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## Cerebral Anoxia and Its Residuals: I. Historical Introduction

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# CEREBRAL ANOXIA AND ITS RESIDUALS\*

## I. HISTORICAL INTRODUCTION

CYRIL B. COURVILLE, M.D.

From the time of Aristotle (384-322 B.C.), who believed that man could not live on Mount Olympus because "he could not respire in that air, otherwise too thin for respiration," to our present "air age," when we are beginning to understand something of cerebral anoxia, stretches the long history of the effects of oxygen want on the human organism. To be sure, it is very doubtful whether Aristotle had any very clear concept of the place of oxygen in the body economy, but it is remarkable that, for his day, he considered the "too thin" air to be the cause of the phenomenon which is now called mountain sickness. It is also very doubtful that with all our increase in knowledge as to the mechanism and effects of anoxia on the brain, we yet fully appreciate all the ramifications of the problem. Therefore to this very old, yet very new subject, we may profitably turn our attention.

But before getting too deep into the historic lore dealing with anoxemia, or *de suffocatione*, as our professional forebears called it, a brief statement of its various causes is in order. Today we recognize that there are many ways in which the cells and tissues of the body may be deprived of their oxygen supply. There may be too little oxygen in the inspired air, fumes, or in the gases used for anesthetic purposes. Mechanical obstruction of the air passages may cause sudden and profound asphyxia by excluding air from the lungs. Pneumonia may interfere with the interchange of oxygen and carbon dioxide through

the alveolar walls. Slowing of the blood stream (stagnation) may lessen the amount of oxygen available to the tissues in a given length of time. Heart failure, even though temporary, may be followed by irreparable brain damage on this basis. Interference with the oxygen-carrying capacity of the hemoglobin, as in the formation of methemoglobin, may likewise result in death, immediate or delayed, or in neurologic residuals of varying degrees of severity. The history of these various clinical conditions which may result in brain damage has, of course, started from widely divergent points in the centuries past, all approaching a modern focus in the pathology of the ultimate cerebral lesion. Only recently has medicine come to recognize in any full sense the nature and mechanism of brain damage due to oxygen lack. In spite of its kaleidoscopic aspects, the story of anoxia proves to be unusually interesting, and a brief survey of its salient features will serve us well as a point of departure for an investigation of its causes and effects.

### THE NOXIOUS GASES OF MINES

Mining is as old as the various civilizations whose very existence was dependent upon its development. The demand for both common and precious metals increased progressively as time went on. Although it is uncertain how soon men became aware of the dangers of asphyxiation, this must have become evident very early to the ancient Egyptians, whose mine galleries, according to Diodorus (4th century B.C.), were narrow and low, and were

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without ventilation. The same applies to the silver-lead mines of ancient Greece, which had already been worked for "many generations" at the time of Xenophon (430-355 B.C.). The shafts were deep, the passages crooked and narrow, and though ventilation was attempted

contemporary of Christ) was perhaps the first to mention the fact that death might follow inhalation of noxious vapors, and advocated the use of a lighted lamp, which was let down into the shaft. If the lamp continued to burn, the miner could descend with safety. Galen (A.D. 131-201) is thought to have been the first physician to call attention to the suffocating effects of fumes so evident, for example, in the copper sulphate mines of Cyprus.

For many centuries apparently little more than this was learned about the asphyxiating gases incident to mining, for we find that Agricola in his famous *De re metallica* (1556) again called attention to noxious gases in mines and mentioned difficulties in respiration, headaches, or actual suffocation resulting therefrom. His illustration of miners descending into pits with their lamps before them suggests their use as a detector of the presence of noxious gases (figure 1). Although others, including Ramazzini (1746),\* had something to say regarding noxious gases and their effects, it is difficult to distinguish in their writings the asphyxial effects of these gases from the metallic poisonings incident to inhalation of vapors.

Throughout the sixteenth and seventeenth centuries the situation did not change. It was not until the demand for coal as fuel became acute in the industrial period of the nineteenth century that the problem of asphyxia by mine gas became a vital problem. It then came to be recognized that the presence of blackdamp, or chokedamp (carbon dioxide and nitrogen), and of firedamp (methane) was a source of danger by suffocation.

The asphyxiating effect of carbon monoxide as experienced in the coal mines of the nine-

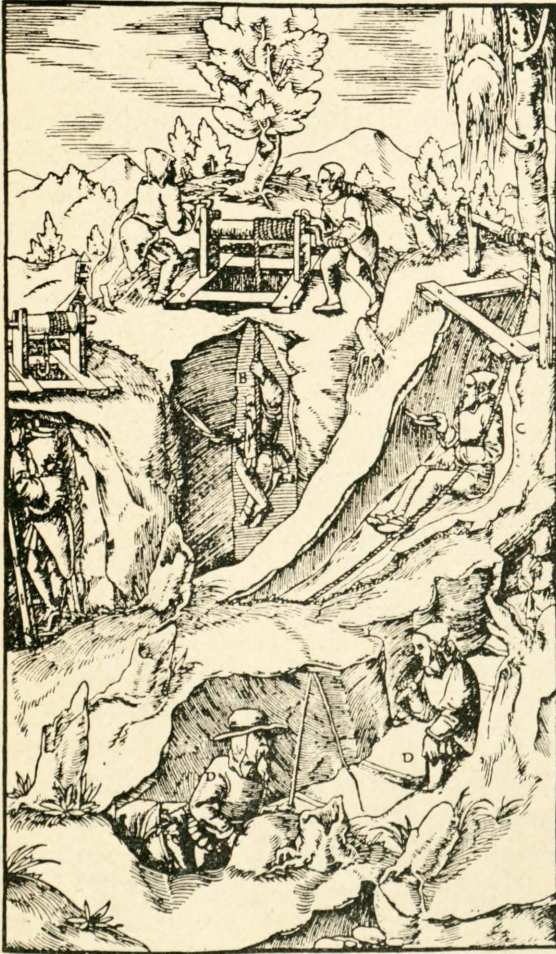


Fig. 1.—Mining operations in the Middle Ages. The use of oil lamps as detectors of asphyxiating gas as well as a source of light is suggested in this woodcut from *De re metallica* (1556.)

teenth century by means of fires, the atmosphere must have been very foul (Rickard, 1932).

It was in the time of the Romans, however, that mining was pushed to the limit of men and matériel. In some mines the galleries were extremely deep and long. Vitruvius (a

\* It is tempting to read the cerebral effects of asphyxia into the following quotation translated from Ramazzini: "[The lungs] suck in the mineral spirits along with the air, and so receive the first injury; after which the same spirits, admitted within the course of the circulation and mingled with the blood, corrupt and taint the natural temperament of the brain and nervous juice, from which spring the tremblings, stupidity, and other disorders above mentioned." It is to be concluded rather that these symptoms are the nervous effects of metallic poisoning.

teenth century is now seen in the fuel gases and automobile exhausts of the twentieth century. Although this story is as yet but recent history, it is worth while mentioning the extensive investigative work on this subject of Barcroft and Haldane in England and Henderson and Haggard in this country. The efforts of these workers have not only served to clear up many of the problems in respiration but have also contributed much to the prevention of asphyxiation and its evil effects by pointing out sources of danger.

But a scant half century after Agricola (1556) recorded his observations on the asphyxial effects of mine gases, men on the other side of the world were beginning to experience another type of anoxemia which manifested itself as "mountain sickness." The history of this type of oxygen want has almost as interesting a history.

#### "MAL DE MONTAGNES"

Just when "mountain sickness" first came to be appreciated is uncertain. But it does seem clear that in the time of Aristotle (384-322 B.C.) it was already appreciated that man experienced difficulty in breathing in high altitudes. It may have been this unpleasantness as well as their superstitions that served as a deterrent to those more adventuresome individuals who might otherwise be interested in exploring the higher reaches of the mountains. However, it may well be believed that in the fastnesses of the Himalayas and the Andes men at this period had already come to accept the rarefied atmospheres of their homelands at its face value.

Be all this as it may, the fact remains that it was the European, with his tendency to record his experiences, who was the first to make note of this mysterious malady which dogged the steps of the adventuresome mountain climber. Close on the heels of the conquistadors, who had the effrontery to assail the

empire of the Incas with a handful of mounted men with firearms, came the emissaries of the Catholic Church, who evidently had more time than the soldiers to analyze their physical experiences and record them. In 1588 the Jesuit, Joseph de Acosta,\* very vividly described the acute symptoms experienced by himself and fellow travelers in the Andes, which report is still one of the classics of medicine (Major, 1932). He attributed the difficulty in breathing, the lack of energy, and the more disturbing nausea to a "subtile and delicate" element of the air, "that is not proportional with the breathing of man, which requires a more grosse and temperate aire." Within the next century after the first edition of Acosta's book was printed (1588), other travelers in the mountains reported similar experiences. The scientists of the seventeenth and eighteenth centuries (among whom may be named Pascal [1647] and Périer [1648]) explained the symptoms of mountain sickness more or less completely on a mechanical basis (Langley, 1943).

There were others who subsequently experienced discomforts of variable degree while climbing mountains, but it was more than 150 years later that Bouger (1744) accounted for mountain sickness by the labored breathing which occurred at high altitudes. A more correct conclusion (among many suggested possibilities) was reached by Saussure (1803) on the basis of his experiences in the Alps, when he stated that the untoward symptoms of mountain sickness—palpitation, dyspnea, muscular weakness, nausea, and even vomiting†—were the result of a depletion of the

\* Acosta, however, was not the first to leave a record of the disturbing symptoms of high altitudes. Jourdanet (1875), who has made an excellent comprehensive review of the problem of mountain sickness, points out that Ordaz, one of the officers in Cortes' force invading Mexico, climbed the mountains around Mexico City only to succumb to fatigue and syncope. Jourdanet states that this is the first time that this condition was called *mal de montagnes*.

† The present writer can testify, as can many other amateur mountain climbers of the West, of the forced respirations, the pounding heart, and the extreme muscle fatigue in a rapid climb even to an altitude of 11,485 feet (Mount San Geronio). Mount Whitney (14,501) will try even the muscle-hardened sportsman.

blood of its "phlogiston." This concept was first definitely stated, however, by Clissola (1823), who concluded that debility in mountain climbers was due to a reduction in the amount of oxygen in the atmosphere.

In spite of all this, many conflicting and contradictory theories came to be propounded in the next few decades, most of which were based on the concept that oxygen consump-

led Paul Bert (1878) to settle the question by intensive experimentation.

A word is in order about the place occupied by balloonists in the discovery of facts regarding the effects of altitude in the production of anoxemia. In 1783 the brothers Montgolfier demonstrated the behavior of lighter-than-air balloons (figure 2). Within four months men began to ascend in these balloons. Although experimentation of barometric pressures and air analysis began within a year (1784), it was twenty years later that any great altitude was reached in this way. In 1804 a French balloonist by the name of Robertson attained the altitude of 26,000 feet and experienced definite symptoms of oxygen want. The same year Gay-Lussac reached an altitude of 23,000 feet, without any great degree of discomfort, however.

There was a lapse of over fifty years (1862) until Glaisher and Coxwell made an ascent for scientific purposes, alleging to have reached an altitude of 29,000 feet. (This was subsequently disputed.) At this height both men experienced disturbances of sight and hearing, and Glaisher became unconscious. Coxwell found himself unable to use his arms and was obliged to pull the valve rope with his teeth, thus saving their lives.

Paul Bert became enthusiastic about barometric pressure, and in 1875 persuaded three fellow scientists—Sivel, Crocé-Spinelli and Tissandier—to undertake a balloon ascension prepared to study the variation of barometric pressure at successive altitudes. At high altitudes these men experienced palpitation, muscular weakness, and somnolence, which preceded loss of consciousness. The balloon ascended to an altitude of 28,200 feet, and then began to descend of its own accord. When the balloon reached the ground, Crocé-Spinelli and Sivel were found to be dead, presenting all the hideous aspects of advanced asphyxia, including hemorrhage from the nose and

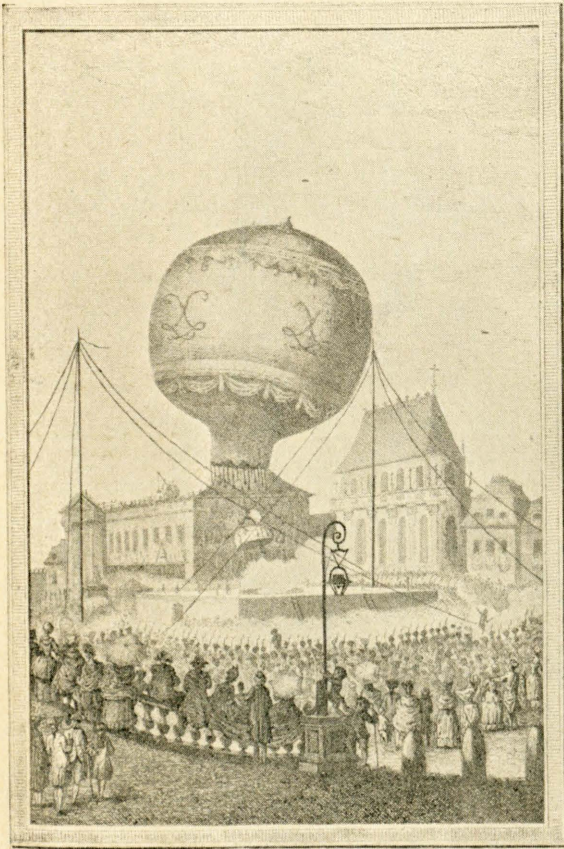


Fig. 2.—The first balloon ascension in 1783. This balloon, constructed by the brothers Montgolfier, carried no human passengers.

tion was purely a physical problem (Payerne, 1851). It remained for Jourdanet (1861) to point out that this was not the case, but rather that the volume of oxygen in the blood was due to its chemical affinity to the elements in the blood stream. This work of Jourdanet and the experiences of contemporary balloonists

mouth. Tissandier, though unconscious, escaped with his life.

It was three years later that Paul Bert (1878) published his memorable monograph on barometric pressure, which shed much light on the problems that had disturbed scientists for

Schneider (1812), who conducted their experiments on Pikes Peak, and Barcroft of England (1925), who studied the effects of altitude in the Teneriffe Mountains of Africa—to write still later chapters in this long search for the cause of mountain sickness.

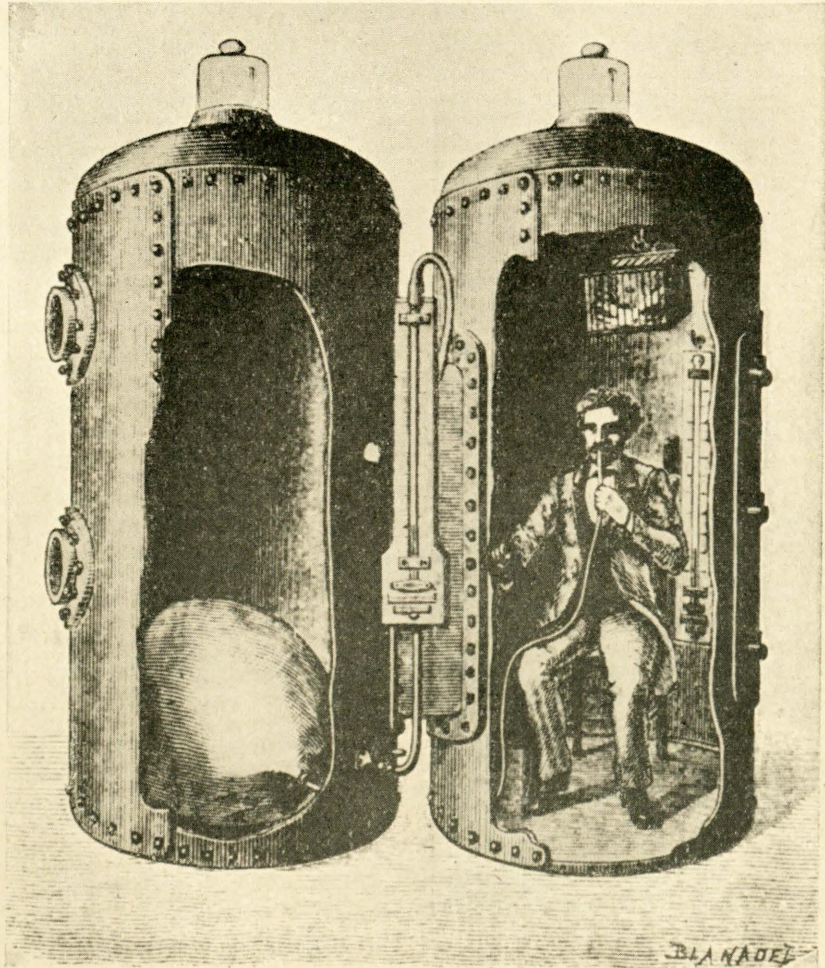


Fig. 3.—Decompression chamber used by Paul Bert in reproducing barometric pressure conditions experienced at high altitudes.

more than two centuries. His work was accomplished with the use of a specially constructed decompression chamber which duplicated conditions in the higher altitudes (figure 3).

It remained for investigators in our country—Douglas, Haldane, Henderson, and

Coming somewhat as an anticlimax to these observations are the recent findings of Monge (1943) in the identical setting of De Acosta—the Andes. After a lapse of almost three and a half centuries, Monge found that in addition to the acute form of mountain sickness there is a subacute and chronic form

(*soroche* is the Quechua Indian word for it), which are now recognized to be true medical entities.

Still another chapter in the history of the effects of altitude has just been written by the aviators and their medical associates during the recent conflict, but the ink on these pages is still too wet for the facts to be available for scrutiny. No doubt there will be found many counterparts of the 1862 tragedy of Sivel and Crocé-Spinelli when the truth is known.

#### "DE SUFFOCATIONE"

The lethal effects of asphyxia, or suffocation, as the ancients described it, have been known since time immemorial, and man in his inhumanity to man has taken advantage of this knowledge to do away with his enemies. Infanticide was often accomplished in the same way. Condemned prisoners were dispatched by the less refined method of garrotting, or slow strangulation, a method that was not infrequently resorted to in the Spanish Inquisition (figure 4). During the recent war Hitler revived this method of capital punishment to deal with some of his personal enemies.

But in its broader aspects we must look into some features of the history of *de suffocatione*, as it was described when Latin was the language of science. Perhaps the first form of suffocation to be recognized was that of drowning, and the Greeks and Romans at least (being close to the sea) apparently recognized that death by this means was the result of interference with the function of respiration. Celsus and Pliny, for example, were well aware of the possibility of death by suffocation in this way. Galen is credited as first using the term *apnea* to describe cessation of respiration. But only when publication of medical treatises came into vogue could any definite concept of this form of asphyxia come to be widely known. Ambroise Paré, Donatus, and

others did describe cases of suffocation by drowning. By this time (as will be shown in a succeeding section) the danger of suffocation by mine gases was already known.

As an example of the status of the question in the seventeenth century we have the comments of John Schenk (1644), who discussed in his large medical treatise something of the



Fig. 4.—Asphyxiation by strangling (garrotting) used in the Spanish Inquisition. After an etching by Goya.

early history of suffocation, notably among the Romans. He mentions in particular asphyxia incident to strangulation, drowning, fainting, and from noxious fumes.

Some thirty-five years later Bonet (1679) published his memorable treatise on pathology and also gave an excellent survey of the more recent history of suffocation, mentioning the reports of Platter (1614), Riolan (1649), Bar-

tholin (1654), Richard Lower (1669), and Wepfer (1724). His discussion of *de suffocatione* is chiefly of medical interest, because he was concerned with those diseases of the heart and lungs which may be associated with, or the cause of, this condition. Morgagni (1766), who started out to write an appendix to Bonet's work but who succeeded in writing a long four-volume treatise of his own on "the seats and causes of disease," also reported a number of cases of suffocation chiefly from a medical viewpoint.

By this time this subject had become one of widespread interest, and a number of tracts, monographs, and reports appeared (Shiller [1753]; Mendel [1776]) to enlighten contemporary physicians. These treatises were concerned with asphyxiation incident to the fumes of liquor, of burning charcoal, and of noxious gas of other types, to drowning, and to those episodes which occur at birth. The last group of contributions is of sufficient interest to be given special attention in a subsequent section; the others will here receive brief mention.

We find that Storcke (1705) published an essay on the asphyxial effects of recently fermented liquor. Similarly, Tannenberg (1729) described instances of "suffocation" following exposure to the vapors of fermenting *musto*. Although it is doubtful that many serious asphyxial accidents occurred on this basis, these contributions give one an interesting sidelight on the subject under consideration.

Exposure to noxious or foul-smelling gases from mines, burning charcoal, or decaying organic materials apparently often resulted in asphyxia. This phase of suffocation was the subject of a monograph by Portal (1775), a book which went through at least six editions and which was translated into German. Portal (1796) also published a book of instruction on the treatment of asphyxia from various causes, including mine gases, which was

widely read. A contemporary, Carminatus (1777), published an interesting study on the suffocating effects of decaying animal matter.

Another designation which came to have common use in these cases of asphyxia was *de suspensa respiratione*, or suspended respiration (Adams, 1796). This term was often utilized to describe drowning in the several monographs on this subject which appeared about this time (Engelmann [1787]; Coleman [1791]; L'Hermitte [1812]; Chevillotte [1816]).

It is pertinent to point out that the introduction of experimentation played an important role in the development of our knowledge of asphyxia. The introduction of the air pump by Torricelli and Guericke had made possible experimentation with the variations in air pressure. Sir Humphrey Davy (1800) and others had utilized the experimental method in their work on the physics and chemistry of air, a subject which will receive more specific mention in a subsequent section.

But from the standpoint of asphyxia in its relation to medicine very little had been done in an experimental way until the time of Goodwyn (1788), whose experimental study on "the effects of submersion, strangulation, and several kinds of noxious airs on living animals; with an account of the nature of the disease they produce" is indeed noteworthy. Moreover, the study by Kay (1834) on the physiology, pathology and treatment of asphyxia "in newborn children, and from drowning, hanging, wounds of the chest, mechanical obstruction of the air passages, respiration of gases" represents an effort to apply the experimental method to the problems of asphyxia in man.

At any rate these problems overflowed their medical confines and gripped the imagination of the laity as well. This is so well portrayed in the painting by Thomas Wright reproduced herewith (figure 5).



In the first half of the nineteenth century a bevy of monographs and articles on the subject of asphyxia came into print.\* This was made possible by the considerable number of new medical journals which came to be published in the various European countries. Of the various phases of the subject then considered, none attracted quite so much atten-

"ASPHYXIA NEOPHYTORUM"

The fact that infants are sometimes born dead or die soon after birth has obviously been known since time out of mind. It is very evident from the silence of earlier available literature that this disaster occurred so often as to be commonplace and scarcely worth mentioning. The question of primary interest in



Fig. 5.—*An Experiment With the Air-Pump*. Oil painting by Thomas Wright now in the National Gallery, London. This picture suggests the grip on popular fancy of animal experimentation with lowered oxygen tensions.

tion as asphyxia of the newborn. To this feature brief attention will be given.

\* In the Index of the Surgeon General's Library there are to be found titles of 100 monographs dealing with asphyxia (including the neonatal variety) which appeared between 1800 and 1850. In the same period 132 articles appeared in medical literature. It is obvious that between 1775 and 1850 there was an awakening of a remarkable interest in the subject of asphyxia in its various aspects.

this connection is to determine when this situation was recognized to be due to "suffocation." And the answer to this question cannot be given exactly. From available sources it appears that medical interest in the problem developed concurrently with the eighteenth century, and the general interest was followed

specifically by attention to asphyxia in the newborn. This condition was described by a variety of terms: suffocation in the newborn (Roederer [1760]); asphyxia neophytorum (Ehrhart [1785]); asphyxia neonatorum (Regnier [1789]); apparent death in newborn Löffler [1792]), all of which terms are accurately descriptive.

In this particular field several names stand out as pre-eminent. Roederer (1760) was one of the outstanding physicians of this period who had given much attention to the ailments of children. It is therefore pertinent that he be one of the first to write on suffocation in infants. Ehrhart (1785, 1789) was also one of the earliest monographers on asphyxia of the newborn. Regnier (1789), de Waldkirch (1793), and Roose (1794) also wrote treatises on the subject.

After the turn of the nineteenth century the contemporary literature was marked by many contributions to the subject of asphyxia in general and to that of the newborn in particular. A number of new methods were also developed in its treatment. But the concept which is of fundamental importance to us today was that introduced by Little (1842, 1853, 1861), which suggested that the spasticities of childhood were the direct consequence of asphyxia at birth. This idea was lost sight of for a full century because of the overemphasis placed on focal hemorrhages caused by birth trauma, but recently it has been reintroduced by Courville and Marsh (1944), who pointed out the objective evidence in the very nature of the cerebral cortical lesions which emphasize their anoxial character. It has furthermore been suggested that some of the other less well-understood cortical degenerations of infancy and early childhood may have a similar genesis (Courville [1945]).

#### RESUSCITATION IN ASPHYXIA

If only the entire story of efforts at resuscitation of asphyxiated individuals could be

known, what an interesting volume in the history of medicine it would be! Regrettably, we know so little of the early efforts in this direction. Indeed, there is but a single item antedating the sixteenth century which is known to the present writer. Garrison calls attention to the fact that in the Babylonian Talmud there is a statement to the effect that a newborn infant who failed to breathe was to be gently swung in a hammock in an effort to restore respiration. This fact seems to point the way that efforts at resuscitation were to take, for attention to therapeutic methods seems to be paramount.

Some sort of effort was almost certainly made to revive miners overtaken by noxious fumes while at their work or those suffocated by drowning; yet the literature prior to the eighteenth century is almost entirely silent on the subject. On the other hand, an early treatise on obstetrics by Pugh (1754) contained methods advocated to resuscitate infants who failed to breathe. From this time on a number of new methods were advocated. One of the first measures used was that known from Biblical times (2 Kings 4:33, 34)—mouth-to-mouth breathing—but whose more modern source is unknown. We find treatises on the subject in one of the earliest of obstetrical journals, the *Archiv fuer die Geburtshilft*, by Wegelin (1789-90) and by Löffler (1792). Monographs by Niemeier (1792), Freteau and Baudelocque ([1799] who advocated section of the umbilical cord), von Frieriep and Schwarzot (1801), and Plenk (1807) also appeared about this time.

It would carry us too far afield to investigate thoroughly this subject of infant resuscitation; however, it is worth while to mention the method described by Marshall Hall (1856) which was destined to be quite extensively (and quite successfully) used in the middle decades of the nineteenth century. This method, which consisted of the alternate

hyperextension of the infant on one hand of the accoucheur and then flexion on the other, is still described in some English textbooks printed today. And with this manual method should be mentioned the swing method of Schultze now referred to only to be condemned. No doubt this measure has been effective in aggravating in many instances subdural hemorrhages which were responsible for the asphyxia in the first place.

To leave the history of this subject of resuscitation with only these few references to neonatal asphyxia would leave a considerable gap in our knowledge. We find that much instruction in both the prevention and relief of asphyxial states of other etiology in the literature of the eighteenth and nineteenth centuries and even before.\*

To turn back to the eighteenth century, we find treatises on resuscitation by Welfroth (1725), Farkas (1762), and de Villiers (1771). Also about this time we have coming to light a series of books of instruction, often addressed to the public as a means of education dealing with the problem of "suspended animation" or "apparent death," as the asphyxial state was then called.† These manuals of instruction (or memorials) were published in Italy (at Firenze, 1772; by Tozzetti,‡ 1773 [figure 6]), in Germany (Munich, 1775), in France (de Gardanne, 1881, *a* and *b*), and in England (Hawes, 1782).

Still other monographs, given to a general

\* An interesting item on the prevention of suffocation in infants is brought to light by Garrison (1937). He called attention to a placard published in the late thirteenth century warning parents not to take infants of less than three years of age to bed with them because of danger of suffocation. In the seventeenth century mothers sometimes deliberately overlay their infants to do away with them. Undoubtedly the old habit of "swaddling" infants with heavy clothing was also an occasional cause of suffocation.

† It is worth while emphasizing the point recently made by Monge (1943) that the rulers of the ancient Incas forbade any mass migrations of captured tribes to altitudes other than those in which they were accustomed to live. It is presumed by Monge that this was done to prevent both the acute and chronic forms of "mountain sickness" which were so physically disabling. This seems to be an example of a prehistoric public health measure!

‡ A copy of this interesting and remarkable complete monograph has recently been added to the library of the Clinical Division of the College of Medical Evangelists through the gift of the Scripps-Remondino Library of Historical Medicine. This book gives considerable information on the history of asphyxia.

consideration of the problem, included a section on therapeutics. Particularly noteworthy in this connection were the treatises of Goodwyn (1788) and of Plisson (1826), the latter containing an important section on the history of asphyxia.\*

The scholarly essay by Kay (1834) may be considered to close the historical period on the therapy of asphyxial states. It is worth while, nonetheless, to note, in passing, those of our own day who have contributed so much to the treatment of anoxic states, viz., Barcroft (1925), Haldane, and associates in England, and Henderson (1924), Haggard (1923), and associates in the United States. To these must be added those (Fulton and associates) who have done so much to make flying in the stratosphere more safe. But this is getting out of the scope of this historical survey of the problem. As we write of either prevention of asphyxia or resuscitation we are brought face to face with a similar specter which has haunted the operating rooms for the past three quarters of a century. When its mask is torn off, we see that it too is asphyxia.

#### ANOXEMIA OF ANESTHESIA

The history of the anoxic effects of the inhalation anesthetics is relatively short. It so happens that these effects were first noted in the case of nitrous oxide, whose identity was early recognized and whose anesthetic action was learned some time before its actual use in surgery. Oddly enough, nitrous oxide was first discovered by Priestley (1774) about the same time that he discovered oxygen. It was Sir Humphrey Davy (1800) who found that nitrous oxide, when inhaled, relieved pain, the discomfort of an erupting wisdom tooth being considerably alleviated. However, his

\*As has already been implied, there are a number of treatises on suffocation or asphyxia, notably those of Schenk (1644), Bonet (1679), and of Tozzetti (1773), which contain valuable material of historical nature. This essay by Plisson and an undated one to appear about half a century later from the pen of Paul Bert are the only specific sources of historical material on this subject. (See figure six.)

suggestion that the gas might be used as an anesthetic in surgical operations, as well as the similar proposal by a young English surgeon, namely Hickman, went unheeded.

The first evidence of the noxious action of nitrous oxide was reported by Stanley (1842) when it was observed that the breathing of the crude gas (made by heating ammonium nitrate) for its exhilarating effects sometimes

were the result of the anoxemia which was an invariable accompaniment of the use of nitrous oxide (Gardner [1902]; Wieland [1922]; Lake and Hertzmann [1924]; and Henderson [1927]).

Of greater interest in view of the cerebral effects of this anoxemia with nitrous oxide was the occurrence of residual manifestations in the form of psychic or psychoneurotic aberrations or rigidities, tremors, speech disturbances, etc. That these signs are due to physical damage to the cerebral cortex and basal ganglia, and that these lesions are the direct result of asphyxia has been proved beyond question (Courville [1936, 1938, 1939]; Lowenberg, Waggoner and Zbinden [1936]; Ford, Walshe, and Jarvis [1937]; O'Brien and Steegman [1938]).

Although not so evident in the case of the other inhalation anesthetics which are less likely to be accompanied by a serious degree of anoxemia, physical damage to the brain, of a similar character, has been shown after delayed death following other inhalation anesthetics. Even in the case of that old standby, ether, the convulsions which sometimes occur in the course of its administration are probably due to cortical anoxia (Courville, 1941).

\* \* \*

And what of asphyxia consequent to exposure to the war gases? Or of those relative anoxemias associated with pulmonary diseases, notably pneumonia, cardiac diseases, and the anemias? Our understanding of these conditions is of recent vintage and of less concern to us in this short survey of the history of asphyxia. The literature dealing with these conditions will be cited in subsequent sections of this study.

But what of the intimate history dealing with the discovery of oxygen and carbon monoxide, the essential chemical fundamen-

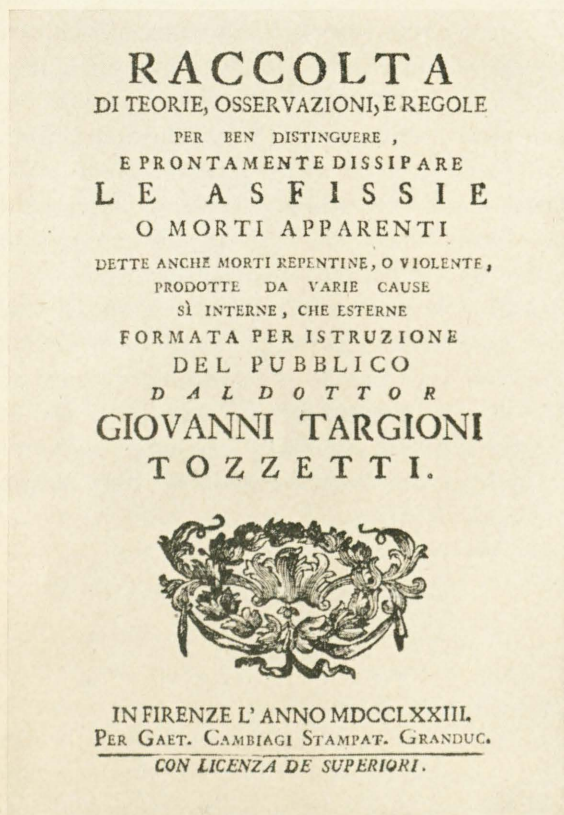


Fig. 6.—Title page of Tozzetti's monograph on asphyxia (or "apparent death") published in 1773. From copy in Scripps-Remondino historical collection.

resulted in forcible and uncontrollable muscular movements. After this gas came to be used as an anesthetic agent, the occasional occurrence of consequent convulsive seizures was reported by Warner (1882), Healy (1926), Evans (1928), and Clement (1928). It was soon suspected that these convulsive move-

tals of the problem, and what of the physical aspects of anoxemia? It has seemed more in order to discuss this phase of asphyxia with the physiology of normal and abnormal respiration to be considered in the following

section of this essay. To this phase of the subject we will now give attention.

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NOTE.—The bibliography will appear at the end of the completed article.

*(To be continued)*