealing with everyday life than what had come before, and the consequent realization that things change, laid the foundation for the possibility that the

¹⁰⁸³Shrady, "The Curability of Cancer by Operation," 85.

¹⁰⁸⁴Adam was fully formed when God breathed life into him. (*Genesis II: 7*)

traditional approach to the world was not the only (and likely not the best) approach to health, well-being, and progress. And progress was the goal, not only in medicine but in manufacturing (post-Adam Smith, pre-Henry Ford serial production), education (Horace Mann's universal public education), and even religion (utopian perfectionism). New ideas, interpretations, and conclusions about the world became not only possible but necessary.

To experimental philosophy, founded in this our own age, we owe everything that distinguishes today's [medical] theory from its rude state in former times.

-Giorgio Baglivi (1704)¹⁰⁸⁵

Into this new world of the mid-nineteenth century came anatomists, physiologists, and physicians whose contrasting outlook compared to those who came before them on how to solve problems became rooted in this notion of constant change and endless possibilities toward the betterment of mankind.

First in Europe and then in the United States, men like John Hunter via his empirical surgical studies, Johannes Müller with his focus on nature seen through the microscope, Matthias Schleiden (a contemporary of Müller who worked in Müller's laboratory) who updated the concept of Robert Hooke's "cells" in plants to add function to structure, and Müller's students Theodor Schwann and Rudolf Virchow (among others) who, with their minds and microscopes, conceived and then taught that the body was not indivisible and did not depend for life upon an ineffable vital spirit suffused throughout the whole that spontaneously generated new complete beings. Instead, they insisted, the body was itself composed of smaller working units, and that those smaller units – be they organs, tissues, or cells (in chronological order from Morgagni to

¹⁰⁸⁵Giorgio Baglivi, Laurent Anisson, and Claude Duflos, *Georgii Baglii medic theoric. in Romano archilyc. prof. societatis Regiæ Londinensis, academ. imp. leop. & c. collegæ : opera omnia medico-practica et anatomica*, Hac 6. ed. (Lugduni: Sumptibus Anisson, & Joannis Posuel, 1704).

Bichat to Schleiden, Schwann, and Virchow) – had a function far beyond their anatomy. In essence, the cell became the unit of life.

It is impossible to overemphasize the facts that Schleiden's idea that the cell was the unit of plant life, that Schwann's tangential notion that the cell was the unit of animal life, and that Virchow's statement that the cell was the origin of all cells, were not born *de novo* fully conceived nor in a historical vacuum. Instead, their ideas – although quite revolutionary at the time – had all been proposed earlier. However, the world into which they re-introduced these different ways of looking at life was more prepared to accept the newly-conceived cell than at any earlier time.¹⁰⁸⁶

People have absolutely no conception of the progress made by the natural sciences in the last thirty years. For physiology the decisive factors have been, firstly the tremendous development of organic chemistry, and secondly, the microscope, which has been properly used only for the last twenty years....The main thing which has revolutionised the whole of physiology and for the first time made comparative physiology possible is the discovery of the cell-in plants by Schleiden and in animals by Schwann (about 1836). Everything is a cell.

-Friedrich Engels to Karl Marx, July 14, 1858¹⁰⁸⁷

This new fertile soil, founded in but not necessarily of a world of science, allowed seeds strewn long before to take hold, grow, and thrive. Culture, philosophy, and a new pragmatism reinforced by technology contributed as much or more to the willingness of this post-Hegelian world to accept these radical notions than any advances in science, including the microscope. For seeing is important, but being able to interpret what is seen with fresh eyes leading to new discoveries is more important.¹⁰⁸⁸ The cell, visible to Robert Hooke through his microscope in

¹⁰⁸⁶Rather, Rather, and Frerichs, *Johannes Muller and the Nineteenth-Century Origins of Tumor Cell Theory*.

¹⁰⁸⁷I. B. Lasker, ed. *Marx-Engels Selected Correspondence*, 3rd rev. 1975 ed. (Moscow: Progress Publishers, 1955), 101.

¹⁰⁸⁸The cell was always there, but few approached its true meaning before Schleiden, Schwann, and Virchow.

the seventeenth century as a remarkable collection of "a great many little boxes," (Hooke thought cells accounted for the light weight of cork),¹⁰⁸⁹ became to Virchow by the mid-nineteenth century a source of life through cells ("*omnis cellula e cellula*") and a locus of pathology.¹⁰⁹⁰

If cancer be at its onset and often for a long time a local disease, it must be possible to cure it at that stage by local treatment.

-Rudolf Virchow¹⁰⁹¹

The conceptual leap from anatomical pathology to cellular pathology was enormous, for the seeds of disease under traditional constitutionalism permeated all cells in all parts of the body with cells being at best ancillary beneficiaries of the largesse of the whole. Pre-Virchow pundits realized that diseases affected some organs, tissues, and cells more than others, but the root cause of the pathology was the being, not the cell. Virchow's studies in cellular pathology changed this focus to the microscopic cell. As such, he deserves credit for the revolutionary notion of the diseased cell as the unit of pathology, for it proclaimed a new way of looking at disease – at the cellular rather than the organismic level.

The reach of Virchow's revolutionary view of disease at the cellular level was far and wide. Over the span of a single generation, diseases previously defined at the gross anatomic level were seen in a whole new light at the microscopic level. Pathologies of organs and even tissues became diseases of cells. Virchow and his followers redefined scores of diseases in this manner. Gout became a disease of microscopic crystalline deposits in joints rather than gross

¹⁰⁸⁹Hooke could not be sure of the function of the little "chambers" that he saw, but he surmised that the "cells" accounted for the light weight of cork. Robert Hooke, *Micrographia: or some Physiological Descriptions of Minute Bodie Made By Magnifying Glasses with Observations and Inquiries thereupon*, Special ed., The Classics of Medicine Library (London: Jo. Martyn and Ja. Allestry, 1665; repr., 1996). 113.

¹⁰⁹⁰Or, as the title of Virchow's most famous text explains: "Cellular Pathology as based upon Physiological and Pathological Histology." Virchow, *Cellular Pathology*. In other words, his work considered the disease of cells as derived from the (microscopical) examination of normally functioning as well as diseased tissues and cells.

¹⁰⁹¹Quoted by Semon (circa 1903) from his teacher, Rudolf Virchow. David Charles Schechter and H. Mason Morfit, "The evolution of surgical treatment of tumors of the larynx," *Surgery* 57, no. 3 (1965): 470-71 and see footnote 96 on page 78.

tophi in toes.¹⁰⁹² Inflammation – differentiated from other ailments since ancient times by its four cardinal features [red (rubor), hot (calor), swollen (tumor), and pain (dolor)] through the lenses of Virchow's microscope became a mass of mucous fibrinous exudates, leading upon further analysis to white blood cells of even more highly differentiated natures (polymorphonuclear leukocytes, monocytes, etc.) that even today remain the defining elements of inflammation at the cellular level. Cellular pathology was indeed a whole new method of analyzing diseases of the human body, as Andreas Vesalius' 1543 opus on anatomical dissection, *De Humani Corporis*, had shattered accepted wisdom engendered by Galen more than a millennium earlier.¹⁰⁹³

One Cancer, One Site of Origin

Of the avalanche of microscopical and cellular analyses of the world of disease inspired by Virchow's focus on the pathology of the cell, none were more auspicious than their implications for the treatment of cancer. None effected a more profound change in the treatment of a disease than did the microscopical view of cancer.¹⁰⁹⁴ For the pathology of cancer as seen through the life and death of the microscopical cell argued convincingly that cancer arose in one spot and not in many, even over time. The local origin of cancer was one of the most profound and productive discoveries in the history of medicine. For if cancer originates at the cellular level, "it must," as Virchow wrote, "be possible to cure it at that stage by local treatment."¹⁰⁹⁵

¹⁰⁹²Virchow, *Cellular Pathology*: 213-14.

¹⁰⁹³I have purposely used part of the title of Vesalius' sixteenth century masterpiece, *De Humani Corporis Fabrica* (*On the fabric of the human body*) to stress how revolutionary was Virchow's spotlight on the cell for the study of *the human body*.

On Virchow's analysis of inflammation, see *ibid.*, 386-94, especially pages 89-90.

¹⁰⁹⁴One could surely argue for profound changes wrought by Virchow's cellular pathology for the treatment of other diseases, but to me the effect of the cellular analysis of cancer was the most important because it led real changes in therapy rather than theoretical considerations.

Surgeons, emboldened by the localistic implications of Virchow's cellular pathology for the surgical treatment of cancer, applied anesthesia, antisepsis, and the other new tools of the industrial age to dramatically increase the number of surgeries for cancer from the 1840s to the 1920s. Between 1822 and 1851, for example, physicians at the Massachusetts General Hospital (MGH) performed surgery for the treatment of cancer on 76 patients.¹⁰⁹⁶ By the last decade of the century, surgeons at the MGH operated to remove cancer on hundreds of patients annually. In the first two decades of the twentieth century, the number of cancer operations increased further. Hundreds of papers I have read from the era lead to the same conclusion that can be tersely summarized as: "A chance to cut is a chance to cure."

Why THE Golden Age of Surgery?

A "golden age" may be defined as "a period of great happiness, prosperity, and achievement."¹⁰⁹⁷ The OED adds that it is "the first and best age," implying an era long ago envisioned through the gossamer fabric of time.¹⁰⁹⁸ The golden age of cancer surgery, extending from the waning decades of the nineteenth century into the first decades of the twentieth gave the promise of hope to patients with cancer in the Western world. More patients survived cancer as a result of surgery than had survived with previous therapies. More patients survived the onslaught of surgical excision and the perils it created than ever before.

¹⁰⁹⁵ Schechter and Morfit, "The evolution of surgical treatment of tumors of the larynx," 470-71.

¹⁰⁹⁶ Samuel David Gross, M. D. (1805-1884), *On the Results of Surgical Operations in Malignant Diseases*, *National Library of Medicine* (Philadelphia: T. K. and P. G. Collins, Printers, 1853), Microfilm, 161 pages, NLM 01613193 2.

¹⁰⁹⁷ [www.merriam-webster.com/dictionary/golden age](http://www.merriam-webster.com/dictionary/golden%20age)

¹⁰⁹⁸ Second edition, 1989; online version June 2012. <<http://www.oed.com/view/Entry/79777>>; accessed 23 August 2012. Earlier version first published in *New English Dictionary*, 1900.

As a result of the higher cancer survival rates afforded an increasing number of cancer patients through surgery, word spread via medical societies,¹⁰⁹⁹ medical journals,¹¹⁰⁰ popular magazines,¹¹⁰¹ and the like that cancer was curable, if only it could be detected early (i.e., before it spread). But even if the patient's cancer was not detected in a timely fashion, surgery offered palliation – not a good death (in the sense of Philippe Aries),¹¹⁰² but a more comfortable one.

How surgery had changed the treatment of cancer! Before the golden age, surgery for cancer was as close to a death sentence as one could imagine, for the watchword of cancer was "incurable" – as Samuel David Gross made very clear in 1853.¹¹⁰³ Only fools and those hoping for miracles would undertake the surgical treatment of cancer for any reason short of a last-ditch effort to palliate the unpalliable or to extend survival of the hopeless. Only a few decades later, by the late 1880s and 1890s, surgery had become the treatment of choice for cancer.

We have come full circle. Surgery was never considered a viable treatment option for General Ulysses S. Grant's throat cancer in 1884-5. Only a few years later, in 1887-1888, Dr. Ernst von Bergmann did indeed propose surgery to remove Crown Prince Friedrich's laryngeal

¹⁰⁹⁹ The American Medical Association first became involved in the diagnosis and treatment of cancer with a concerted effort begun in 1905 when Dr. Lewis McMurry, then President of the AMA, appointed Dr. John Clark and Dr. Frank Simpson to investigate "the cancer problem." Not long thereafter, the American College of Surgeons appointed a committee of its own to promulgate information about the treatment of cancer to its members and the public. New York City Cancer Committee, *History of the American Society for the Control of Cancer 1913-1943* (New York: New York City Cancer Committee, 1944). no pagination.

¹¹⁰⁰ Witness the astounding growth in the number of articles on the surgical treatment of cancer from the inception of the *Index Medicus* in 1879 through 1920 (and beyond).

¹¹⁰¹ One of the best popular articles I have found regarding the education of the public on the diagnosis and treatment of cancer resulted from the efforts of Drs. Thomas Cullen and Howard Kelly, both gynecologists at Hopkins. The article focused on cancers of women, not surprisingly. In the early twentieth century, before male deaths attributed to cigarette smoking skyrocketed, cancer was still considered very much a woman's disease. Samuel Hopkins Adams, "What Can We Do About Cancer?," *Ladies Home Journal*, May 1913.

¹¹⁰² See Philippe Aries, *The Hour of Our Death*, trans. Helen Weaver (New York: Oxford University Press, 1981; repr., 1991).

¹¹⁰³ Gross, *On the Results of Surgical Operations in Malignant Diseases*.

cancer, but Drs. Morrell Mackenzie and the by-then-renowned Rudolf Virchow advised against this aggressive undertaking, noting that the odds of surgical failure were too great. Yet, by 1893, when President Grover Cleveland's "rough place" on the roof of his mouth was discovered on the basis of biopsy and microscopical analysis to be cancer, Drs. R. M. O'Reilly and Joseph Bryant did not hesitate to advise the President that surgery was the treatment of choice for the cancer. And the surgical treatment of cancer had advanced so much in those few years between the final years of the 18th President of the United States and the first years of the 24th President that even the vigilant press corps could hardly detect that Mr. Cleveland had undergone surgery.

The End of the Golden Age of Cancer Surgery

All golden ages come to an end. Indeed, few mortals have the perspicacity to realize that they are living in a golden age. Golden ages are described retrospectively. Things change. And so it was with the surgical treatment of cancer. The halcyon days when surgery appeared to offer a chance of cure for all cancer patients were short-lived. Increased data accumulation and statistical analyses revealed that some cancers were more amenable to surgical cure than others – and other cancers not at all.

The wrappings of surgery also showed their true faces. Anesthetics and their administration improved, but some patients still died from anesthesia. Post-surgical wounds, although much less frequent than had occurred during the days of the four horsemen of death, sometimes still became infected and some patients still died of sepsis. Medications became better to treat the complications of surgery – bleeding, infection, and the like – but unmet needs persisted that surgery could not satisfy.

The golden age, when all roads led to surgical treatment of cancer, also ended because other types of cancer therapy became available. The physicist Wilhelm Röntgen's discovery

with his cathode ray tube in late 1895 of what he called X-rays (so named because he did not know what they were, so he used the symbol X for unknown) led by the next year to their use for medical diagnosis (as today) and, shortly thereafter, as a treatment for cancer – radiation therapy or radiotherapy.¹¹⁰⁴ The discovery of the radioactive element, radium, by Pierre and Marie Curie in late 1898 furthered the use of radiation therapy for the treatment of cancer.

Paul Ehrlich's discover of Salvarsan, Compound 606, for the treatment of syphilis in 1909 may be said to be the origin of science-based chemotherapy. Since then, the use of chemicals as therapies for diseases has diverged in many directions. Two of the best known derivatives, synthetic antibiotics and cancer chemotherapy, are targeted to treat specific cancers, much as Ehrlich used Salvarsan to treat syphilis. Many medical "advances" have occurred in wartime, and the discovery of cancer chemotherapy was no exception. Nitrogen mustard was one of the most common poisons used to kill soldiers (and others) during the trench warfare of the First World War. Two American pharmacologists, Goodman and Gilman, serendipitously discovered that this high toxic chloroethylamine profoundly suppressed the division of certain hematopoietic (blood) cells in the body – the same cells found in overwhelming quantities in lymphomas and leukemias.¹¹⁰⁵ By 1946, they and others published articles that became classics in the history of the use of chemicals to treat cancer – the birth of modern chemotherapy.¹¹⁰⁶

¹¹⁰⁴One of the first effects of radiation on humans was found to be skin burns – not dissimilar in appearance from those caused by plasters and poultices used to treat cancer in the first years of the nineteenth century. Hence, as a form of medical inertia, radiation was first used to treat those conditions previously treated by plasters and poultices; viz., everything from infections like tuberculosis to stomach ulcers. Not long thereafter, however, patients and physicians began to notice the adverse effects caused by these "invisible rays."

¹¹⁰⁵Soldiers exposed to nitrogen mustard who did not die within a few hours from lung toxicity instead died days later from pancytopenia – the inability of the body to continuously produce cells necessary for life. Since many of the blood cells (red blood cells and platelets in particular) have short half lives (i.e., they "die" in a few days and must be replaced by new blood cells propagated especially in the bone marrow), soldiers who developed pancytopenia as a result of nitrogen mustard exposure died from their inability to resist infection – a major function of white blood cells.

The use of the body's own immune system to fight cancer – immunotherapy – is a strategy that has been used for more than a century. Physicians in Germany noted as early as the 1850s that a patient's cancer would occasionally shrink if it became infected.¹¹⁰⁷ By the early 1890s, William Bradley Coley, who treated the sarcoma of Bessie Dashiell (whose close childhood friend, John D. Rockefeller Jr. claimed that her death from cancer at the age of 17 sparked his interest in funding cancer research and what became the Memorial-Sloan Kettering Cancer Center in New York), found that infections and high fevers sometimes led to cancer regression. His combination of two bacteria, *Streptococcus pyogenes* and *Serratia marcescens*, became known as Coley's Toxins and was sold as an immune-stimulating treatment for cancer from 1893 until the 1960s.¹¹⁰⁸ Many other efforts to harness the powerful immune system of the human body to fight against its own cancer cells have been made with variable success. One of the most recent, Provenge (sipuleucel-T), induces an immune response against prostatic acid phosphatase, an enzyme found commonly in high concentrations in prostate cancer, the second leading cause of death in men today (behind lung cancer).

The many decades since the advent of the golden age of surgery have been witness to many additional attempts to rid the body of cancer. From some of the older scientific treatments, like hormonal therapy, to some of the newest, like antibodies targeted against specific constitutive (always turned on) enzymes in cancer cells, there has been lacking a foundational

¹¹⁰⁶Louis S. Goodman et al., "Nitrogen Mustard Therapy: Use of Methyl-Bis(Beta-Chloroethyl)amine Hydrochloride and Tris(Beta-Chloroethyl)amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders," *Journal of the American Medical Association* 132, no. 3 (1946).

Louis Goodman and Alfred Gilman are the same pharmacologists whose 1941 textbook and later editions of *The Pharmacological Basis of Therapeutics*, has been studied by tens of thousands (hundreds of thousands?) of medical students and is now (under different editorship but with a similar focus) in its 12th edition.

¹¹⁰⁷<http://info.cancerresearchuk.org/cancerandresearch/all-about-cancer/what-is-cancer/treating-cancer/history-of-immunotherapy/immunotherapy2> accessed August 23, 2012.

¹¹⁰⁸William Bradley Coley, "The treatment of malignant tumors by repeated inoculations of Erysipelas, with a report of ten original cases," *American Journal of Medical Sciences* 105(1893).

piece in the puzzle whose solution may possibly lead to its ultimate cure – knowledge of the cause of cancer.

There have been enormous advances toward the discovery of the etiology of cancer since World War II, but the answer continues to elude those who seek it. Lost in the discussion, however, is the subject of this paper; viz., how physicians and the public came to understand and approach the problem of cancer as they do, and how this foundation of modern cancer, based firmly at the critical turning point in cancer history – the late nineteenth century – continues to influence the diagnosis, treatment, and investigation of cancer in the twenty-first century.

CONCLUSION

The End of the Beginning

This dissertation has demonstrated the critical importance of the late nineteenth century to the development of a new, radical approach to cancer. This was not a gradual historical development that could have been predicted by what had come before. Instead, the late nineteenth century was a revolutionary turning point that totally changed mankind's approach to cancer, from the perception of the disease by society to the diagnosis and treatment of the malady in individual patients by practitioners. This watershed era occurred over the course of a mere two decades. Like other short periods of intense change, the subject of that change was never perceived, diagnosed, or treated the same afterwards, and all subsequent developments can be traced back to those seminal years. Modern cancer is as different from traditional cancer as the day is from the night, for although the biological entity called "cancer" may not have undergone marked evolution over the course of human existence, cancer as it is thought of in 2013 – diagnosis, treatment, and prevention – dates back only to the end of the nineteenth century.

A few new thoughts and actions led to enormous transformations. In the case of cancer, the advent of the medical microscope, histological pathology, and human chemistry in the nineteenth century were fundamental. But these derivatives of the application of science to medicine would have been insufficient to create the watershed period of the late nineteenth century without the human element – seemingly far removed from developments in medical science. Like other endeavors of mankind, science and medicine require proponents (and opponents) to carry ideas forward and make them part of the fabric of society. In the history of cancer, individuals – from obscure names like John Parsons, Joseph Bryant, and Ernst Abbé, to

names well-known for other achievements, like Paul Ehrlich, Sigmund Freud, and Oliver Wendell Holmes, Sr., to easily recognized names like Ulysses S. Grant, and Grover Cleveland – provided the spark that thrust cancer from a relatively obscure but feared disease to an everyday household word of deadly connotation. This dissertation has demonstrated when, where, what, how, and, oftentimes, the why of the making of modern cancer.

The treatment of cancer has changed dramatically since William Rockefeller peddled his proprietary cancer elixirs throughout the old Northwest during the middle years of the nineteenth century. As demonstrated in the first section of this work, but omitted or marginalized by historians of cancer including James Patterson, Barron Lerner, and Siddhartha Mukherjee, the diagnosis and treatment of traditional cancer relied on an eponymous and grossly descriptive nomenclature that made comparisons of tumors between patients problematic and did little to advance the uniformity and standardization of diagnosis. Treatment depended on the presumption of constitutionalism, the millennia-old notion that cancer was part and parcel of the entire being; i.e., intrinsic to the afflicted human body. Eradication of a growth in one part of the body merely foretold subsequent growths elsewhere in the body. Traditional cancer, therefore, was incurable. The fact that cancer was stigmatized as a punishment for sin contributed further to the incurability of cancer, for it relegated treatment to only the most advanced cases when the choice was between temporary palliation or certain death.

The birth of cell theory in the chambers of Müller, Schleiden, and Schwann and the subsequent development of histopathology began to turn the focus on the problem of cancer from that of a gross disease to a disease of cells and tissues. Rudolf Virchow, one of Müller's students, contributed immeasurably to cellular pathology, as he applied an instrument only recently refined into a tool of consistent reliability for the analysis of disease – the microscope.

Through Virchow's microscope may be witnessed the seeds of the overthrow of constitutionalism.

The medicalization of cancer could not have led to a new conceptualization of the disease without its destigmatization and subsequent legitimization as a natural phenomenon rather than a punishment from the Almighty. The application of science to medicine contributed to cancer's destigmatization. Moreover, the institutionalization of cancer and its personification in revered figures like General Ulysses S. Grant, transformed the disease from a sentence of silent suffering to a challenging object of scientific and medical research.

The New York Cancer Hospital, in 1884, was founded on the personal tragedies of Elizabeth Hamilton Cullum and Charlotte Augusta Astor and the quest to contain the perceived contagiousness of cancer. Although initially mired in the racism, Victorian sexism, and hospital-as-almshouse mindset of the past, the cancer hospital represented a momentous development for it institutionalized the dread disease and made its treatment a collective effort in the research laboratories and operating suites of the hospital. Thus, the cancer hospital further served to destigmatize and legitimize the diagnosis and treatment of cancer.

The 1880s represented a transitional time in the transformation of traditional to modern cancer. For many older practitioners, the diagnosis and treatment of cancer were very much as they had been for their entire careers, frozen in a temporal quagmire of gross anatomy and superficial treatments founded in a theory of constitutionalism that led to stubbornness on the part of patients against seeking early diagnosis and consequently led to poor outcomes.

General Ulysses S. Grant is an excellent example of this late-stage traditional cancer mentality. He delayed seeking definitive diagnosis, and, in conjunction with his physicians' antiquated approach, delayed treatment. Contrast this with President Grover Cleveland's rapid

diagnosis and treatment, orchestrated by a newer generation of physicians less than a decade later.

Whereas almost five months passed from the onset of Grant's symptoms to his clinical diagnosis, Cleveland's physicians diagnosed his cancer accurately seven weeks after his symptom onset. While Grant's cancer was not examined under the microscope until eight months after symptom onset and four months after he received a clinical diagnosis of cancer, Cleveland's physicians biopsied his tumor immediately upon discovery and confirmed a diagnosis of cancer shortly thereafter. Grant's physicians, steeped in old-school traditional cancer and constitutionalism, dismissed a surgical treatment, but Cleveland's new-age physicians, learned in the avant-garde diagnostic and therapeutic techniques based upon localism and founded in Germany and England, advised immediate surgery – despite the need for precautions for a sitting President in the midst of an economic crisis. Whereas Grant never had surgery for his malignancy, Cleveland underwent three operations over the course of four and a half months. Although Grant received red-clover and other questionable medicinals, the medications that Cleveland received were anesthetics that made surgery tolerable, antiseptics that made surgery safer, and post-operative analgesics that made recovery bearable. Whereas Grant's palliative therapy included attention to the meteorological and other perceived salubrious portents of the day despite his waning voice and failing body, a prosthodontist fitted Cleveland shortly after extirpative surgery with a rubber prosthesis that allowed him to speak clearly for the remainder of his cancer-free, natural life.

The contrast between the diagnosis and treatment of General Grant's cancer and President Cleveland's could not be more striking. While Grant was a victim of the failings of traditional cancer that led to late diagnosis and inadequate treatment, Cleveland, only a few years later,

benefited from the advances of modern cancer to undergo rapid diagnosis and definitive surgical cure.

Nonetheless, the contribution of Grant to the history of cancer cannot be overemphasized, for the General, by publicizing his illness, served to destigmatize and legitimize the diagnosis of cancer. As traditional cancer was hidden within the confines of family and Church to the disadvantage of the afflicted, the publicity surrounding the former President's cancer removed it from the shadows of suppression. Ironically, the successful treatment of President Cleveland's cancer could have further advanced publicization of the benefits of the early diagnosis and treatment of cancer – hallmarks of modern cancer. But politics and economics – not religion and social stigma – shrouded Cleveland's cancer and its treatment in secrecy until long after others had taken up the cause for early cancer diagnosis and treatment.

The foundations of modern cancer are the medical microscope and the advent of modern surgery. Both came to fruition in the late nineteenth century, the microscope via refinements in optical technologies, slide preparations, and cellular pathology and surgery via anesthesia and antisepsis.

The medical microscope is critical to the diagnosis and treatment of modern cancer. Although the compound microscope was invented during the Renaissance, optical aberrations prevented its use as a medical instrument until well into the nineteenth century. Distortions of colors and shapes by early microscopes made the visualization of images through the microscope so strange and inconsistent that the microscope remained more toy than tool. Even after Joseph Jackson Lister and others refined the optical lens system in the first half of the century, however, many medical practitioners refused to use the microscope and denigrated findings made with its use.

The growing acceptance of cell theory and then cellular pathology enhanced the value of the microscope to medicine. Virchow's demonstration that cancer was a disease of cells, a conception that began with his teacher Müller's "Nature of Cancer," revolutionized the perception of the disease. Scientists of cancer switched their focus from the macroscopic to the microscopic. A new understanding of the disease followed. Among many other changes, pathologists revised the nomenclature of the disease (e.g., from gross-level scirrhus to microscopic-level adenomatous) and a new generation of physicians, schooled in the use of the compound microscope as an instrument of medicine, challenged the long-accepted constitutional nature of the disease.

Optical physics and its application to lens manufacturing were critical to the structure and function of the microscope, but the transformation of the instrument into an essential tool for medical decision-making and cancer treatment required prepared specimens viewed through the microscope. Paul Ehrlich, best known in medical history for his "lock and key" theory of immunology and for Salvarsan, one of the first scientifically-based chemotherapeutic agents, was a chemist at heart. A youthful experimentation with different dyes on living tissues paid enormous dividends when he found that different cells – and even organelles within cells – colored distinctly with various dyes. The recognition that leukemia, so named for the white appearance of the blood in patients with the disease, was a cancer that consisted of innumerable cells that Ehrlich could highlight with his stains, was just one of his many discoveries in what came to be called staining.

Finely-ground lenses situated precisely in the optical microscope so as to eliminate distortion, chemical staining of tissues, and microscope slide preparation with microtomes combined to make the microscope an essential tool of cancer medicine. All of these factors

came to the fore in the case study of Emperor Friedrich III of Germany, King of Prussia, whose microscopical diagnosis of cancer and subsequent interpretations by his physicians may have altered the course of history, culminating in World War I.

Modern cancer could no more have come about without scientific surgery than it could without the medical microscope. As is argued in the final chapter of this work, the evidence shows that the development of surgery into the treatment of choice for cancer at the end of the nineteenth century was greatly influenced by the application of chemistry to human biology in the form of anesthetics to eliminate the pain of surgery and antiseptics to prevent postoperative infection. Surgery prior to these twin innovations was unbearable and exceedingly dangerous, as even the most stalwart patients risked their lives with minor skin excisions. And it is not without significance that the first patient operated upon with Morton's Letheon anesthetic had a tumor removed.

Anesthesia and antisepsis were necessary to the rise of surgery as the treatment of choice for cancer, but they were not sufficient. Undergirding surgery as the preferred treatment for cancer was a presumption of the validity of localism. Indeed, the concept that cancer began in one place and spread outward was a radical inversion of constitutionalism, that held that all tissues in the cancerous body had a propensity to develop cancer. Once cancer, always cancer. Surgery held no long-lasting value under such a mindset. With a localistic conception of the disease, however, surgery offered the possibility of cure, an idea radically different from the collective wisdom expressed by the eminent Dr. Samuel Gross only a few years earlier in 1853 that cancer was incurable.

By the late nineteenth century, it was clear that the diagnosis, treatment, and investigation of cancer had undergone revolutionary changes. Built upon an intellectual framework that relied

upon new insights and tools, the diagnosis of cancer was sought sooner rather than later; the treatment of cancer was by surgical excision; and the investigation of cancer became microscopic rather than macroscopic.

Unrecognized by those who write cancer history in the 21st century, including James Olson and Mukherjee, the paradigm shift in cancer occurred not in the post-World War II period, but more than half a century earlier in the late nineteenth century. For without the pathological turn from gross to microscopic anatomy, recognition of the cellular and molecular basis of cancer so widely accepted would not be the same. Without the stains, "magic bullets," and "lock and key" antibodies of Ehrlich, neither chemotherapy nor immunotherapy would be the same. Without the anesthetics and antiseptics developed in the nineteenth century, there would be no surgery. And without the seminal application of science to medicine rooted in the nineteenth century, there would be no intellectual framework for the prevention, diagnosis, treatment, and, ultimately, cure of cancer. The great revolution in cancer took place in the late nineteenth century and gave birth to modern cancer and all that came after.

EPILOGUE

The Beginning of the End

By the early twentieth century, cancer had become a much greater concern in the collective professional and public mindset than it had ever been earlier. The disease had always been a foe for those relatively few unfortunate to develop it, but in its new guise as modern cancer from the late nineteenth century onward, it had become sufficiently prevalent that it engendered a heightened level of investigation and fear on the part of professionals and the public alike.¹ There were enormous strides in the treatment of cancer following World War II, but they were no more meaningful than those made during the preceding century. This epilogue seeks to carry the story of modern cancer forward into the twenty-first century to demonstrate how the present view of cancer is a consequence of the revolutionary changes that occurred during that period rather than *sui generis* to the twentieth century.

GETTING THE WORD OUT: DIAGNOSE CANCER EARLIER?

The most important change was the earlier diagnosis of cancer.² In the early decades of the nineteenth century, a cancer diagnosis was reactive rather than proactive. People neglected lumps, bruises, and/or changes in bodily functions (e.g., cough, change in bowel movements, bloody emissions) preferring to hope that it would go away. This was with good reason, for cancer then was tantamount to a death sentence.

¹One method of evaluating the effect of the increased prevalence of cancer on the medical community is via the approach to cancer in medical textbooks. In William Osler's formidable *Principles of 1892* (William Osler, *The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine*, The Classics of Medicine Library (New York: D. Appleton and Company, 1892; repr., 1978)., the diagnosis and treatment of cancer was little more than a footnote to Osler's analysis of organ-based diseases (stomach, lung, etc.). By 1919, when James Ewing published *Neoplastic Diseases*, entire textbooks were devoted strictly to cancer. (James Ewing, *Neoplastic Diseases, a Treatise on Tumors* (Philadelphia: W. B. Saunders, 1919).

²Dr. Paul Marks, then head of the Memorial Sloan-Kettering Cancer Center, made this point repeatedly to me in a personal interview in the late 1990s.

As surgery improved toward the end of the century more practitioners began to realize that early diagnosis could, in some circumstances, even lead to cure. Word of the value of early diagnosis (breast, uterus, skin, etc. – and eventually X-rays) spread. Popular magazines like the *Ladies Home Journal* encouraged routine physical examinations for cancer.³ Men became interested in screening, especially as the incidence of lung, throat, lip, and other cancers grew.

By 1913, physicians, groups, and even life insurers decided to attack the problem in an organizational manner. New Yorkers formed the American Society for the Control of Cancer (ASCC).⁴ Thirty years later, the ASCC morphed into the American Cancer Society (ACS), a formidable force in cancer education, prevention, surveillance, diagnosis, treatment, and research.⁵

At the same time, statisticians, who worked for institutions life insurance companies, took notice of the rising incidence and prevalence of cancer deaths. Frederick Ludwig Hoffmann, a statistician who worked for Prudential Insurance Company of America beginning in 1891, published broad tracts exclaiming the rise of global cancer mortality.⁶ As cancer touched more families, awareness increased and attention to cancer screening followed with resultant earlier diagnosis.

THE SCIENCES DOMINANT:

TWENTIETH-CENTURY CANCER MEDICINE

³Samuel Hopkins Adams, "What Can We Do About Cancer?," *Ladies Home Journal*, May 1913.

⁴New York City Cancer Committee, *History of the American Society for the Control of Cancer 1913-1943* (New York: New York City Cancer Committee, 1944). Also see Victor A. Triolo and Michael B. Shimkin, "The American Cancer Society and Cancer Research: Origins and Organization: 1913-1943," *Cancer Research* 29(1969).

⁵Donald Shaughnessy's doctoral dissertation is particularly comprehensive on the ACS, if now over fifty years old. Donald Shaughnessy, "The Story of the American Cancer Society" (1957).

⁶Frederick L. Hoffman, *The Mortality from Cancer Throughout the World* (Newark: Prudential Press, 1915).

Over the course of the twentieth century, medical and surgical practitioners of cancer became more specialized and investigated specific targets in their quest to understand and treat cancers. Some of the paths followed by twentieth century researchers included experiments in hormonal regulation, penetrating rays, chemotherapy, and immunotherapy – among several others. Although potions and pills have been used to treat cancer from time immemorial, it is difficult to classify these "treatments" as scientific. The first scientific researches into the nature and treatment of cancer, therefore, were hormonal.

Magical Chemical Messengers

In 1878, George Thomas Beatson (1848-1933), a young graduate of the University of Edinburgh removed the ovaries (oophorectomy) of rabbits and discovered that the rabbits stopped producing milk! How strange, he felt, "that one organ [could hold] control over the secretion of another and separate organ."⁷ He extrapolated this finding to conclude that "the ovaries may be the exciting cause of [breast] carcinoma" and in 1896 published his findings on hormonal ablation in the venerable British medical journal, *The Lancet*.⁸

As Lister did not know why his antiseptic method was successful, neither did Beatson realize why the removal of the ovaries could treat breast cancer. Nonetheless, it worked in many cases, demonstrating once again that empiric success without causal understanding is more desirable than understanding without treatment success. Thirty years later, in 1929, Adolf Butenandt and Edward Adelbert Doisy independently isolated and determined the chemical structure of estrogen – the hormone that Beatson had unwittingly reduced by removing the

⁷ <http://www.cancer.org/cancer/cancerbasics/thehistoryofcancer/the-history-of-cancer-cancer-treatment-hormone-therapy> accessed November 8, 2012.

⁸George Thomas Beatson, "On the Treatment of Inoperable Cases of Carcinoma of the Mamma: Suggestions for a New Method of Treatment, with Illustrative Cases," *The Lancet* 148, no. 3803 (1896).

ovaries. By the 1930s, hormone therapy was the rage, but it was only the first of many chemical therapies to come, including anti-estrogenic compounds. In 1940, an American urologist, Charles Huggins, discovered that male castration caused the regression of prostate cancer. Since then, many chemical inhibitors of hormonal actions have been used to halt the growth of, or even cause regression of, cancers. Thus, hormonal cancer therapy has led to changes in the objectives of cancer surgery for, ironically, cancer surgery – founded on principles of localism – cannot reach beyond the scalpel's blade. Hormones, carried to all cells of the body via the bloodstream, can.

Invisible Rays

More than two centuries after Isaac Newton published his *Principia* (1687) revealing that invisible forces like gravity could work on bodies at a distance without a tangible connection between them, Wilhelm Röntgen, a German physics professor, discovered that he could produce invisible rays that could penetrate seemingly impenetrable objects without visibly altering them. He named these unknown *strahlungen* X-rays. One of his first uses of this mysterious type of electromagnetic radiation was a never-before-seen look at his wife's hand.



Figure 14. The Left Hand of Frau Röntgen (1895)⁹ (Note wedding ring on the fourth finger)

⁹ http://quibb.blogspot.com/2011_02_01_archive.html accessed November 8, 2012.

The medical value of the X-ray was rapidly realized. By early 1896, the X-ray had become well known the world over (Röntgen would be awarded the Nobel Prize only five years later) and was already being used for diagnostic purposes, starting with fractured bones. From this early imaging of the inside of the body from without developed other imaging techniques, including ultrasound (sonography), computerized tomography (CT scans of sliced X-rays), magnetic resonance imaging (MRI), and proton emission tomography (PET scans) that could reveal function in addition to the structure of the tissue under examination.

Within a few years, X-rays were being used to treat cancer. Some cancers melted away, but, as with so many other therapies, the cancer returned weeks and months later.

Only a few weeks after Röntgen's discovery of X-rays, Henri Becquerel, also a physicist, found that if he exposed phosphorescent substances – like uranium salts – to sunlight, a powerful, penetrating X-ray-like emission might follow. Repeated experiments confirmed this amazing finding, but radiation was different from that of the X-ray. Becquerel's doctoral student, Marie Sklodowska Curie (1867-1934) (who had married Pierre Curie only a few months earlier), discovered that two other elements, polonium and radium, were also radioactive. Within a short time, radioactive elements were also, like X-rays, in great demand for the treatment of cancer. But radium was hard to procure and extremely expensive, limiting its medicinal use.

Radiation therapy had drawbacks. Unrecognized at the time, X-rays damage DNA and other essential cellular organelles. Thus, radiologists in the first years of the twentieth century, who calibrated the dose of radiation just strong enough to turn their skin pink (an "erythema dose"), discovered they were developing leukemia (blood cancer) in exceptional numbers. Even when the radiation dose was insufficient to induce a radiation burn, there was no way in the early years to shield the non-cancerous tissue from the cancerous tissue. Wide exposure led to adverse

radiation effects ranging from nausea, vomiting, and diarrhea to bone marrow suppression and a lack of blood cells to carry oxygen to the tissues (red blood cells), help protect against infection (white blood cells), and aid blood clotting (platelets). Madame Curie died of aplastic anemia, a form of bone marrow suppression, as a result of her many years of exposure to radiation.

World War II advanced the use of radiation therapies for the treatment of cancer. Stereotactic radiation therapy, using high-intensity rays, enhanced cancer cell death while reducing exposure of the surrounding tissues and thus unwanted side effects of the radiation. Computers raised radiation therapy to a fine art, exceeded perhaps only by lasers, which are themselves highly concentrated forms of energy. Advances in basic physics led to the advent of proton beams for cancer therapy. Protons, unlike X-rays, and the alpha and beta rays of radioactive decay, are parts of the nucleus of the atom that cause little change in cells and tissues through which they pass while they are lethal to the cells at the end of their short beam. Hence, targeted therapy is also possible with proton beams, sparing non-cancerous tissues surrounding a cancer.

As the dream of the precise, invisible knife for the extirpation of cancer continues to elude the medical community, one must remember that the advances of the past were all made possible by the a happy confluence of physics, chemistry, biology, and medicine, driven by the scientific method and the quest to cure cancer. One can only hope that a future combination of disciplines through focused methodologies will lead to invisible rays that cure cancer.

One Pill, Taken Once – The Dream of the Magic Bullet

The treatment of choice for most cancers from the end of the nineteenth century until World War II was surgery. For the remainder of the twentieth century, chemotherapy became the treatment of choice – with or without surgery.¹⁰

Chemotherapy is the use of chemicals to kill cancer cells. The difference between chemicals and chemotherapy is that chemotherapeutic agents are chemicals that are therapeutic. Simple as that sounds, it means that chemicals thought to have efficacy against cancer cells are shown through rigorous clinical trials to be safe as well as effective against a particular type of cancer. This is the difference between the cancer elixirs of William Rockefeller (and so many, many others) and the agents used against cancer in 2013.

Chemotherapy was forged in the trenches of the World War I, and substantiated in bodies of numerous adults and children with cancer following World War II. Chemotherapy need not imply a term used solely for cancer treatment, but it is often used that way. The result of Paul Ehrlich's 606th attempt to find a chemical to treat syphilis, known since then as Salvarsan (arsphenamine), is chemotherapy. So is the antibiotic taken for a serious infection, or the drug to reduce or prevent vomiting following cancer chemotherapy.

Toward the end of World War I, the German Army began using a form of chemical warfare with an agent known as Sulfur Mustard (mustard gas). By 1919, it was known that many soldiers exposed to Mustard developed a decline in their white blood cells, especially infection-fighting lymphocytes. During World War II, the United States Army, fearful of a German return to chemical warfare, experimented on Nitrogen Mustard and similar agents.

Louis Goodman and Alfred Gilman (famous for their publication of *The Pharmacological Basis*

¹⁰There are many, many exceptions. Small, localized, accessible tumors remained the province of the surgeon. Generalized cancers, like leukemia or Hodgkin lymphoma, were never (almost never) the surgeon's territory.

of Therapeutics), found that lymphoid tissue was sensitive to mustard. Several patients with lymphoma tested soon thereafter had remarkable reductions in their lymphoid tissue mass.¹¹ For reasons of military secrecy and the Cold War, the real story of this watershed discovery was not released to the public until 1963.¹² Mustard was the first of a class of cancer chemotherapy drugs known as alkylating agents, but it would not be the last. Over the ensuing decades, medical scientists discovered many more alkylating agents as well as drugs that worked to halt the growth of cancer cells – a story and a quest that are far from over. For until a patient with cancer can take a pill to cure one or many cancers, the story will continue. If war is a story of blood and treasure, then cancer chemotherapy is a story of research and redemption.

Who Owns Cancer?

The Golden Rule: He who has the Gold makes the Rules.

-Unknown

As the incidence of cardiovascular diseases declines, cancer's share of the healthcare budget will increase, *ceteris paribus*. Who benefits? To what end? The end should be clear – the restoration of the health of the patient through the eradication of cancer. But how is that achieved? By whom? What value does a society place on such an achievement? And who will pay for it?

Although cancer is as old as man, society did not quantify cancer as a major health problem until the end of the nineteenth century. Prior to that time, the leading causes of death were infectious, and these took their toll on those of any age. As the lifespan of citizens of the more developed countries increased from the nineteenth into the twentieth century – and

¹¹Louis S. Goodman et al., "Nitrogen Mustard Therapy: Use of Methyl-Bis(Beta-Chloroethyl)Amine Hydrochloride and Tris(Beta-Chloroethyl)Amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders," *Journal of the American Medical Association* 132, no. 3 (1946).

¹²Alfred Gilman, "The Initial Clinical Trial of Nitrogen Mustard," *American Journal of Surgery* 105, no. 5 (1963): 574-78.

especially with the advent of antibiotics beginning in the 1930s – acute infections began to take a back seat to chronic diseases, including heart disease and cancer. Society and government took notice.

The age of traditional cancer witnessed little regulation of treatments. Most experimentation and research was either self-funded, as in the eighteenth century or funded through hospitals and associated medical schools beginning later in the nineteenth century. The 1906 Pure Food and Drug Act was a Progressive endeavor to eliminate the snake oil salesmen of cancer cures and establish standardization within the growing pharmaceutical industry. But it established no clear path for the treatment of cancer, and most research continued to be funded through private institutions such as universities.

By the 1930s, however, cancer became recognized as a public problem. The National Cancer Act of 1937 established the National Cancer Institute "for the purposes of conducting researches, investigations, experiments, and studies relating to the cause, diagnosis, and treatment of cancer."¹³

The politics of cancer in the twentieth century is a story unto itself, but suffice it to say that for any piece of legislation there is a driving force – usually one or more very interested parties. The proponents of legislation may be any part of the iron triangle: the government agency, the legislative committee, or the interested lobbying group.

Mary Lasker (1900-1994) lobbied hard for government funding of many healthcare issues. Her advocacy reached to many diseases in addition to cancer, but the death of her wealthy advertising executive husband, Albert Lasker (who played a major role in the advertising slogan: "L.S.M.F.T. – Lucky Strike Means Fine Tobacco), from colorectal cancer at the prime of her life surely had something to do with her advocacy for the increased funding of

¹³ <http://legislative.cancer.gov/history/1937> accessed November 9, 2012.

cancer research.¹⁴ Perhaps Mrs. Lasker's greatest single act of lobbying was in favor of and gaining the passage of the National Cancer Act of 1971, otherwise known as the Nixon's "War on Cancer." The words of Neen Hunt, former President of the Lasker Foundation, neatly sum up Mrs. Lasker's efforts:

Mary used to say that she was opposed to cancer, stroke and heart disease the way that she was opposed to sin. This was her axis of evil and she began her front in the battle against disease by attacking cancer, the most feared killer in the 1950s. At that time, if someone was diagnosed with cancer, it was referred to as a "death sentence." Cancer victims often were not told that they had the fatal disease, and families did not dare to utter the dreaded "C" word [sic] to even themselves.¹⁵

Mary, with Albert's support, helped to change attitudes toward cancer from a killer that was too horrible to imagine to a threat that could be thwarted. She helped organize the American Cancer Society, convinced RCA president David Sarnoff that "cancer" could be said over the radio, pressured *Reader's Digest* to publish a series of cancer-related articles, and lobbied Congress and several presidents to create the National Cancer Institute. In 1971, after what Neen Hunt and others describe as Mary's "furious lobbying," the National Cancer Act became law.

As President Nixon wrote Mary: "I feel that with the procedures set up under this bill, we are now in a position to make a total commitment to the conquest of cancer."¹⁶

¹⁴The Lasker Award, presented by the Lasker Foundation founded by Mary and Albert Lasker in 1942, is perhaps the most prestigious medical research award in the United States. A high percentage of Lasker Award winners subsequently receive a Nobel Prize. See <http://www.laskerfoundation.org/awards/index.htm> accessed November 9, 2012.

¹⁵Ibid.

¹⁶<http://www.laskerfoundation.org/media/firstlady.htm> accessed November 9, 2012.



Figure 15. Mrs. Mary Lasker (1900-1994) on a stamp issued by the government she fought so hard to influence.

The National Cancer Act of 1971 minced no words. "There is broad agreement," wrote the Committee that authored the bill, "that cancer research has advanced to the stage where a substantial increase in resources and effort could be very productive."¹⁷ The Act sought to provide those resources, and so it did. Increased funding gave rise to new cancer institutions and extensions of old ones. It increased the number of researchers and enticed many young physicians to follow a career in oncology.

But the Act did not achieve for cancer what the Space Program or the Federal-Aid Highway Act of 1954 achieved toward their objectives. Nevertheless, the Act did foster an explosion in cancer research to new approaches to the disease. Among them were a shift in theories of causation from externalities (like radium-painted watch dials, asbestos, viruses, radio waves, and so many more) to internalities related to oncogenes and other genetic propensities to cancer. Above all, however, cancer research in the 1970s fostered a new respect for the body's own defenses against "foreign invaders."

Immunotherapy: The Battle for and against Self

¹⁷ <http://legislative.cancer.gov/history/phsa/1971> accessed November 9, 2012.

Evolution presupposes change. If change allows the organism to adapt to a changed environment, we say that it is for the good. If change fails, it is not good. How then can an organism adapt to its changing surroundings without itself changing? It cannot. But in the process of changing, it exposes itself to a potentially dangerous environment. It must have a means to protect itself against a hostile, external environment, and against those invaders that breach its defenses. That means is the immune system.

Emil von Behring discovered in 1890 that the blood of animals infected with germs contained molecules that attacked these invaders and the cells invaded. He named these molecules antibodies. Paul Ehrlich found that his histological stains colored some cells but not others, implying that some cells had something that could attach or receive the stains (cell surface receptors) and others could not. He called foreign invaders antigens and hypothesized that something about the structure of antibodies, that he found were made by certain cells in profusion upon exposure to an antigen, attached to the antigen, rendering it harmless. This led to his side chain theory (receptors on antibodies), whereby the unique antibody structure grabs on to a specific antigen and maintains its grip. The production of antibodies by the host and its attack on the antigen he called the immune response, meaning "protection from disease."¹⁸

Coley's toxins, named after New York Cancer Hospital surgeon William Bradley Coley (1862-1936), were early attempts to use the immune system stimulated by infection to fight cancer. Coley was not the first to do this, but his mixture of two bacteria, *Streptococcus pyogenes* and *Serratia marcescens*, beginning in 1893, was used to treat cancer in the United States until 1963 and in other European countries for almost thirty years thereafter. The connections between infection, cancer, and the immune system are enormous and complex, as

¹⁸ <http://www.etymonline.com/index.php?term=immunity> accessed November 9, 2012.

evidenced from Virchow's chronic irritation cancer causation theory to the knowledge that viruses such as the Hepatitis B virus can insinuate itself into human DNA to cause cancer.

What if researchers could harness the power of antibodies to attack cancer cells? Would this not be an ideal treatment, because it is "natural"? It would kill the targeted cells but not normal cells, and would obviate the need for potentially deforming surgery. These, then, would be magic bullets.

Technology in the 1970s allowed the production of vast quantities of antibodies of the same structure from the same nidus – monoclonal antibodies. As basic scientists elucidated the structures, functions, and pathways of the immune system and cancer cells, these targeting monoclonal antibodies could be injected into the cancer patient and, presumably, kill the cancer without harming the host.

Reality, however, is different from theory, because the efficacy in killing cancer cells has not always reached the expectation and adverse effects of these monoclonal antibodies can be intolerable. Improved recombinant DNA technologies have improved the effectiveness of these targeting antibodies, but adverse effects remain limiting.

Infused monoclonal antibodies, like Rituxan (rituximab – drugs have both brand names and generic names, the latter in parenthesis here) for lymphomas and other diseases and Herceptin (trastuzumab) for certain types of breast and stomach cancers, have revolutionized the field of cancer therapy, representing a strong claim for the development of pharmaceuticals based upon the findings of basic science.

But what if, instead of introducing an external chemical immune molecule to prevent the cancer cell from dividing, one could inject a substance that stimulates the organism's own immune system to attack the cancer cells – like a vaccine? Vaccines can be preventive (such as

the common mumps, measles, and Hepatitis A & B vaccines) or therapeutic (i.e., treat an existing disease). In 2010, the Food and Drug Administration approved just such a therapeutic vaccine – Provenge (sipuleucel-T) for advanced states of prostate cancer. In a marvelous amalgam of science and engineering, Provenge is actually made from the patient's own immune cells. Blood is withdrawn from the patient (not to remove it from the body as in days of old, but rather to concentrate some of its components and treat them for later re-infusion). Special cells of the immune system (antigen presenting cells, or APCs) are separated from other blood components, cultured with special antigens (prostatic acid phosphatase, PAP and an antigen that stimulates white blood cell proliferation, GM-CSF) that lead the APCs to "express" fragments of these antigens on their cell surface. The cells are then re-infused into the patient (now as Provenge) and activate the cancer patient's own immune cells (T-lymphocytes) to attack the prostate cancer cells. Compelling as are the theoretical underpinnings for the use of Provenge, overall survival is extended by only 4 months (from 21.7 to 25.8 months after diagnosis) and adverse effects can be severe.¹⁹ And Provenge is extremely expensive, costing almost \$100,000 for the standard three treatments.

The production, structure, and function of the immune cells are some of the most fascinating processes known – and the basis for an entirely different method for treating cancer; i.e., immunotherapy. Efficacy, safety, cost, and other issues remain to be refined.

A Good Beginning

The nineteenth century, with its turn from a didactic, empirical approach to the problem of cancer toward a scientific analysis of the diagnosis and treatment of the disease, marked the end of the beginning in the fight against cancer. The growth of specialization throughout

¹⁹Philip W. Kantoff et al., "Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer," *The New England Journal of Medicine* 363(2010).

medicine in the twentieth century, combined with interdisciplinary cooperation among physicists, chemists, biologists, physicians, and others, led to new ways of treating the disease beyond surgery. Chemotherapy, radiotherapy, and immunotherapy are just some of the non-surgical therapies that have improved patient outcomes since the last decades of the nineteenth century.

The prevention of cancer may have temporarily become secondary to its treatment during the twentieth century, but a groundswell of opposition in the early twenty-first century to the economically-driven, politically-inspired, and medically-enabled emphasis on treatment rather than prevention may reverse that trend.

None of these twentieth-century developments in the diagnosis and treatment of the disease could have occurred without the revolution in cancer medicine that came about during the late nineteenth century.

Waiting on a Happy Ending

As we delve deeper into the complexities of cancer in the twenty-first century, we see that past is prologue: that the present builds upon the knowledge of past. The decades since the cancer revolution of the late nineteenth century have witnessed significant advances in cancer medicine, but those developments derive from the critical juncture of that earlier period and could not have occurred without them. It is like marveling at the newest leaves of a tree without knowing its roots, for the roots give meaning and understanding to the entire tree.

The end of cancer is not near. Careful documentation by countless observers over the centuries, however, has pointed the way to diagnosis. The achromatic, aspherical microscope has been the single greatest tool toward an explanation of the mystery that is cancer. General Grant did not die in vain. His death augured the end of an old disease and the beginning of a

new one. President Cleveland ultimately became the poster child for that new disease. The epic nineteenth-century battle in the minds and hearts of the older and younger generations between constitutionalism and localism, between pain and anesthesia, between sepsis and antisepsis, and between taking medicines versus undergoing surgery, became well decided and their divisiveness put to rest, at least for a while.

The money spent on the treatment of cancer since the revolution of the nineteenth century has yielded invaluable results. Unfortunately, these newer therapies involving radiation, hormones, chemicals, immune system modulators, targeted pharmaceuticals, and much-improved surgeries with safer anesthetics have yet to lead to a bright future for many cancer patients.

This is the hardest story that I've ever told
 No hope, no love, no glory
 Happy endings gone forever more
 I feel as if I'm wasted
 And I'm wastin' every day.

This is the way you left me,
 I'm not pretending.
 No hope, no love, no glory,
 No Happy Ending.

-Mika, *Happy Ending* (2007)²⁰

As yet, there is no happy ending.

²⁰Mika, "Happy Ending," (Casablanca Music, LLC, 2007).

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