1984

Cancer and Toxic Substances: The Problem of Causation and the Use of Epidemiology

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CANCER AND TOXIC SUBSTANCES: THE PROBLEM OF CAUSATION AND THE USE OF EPIDEMIOLOGY

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I. INTRODUCTION

Cancer, a disease characterized by the progressive and unrestrained growth of populations of abnormal cells,[1] is probably the most feared disease process in the United States today.[2] The reasons for this are numerous. First, and most obvious, is that except for the non-melanoma skin strain, cancer is frequently fatal,[3] and when it is not, it requires ag-

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[1] OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION, IDENTIFICATION, CLASSIFICATION, AND REGULATION OF POTENTIAL OCCUPATIONAL CARCINOGENS, 45 Fed. Reg. 5,016-17 (1980) (to be codified at 29 C.F.R. § 1990 (1980)) [hereinafter cited as OSHA CARCINOGEN POLICY], points out that cancer is actually a large group of different disease processes which share certain common features. These features include (1) uncontrollable growth of cells; and (2) killing the host cell by either a local extension into the tissue from which it arose (invasion) or by spreading to distant sites (metastasis). J. WYNGAARDEN & L. SMITH, CECIL TEXTBOOK OF MEDICINE 1010 (16th ed. 1982).

[2] Once cancer is understood, another disease will inevitably replace it as the most feared. One author notes that in early biblical times, leprosy was such a disease. In late medieval times, that distinction focused on the bubonic plague or the "black death." In the 19th, tuberculosis, the "white death," was most commonly associated with human suffering. H. PITOT, FUNDAMENTALS OF ONCOLOGY 1 (1978).

[3] In 1980, the American Cancer Society (ACS) estimated that 815,000 new cases of cancer (excepting non-melanoma skin cancer) would be diagnosed in 1981. The ACS also estimated 420,000 (more than 1,000 per day) people would die from cancer in 1981. Although the cancers diagnosed in a given year are not necessarily reflected by the deaths that year

gressive and expensive therapy that is generally most unpleasant.[4] Second, over the last several decades, cancer has become an increasingly common cause of death and disease. Cancer is the second leading cause of death in the United States today.[5] Third, despite the expenditure of billions of dollars on research,[6] the causes of cancer in humans are really not known, nor are the mechanisms by which cancer develops.[7]

There are a number of factors which contribute to the frequency with which cancer is observed today. One reason that cancer is so common is that other causes of death are relatively less prevalent. In 1900, cancer was the eighth leading cause of death, accounting for only four percent of deaths, with infectious diseases such as influenza, pneumonia, tuberculosis, and infectious gastrointestinal disease far outranking it.[8] With the introduction of antibiotics and improvements in sanitation and nutrition, death from infectious disease became relatively less common, and death from cancer became relatively more so.[9] Additionally, with the reduction of other types of disease, people live longer, thereby allowing more to reach the age at which cancer traditionally has been a greater risk.[10] Finally, with the advent of improved diagnostic techniques, cancer is recognized more frequently than it was in the past.[11]

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from cancer, the proportion of deaths from given types of cancer is instructive. For example, there were estimated to be 122,000 new cases of lung cancer in 1981. There were estimated to be 105,000 lung cancer deaths. AMERICAN CANCER SOCIETY, CANCER FACTS AND FIGURES (1980).

[4] Direct costs for all cancers (doctor and hospital care) amounted to 7% of the costs incurred for all illnesses. Indirect costs (based on a lost earnings approach) amounted to 19% of total indirect costs. OFFICE OF TECHNOLOGY ASSESSMENT, ASSESSMENT OF TECHNOLOGIES FOR DETERMINING CANCER RISKS FROM THE ENVIRONMENT 33 (1981) [hereinafter cited as OTA REPORT]. The cost for medical care for cancer patients in 1977 was $5.5 billion. The expected future earnings of those who died that year was $14.6 to $18.5 billion. OSHA CARCINOGEN POLICY, *supra* note 1, at 5,016.

[5] PUBLIC HEALTH SERVICE, HEALTHY PEOPLE: THE SURGEON GENERAL'S REPORT ON HEALTH PROMOTION AND DISEASE PREVENTION 60 (1979) [hereinafter cited as HEALTHY PEOPLE]. Cancer accounts for about 20% of total U.S. mortality, second only to heart disease which accounts for 38% of deaths. OTA REPORT, *supra* note 4, at 31.

[6] In the 1974 fiscal year alone, the National Cancer Institute reported expenditures of $100 million for research on the environmental causes of cancer. GENERAL ACCOUNTING OFFICE, FEDERAL EFFORTS TO PROTECT THE PUBLIC FROM CANCER CAUSING CHEMICALS ARE NOT VERY EFFECTIVE (1976).

[7] The OSHA Carcinogen Policy states: "The early cellular and molecular events of the disease and the mechanisms leading to its initiation are not fully understood." OSHA CARCINOGEN POLICY, *supra* note 1, at 5,016.

[8] HEALTHY PEOPLE, *supra* note 5, at 4. If the mortality rates today were the same as they were in 1900, 400,000 people a year would die from tuberculosis, almost 300,000 from gastroenteritis, 80,000 from diphtheria and 55,000 from polio. *Id.* at 3. *See also* OSHA CARCINOGEN POLICY, *supra* note 1, at 5,033.

[9] OTA REPORT, *supra* note 4, at 32.

[10] OSHA CARCINOGEN POLICY, *supra* note 1, at 5,026.

[11] OTA REPORT, *supra* note 4, at 32.

The legal system's difficulty in dealing with cancers is largely caused by the medical community's lack of understanding of what causes cancers and how they develop. While a number of theories of cancer causation exist, there is no certainty as to which theory is correct. Epidemiologists observe working and environmental conditions and attempt to determine any association between increased incidences of cancer and work and environmental factors. There are almost always imperfections, however, in the epidemiological studies, since multiple factors may be involved, and increased incidences may be coincidental. Because of these uncertainties, courts have had difficulty in accepting epidemiological evidence. Most medical opinions, however, are based on probability, not certainty. Medicine is, after all, sometimes more an art than a science. Thus, if epidemiological studies are carefully performed and show material and substantial evidence of causation, such evidence should be accepted by the courts subject, of course, to rebuttal evidence.

II. THEORIES OF CANCER CAUSATION

Though cancer was known in antiquity, and the term carcinoma was coined by Hippocrates in the fourth century b.c.,[12] it was not until the nineteenth century that cancer began to be studied systematically and intensively.[13] During the nineteenth century, there were three general lines of investigation. One centered on the theory that cancer was the result of a chronic physical irritation of cells. Cancers which developed in and around scars or ulcerations and those which occurred after acute or chronic injury were cited in support of this hypothesis. Essentially, this theory assumed that normal cells are converted to cancer cells.[14] The second theory, which also assumed that normal cells could become cancerous, stated that some infectious agent causes cancer. While some type of bacterial agent was sought in the nineteenth century, twentieth century research has focused on viruses as etiologic agents.[15] Interestingly, viral causes of cancer have been isolated in animals, but no such agent has been isolated as yet in humans.[16]

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[12] PITOT, *supra* note 2 at 3. *See also* WYNGAARDEN AND SMITH, *supra* note 1, at 1010 (discussing the historical roots about the causes of cancer).

[13] PITOT, *supra* note 2, at 4.

[14] *Id.* at 6. This theory of carcinogenesis is no longer supported by most oncologists. However, chronic irritation may nevertheless produce cells that are a more fertile ground in which carcinogens may act. *Id.* at 42-43.

[15] In the early years of the twentieth century, Johannes Fibiger performed experiments wich evidenced a link between a parasite and the growth of stomach tumors. In 1926, for that work, he was awarded the Nobel Prize in Medicine. One year later, his experiments were shown to be invalid. This resulted in a setback for the infectious agent theory of cancer causation. *See* M. SHIMKIN, CONTRARY TO NATURE 245-46 (1977).

[16] WYNGAARDEN & SMITH, *supra* note 1, at 1011. *See also* PITOT, *supra* note 2, at 46-47 (discussing viral theories of cancer development).

The third theory prominent in the nineteenth century stated that cancer cells exist in the body from the time of embryonic development and express themselves later in life.[17] Presumably, part of the rationale behind this theory is that many cancer cells resemble embryonic tissue, i.e. they are undifferentiated in their appearance.[18]

In the twentieth century, experiments on animals indicated that certain substances were capable of producing cancer by themselves, but that other substances, while not able to produce cancer, were capable of enhancing its development in animals treated with either mild carcinogens, or carcinogens at a dose incapable of producing cancer alone. These experiments and other research lend support to a theory that cancer might be more than a one-step process; some substances may act as initiators while others act as promotors. A single substance may be its own initiator and promotor, or a substance may independently only initiate the process, but not cause cancer unless another substance, the promotor, is present.[19]

Since cancer is the unrestrained growth of individual cells, techniques recently developed to examine individual cells and their components, such as electron microscopy, are being utilized to determine how cancer is caused. Most scientists have directed their attention to the nucleus of the cell because it is there that the critical processes, including cell replication, are controlled.[20] All cells function by means of a vast number of chemical and physical processes. These govern the cells' own metabolism, its differentiation into a certain type of cell, (such as a nerve cell or liver cell), whether and to what extent it proliferates, and whether it produces products used outside the cell, such as antibodies. Each cell must contain and transmit to daughter cells the instructions for these processes. These instructions are contained in molecules of deoxyribose nucleic acid (DNA), which is found almost exclusively in the cell nucleus.

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[17] PITOT, *supra* note 2, at 6.

[18] *Id.*

[19] WYNGAARDEN & SMITH, *supra* note 1, at 1011. *See also* OSHA CARCINOGEN POLICY, *supra* note 1, at 5017-20 (discussing the cumulative contribution of carcinogens). One of those submitting a statement to OSHA said:

> "Initiation" describes s specific and irreversible cellular alteration induced by carcinogenic substances and resulting in a population of latent or dormant tumor cells. "Promotion" describes the proliferation of those cells, a process which is induced by subsequent exposure to the same or a different substance and which results in progression to clinical cancer. Classical initiation-promotion studies illustrate well the synergistic effects of separate exposures which would not have independently produced cancer at the doses involved. It is significant to note that the conditions induced by initiator substances persist; therefore, exposure to a promoting substance even after considerable delay can result in cancer.

OSHA CARCINOGEN POLICY, *supra* note 1, at 5018 (testimony of Dr. Robert Squire).

[20] *See generally* PITOT, *supra* note 2, at 100-04 (discussing cellular replication and the cell cycle).

The basic unit of DNA structure is known as a nucleotide, and it may be that in this structure lies the secret of cancer causation. The nucleotide is comprised of a five-carbon sugar (deoxyribose), with a phosphate group attached to it. This structure is linked to one of four specific molecules, called bases. The four bases are adenine and guanine (known as purines), and thymine and cytosine (known as pyrimidines). Thus, there are four possible nucleotides. These four types of nucleotides are linked together by the phosphate groups which extend from one sugar to the next. This results in long polynucleotide chains. A complete DNA molecule is formed by two polynucleotide chains which are tightly wound about each other with complementary bases pairing with each other, thus forming a double helix. Schematically, the double helix resembles a spiral staircase, with the base pairs forming the steps.

The replication of DNA may occur in two ways. It may "unzip" completely and replicate itself in its entirety during the process of cell division, so that each daughter cell gets a complete copy of all the information in the parent cell. DNA may also partially "unzip," and transcribe certain information to single stranded molecules of ribonucleic acid (RNA). These RNA molecules then convey that information out of the nucleus and into the cell body, where proteins are manufactured. Each set of three bases (a triplet) codes for a single amino acid, many thousands of which are required to construct a single protein.[21] Certain base triplets also are thought to provide "start" and "stop" signals for the production of certain products or processes, including cell replication.[22]

The strands of DNA are collected in chromosomes. Chromosomes functionally are divided into genes, which were originally defined as the hereditary determinant of a single characteristic, but which are now more often defined as segments of DNA which code for a single protein.[23] Attention has focused in recent years on the genes which form the chromosomes.[24] A recent theory postulates that certain genes can be modified, perhaps by as little as the mutation of a single nucleotide, which results in the change of a single amino acid.[25] This change produces an oncogene, a gene which may cause the cell to activate and proliferate

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[21] *See* GENERAL ACCOUNTING OFFICE, PROBLEMS IN ASSESSING THE CANCER RISKS OF LOW-LEVEL IONIZING RADIATION EXPOSURE, 2-20, 8-3 through 8-6 (1981). *See generally* J. THOMPSON & M. THOMPSON, GENETICS IN MEDICINE 32-52 (1980) (discussing the function and structure of chromosones); WYNGAARDEN & SMITH, *supra* note 1, at 7-11 (presenting an overview of biochemical genetics); J. Darnell, *The Processing of RNA*, 249 SCI. AM. 90-100 (Oct. 1983) (describing the transcription of DNA into RNA and the translation of RNA into proteins).

[22] WYNGAARDEN & SMITH, *supra* note 1, at 10-11.

[23] *Id.* at 7.

[24] *See generally* PITOT, *supra* note 2, at 119-121 (describing experiments conducted to determine whether the tendency of cells to become malignant is a dominant or recessive trait).

[25] R.A. Weinberg, *A Molecular Basis of Cancer*, 249 SCI. AM. 26.

without cessation.[26] Some of these oncogenes also have been located in chromosones other than those to which they were originally attached. On these chromosones, the oncogenes are located near genes responsible for the rapid transcription of antibodies.[27] Additionally, it is suspected that more than one process may be necessary in order for a cell to become cancerous. As one author described oncogenes:

> Carcinogenesis appears to be a multistep process. Evidence from a variety of sources indicates that a normal cell must suffer several independent alterations before it becomes a bona fide tumor cell. A point mutation that gives rise to an aberrant version of a single protein represents only a single step affecting a single gene. Presumably the creation of an oncogene fulfills one requirement for making a tumor, but there are other necessary steps; the oncogene may be necessary, but it is hardly sufficient.[28]

The mechanism of cancer causation, when finally elaborated, may have profound consequences for the legal system. If cancer can be initiated by a single event, e.g., the translocation of a single nucleotide, then there is no level of exposure to a carcinogen below which an effect cannot occur, although the chances of the occurrence of that effect become more remote as the dose decreases. That reduction of risk for a "one-hit" theory of carcinogenesis would be linear since there is but one variable in the equation. That is, for any reduction of the dose by half, the effect would be reduced proportionately.[29] (This analysis, of course, greatly oversimplifies the model because factors such as DNA repair which might reduce the risk, or hormonal factors, which might increase susceptibility and risk, are not taken into consideration).[30] However if cancer induction re-

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[26] *Id.*

[27] *Id.*

[28] *Id.* at 140. Cancer as a multiple step process is widely accepted in the scientific community. *See generally* OSHA CARCINOGEN POLICY, *supra* note 1, at 5017-23 (many witnesses testified that cancer progresses through a number of stages of development). One researcher noted: "Cancer seems to develop progressively through a number of stages, each of which can be influenced by chemicals or other environmental factors, interacting with host factors such as nutrition, hormone levels, etc." *Id.* at 5019 (testimony of Dr. Emmanuel Farber).

[29] One scientist testifying before OSHA stated: "If individual cancers arise from an original, single, transformed cell, then the statistical nature of the carcinogenic dose response will be governed by the extreme tail of the "transformation" response distribution. The effect of this is to make virtually any process of discrete events approximately linear at low dose." *Id.* at 5023 (testimony of Mr. Richard Peto). OSHA further noted that even though a number of witnesses disagreed, it would follow from the fact that cancer develops from a single cell that cancer may be initiated by the interaction of a single molecule of the carcinogen with the critical target site in the cell. *Id.* at 5024. Later, speaking of cancer as a failure of DNA repair, OSHA stated: "Strictly speaking, any failure in repair leaves open the possibility of initiation of the carcinogenic process and so precludes the existence of a threshold." *Id.* at 5127.

[30] Scientists testifying before OSHA testified that there may exist a safe level of expo-

quires multiple steps, two or more variables come into play and the chances are more remote that a single dose of the carcinogen will cause all the necessary effects.[31] For example, a recent report on radiation carcinogenesis noted: If two independent single events are required, at different gene loci, to produce malignant transformation, the model would be quadratic (i.e., the effect would increase with the square of the dose). If the order in which the genetic changes must occur is important, an even higher power of dose might be required in the model. However, if the gene loci are close enough together at times, a single event might affect both gene loci, and a linear term might be needed, as well.[32] Under these circumstances, it may become more difficult to prove that a single substance to which someone was exposed "caused" the cancer, in the legal sense.[33]

Although scientists do not know what causes cancer in humans or how it is caused, they do know that those exposed to certain substances appear to develop cancer more frequently than those not exposed. There are two sources cited in support of this theory: observation and experimentation.[34] One of the earliest noted observations was made by Sir Percival

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sure to a carcinogen as for other toxins. OSHA CARCINOGEN POLICY, *supra* note 1, at 5022 (testimony of Dr. Robert Squire). However, non-cancer toxic effects occur early, and the symptoms may be reduced and reversed by reduction of dose. *Id.* at 5023 (testimony of Dr. Umberto Saffiotti). With carcinogenic substances however, no safe level can be assumed because the effect (cancer) is separated from the exposure by such a long latency period, the effect cannot be modified by a reduction of dose (i.e., by the time cancer is discovered, it isn't going to be affectuated by cessation of exposure). Also, because very small amounts of carcinogenic substances can begin the damage that results in carcinogenesis, the determination of a safe level is hindered further.

[31] As one scientist has noted:

> If multistage models are even approximately true, then the incidence rate for each cancer is proportional to a product of more than one event rate, each with different determinants, and it makes little sense to ask for the cause of a particular cancer; each has more than one distinct cause.

OSHA CARCINOGEN POLICY, *supra* note 1, at 5019 (testimony of Mr. Richard Peto).

[32] National Academy of Sciences, Oversight Committee on Radioepidemiological Tables, Assigned Share for Radiation as a Cause of Cancer, 63 (1984).

[33] For example, Dr. Arthur Upton, then Director of the National Cancer Institute, said in testimony to OSHA:

> Cigarette smoking provides an example of the difficulty of quantifying the contribution of a single factor. . . .The incidence of cancer in smokers and non-smokers has been studied extensively; the excess rates of cancer in smokers are well established; and from knowledge of the number of smokers, the total number of excess cancers causally related with smoking can be calculated. . . .It would be reasonable to conclude that smoking is *one* major cause of these cancers, in the sense that they would not have occurred in the absence of smoking. However, it would not be reasonable to conclude that smoking is the *only* cause. It is known, for example, that at least two agents—alpha radiation and asbestos—act synergistically with cigarette smoking in causing lung cancer in exposed workers. OSHA CARCINOGEN POLICY, *supra* note 1, at 5020 (testimony of Dr. Arthur Upton).

[34] A. LILIENFELD & S. LILIENFELD, FOUNDATIONS OF EPIDEMIOLOGY 191 (2d ed. 1980)

Pott, a British surgeon, who in 1775 observed that chimney sweeps had a high incidence of cancer of the skin of the scrotum. Dr. Pott believed that the soot, which lodged in the trousers of these workers, must have caused the cancers.[35] In the late nineteenth century, other scientists observed that in particular populations the occurrence of certain tumors seemed excessive. Aniline dye workers, for example, were observed to suffer from cancers of the bladder[36] more often than the general population. In the early twentieth century, it was observed that people who worked around x-rays or other forms of radioactivity developed various types of cancer in apparent excess.[37] In 1935, scientists diagnosed two cases of lung cancer in asbestos workers.[38] However, as the debate concerning asbestos and cancer causation demonstrates, it is not enough, from either a scientific or a legal standpoint, for scientists simply to make an observation that two events appear associated. More rigorous proof is necessary[39]—proof which may be provided by the science of epidemiology.

III. Occupation and Other Environmental Factors in Cancer Causation

An issue which has been debated at length is the extent to which cancer is produced by environmental, including occupational, factors as opposed to factors that are genetic. Environmental factors, which are generally include habits such as smoking, alcohol use, lifestyle, diet, and occupation, have been said to account for the majority of cancers.[40] Part of this hypothesis stems from studies of worldwide cancer rates that analyze how cancer rates vary in different geographical locations and among different populations. Though some cancers tend to occur more in partic-

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[hereinafter cited as Lilienfeld]; OTA Report, *supra* note 4, at 113. Experimental studies require the deliberate giving or withholding of a factor and observing the occurrence or lack of occurrence of an effect. Ethical considerations, of course, preclude the administration of suspected carcinogens to people, but it is possible to test agents thought to aid in prevention or hoped to aid in treatment. OTA Report, *supra* note 4, at 137. Observations may be the result of case reports or epidemiological studies. OSHA Carcinogen Policy, *supra* note 1, at 5044.

[35] Schottenfeld & Haas, *Carcinogens in the Workplace*, 29 CA—A Cancer Journal for Clinicians 145-46 (May/June 1979).

[36] M.B. Shimkin, *supra* note 15, at 165-66 (1977).

[37] *Id.* at 247-50.

[38] Gloyne, *Two Cases of Squamous Carcinoma of the Lung Occurring in Asbestosis*, 17 Tubercle 5-10 (Oct. 1935).

[39] The observation of isolated cases of cancer in relation to a specific environmental factor may be misleading, as subsequent statistical evaluation of the data may show. Pitot, *supra* note 2, at 75.

[40] Schottenfeld & Haas, *supra* note 32, at 144. Various other sources have similarly asserted this. A listing of the sources is collected at OTA Report, *supra* note 4, at 65, and OSHA Carcinogen Policy, *supra* note 1, at 5027.

ular racial or ethnic groups, most affect all groups equally.[41] Furthermore, when certain migrant populations relocate, their cancer rates for numerous organs begin to approximate the rates in the geographical area into which they move. This type of change has been attributed to changes in lifestyle. If genetic factors were responsible for the international differences in risk, the rates among population groups that migrate essentially would remain fixed.[42] Thus, there appears to be less dispute regarding the percentage of environmentally-induced cancers than about the percentage of the subset of that group, occupationally-caused cancers.

The percentage of cancers believed to be the result of one's occupation varies considerably. A frequently quoted figure is from one to five percent.[43] Other estimates range upwards to ten percent,[44] and one widely-quoted study indicated that a reasonable projection for the consequences of past exposure to carcinogens in the workplace would be twenty-three percent to thirty-eight percent of the overall cancer total; of that overall sum, the projected asbestos related cancers would comprise thirteen to eighteen percent.[45] However, this particular report, which has never been published, has been the subject of rather extensive criticism.[46]

IV. EPIDEMIOLOGY

As pointed out, as a result of the lack of knowledge about what causes cancer, or how it is caused, the only way to identify substances as carcinogens in humans is to observe a particular population with exposure to a substance and determine if that population develops a greater number of cancers than would be expected. In fact, one proposed definition for carcinogen states the following:

> A carcinogen is an agent whose administration to previously untreated animals leads to a statistically significant increased incidence of malignant neoplasms as compared with that in untreated appropriate control animals, whether the control animals have low or high spontaneous incidences of the neoplasms in question . . . . Some agents, including promoters and immune suppres-

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[41] Weisburger & Williams, *Metabolism of Chemical Carcinogens*, in CANCER - A COMPREHENSIVE TREATISE 241-42 (F.F. Becker 2d ed. 1982). *See also*, Fraumeni, GENETIC DETERMINANTS OF CANCER, in HOST ENVIRONMENT INTERACTIONS IN THE ETIOLOGY OF CANCER IN MAN 7 IARC SCIENTIFIC PUBLICATIONS (1973). The interaction of an environmental and so-called "host factor," such as genetic make-up (including immunologic and DNA repair factors), age, and hormonal and nutritional status, is the subject of much investigation. See HOST FACTORS IN HUMAN CARCINOGENESIS, 39 IARC SCIENTIFIC PUBLICATIONS (1982).

[42] Schottenfeld & Haas, *supra* note 32, at 144.

[43] *Id.* at 145.

[44] The study estimates are collected at OTA REPORT, *supra* note 4, at 86-7, 108-9.

[45] DEPARTMENT OF HEALTH, EDUCATION AND WELFARE, ESTIMATES OF THE FRACTION OF CANCER IN THE UNITED STATES RELATED TO OCCUPATIONAL FACTORS (1978).

[46] *See* OTA REPORT, *supra* note 4, at 87-88.

> sants, can increase the incidence of malignant neoplasms in tissues previously treated with subcarcinogenic doses of carcinogens; such agents should not be termed carcinogens.[47]

Although this definition was developed with reference to experimental animals, it applies with equal validity to human studies. The only difference, as noted, is that human epidemiology provides direct evidence about cancer in man, and positive animal studies determine only that the substance is a carcinogen in that species, indicating only that the substance is a potential human carcinogen.[48]

Epidemiology is the study of patterns of disease occurrence in populations and factors which influence those patterns.[49] Human epidemiologic studies essentially are comprised of two types. In the first type, a prospective study,[50] scientists identify a substance or agent, the effects of which they seek to investigate, for example, benzene. A population which has been exposed to that substance is then identified and followed in order to verify the health outcomes of that group. These outcomes are then compared with those of people who have not been exposed to the substance at issue. A good example of a prospective study is that involving the survivors of the atomic bombs at Hiroshima and Nagasaki.[51] That study, which focused on radiation, identified as many persons as possible who had been exposed to radiation from the bombs and has followed the group to note what outcomes have occurred.[52] However, rather than merely following a group, an investigator may choose a population for study, go back in time to a given date, identify the group as of that date, and then trace it over time, usually to the present. This type of study is known as a nonconcurrent or historical prospective study.[53]

In the second type of study, the retrospective or case-control

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[47] PITOT, *supra* note 2, at 29-30. *See* E.C. Miller & J.A. Miller, *Mechanisms of Chemical Carcinogenesis: Nature of Proximate Carcinogens and Interactions with Macromolecules*, 18 PHARMACOLOGICAL RESEARCH 805 (1966). Other authors have taken a much broader view of what constitutes a carcinogen. Richard Peto defines a carcinogen as any external agent that directly or indirectly increases the likelihood that a transformed cell will pass through one of the stages involved in the process of development of cancer. OSHA CARCINOGEN POLICY, *supra* note 1, at 5022. The NCAB Subcommittee on Environmental Carcinogenesis pointed out that the term "carcinogen" should be used in the broad sense, because it is not possible to differentiate clearly between initiating agents and certain modifying factors. OSHA CARCINOGEN POLICY, *supra* note 1, at 5022.

[48] OTA REPORT, *supra* note 4, at 114 (Table 23).

[49] LILIENFELD, *supra* note 31, at 3.

[50] *Id.* at 226-7; *see also* OTA REPORT, *supra* note 4, at 138; Schottenfeld & Haas, *supra* note 32, at 147.

[51] *See* LILIENFELD, *supra* note 31, at 227; Schottenfeld & Haas, *supra* note 32, at 147.

[52] *See, e.g.*, G.W. Beebe, H. Kato & C.A. Land, *Mortality Experience of Atomic Bomb Survivors 1950-1975*, LIFE SPAN STUDY REPORT 8 (1978).

[53] LILIENFELD, *supra* note 31, at 227.

study,[54] scientists identify certain outcomes about which they are interested, for example, leukemia. A population, all of whose members have the particular outcome, is then selected and is matched with another population which is similar in as many respects as possible to the study population, except that its members do not have the outcome. Comparing the members of the two populations, the scientists determine whether the study population was exposed to anything different prior to the development of the outcome than was the so-called "control" population. An example of a case-control study is the Oxford Survey of Childhood Cancer, which identified all English children under the age of ten who had been diagnosed with cancer. A control group was then selected and matched for age and a variety of other factors; the controls differed only in that they did not have cancer. The cases and controls were then traced in order to identify any differences. In the Oxford Survey, the researchers found that the only real difference was that the cases were exposed to more radiation while they were still fetuses than the controls. This prompted the researchers to suggest that pelvic irradiation was the cause of cancer in the cases.[55]

There are two types of problems commonly associated with epidemiological studies. These problems may be divided into those of establishing an association between an agent and a cancer, and, if an association is established, problems of determining whether the association so established is a causal one, i.e. whether the exposure caused the disease.

A. Problems of Establishing an Association

One of the major problems with establishing an association is determining if the number of cases observed is statistically and significantly different than the number of cases expected. A discussion of the limitations of the statistical method is beyond the scope of this article. However, some general comments may be in order. A particularly difficult problem with attempting to detect the effect of a weak carcinogen (or low doses of any carcinogen) is that a large study population is necessary. As Dr. Robert Hoover of the National Cancer Institute testified before the Occupational Safety and Health Administration (OSHA):

> [Epidemiology] is quite weak at identifying the causes of very low levels of risk. Very small differences in risk between a group exposed to some substance versus that in a group not exposed to it could be due to a variety of reasons: for example, chance, or other differences between the exposed and unexposed which we either do not know about or cannot adequately control for. Because of

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[54] *Id.* at 194. *See also* OTA REPORT, *supra* note 4, at 138.

[55] A. Stewart, J. Webb & D. Hewitt, *A Survey of Childhood Malignancies*, I BRIT. MED. J. 1495-1508 (1958).

> this, it becomes next to impossible to say with any assurity [sic] that a very low level of risk is caused by a similarly low level exposure to some substance.[56]

Dr. Hoover further stated that the lowest excess cancer risk, that was directly observable in a group of exposed persons and is generally accepted as being due to that exposure, is the thirty percent excess risk of childhood leukemia found in children exposed to radiation in utero during the last trimester of pregnancy.[57] In fact Dr. Hoover said: "Indeed, it has taken us some 20 years to become reasonably convinced of this 30% excess risk."[58] Another witness before OSHA pointed out that "[f]ew epidemiological studies of occupational cancer have been of adequate sensitivity to detect anything smaller than a 50% increase in the incidence of cancer over that found in the general population."[59] A study of the risks posed by saccharin, conducted by the National Academy of Sciences, indicated that "assuming that saccharin is a carcinogen of low potency in humans . . . the number of bladder cancers studied have been too small . . . to demonstrate a statistically significant difference [between the cases and the controls]."[60] Another witness before OSHA, commenting on the insensitivity of methods for detecting an association between a chemical exposure and cancer, noted that such an association has only been made when "an increased incidence of a tumor of an unusual type was noted or when an unusual clustering of a common tumor occurred in a particular population."[61]

The problem is illustrated further by an example from a report to the Nuclear Regulatory Commission on the feasibility of epidemiologic studies of the effects of low levels of ionizing radiation (the "Dreyer Report"). The report took one theoretical model that predicted a single dose of ten rems[62] of radiation to a population of 100,000 would produce 200 excess cancers. Noting that the Third National Cancer Survey projected an occurrence of 20,000 cancers in the same population (making the excess .2%), the authors of the report concluded that it would be "practically impossible to distinguish such an increment . . . ."[63] The authors did

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[56] OSHA CARCINOGEN POLICY, *supra* note 1, at 5040 (testimony of Dr. Robert Hoover).

[57] *Id.*

[58] *Id.*

[59] *Id.* at 5049 (testimony of Dr. Richard Bates).

[60] NATIONAL ACADEMY OF SCIENCES, COMMITTEE FOR A STUDY ON SACCHARIN AND FOOD SAFETY POLICY 3-89 (1978).

[61] OSHA CARCINOGEN POLICY, *supra* note 1, at 5044 (testimony of Dr. Peter Goldman).

[62] A rem is a measure of radiation dose. It is equivalent to the absorbed dose in rads times a quality factor to equalize biologic effects. The major quality factor is generally to correct for the linear energy transfer (LET). A rad represents an absorbed energy of 100 ergs per gram of tissue. R. SCHEELE & WAKLEY, ELEMENTS OF RADIATION PROTECTION (1975).

[63] N.A. DREYER, THE FEASIBILITY OF EPIDEMIOLOGIC INVESTIGATIONS OF THE HEALTH EFFECTS OF LOW LEVEL IONIZING RADIATION 36, 54 (1980).

note that: "To establish that a difference in cancer rates of 0.2% is statistically significant at the .05 level in a single tail test with 0.9 power would require a sample size of about 700,000 each, exposed and unexposed."[64] The Dreyer Report also pointed out that the sensitivity of the analysis could be greatly improved if most of the excess cancers were of a type that is normally rare and which, thus, represented at least a fifty percent or greater increase in the rate of that type, instead of a one percent increase.[65]

With respect to some exposures, such as radiation, there is evidence of an association (and causation) at high doses because the effect is pronounced, i.e. many cancers of various types occur when a few would be expected. However, as the dose of radiation decreases, so does its effect,[66] and, as stated, any sort of effect is much more difficult to detect at low dose levels. As one report evaluating saccharin stated: "Humans are usually exposed to carcinogens in doses far smaller than are used in animal experiments. The effects are consequently less frequent, and the number of people whose experience needs to be judged to detect the cancer effect is much greater."[67]

Efforts have been made to extrapolate from the effects of high doses of some of these substances or agents to the possible effect at low doses, although no data exists for the lower levels, and construct dose-response curves for these low levels of exposure.[68] These efforts have been hampered because it is not known to what extent DNA repairs itself at low levels of exposure[69] or to what extent fractionation of dose reduces the effect of carcinogens.[70]

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[64] The concept of statistical significance is discussed in the OSHA CARCINOGEN POLICY, *supra* note 1, at 5096-100. In this example, the .05 is known as the p-value:

> The role of chance is assessed by the p-value, which indicates the probability that an observed association exists by chance alone. A small p-value implies that chance is an unlikely explanation. Yet, no matter how small the p-value, the results can still be due to chance. Since rare events do occur spontaneously, other problems in interpreting p-values involve the adequacy of the sample size and sufficiency of the power of the statistical test used.

DREYER, *supra* note 60, at 54.

[65] DREYER, *supra* note 60, at 54.

[66] This phenomenon occurs with any agent in which there is a dose-response relationship. The higher the dose, the greater the effect. Inversely, the lower the dose, the more minimal the effect.

[67] OSHA CARCINOGEN POLICY, *supra* note 1, at 5048.

[68] *See, e.g.*, THE EFFECTS ON POPULATION OF EXPOSURE TO LOW LEVELS OF IONIZING RADIATION: 1980, THE REPORT OF THE NATIONAL ACADEMY OF SCIENCES, COMMITTEE ON THE BIOLOGICAL EFFECTS OF IONIZING RADIATION 136-37 (1980) (BEIR III).

[69] PROBLEMS IN ASSESSING THE CANCER RISKS OF LOW-LEVEL IONIZING RADIATION 5-18, 5-19 (1981).

[70] *See also* NATIONAL COUNCIL ON RADIATION PROTECTION AND MEASUREMENTS, INFLUENCE OF DOSE AND ITS DISTRIBUTION IN TIME ON DOSE-RESPONSE RELATIONSHIPS FOR LOW LET RADIATIONS, NCRP REPORT No. 64, 170-74 (1980).

Another problem in establishing the association is that there may be a prolonged latent period between exposure to a carcinogen and the development of a frank cancer. Failure to follow up on study groups for long periods of time may lead to "false negative" results,[71] i.e. those which show no effect although one actually exists. One of the witnesses who testified before OSHA noted that "[i]t may be that 40 years continued exposure is extremely dangerous, but that 15 years of continued exposure confers what is a negligible risk until further time has elapsed."[72]

Problems associated with both group size and latency periods were addressed before OSHA by Dr. Irving Selikoff:

> I think that Dr. Nicholson's mention before of the asbestos related cancer of the lung in non-smoking asbestos workers teaches us a great deal. We looked at a fairly good sized group in New York City of the 370 men. They were all more than 20 years from onset . . . and yet, by 1967 we did not see a single case of lung cancer among the non-smokers . . . . It was not until we followed 2,000 people for 10 more years that we were able to find eight cases against 1.82 expected.[73]

Therefore, as summarized in the Dreyer Report:

> The general approach to the analysis of epidemiologic studies is similar for both case-control and cohort studies. This involves estimating a measure of association . . . between the disease and exposure, statistical testing of that estimator (hypothesis testing), calculating of a confidence interval around the estimate, and adjusting for confounding variables.[74]

The measure of association discussed by the Dreyer Report is generally couched in terms of "relative risk." As noted, even if an epidemiological study has been conducted in accordance with accepted principles, all that can be shown is that the risk associated with exposure to a given agent exceeds that which occurs in a control population. The ratio of the observed cases to the expected cases is called the risk ratio or the relative risk. For example, assume that the naturally occurring incidence of a given cancer in a given population (adjusted for age and sex) is six. Assume further that for the population under study, the incidence of that cancer was nine. Of these nine observed cases, six could be said to have

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[71] OSHA CARCINOGEN POLICY, *supra* note 1, at 5050.

[72] *Id.* (testimony of Mr. Richard Peto).

[73] *Id.* at 5049-50.

[74] DREYER, *supra* note 60, at 259. A study is positive when the upper confidence limit of the frequency of the effect observed in the comparison population falls below the lower confidence limit of the frequency of that effect observed in the study population, and the difference is not explained by limitations in the design of the study, biases, or confounding variables. *See* OSHA CARCINOGEN POLICY, *supra* note 1, at 5046.

been "expected" and the ratio of observed to expected (nine divided by six) is 1.5. However, if the disease under study is one that occurs in the general population, as does cancer, and is not distinguishable as being induced by a given substance or agent, there is no way to determine which cases occurred naturally and which occurred by virtue of whatever caused the excess.

Therefore, epidemiology alone is not satisfying to those who want to establish the probability that a given case is related to particular exposure. It is for this reason that the concept of probability of causation or percentage probability was developed. By means of this formula, the proportion of all cases of the disease in the total population attributable to a specific exposure may be calculated. The formula is:

$$\text{percentage probability} = \frac{RR - 1}{RR}$$

where RR = relative risk.[75]Utilizing the numbers from the above example (a 1.5 relative risk), it may be calculated that the percentage of the risk of cancer in the exposed population attributable to the agent is 33⅓ percent (1.5 minus 1 divided by 1.5). This also reflects the chance that any given individual in the population developed his or her cancer as the result of exposure to a particular agent.

By inserting several numbers into the formula, it can be seen that any time the relative risk exceeds 2.0, the chances that the agent caused the cancer in a given person is greater than 50 percent, i.e., more likely than not. However, the most that can be said about this analysis is that, as a matter of statistical probability, the chances that the individual acquired cancer due to the agent are whatever is shown by the attributable risk. Even with a relative risk greater than 2.0, an individual could be a naturally occurring case. Conversely, with a relative risk of less than 2.0, the cancer could still be agent-induced.

B. Problems With Establishing Causal Significance

Even if an increased relative risk is identified in a given population, however, it must still be determined whether the established association is of causal significance. As one of the witnesses testified in the OSHA Carcinogen Policy hearings:

> A point that has not come out, really, is that there is no such thing as proof, and the acceptance or rejection of a hypothesis is really a subjective phenomenon based as much as possible on ob-

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[75] The confidence limit, or interval, is the range of values which could be right at the level of statistical significance decided upon. LILIENFELD, *supra* note 31, at 331-38. P.E. Enterline, *Attributability in the Face of Uncertainty*. 78 CHEST, No. 2, p. 377 (Aug. 1980 Supp.)

jective data . . . .

One of the criteria you have to build in . . . is does the study make sense. There are far more problems in the design of the study and the data collection than there are in the statistical tests.[76]

Similarly, the first Surgeon General's Report on Smoking and Health stated: "The causal significance of an association is a matter of judgment which goes beyond any statement of statistical probability."[77] There are a variety of criteria for determining whether a given result "makes sense." These are summarized in the OSHA CARCINOGEN POLICY.[78] One widely accepted set of criteria indicate that the factors most appropriate for evaluating an association are consistency, strength, temporal relationship, coherence and specificity.[79] Essentially, consistency means repeatability or experimental replication, but it may also be demonstrated by showing diverse investigative approaches which produce similar results. The strength of an association may be expressed in terms of relative risk or odds ratio. Temporal relationship means that the presumed cause always precedes the observed effect. Coherence embraces the concept of biological plausibility. The criterion of specificity implies that there is a predictive pattern of effects likely to occur with a frequency greater than random chance if the antecedent event is of causal significance.[80]

The International Agency for Research on Cancer (IARC), in the preamble to its monograph series on carcinogens, indicates that a study which shows a positive association between an agent and a cancer "may be interpreted as implying causality, to a greater or lesser extent," if five criteria are met:

1. There is no identifiable positive bias.

Positive bias means that factors in the design or the execution of the study lead erroneously to a more strongly positive association between an agent and disease than, in fact, exists. An example of positive bias in a case-control study would be more nearly complete ascertainment of exposure to the agent in the cases studied than in the controls. An example of positive bias in a cohort study would be more nearly complete detection of cancer in individuals exposed to the agent than in individuals not exposed to the agent.

2. The possibility of positive confounding has been considered. Confounding refers to the extraneous influence of factors, other than the one sought to be measured, in the association with the

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[76] OSHA CARCINOGEN POLICY, *supra* note 1, at 5051 (testimony of Dr. Robert Morgan).

[77] SMOKING AND HEALTH, REPORT OF THE ADVISORY COMMITTEE TO THE SURGEON GENERAL OF THE PUBLIC HEALTH SERVICE 20 (1964).

[78] OSHA CARCINOGEN POLICY, *supra* note 1, at 5044-46.

[79] Schottenfeld and Haas, *supra* note 32, at 147.

[80] *Id.*

> risk of cancer. Positive confounding refers to the situation in which the association between the agent and the disease is rendered more strongly positive than it really is as a result of an association between the agent and another agent which either causes or prevents the disease. One of the best examples of positive confounding is the positive association between coffee consumption and lung cancer. Drinking coffee does not, to anybody's knowledge, in fact, cause lung cancer, but the association between the two results from their joint association with cigarette smoking.
> 3. The association is unlikely to be due to chance alone.
> 4. The association is strong.
> 5. There is a dose-response relationship.[81]

The IARC Preamble further states:

> In some instances a single epidemiological study may be strongly indicative of a cause-effect relationship, however, the most convincing evidence of causality comes when several independent studies done under different circumstances result in "positive" findings.[82]

Keeping these criteria in mind, it may be useful to review some of the advantages and disadvantages of the retrospective (case-control) studies, and the prospective (cohort) studies. The retrospective study requires a smaller sample since the disease under study is already identified. The time involved in doing the study is also short since the pertinent events have already occurred. The size of the sample depends on the prevalence of the exposure to the "causal" factor or factors, the relative risk of disease the investigators deem it important to detect, and the acceptable levels of false positive and false negative results.[83] This type of study is more useful in studying rare diseases because confirmed cases constitute the study group. If the association between the factor and the disease is relatively strong, the number of cases necessary to show a significant increase is correspondingly small.

Some of the major problems in retrospective studies include: (1) bias -

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[81] OSHA CARCINOGEN POLICY, *supra* note 1 at 5044 (citing 17 IARC 18 (1978)).

[82] *Id.* In an editorial comment printed in the New York Times on the subject of the alleged use of toxic chemicals in Southeast Asia, the writer set out four rules of thumb that are applicable to epidemiological studies: (1) Science is founded on careful observation; (2) A difficult test or measurement must be repeated by a second scientist in case the first scientist made an error; (3) Science is cumulative and to ignore what is on the record is to build on air; and (4) Controls must be properly matched or conclusions are invalid. New York Times, Feb. 14, 1984, A26, Col. 1.

[83] False positives result when there is, in fact, no effect from the agent, but statistical tests show there is an effect. False negatives result when there is actually an effect of the agent, but the study shows none. Schottenfeld & Haas, *supra* note 32, at 148-50.

the subject's recall of earlier events may be distorted by knowledge of the disease; (2) lack of information - necessary information may be lost or incomplete, or the subject or his family may not be able to recall the critical information; and (3) control selection - controls must be selected to match as many characteristics of the cases as possible. Ideally, controls should be selected from the same population as the cases. On occasion, multiple control groups must be used. These may come from the same hospital, neighborhood, family or workplace.[84]

Prospective studies present yet another set of problems. They are more expensive since most of the data must be recorded, and a larger sample is usually needed since the outcomes are not known. Furthermore, due to the long latent period which occurs between exposure and the occurrence of some diseases, a long follow-up period is often required. As with retrospective studies, to determine sample size, the investigators must decide what level of false positives and false negatives they are willing to accept and what relative risk they regard as important. However, the sample size also depends on the expected incidence of the disease in those not exposed. If the incidence of the disease is low in the exposed and unexposed group, a very large sample will be needed to show significant differences between the groups. In a prospective study, as in a retrospective study, the incidence of disease is compared with what is "expected." Thus, the selection of the "normals" must be made with care. Additional problems include study subjects who may be unable to follow-up, or in the noncurrent (historical) approach, documentation of past exposures or the tracing of individuals may prove incomplete.[85] Finally, diagnostic criteria and methods may change over time.[86]

One author on the subject of epidemiological studies has suggested that the retrospective (case-control) study is the most suitable for the examination of rare diseases, in "fishing" for multiple factors of uncertain significance and for the initial exploration of a specific hypothesis regarding causation. The prospective (cohort) study, by directly measuring the risk of persons with a particular characteristic, is more suitable for testing hypotheses that have been developed from prior retrospective studies.[87]

In summary, then, two points should be made about epidemiological studies. The first is that even if an association is found between a factor and a disease, it is still a matter of judgment whether that association is of causal significance. The second point is that epidemiology, by defini-

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[84] *Id.* at 148.

[85] Incomplete exposure histories may result in an understatement of the effect of the factor. Incomplete tracing of individuals may result in understatement of the effect of the factor (if, for example, untraced individuals exposed to the factor have the disease) or overstatement of that effect, (if, for example, untraced individuals exposed to the factor don't have the disease).

[86] Schottenfield & Haas, *supra* note 32, at 149.

[87] *Id.* at 147.

tion, is a study of populations, not individuals. Even if an association of causal significance is found, the question still remains: did the substance or agent in question cause the disease in the particular person in whom the legal system is interested? As noted, the answer to that question can only be a statistical one. Therefore, from a scientific point of view, the major problems of primary importance in any analysis of the validity of epidemiological studies are the problems of determining whether an association is causal and the problems associated with statistical analysis. From a legal point of view, however, even if a causal association is established, can it ever be said with reasonable medical certainty (i.e. more likely than not), that a particular person developed the disease from the factor in question? The next section will examine how courts have dealt with this problem.

V. JUDICIAL TREATMENT OF EPIDEMIOLOGY

Courts faced with diseases of unknown etiology may either consider unfamiliar medical methodology or disregard it in favor of familiar legal theories. The resulting situation is an anomalous one—a judicial system requiring legal certainties yet dealing with claims fraught with medical uncertainty.

Such tension stems from the difficult problems of proof presented by diseases of unknown causes. Under precepts of traditional tort law, plaintiffs are required to establish the element of causation "by preponderance of the evidence."[88] In disease-related cases, this translates into proof of causation to a "reasonable medical certainty." Yet, because the cause of some diseases, such as cancer, is unknown, plaintiffs must rely on proof other than direct evidence as a basis for establishing an action.

The introduction of epidemiological studies is one means by which plaintiffs may satisfy the causation burden. Case law on cancer and epidemiology is scarce. Courts have considered epidemiology in other, related contexts, however, and their reception to this type of proof may guide future attempts for litigating cancer-related injuries.

Epidemiological proof was considered extensively in cases involving the swine flu vaccine and Guillain-Barre Syndrome (GBS).[89] In *In re [Swine*

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[88] *See* PROSSER, HANDBOOK OF THE LAW OF TORTS § 236 (4th ed. 1971).

[89] GBS is a disease affecting the peripheral nervous system. It has been defined as "a syndrome described as encephalitis of virus origin consisting of absence of fever, pain or tenderness in the muscles, motor weakness, abolition of tendon reflexes, and great increase of protein in the cerebrospinal fluid without increase in cells." Alvarez v. United States, 495 F. Supp. 1188 (D. Colo. 1980) (citing DORLAND'S MEDICAL DICTIONARY (1965)). The bulk of cases discussing GBS are linked to the swine flu vaccination program. In 1976, the federal government began the Swine Flu Immunization Program in an attempt to avoid a swine flu epidemic. 495 F. Supp. at 1190. One third of the adult population was vaccinated. *Id.* The program began pursuant to the Swine Flu Act, which also provided for a cause of action against the government for any personal injury or wrongful death attributable to the vac-

Flu Immunization] Products Liability Litigation, Alvarez v. United States,[90] the federal district court in Colorado considered a claim under the Federal Tort Claims Act.[91] A sixty-three year old woman alleged that the United States was liable for her diagnosed condition of GBS; it was not disputed that she suffered from GBS.[92] The issue facing the court, instead, was whether the plaintiff's GBS was caused by her swine flu vaccination. The court considered neurological, virological, immunological, epidemiological, and pathological evidence before finding in favor of the United States.[93]

The court recognized that because the exact cause of GBS remains unknown, "we must consider epidemiologic studies to determine if the disease is causally related to an antecedent event."[94] In particular, the court considered testimony of Dr. Lawrence Schonberger,[95] defendant's expert, who had previously authored a study concluding that an etiological relationship existed between the swine flu vaccine and GBS.[96] His study revealed that GBS was expected to occur in nine to nineteen persons per million population each year in the United States,[97] compared to the incidence of GBS among the vaccinated population of seven times

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cine, an exclusive remedy, and application of the Federal Torts Claim Act to such suits. 42 U.S.C. § 247(b)(K)(2)(A) (1976).

A surveillance program was also instituted to consider possible problems from the vaccination program. The Center for Disease Control in Atlanta, Georgia compiled statistics on the incidence of GBS among the vaccinated and unvaccinated population during the course of the program. A statistical correlation resulted from this surveillance which showed that the risk of incurring GBS among the vaccinated population was seven times greater than the risk of incurring the disease among the general unvaccinated population. These results led to the eventual cessation of the program. Subsequently, over a hundred suits were brought alleging injury pursuant to the program. 495 F. Supp. at 1191.

[90] 495 F. Supp. at 1188.

[91] 28 U.S.C. §§ 2671-80 (1982).

[92] 495 F. Supp at 1191. In addition, it was not contested that the epidemiological studies showed an association between the swine flu vaccine and GBS. The district court relied upon the final pretrial order of the multi-district litigation panel for this conclusion. *See In re* Swine Flu Immunization Products Liability Litigation, 464 F. Supp. 949 (D.D.C. 1979), which provided that when the government stipulated to the plaintiff having GBS, the plaintiff need not assert a theory of liability but only proof of causation. *Id.* at 953.

[93] 495 F. Supp. at 1207.

[94] *Id.* at 1203. Unlike cancer, GBS is associated with various antecedent events including viral infections (respiratory or gastroenteric), bacterial infections, surgery, fever treatment, malignant diseases and vaccines, thus facilitating proof of an association with the vaccine and GBS. *Id.* at 1195 (citing DYCK, PERIPHERAL NEUROPATHY 1114 (1975)).

[95] Schonberger relied upon the article, which he principally authored, *Guillain Barre Syndrome Following Vaccination in the National Influenza Immunization Program, U.S. 1976-77*, 110 AM. J. EPIDEMIOLOGY 105-122 (1979), in which 1098 cases of GBS were analyzed. 495 F. Supp. at 1203. Schonberger and his colleagues found that there was "an etiologic relationship between the swine flu vaccine and GBS, but that such relationship extended for ten weeks at most." *Id.* at 1203.

[96] *Id.*

[97] *Id.*

that amount.[98] (This would produce a relative risk of 7, or a vaccine induced probability of causation in any one patient of 6/7, or 85%.)

The issues raised regarding the epidemiologic study concerned its reliability on a temporal basis. The study showed a return to the normal incidence of GBS in the vaccinated population after a period of ten weeks from the date of vaccination. Plaintiff, however, was not diagnosed as having GBS until seven months after her vaccination, and thus, her GBS did not fall within the range of the noted association. Notwithstanding plaintiff's attempts to undermine the epidemiological statistics, the court ruled that plaintiff's GBS was not causally related to her vaccination.[99]

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[98] *Id.*

[99] Plaintiff argued that the epidemiologic study was inconclusive and of limited value as applied to her case of GBS because (1) the study was not intended to determine for how long a causal connection existed, and (2) only a limited number of people could have been analyzed past the ten week point. The court, however, ruled that a substantial number of cases had been analyzed and that a drop-off in the incidence of GBS beyond a certain time period became apparent as a result of determining the causal connection between the vaccination and GBS. Furthermore, the time of the association need not have been the primary focus of the study in order to be conclusive. *Id.* at 1205.

Other courts considered similar attacks on the study to those raised in *Alvarez*, but courts were steadfast in their adherence to the ten week limit. The study was later revised to reflect adjustments in reporting; these changes, however, did not alter the time limitation attributable to the return of the incidence of GBS among the vaccinated population after ten weeks to normally expected rates. For example, plaintiff in one case demonstrated the manipulation of the epidemiological statistics. In Varga v. United States, 566 F. Supp. 987 (N.D. Ohio 1983), plaintiff's expert attempted to undermine the temporal cut-off for establishing a causal relationship between GBS and swine flu vaccine subsequent to the revised study. First, plaintiff's expert noted that the observed rate of GBS in the unimmunized population was not necessarily the "true rate." *Id.* at 993. By changing the baseline rate number of GBS occurrence in the unimmunized population, plaintiff's expert concluded that an "enhanced relative risk" of incurring GBS after a swine flu shot existed during the eleventh and twelfth week after vaccination. *Id.* at n.8. Notwithstanding defendant's expert's testimony that his own studies had "many opportunities for error," the court rejected the plaintiffs' expert's testimony of a re-estimated baseline, his contention of underreporting, and his arguments of bias within the subjective analysis of symptoms from cases designated as having insufficient information, and denied recovery. *Id.* at 995-96, 1012. *See also* Gates v. United States, 707 F.2d 141 (10th Cir. 1983) (GBS developed eleven months after vaccination; relief denied because of failure to prove causation); Padgett v. United States, 553 F. Supp. 794 (W.D. Tex. 1982) (denial of recovery for GBS developed sixteen weeks after shot); Cook v. United States, 545 F. Supp. 306 (N.D. Cal. 1982) (twelve and one-half weeks); Migliorini v. United States, 521 F. Supp. 1210 (N.D. Fla. 1981) (denied recovery because developed GBS twenty-one weeks after vaccine); Lima v. United States, 508 F. Supp. 897 (D. Colo. 1981) (sixteen weeks); Hixenbaugh v. United States, 506 F. Supp. 461 (N.D. Ohio 1980) (fifteen months).

These courts all accepted as persuasive the epidemiological study authored by the Center for Disease Control and relied upon the statistics as proof of causation and its temporal restrictions to deny recovery to the GBS victim. At least one court, however, noted that it did not rely on the epidemiological proof and instead based its decision to deny recovery solely on clinical and neurological proof. Robinson v. United States, 533 F. Supp. 320 (E.D. Mich. 1982). In *Robinson*, plaintiff developed GBS seventeen weeks after receiving the vac-

The swine flu vaccine also presented the courts with more opportunities to consider epidemiological proof when plaintiffs began attributing other ailments to the swine flu vaccine; unlike the GBS cases, however, defendants in those cases forcefully contested the epidemiological proof.

For example, in *Szczepaniak v. United States*,[100] the plaintiff offered an epidemiological study as proof of a causal relationship between the swine flu vaccine and transverse myelitis.[101] The government denied that the vaccine caused any of plaintiff's injuries. The court considered testimony from six medical expert witnesses, including plaintiff's epidemiology witness, Dr. Goldfield. Dr. Goldfield testified that the number of cases of transverse myelitis actually observed in the vaccinated population was significantly greater than the number that would be expected,[102] and concluded that Szczepaniak's transverse myelitis was "caused" by the administration of the swine flu vaccine.[103]

The court specifically rejected the epidemiologic proof,[104] however, and

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cination. The court denied damages, and explained its reason for not following the lead of the other swine flu courts: "I would reach the same result if the epidemiological data were entirely excluded since statistical evidence cannot establish cause and effect." *Id.* at 330. The court was evidently dubious about the reliability of the statistical evidence presented; defendant's own expert testified to the questions surrounding the use of epidemiological proof:

> [T]here is no epidemiological or biostatistical method which definitively establishes whether an individual case of GBS is caused by the individual's receipt of the swine flu vaccine or by other factors. At most, one can examine statistical correlation and then within a chosen interval of error, determine whether GBS is more likely than not associated with swine flu vaccine in a particular period after receipt of the vaccination.

Id. at 326.

[100] No. 80-990 (D. Mass. 1983) (available June 1, 1984 on LEXIS, Genefed library, cases file).

[101] Transverse myelitis is a neurological disorder in which a lesion is produced across the spinal cord. In *Szczepaniak*, plaintiff suffered from the condition as a result of unknown causes. He experienced numbness and weakness on one side, difficulty with his bowel and bladder, and episodes of incontinence and sexual problems. Plaintiff also testified to bouts of frustration and depression as a result of his condition. *Id.*

[102] *Szczepaniak*, No. 80-990, slip op. at 10.

[103] *Id.* The court also considered two other experts for plaintiff: Dr. Locke, a treating physician, who concluded that a causal relationship existed on the basis that the plaintiff's symptoms developed soon after the vaccine and "stabilized" soon thereafter, and Dr. Poser, a neurologist, who based his conclusion of a causal relationship on medical literature, his examination of the plaintiff, and the plaintiff's medical records. *Id.* at 9, 12-13. The court found most persuasive the former's testimony. He dismissed the neurological expert opinion because the only medical literature upon which the expert based his opinion was of his own authorship. *Id.* at 13.

[104] The court stated:

> I can accept that Dr. Goldfield's epidemiological studies might be of some interest and probative value in the medical field, as they tend to show a statistical association between the occurrence of transverse myelitis and administration of the swine flu vaccine. However, while I accept that this is a valid technique in the field of

concluded that under Massachusetts law, more than "expert recognition of mere possibility" is required for establishment of proximate cause. The court accordingly denied relief.[105]

Epidemiologic studies fared far better in a case involving a connection between a product and the introduction of a disease-causing bacteria. In *Kehm v. Proctor & Gamble*,[106] the Eighth Circuit Court of Appeals accepted epidemiological studies as proof of the connection between toxic shock syndrome (TSS) and defendant's product, Rely tampons.[107] The lower court in *Kehm* considered plaintiffs' claim that Rely tampons were defective and unreasonably dangerous and that Proctor & Gamble failed to warn Rely users of this.[108] The appellate court affirmed the lower court's judgement and verdict against the defendant-manufacturer for $300,000.

On appeal, Proctor & Gamble contested the trial court's admission of

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> epidemiology, *I do not find bare statistics to be of great probative value in establishing causation in the matter at hand.* Epidemiology . . . does not as a discipline purport to isolate the sole cause for a single individual's medical ailment. However useful it may be as a diagnostic, therapeutic, or preventative tool, the broadbased statistical conclusions that are its product do not alone establish the legal causation necessary for demonstrating liability in a court of law.

Szczepaniak, slip op. at 10-11 (emphasis added).

[105] Courts, when considering epidemiology as proof of causation, are often ambivalent in their acceptance of these studies. An offer of epidemiological proof to the *Szczepaniak* court, led to an admonishment of the plaintiff for relying on medical evidence in a court of law, while the failure to provide such statistics, in other forums, led to a failure for lack of proof of causation. *See* Marneef v. United States, 533 F. Supp. 129, 134 (E.D. Mich. 1981) (no epidemiological basis for concluding relationship between swine flu vaccine and peripheral neuropathy); Adelson v. United States, 523 F. Supp. 459 (N.D. Cal. 1981) (insufficient evidence of statistical correlation showing causal relationship between swine flu vaccine and chronic inflammatory polyradiculoneuropathy led court to conclude no proximate cause). *But see* Ferebee v. Chevron Chem. Co., 736 F. 2d 1529, 1535-6 (D.C. Cir. 1984) (a cause-effect relationship need not be clearly established by animal or epidemiological studies before a doctor can testify that, in his opinion, such a relationship exists . . . . Products liability law does not preclude recovery until a "statistically significant" number of people have been injured.)

[106] Kehm v. Proctor & Gamble Mfg. Co., 724 F.2d 613 (8th Cir. 1983).

[107] Rely tampons were manufactured and placed on national markets by Proctor & Gamble during late 1979. According to facts found by the lower court, TSS was first identified in November of 1978. *Id.* at 616. It is typically associated with staphylococcus aureoles and its symptoms include fever, vomiting, diarrhea, low blood pressure, rash, and skin-peeling. In May of 1980, the Center for Disease Control published a report indicating a link between TSS and menstruation, and later found a relationship between tampon use and TSS. It was not until August of 1980 that Proctor & Gamble learned of a Minnesota study showing that twice the percentage of Rely users had TSS than did those in a control group; CDC issued similar findings on September 19, 1980. *Id.* at 617. Unlike cancer or GBS, the cause of TSS is known, and thus, the epidemiological studies were offered not as inferential evidence of cause per se, but instead to establish a link between the product and the growth of the causative agent.

[108] Plaintiff in *Kehm* died of TSS on September 6, 1980. 724 F.2d at 617. Proctor & Gamble withdrew the product from the market on September 22, 1980. *Id.*

reports prepared by the Center for Disease Control and various state health departments on the grounds of hearsay.[109] The district court had admitted into evidence reports of epidemiological studies and had allowed plaintiffs' expert to testify about the studies. Each of the reports analyzed the statistical association of tampon use and TSS.[110] Proctor & Gamble claimed that the statements were not "factual findings," that the preparers did not have first-hand knowledge of the matters asserted, and that the statements were not trustworthy, thus precluding their admission as an exception to the hearsay rule. The appellate court ruled that merely because the findings were conclusory did not preclude them from being factual; as long as the reports were prepared pursuant to an investigation authorized by law, trustworthiness was the only real inquiry.[111]

In response, Proctor & Gamble asserted that the studies were not trustworthy because of the existence of particular biases inherent in compiling the data. Moreover, the unavailability of the preparers for cross-examination made it impossible for Proctor & Gamble to discover and adjust for the biases. This attack on the admissibility of the epidemiological studies, however, was not successful.[112] The court instead ruled that the evidence on both sides was sufficient to permit the jury to resolve the question of fact.

This "balanced" approach, one in which the court permitted the use of epidemiologic studies on the condition that the complaining party had opportunity to proffer question and to offer contradictory studies, and one in which the probativeness of the statistics offered is a question to be

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[109] *Id.* Proctor & Gamble also based its appeal on errors made by the district court in its jury instructions, its refusal to grant a limiting instruction, its admission of evidence on punitive damages, and, finally, because the court permitted an in-court demonstration. The Eighth Circuit affirmed the district court. *Id.* at 628.

[110] The district court based the introduction of the epidemiological evidence on FED. R. EVID. 803 (8)(C), an exception to the hearsay rule, which permits admission of investigative or "evaluative" public records and which specifically covers "factual findings." 724 F.2d at 618.

[111] *Id.*

[112] The court stated:

> Allowing such cross examination as a condition of admissibility in cases like this would not only threaten individual patient's privacy, it would also inhibit agencies' efforts to collect data and inform the public in accordance with their statutory mandate.
>
> Moreover, though Proctor & Gamble could not cross-examine individual patients and interviewers, it presented expert testimony of its own challenging the methodology of the government reports, and evidence rebutting the conclusion of those reports. It thus has ample opportunity to attack the probative value of the . . . reports. The jury was therefore fully aware of the parties' conflicting assessments of the reports, and we believe, fully capable of evaluating the evidence on both sides.

Id. at 619. The court cited Migliorini v. United States, 521 F. Supp. 897 (D. Colo. 1981), as support for the introduction of epidemiological studies as long as balanced testimony is presented.

resolved by the jury, has also been found to be appropriate by courts considering a more difficult causation issue.[113] For example, two recent courts considered and implicitly approved the use of epidemiologic studies as proof of causation of cancer. Subsequent appellate rulings, however, have placed in doubt those decisions as bases for the judicial acceptance of epidemiological proof. Both cases involved the causal relationship between prenatal exposure to diethylstilbestrol (DES) and clear-cell adenocarcinoma. In *Mertan v. E.R. Squibb & Sons*,[114] plaintiff complained that her mother had ingested doses of DES during her pregnancy; at age 19, plaintiff experienced symptoms of, and was subsequently diagnosed as having a rare form of vaginal and cervical cancer. She sued several manufacturers of DES, and at trial offered epidemiologic studies by an expert

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[113] Cases concerning cancer and the causation problems associated with it have not yet flooded the courts. Instead it is instead in the workmen's compensation area that case law on the subject maybe found. Cases in this area illustrate judicial acceptance of epidemiological studies as the primary means for establishing causation. For example, statistics demonstrating a causal connection between peritoneal mesothelioma and asbestos employment have led to recovery. *See, e.g.*, Osteen v. A. C. & S., Inc., No. 43692 (Neb. Workmen's Comp. Ct. June 26, 1981) (Employed as insulator for forty years, a worker developed peritoneal mesothelioma. Appellant employer claimed absence of competent medical evidence to establish that it was a compensable occupation disease. Under a statute permitting recovery for all diseases except those occurring in "ordinary life," the workers' compensation panel held that epidemiological evidence that peritoneal mesothelioma was negligible in the population at large, but approached 7% among asbestos workers, was sufficient and competent medical evidence to establish causation.); Powell v. State Workmen's Compensation Comm'r, 273 S.E.2d 832 (W. Va. 1980) (recognized lung cancer as an occupational disease even though it is an ordinary disease of life. The court cited medical journals and doctor's testimony as support for causation; the court also stated that claimant need not negate all possible non-occupational causes of an alleged disease. *Prima facie* case of causation is established once exposure to hazard and suffering from it are thereby established, as long as studies and research "clearly link" a disease to particular workplace.) Because the burden of proof in workers' compensation cases is much less difficult to meet, application of these precedents to common law torts is questionable. However, it does explain that this area is in the forefront in terms of accepting epidemiological studies as proof of causation.

One of the few cases in which causation was shown by epidemiologic proof in an area other than workmen's compensation is Pritchard v. Liggett & Myers Tobacco Co., 295 F.2d 292 (3d Cir. 1961). In *Pritchard*, plaintiff claimed that his lung cancer was caused by smoking Chesterfield cigarettes for over thirty years. His cause of action was for negligence and breach of warranty; defendant cigarette manufacturer had advertised that its cigarettes were "pure" and that they would not cause harm to a smoker's nose, throat or other affected areas. *Id.* at 296-97. Plaintiff supported his proof of causal relationship by the testimony of five medical experts, one of whom was a specialist in the epidemiology of cancer. All testified that plaintiff's cancer was caused by smoking and that the chance of having lung cancer was 4 to 11 times greater in smokers than in nonsmokers. The defendant responded that such opinions had no validity, since no proof existed that his causal relationship had been accepted by the medical profession. The district court ruled that this was a question for the jury. On appeal, the decision was affirmed. *Id.* at 296. The case is of little significance today in light of the Surgeon General's warning which appears on all packages of cigarettes and which established plaintiffs' assumption of the risk.

[114] 141 Cal. App. 3d 511, 190 Cal. Rptr. 349 (Ct. App. 1983).

witness to establish the causal connection between DES and this form of cancer. Despite defendants' protestations, the court admitted statistical evidence demonstrating that a relative risk of 675 to one existed for DES ingestion and cancer.[115] The jury was not persuaded, and the defendants prevailed.

When reviewing the record below, the appellate court noted the expert testimony introduced concerning the causal relationship between ingestion of DES by mothers and the incidence of clear-cell adenocarcinoma in their daughters. The court did not, however, choose to rule on the error or propriety of the introduction of the studies. The appellate court instead reversed the decision below on other grounds.[116]

Similar studies were introduced and admitted with sound approval by the federal district court in *Needham v. White Laboratories, Inc.*[117] Plaintiff, as in *Mertan*, suffered from clear-cell adenocarcinoma; her mother had also taken DES while pregnant. Plaintiff introduced medical expert and statistical evidence that her mother's ingestion of DES caused the cancer. The statistics offered as proof established an association between artificial estrogen (like DES) and genital tract diseases; another

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[115] *See* Dickson, *Medical Causation by Statistics*, 17 FORUM 792, 805 (1982). The author Robert L. Dickson, represented one of the defendants in *Mertan*, and in this article describes the presentation of statistical proof at trial. He also offers criticism of the admission of the epidemiological studies by the trial court judge. According to Dickson, plaintiff's epidemiologist based his conclusion of a connection between DES and cancer on studies of forty women and thirteen cases of clear-cell adenocarcinoma conducted during the early 1970's. *Id.* at 805. Additional data, including a study undertaken to determine the number of pregnant women who had taken DES, was reviewed and analyzed to corroborate the ratio and an analysis was prepared comparing DES sales in a geographic area with the incidence of clear-cell adenocarcinoma in that area. *Id.* at 806.

[116] The court found that the trial court's failure to authorize an amendment of the complaint to reflect a recent California Supreme Court decision was prejudicial error. That decision, Sindell v. Abott Laboratories, 26 Cal. 3d 588, 607 P.2d 924, 163 Cal Rptr. 132, *cert. denied*, 449 U.S. 912 (1980), provided that a plaintiff may recover even if unable to identify the manufacturer of the DES ingested by her mother. Plaintiff in *Mertan*, at time of the *Sindell* decision, had been unable to identify defendant responsible for the manufacture of DES taken by her mother and had not amended the complaint to reflect the *Sindell* decision due to the possibility of exceeding a mandatory statute of limitations. 141 Cal. App. 3d at ____, 190 Cal. Rptr. at 351. The nearest the court on appeal in *Mertan* came to passing on the admissibility of the epidemiological evidence was its commentary on admitting testimony of another expert witness:

> We need not reach the issue of whether allowing the testimony of Tobias Klinger, as an expert witness without prior notice to plaintiff, was in violation of Code of Civil Procedure section 2037. If error was committed, it was harmless. The testimony which was presented to the jury, *as distinguished from the testimony at the Evidence Code section 402 hearing*, consisted of a recitation of the procedures followed in submitting a new drug application. . . .

Mertan, 141 Cal. App. 3d at ____, 190 Cal. Rptr. at 354. (emphasis added).

[117] 639 F.2d 394 (7th Cir. 1981). For a discussion of the lower court opinion, and other issues of causation, see *Phelan, Proof of Cancer From a Legal Viewpoint*, in PLI HANDBOOK, TOXIC SUBSTANCES PROBLEMS IN LITIGATION 133 (1980).

study indicated that the likelihood of the relationship between the ingestion of DES and the subsequent development of clear-cell adenocarcinoma being "accidental" was only one in one hundred thousand.[118]

Plaintiff prevailed on the merits and was awarded $800,000.[119] Defendants moved for a judgment notwithstanding the verdict based primarily on the grounds that the jury verdict was based on "speculation."[120] The court denied the motion and stated its sound approval for the use of statistical data for establishing causation, and affirmed the jury verdict.[121]

Notwithstanding the district court's approval of the use of epidemiological proof, the decision was reversed, thus leaving in doubt the precedential value of that decision. On appeal, defendants claimed error in the district court's introduction of evidence that the drug was ineffective for its intended purpose. The appellate court agreed, ruling that the lower court had erroneously interpreted section 402A of the RESTATEMENT (SECOND) OF TORTS.[122] Defendants also claimed error in the district court's admission into evidence of a list of medical journal titles by plaintiff's expert witness. The appellate court found that this was an abuse of dis-

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[118] *Phelan, supra* note 116, at 148.

[119] 639 F.2d at 397.

[120] *Id.*

[121] In response to the defendant's contention that the statistics were speculative, the court stated:

> Specifically, the jury was entitled to conclude on this record that maternal ingestion of synthetic estrogens during pregnancy is one such condition. It was also entitled to conclude that reputable statistical analysis of confirmed data has led qualified experts to believe that the coincidence of this potentially carcinogenic condition with the actual fact of a case of clear cell adenocarcinoma makes "the chances of a causal relationship extremely high." Finally, the jury was entitled to conclude, by crediting Dr. Shimkin's testimony to this effect, that such statistically well established generalizations are equally reliable as, and functional equivalents of, flat causal pronouncements. These propositions taken together make the causal link between Anne Needham's condition and her mother's use of dienestrol more than a mere possibility. Certainly the jury conclusions to this effect was far removed from the acts of imagination, speculation [and] mere conjecture disapproved by *Teffin*. Accordingly, the court holds that there was sufficient evidence to support the jury finding of causation.

Phelan, *supra* note 116, at 149.

[122] 639 F.2d at 401. The district court admitted evidence on the effectiveness of DES on the grounds that it was relevant to refute an affirmative defense under comment k of Section 402A (risk of danger with product outweighs apparent usefulness). Alternatively, the district court admitted the evidence on the grounds that it established that the product was ineffective. *Id.* at 402. The court relied on a prior case which held that an ineffective product is a defective product. *Id.* The district court had instructed the jury to return a verdict for the plaintiff if it found that defendant knew or should have known that DES could cause cancer in the children of users, or if the jury found that DES was ineffective. *Id.* The jury did not return a special verdict, and accordingly, the appellate court was unable to determine the basis for its decision. *Id.* Consequently, it is not possible to determine whether the appellate court would have agreed with the district court's ruling on the epidemiological studies as being probative of causation.

cretion, for plaintiffs had failed to lay an adequate foundation for admission of the list and also had failed to establish the accuracy of the journals.[123]

VI. BENDECTIN

The lack of certainty of statistics is a burden facing plaintiffs in other areas. Recently, plaintiffs have used epidemiological proof in cases concerning the alleged association between Bendectin and birth defects, but have not been successful due to the uncertain nature of the statistics. At least one court has dealt with this uncertainty by imposing a ninety-five percent confidence level before allowing use of epidemiological proof of a connection between Bendectin and birth defects.[124] In *Oxendine v. Merrell Dow Pharmaceuticals*,[125] plaintiff alleged that her mother's ingestion of Bendectin during her pregnancy with plaintiff caused her resulting birth defect. Plaintiff buttressed her case against Merrell Dow with testimony on causation from Dr. Alan K. Done.[126] In spite of Dr. Done's testimony that an association existed between the birth defect at issue and Bendectin, defendants were successful on a motion for ajudgment notwithstanding the verdict.[127] At trial, defendants led Dr. Done to admit that statistics were never 100% correct and that proof of an objective conclusion was not possible in medicine. The defendants argued that plaintiff's expert testimony on Bendectin passed the bounds of a "reasonable medical certainty" and entered the realm of speculation. The court agreed.

VII. RADIATION EXPOSURE

An example of the use of undisputed epidemiologic proof can be found in the recent landmark decision, *Allen v. United States*.[128] In that case,

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[123] 639 F.2d at 403. The articles were offered for the limited purpose of showing that defendant should have known in 1952 that DES could cause cancer. *Id.* The plaintiff's witness, however, had not read all the articles nor could he testify that all of them were relevant to demonstrate a relationship between DES and cancer. *Id.*

[124] Kollar v. Richardson-Merrell, Inc., C.A. No. 80-1258 (D.D.C. 1983). A ninety-five percent confidence level simply means that the odds of the result having occurred as the result of chance are less than five in one hundred.

[125] Oxendine v. Merrell Dow Pharmaceuticals, Inc., C.A. No. 1245-82 (D.C. Super. Ct. 1983).

[126] Plaintiff suffered from limb reduction at birth. Defendants' Memorandum of Points and Authorities in Support of Motion for Judgment Notwithstanding the Verdict, or in the Alternative, Motion for New Trail filed June 6, 1983 [hereinafter cited as *Defendant's Memo*] in Oxendine v. Merrell Dow, supra, note 124.

[127] *Defendant's Memo*, supra note 125, at 2.

[128] Allen v. United States, No. C79-0515-J (D. Utah 1984). The Allen case consolidated 24 claims for alleged radiation induced cancers caused by fallout from atmospheric nuclear weapons tests conducted at the Nevada Test site from 1951-1962. *Id.* at 3. The claims, which were representative claims from the more than 1100 filed, were brought against the

Judge Jenkins of the district court in Utah considered the issue of cancer causation in the context of radiation exposure. Recognizing that the cause of cancer is not known in fact, Judge Jenkins nevertheless permitted the radiation exposure cases to proceed according to this remedial framework:

> [T]his court now holds as follows:
> Where a defendant who negligently creates a radiological hazard which puts an identifiable population group at increased risk, and a member of that group at risk develops a biological condition which is consistent with having been caused by the hazard to which he has been negligently subjected, such consistency having been demonstrated by substantial, appropriate, persuasive and connecting factors, a fact finder *may* reasonably conclude that the hazard caused the condition absent persuasive proof to the contrary offered by the defendant.[129]

Using this framework, the court cited the appropriate factual connecting factors upon which a finding of causation could be based. These factors included the presence of an observed statistical "incidence of the alleged injury greater than the expected incidence in the same population."[130] Indeed, the court also recognized that statistical evidence, under the present facts, would be the "strongest evidence" available.[131] While recognizing the inherent problems with statistics, including the appropriate-

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government under the Federal Tort Claims Act. 28 U.S.C. §§ 2671-2680 (1976). Therefore the basis for liability was negligence. *Allen*, No. C 79-0515-J, at 4. The court found negligence in the government's failure to adequately warn residents in the affected areas of the dangers of radiation and how they could protect themselves, and its failure to monitor radiation dose levels, in localities near the test site, on a person-specific basis, or its equivalent. *Id.* at 416-17.

[129] *Id.* at 343-44 (citation omitted). Judge Jenkins likened the radiation cancer causation issue to the common law tort cases wherein two hunters negligently fire and one pellet hits an innocent bystander. *Id.* at 333-35. Notwithstanding the fact that only one hunter could in fact be responsible, the burden was shifted to the defendants to establish the absence of substantial factual connection to the injury on their part.

[130] *Id.* at 344. The other factors which Judge Jenkins considered included:

> (1) the probability that plaintiff was exposed to ionizing radiation due to nuclear fallout from atmospheric testing at the Nevada Test Site at a rate in excess of natural background radiation; (2) that plaintiff's injury is of a type consistent with those known to be caused by exposure to radiation; and (3) that plaintiff resided in geographical proximity to the Nevada Test Site for some time between 1951 and 1962. Other factual connections may include but are not limited to such things as time and extent of exposure to fallout, radiation sensitivity factors such as age or special sensitivities of the afflicted organ or tissue, retroactive internal or external dose estimation by current researchers, a latency period consistent with a radiation etiology, or an observed statistical incidence of the alleged injury greater than the expected incidence in the same population.

Id.

[131] *Id.* at 346. The court stated that the study of the incidence of diseases is the "classic approach" to researching radiation caused by cancer. *Id.* at 347.

ness of their use with small populations such as the one at issue, the court nevertheless concluded that epidemiologic proof was credible evidence:

> That data from small populations must be handled with care does not mean that it cannot provide substantial evidence in aid of our effort to describe and understand events. Mathematical or statistical evidence, when properly combined with other varieties of evidence in the same case can "supply a useful link in the process of proof." *If relied upon as a guide rather than as an answer, the statistical evidence offered in this case provided material assistance in evaluating the factual connection between nuclear fallout and plaintiffs' injuries.*[132]

The federal government did not dispute the epidemiologic proof presented,[133] and the court ruled that ten of the twenty-four plaintiffs prevailed.[134] In accordance with Judge Jenkin's prediction, the epidemiologic proof was found to be the persuasive connecting factor of the cases.[135]

In a more recent decision involving allegations of radiation induced acute myeloid leukemia, *Roberts v. United States*,[136] Judge Foley, of the District Court of Nevada, rejected the plaintiffs attempts to prove their case by use of a study comprised of only eighty-six subjects. The judge criticized the methodology and noted that other, larger studies had found no effect.[137]

The decisions in which courts have considered epidemiological studies as indirect evidence of causation provide little guidance for future use. Some courts seemingly are comfortable only with those studies bearing indices of credibility, such as the government-approved statistics offered and unsuccessfully challenged or supplemented in the swine flu cases.[138]

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[132] *Id.* at 352 (citation omitted).

[133] The epidemiologic proof included the studies conducted of victims of radiation exposure suffered during the attacks of Hiroshima and Nagasaki and federal government reports. *Id.* at 375-407.

[134] *Allen*, No. C79-0515-J at 407.

[135] *Id.* at 375-406. The majority of the unsuccessful plaintiffs failed because in the court's words, their cases showed a "paucity of statistical evidence [needed to] demonstra[te] an increased incidence of cancer of the bladder, the pancreas, . . .melanoma and Hodgkins disease" attributable to radiation exposure. *Id.* at 382. A few plaintiffs failed either due to their inability to rebut the government's supporting and finding arguments, or their failure to plead sufficient facts of injury. *Id.*

[136] Roberts v. United States, Nos. Civil LV 1766 and 76-259 RDF (D. Nev. 1984).

[137] *Id.* at 95-97.

138 The "swine flu" decisions are somewhat anamolous and demonstrate an apparent willingness on the part of some courts to embrace epidemiological studies as proof of causation. Notably, the defendant United States was the source of the epidemiologic studies found persuasive in those cases. It is also of interest that courts considering swine flu vaccine claims did not venture past the bounds of the government's own study, evidencing a judicial hesitancy to venture far into the epidemiological frontier.

Appellate courts have managed to avoid the issue of the propriety of epidemiological studies as proof of causation by failing to address the question,[139] and district courts considering them either permit their admission as sufficient to raise questions for the jury (if the complaining party has an opportunity to refute them) or, alternatively, criticize them for the studies' inability to prove conclusively a cause and effect.[140]

This ambivalence perhaps may be attributed to the nature of epidemiological studies. As case law demonstrates, statistics may be probative. However, they can also be manipulated, thereby undermining the probative value and reliability of the conclusions drawn.[141] Moreover, the form of the epidemiological proof offered presents evidentiary problems. The studies themselves present problems of authentication and cross-examination; opponents of this type of proof claim that they are unable to cross-examine the authors for any biases, assumptions, or the validity of the studies.[142] The problems of authenticity and cross-examination are

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[139] *See* cases cited *supra* note 104.

[140] *Compare* cases cited *supra* note 98 with those cited *supra* note 104.

[141] Dickson notes the problems attributable to the size of the sample. Only forty women were the subject of the clear-cell adenocarcinoma analysis, which the author contrasts to the "thousands of cases studied in order to make the causal connection between smoking and lung cancer." Dickson, *supra* note 114, at 805.

[142] *See* McGovern, *Toxic Substances Litigation in the Fourth Circuit*, 16 U. RICH. L. REV. 247, 296-98 (1983). The author notes:

> Experiments, studies, articles, documents and expert witnesses have created substantial difficulties for the trial judge . . . . Although some attorneys have been successful in introducing epidemiological and other studies into evidence, they must, however, overcome arguments suggesting that these studies are unreliable, irrelevant, unnecessary, hearsay and not subject to cross-examination . . . . Defendants have argued that this type of testimony is inherently prejudicial because the defense cannot cross-examine the witness upon the controls, assumptions, soft variables, validity and other factors inherent in the studies that form the basis of the expert opinion.

The author also suggests that the nonexamining expert should only be permitted to testify to the conclusions of his studies. "However, such an expert witness should not be allowed to draw conclusions about the particular plaintiff because the witness had neither the ability nor the opportunity to give the plaintiff a medical examination to establish specific causation." *Id.* at 298.

Author Dickson, in his criticism of the superior court in *Mertan*, also notes the bias in that case which may have altered the conclusions drawn from the study offered as proof of causation. In that analysis, the control group was heavily represented by women without a history of prior pregnancy losses, thus raising the question as to the reliability and applicability of the results of the study to women with prior pregnancy-related problems. Dickson, *supra* note 114, at 806.

As for the possibility that the compilers' assumptions may skew statistics, Dickson also questioned the assumption in *Mertan* that one company's sales of DES remained constant throughout the years of DES sales. Moreover, he soundly criticizes the studies used in the trial court in Mertan for other deficiencies:

> These examples of possible deficiencies in the analysis performed in [*Mertan*] illustrate some of the major problems involved in an epidemiologist's reliance on

exacerbated when one considers that the expert testifying to the results of the epidemiological proof usually has no experience with the individual plaintiff.

The most glaring problem with epidemiology as proof of causation, however, is attributable to the nature of statistics; they do not account for an individual's ailment. Neither do they refer to an individual's idiosyncracies, sometimes called the "host factor."[143] Because epidemiological proof, by definition, does not "purport to isolate the sole cause for a single individual's medical ailment,"[144] it is limited in its application to individual legal claims. Lacking capacity to be applied to individuals, epidemiolgical studies are hardly a fail-safe substitute for direct proof of causation.[145] However, to assist courts in their use of epidemiological proof, legislation has been considered.

VIII. Proposed Legislation

Since the mid 1970's, there have been numerous attempts to legislate compensation for victims of disease resulting from toxic substances, either as result of occupational exposure or of environmental exposures, such as toxic waste dumps. In the first session of the 98th Congress alone,

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> retrospective studies. The studies reviewed are medical in nature and often give little or no indication of the existence of necessary statistical controls or whether they were constantly applied. As my discussion earlier of the smoking-lung cancer association indicated such controls are considered to be critical and because of their sensitivity and complexity often cannot be achieved through retrospective studies. As a result the epidemiologist is forced, out of necessity, to make assumptions about how certain tests were performed, how certain controls were imposed, and probably most importantly, what assumptions may have been made which do not appear in the text of the studies relied upon.

Id. at 806-07.

[143] *See* Henderson, *Medical Causation in Product Liability Disease Litigation*, 18 Trial 53 (July 1981) (other factors, such as genetic background, can affect plaintiff's propensity for acquiring a disease). The realization that one's genes can affect the appropriateness of applying general probabilities to an individual, is applicable to other personal habits, such as smoking, life style, occupational history, or past illnesses. These characteristics inherently make one person different from another, and accordingly, render general population statistics more or less appropriate for determining the cause of an individual's ailment.

[144] Szczepaniak v. United States, No. 80-990 (D. Mass. 1983).

[145] Author Michael Dore suggests that courts today use epidemiological studies too frequently and often incorrectly. Because of the noted failings of epidemiological proof, Dore suggests that this type of proof be used only under controlled circumstances, such as judicial determinations of study reliability, so-called "quality control," and limiting jury instructions, which he deems to be "jury control." Dore, *A Commentary On the Use Of Epidemiological Evidence in Establishing Cause-In-Fact*, 7 Harv. Envtl. L. Rev. 429, 438-40 (1983). Notwithstanding the obvious limitations of the use of epidemiological proof, some critics see its benefits as far outweighing its drawbacks. Thus, Hall & Silbergeld, in their response to Dore's article, conclude that epidemiological proof "can play a legitimate role as relevant circumstantial evidence in showing causation." Hall & Silbergeld, *Reappraising Epidemiology: A Response to Dore*, 7 Harv. Envtl. L. Rev. 441, 448 (1983).

nine such bills were introduced.[146] A compensation program for those injured by environmental chemical exposure was actually a part of the bill which, as revised, became the "Superfund" Act.[147] Although that program was dropped before the bill became law, the Act did provide for the appointment of a study group to review remedies for damages due to hazardous wastes.[148] The study group was required to analyze any problems with those remedies and to recommend change to the system so as to obviate those problems.[149] Although at least one legislative proposal has incorporated many of those recommendations,[150] neither that proposal nor any other victim compensation proposal has been passed by Congress.

In the first session of the 97th congress, Senator Orrin Hatch and others[151] proposed what appears to be the first effort by Congress to deal specifically with the problem of compensation for cancer.[152] The Hatch Bill[153] sought to amend the Federal Tort Claims Act[154] in order to render

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[146] The Senate bills include: 1) S. 1155, 98th Cong., 1st Sess. (1983) (to compensate those with brown lung disease, resulting from cotton dust exposure); 2) S. 946, 98th Cong., 1st Sess. (1983) (to provide a complete compensation system for victims of environmental chemical exposures); 3) S. 945, 98th Cong., 1st Sess. (1983) (to provide for compensation for medical expenses for victims of environmental chemical exposures); 4) S. 921, 98th Cong., 1st Sess. (1983) (to provide compensation for certain uranium miners and those exposed to fallout from atomic weapons testing).

The House bills include: 1) H.R. 4303, 98th Cong., 1st Sess. (1983) (to compensate victims of environmental pollution pursuant to an amendment of the Toxic Substances Control Act); 2) H.R. 3175, 98th Cong., 1st Sess (1983) (to compensate individuals with occupationally related asbestos diseases); 3) H.R. 2582, 98th Cong., 1st Sess. (1983) (to compensate victims of environmental pollution); 4) H.R. 2482, 98th Cong., 1st Sess. (1983) (to compensate victims of environmental pollution).

[147] S. 1480. 96th Cong., 1st Sess. § 4 (1980). The enacted legislation, known as the Superfund Act, is the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, Pub. L. No. 96-510, 94 Stat. 2767 (codified at 42 U.S.C. §§ 9601-59 (Supp. V 1981)). *See generally* Nute, *Compensation for Exposure to Hazardous Substances*, 7 CHEMICAL TIMES & TRENDS 27 (1984).

[148] 42 U.S.C. § 9651(e) (Supp. V 1981).

[149] *Id.* An example of the study group's required reports is *Superfund Section 301(e) Study Group 97th Cong., 2nd Sess. Injuries and Damages from Hazardous Wastes - Analysis and Involvement of Legal Remedies*, (Comm. Print 1982) (available on microfiche: Cong. Information Serv. 1982).

[150] *E.g.*, S. 946, 98th Cong., 1st Sess. (1983).

[151] S. 1483, 97th Cong., 1st Sess. (1981). Co-sponsors were Senators Kennedy, Garn, Cannon, Laxalt, DeConcini, Randolph, Inouye, Hawkins, Metzenbaum, Pell, Hatfield, Matsunaga, Moynihan, Denton, and Mathias.

[152] Congress had earlier enacted a comprehensive legislative scheme for the compensation of coal worker's pneumoconiosis. *See* authority cited *infra* note 159. After the introduction of this bill, Congressman George Miller and others introduced legislation to compensate victims of asbestos related disease, one of which was asserted to be lung cancer. H.R. 3175, 98th Cong., 1st Sess. (1983).

[153] S. 1483, 97th Cong., 1st Sess. (1981).

[154] 28 U.S.C. §§ 2671-2680 (1976).

the United States liable for damages caused by particular types of cancer. The eligible individuals had been exposed to radioactive fallout resulting from nuclear tests at the Nevada test site and to radionuclides certain uranium mines.[155]

As originally proposed, the bill merely sought to introduce a rebuttable presumption in any suit for damages against the government for radiation-caused injury under the Federal Tort Claims Act.[156] The rebuttable presumption was that the damages alleged were caused by exposure to radiation which resulted from a nuclear detonation or exposure to uranium. The presumption would be invoked upon proof of two facts:[157]

> (1) That the individual on whose behalf suit is brought lived or worked within a defined "affected area" for a certain minimum time period during the nuclear testing program (or worked in a uranium mine for that period of time).[158] (2) That the individual on whose behalf suit is brought has one of the cancers defined in the bill, or any other cancer identified by an Advisory Panel established by the statute, as being related to radiation exposure.[159]

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[155] S. 1483, 97th Cong., 1st Sess. § 2 (1981). The necessity for the compensation remedy provided by the bill was the result of nuclear weapons testing from 1951 to 1962 at the Nevada test site. *Id.*

[156] *Id.* § 2(b).

[157] The bill provided that the presumption arises "[i]f the court determines that the plaintiff meets such requirements." *Id.* It is not certain from this language whether the court is obliged to rule in plaintiff's favor as to the satisfaction of these requirements or whether the factfinder may just hold the plaintiff has made a prima facie case before invoking the presumption.

[158] *Id.* § 2(a)(1)-(3). Affected areas include those areas "shown to have received a significant level of fallout as a result of the nuclear detonation[s] at the Nevada test site between January 1, 1951, and October 31, 1958, or between June 30, 1962, and July 31, 1962." *Id.* § 2(e)(1)(A). That determination is to be made from the "best available fallout maps, as determined by the Secretary [of Health and Human Services]." *Id.* Other affected areas as a result of the same nuclear testing may also be identified by an Advisory Panel on the Health Effect of Exposure to Radiation and Uranium which would have been created by this legislation. *Id.* § 2(e)(1)(B). Plaintiffs seeking damages because they have developed cancer as a result of living in an affected area between January of 1951 and October of 1958 must have lived in the area for at least one year. *Id.* § 2(a)(1).

[159] For those residing in the areas determined to have received a significant level of fallout, the listed disease are the acute leukemias, chronic myelogenous leukemia, thyroid carcinoma, pulmonary carcinoma and osteogenic sarcoma. *Id.* § 2(a)(1). Also potentially compensable are any cancers identified by the Advisory Panel on the Health Effects of Exposure to Radiation and Uranium. These cancers are "those types of cancer . . . that are more likely than other cancers to develop in human beings after exposure to low level radiation." *Id.* § 4(b)(1)(A). For uranium miners, the listed diseases are lung cancer (the bill never addresses whether lung cancer and pulmonary carcinoma are the same) and "significant pneumoconiosis." *Id.* § 2(a)(3). In addition, the Advisory Panel may identify other compensible diseases and illnesses "that are more likely than other diseases and illnesses to develop in human beings who worked in uranium mines for at least a year between January 1, 1947,

Once the presumption was invoked, the court was directed by the bill to "admit and hear evidence" rebutting such a presumption.[160]

Presumptions of compensability are fairly common devices in compensation statues. Typically, the presumptions are contained in a number of state laws which state that heart (and sometimes lung) disease in a police officer or firefighter is work-related.[161] Presumptions are also in use in two federal compensation schemes. The first is the Black Lung Benefits Act[162] which, with its accompanying regulations provides a fairly comprehensive set of presumptions.[163] The second scheme, in the Longshoremen's and Harbor Workers' Compensation Act,[164] merely provides that it will be presumed "in the absence of substantial evidence to the contrary. . .[t]hat the claim comes within the provisions of this [Act]."[165] The exact operation of a presumption of compensability has been much debated, and its uses have been discussed in detail elsewhere.[166] It is sufficient to say that at least under the Longshoremen's Act, once substantial evidence is introduced by the defendant, the presumption drops from the case, and the factfinder weighs the evidence to arrive at a conclusion.[167]

The presumption is a mechanism for shifting the burden of production on an issue. The function of a presumption in the context of cancer causation is to shift the initial burden of coming forward with proof which shows that it is more likely than not one's condition is due to the substance alleged to have caused it, and to place the burden on the defendant to come forward with some level of proof that the condition was not due to the substance alleged to have caused it.[168] Once this occurs, no presumption exists for the case.

In October of 1982, during the course of the testimony on the Hatch

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and December 31, 1961." *Id.* § 4(b)(1)(B). Since pneumonconiosis generally occurs only in worker populations and epidemiology is usually not used to determine if it is work related, pneumoconiosis will not be addressed further in this article.

[160] *Id.* § 2(b).

[161] *E.g.*, V. CODE § 65.1-47.1 (Supp. 1983).

[162] Black Lung Reform Act of 1977, Pub. L. No. 95-239, 92 Stat. 95 (1978), *amended by* Black Lung Benefits Amendments of 1981, Pub. L. No. 97-119, 95 Stat. 1643 (1981) (codified at 30 U.S.C. §§ 901-945 (1976 Supp. V 1981)).

[163] 30 U.S.C. § 921(c) (Supp. V 1981); 20 C.F.R. 727 200-06 (1983). The Black Lung Benefits Amendment prospectively eliminated three of the presumptions contained in the predecessor to § 921(c). *See* 30 U.S.C. § 921(c) (Supp. V 1980).

[164] Pub. L. No. 92-576, 86 Stat. 1263 (1977), *amended by* Act of Nov. 6, 1978, Pub. L. No. 95-598, 92 Stat. 2679 (codified at 33 U.S.C. §§ 901-950 (1976 & Supp. V 1981).

[165] 33 U.S.C. § 920(a) (1976).

[166] *E.g.*, McElveen & Postol, *Compensating Occupational Disease Victims Under the Longshoremen's and Harbor Workers' Compensation Act*, 32 AM. U. L. REV. 717 (1983).

[167] *See, e.g.*, Del Vecchio v. Bowers, 296 U.S. 280, 285-87 (1935) (presumption); United States Steel Corp. v. Gray, 588 F.2d 1022, 1076-28 (5th Cir. 1979) (presumption in Black Lung Benefits Act).

[168] *See generally* FED. R. EVID. 301 (effect of presumption in civil actions).

bill, the use of a presumption in the radiation exposure context was criticized.[169] For example, Dr. Victor Bond of the Brookhaven National Laboratories stated:

> The bill provides that for any individual developing certain types of cancer [and] who was in the region of fallout in certain time periods, there would be a legal presumption that such cancers were caused by fallout from government weapons testing, with no reference to dose magnitude or other factors related to causation . . . . However, the virtually "automatic" liability of the government proposed in the bill is seriously defective with respect to the scientific basis for the problem involved.[170]

Dr. Bond also pointed out that the risk of getting cancer from radiation is related to a variety of factors including age, sex, personal characteristics, latent and plateau periods for the tumor in question, radiation dose, and origin of the radiation.[171] Dr. Bond indicated that two related approaches can and should be undertaken together in order to account for the factors in any compensation scheme. The first approach is epidemiology, which should be used to determine "the magnitude of the community health problem," i.e. the number of additional cancer cases and deaths that must be taken into account by community health officials.[172] The second approach is the method of estimating the odds that any given cancer may be causally related to a specific exposure of an individual.[173]

Based in part on testimony such as that of Dr. Bond, Senator Hatch and others revised the proposed mechanism for compensation in the bill by adopting an approach that incorporated Dr. Bond's suggestions. By so doing, the bill attempted to utilize the science of epidemiology and the concept of probability of causation.

The revised Hatch bill directed the Secretary of Health and Human Services to determine and publish a list of radiation-related cancers.[174] It also instructed the Secretary to devise and publish radio-epidemiological tables that estimate the likelihood that persons who have (or had) any of the radiation-related cancers and who have received specific radiation doses before the development of any of those cancers, got the cancer as a result of the radiation dose.[175] The Secretary was directed to establish

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[169] *Hearing Before the Comm. on Labor and Human Resources, United States Senate on S.1483*, 97th Cong., 1st Sess. (1981).

[170] *Id.* at 247.

[171] *Id.* at 252 (testimony of Dr. Victor P. Bond).

[172] *Id.* at 247.

[173] *Id.* at 247-48.

[174] S. 1483, 97th Cong., 2d Sess., §(4)(a) (Comm. Print) (1981).

[175] Section 7(b) of the Orphan Drug Act, Pub. L. No. 97-414, 96 Stat. 2049, 2060 (1983) (to be codified at 42 U.S.C. 241), referred to in S. 291. provided the detailed requirements of radioepidermiological tables.

such probabilities of causation in percentages for doses from one millirad to one thousand rads, taking into account age at time of exposure, sex, time from exposure to the onset of the cancer, and other appropriate factors.[176]

The bill further provided that any individual subjected to radioactive fallout from nuclear weapons testing who could establish that his or her probability of causation exceeded fifty percent was entitled to an award of actual damages from the United States of not more than $500,000.[177] Any individual who established a probability of causation of from ten to fifty percent was entitled to an award of damages of not less than $50,000 and not more than the product of his individual probability of causation as multiplied by $500,000.[178]

This bill presented a complete departure from earlier compensation legislation and the common law of torts in two ways: (1) It mandated that the courts use radioepidemiological tables as the standard for judging the merits of the case; and (2) It permitted damages to be awarded to individuals whose demonstrated probability of harm was less than fifty percent.

The revised version of Senator Hatch's bill did not pass Congress in the 97th session and was reintroduced in the 98th.[179] One portion of the bill did, however, become law as a rider to the Orphan Drug Act.[180] That portion which was passed provided that, within one year of passage of the Act, the Secretary of Health and Human Services was to develop and publish radioepidemiological tables.[181] Those tables are to be used to estimate the likelihood that persons who have developed any of the radiation-related cancers and who had specific radiation doses prior to the onset of that disease developed the cancer as a result of these doses.[182] Though these probabilities will have no immediate legal effect, courts and administrative bodies may refer to them for assistance in determining whether given cancers may be related to radiation exposure. They may also serve as a model for efforts to quantify the risks of other carcinogens.

If the probability tables are used, there is an obvious problem in regard to dose measurement. Whereas radiation doses, in the occupational context at least, have been rather carefully measured, doses of other suspected cancer-causing agents, often inhaled or ingested decades ago, have not been measured at all. Epidemiologic studies that have sought to measure the effect of doses have often divided the study population into groups, depending on length of time spent at the job. If there is a dose-

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[176] S. 1483, *supra* note 171, at § 4(b).
[177] S. 921, 98th Cong., 1st Sess., § 8(a)(1) (1983).
[178] *Id.*
[179] S. 921, 98th Cong., 1st Sess. (1983).
[180] Pub. L. No. 97-414, 96 Stat. 2049, 2060 (1983) (to be codified at 42 U.S.C. 241).
[181] *Id.*
[182] *Id.*

response relationship and relatively constant exposure to the substance in question, a person's risk continues to increase the longer they continue to work.

IX. Conclusion and Recommendation

Despite the limitations of epidemiologic proof in particular and statistical analysis in general, courts should permit the use of epidemiologic proof. The argument raised against its use—the imprecision of probabilities—is weak considering that medical science is rarely, if ever, a precise science. The popular assumption that medical diagnosis is based on medical certainties is undoubtedly a false one; many clinical medical diagnoses are instead rooted in medical probabilities. This imprecision further applies to the medical diagnosis of the cause of the identified condition. As a result, the excuse given for not using epidemiologic proof of causation—its reliance on probabilities—loses force in light of the inherent reliance on probabilities in every aspect of medical science.

The recommendation that courts accept epidemiologic proof is subject to the qualifications discussed in this Article. Each study should be evaluated for its reliability and validity prior to its introduction as sound evidence. A high confidence level should be required, such as the 95% level of confidence mandated by the court in *Kollar*.[183] In sum, "quality controls" such as those suggested by other critics, and indeed by the medical profession, must be verified prior to judicial use.

Once accepting the recommendation to use epidemiological data, courts are faced still with the choice of a rational *procedural* scheme by which to consider the proffered evidence. Courts first ought to consider whether the epidemiologic study at issue demonstrates a statistically significant increase in the relevant disease. In particular, the absence of such a study should sway the court when considering a summary judgment motion. Such an absence should be particularly determinative when the burden of proof is imposed by statute. Although the view that a failure to produce credible epidemiologic proof should be determinative of case outcome may seem harsh, at least one tribunal has approved of it and stated:

> The employee meets his burden where medical science has progressed to the point where, as here, epidemiological studies establish a higher than expected incidence of the disease among workers exposed to the harmful stimulae. In cases where no such relationship exists or where medical science has not yet discovered the relationship, the employee may not be able to show that working conditions could have caused the harm . . . . We are aware that once the presumption is invoked, the subsequent allocation of the burden of proof may in many instances be determi-

[183] *See* note 123 and accompanying text.

native of liability.[184]

In the above cited workers' compensation case, a statutory presumption of compensability was invoked if the claimant was able to show harm and a work-related factor that could have caused that harm. In that case, the statement by means of an epidemiologic study was able to invoke the presumption. Thus, the failure to offer a sound epidemiological study in defense was outcome-determinative. This scheme in areas other than workers' compensation could, however, lead to failure of proof for plaintiffs as well.

Conversely, the mere proffer of a study showing a statistically significant increase in the incidence of disease should not lead automatically to success on a summary judgement motion by its proponent. Certainly, the existence of an epidemiological study which shows no excess incidence should cause the case to be decided by the finder of the fact. Similarly, a study which shows a relative risk of less than 2.0 should result in submission to the factfinder. Even if there are only studies which show an excess incidence of more than 2.0, the decision as to the credibility and weight to be given such proof should still remain with the finder of fact. As pointed out, even in the situation of a statistically significant increased disease incidence, the chance remains that the disease was not caused by the agent. Sometimes, this chance is quite high. Furthermore, the category in which the plaintiff falls is always a question for the trier of fact. Yet, if there is no statistically significant increase, there is no evidence to present to the trier of fact on the issue of causation. Such a failure on the part of a party which has the burden of proof will undoubtedly result in a summary judgment on that issue.

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[184] Compton v. Pennsylvania Avenue Gulf Serv. Center, 14 BEN. REV. BD. SERV. 472, 481 (1981).