Carbon Dioxide

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On May 9, 1794, during the Reign of Terror, Antoine-Laurent Lavoisier died by the guillotine. This event closed the first and greatest chapter in the physiology of carbon dioxide: for the principle of the production of carbon dioxide and its relation to oxygen in fire and in life which Lavoisier had discovered shortly before his death was, and still is, the most fundamental of all contributions to knowledge in this field. Truly, as his colleague Lagrange said: "It took but a moment to cut off a head, the like of which a hundred years may not reproduce."

Likeness of Life to Fire

Lavoisier's supreme contribution to science, and particularly to physiology was the demonstration that, in their broad outlines, combustion in a fire and respiratory metabolism in an animal are identical. Both consist in the union of oxygen from the air with carbonaceous material: and both result in the liberation of heat and the production of carbon dioxide. Carbon dioxide had, indeed been discovered previously by Black in 1757, and oxygen had been described by Mayow, Scheele and Priestly. But it was Lavoisier who first showed the part played by oxygen and the process by which carbon dioxide is produced.

A century later the standard textbook of physiology in the English language was that of Sir Michael Foster of Cambridge University. This book supplied the early training of many of the physiologists who during the past 35 years have contributed to the development of respiration and to the increasing recognition of the part played in the economy of the body by carbon dioxide. The facts and conceptions presented by Foster show, therefore both the advance of 100 years from Lavoiser and the starting point of modern investigation. If the first chapter of the physiology of carbon dioxide was contributed by Lavoisier and closed with his death, the second chapter is presented by Foster, and is nearly coextensive with the 19th century; which the third chapter, with which this paper will chiefly deal, is the product of the generation that has done its experimental work in the first 3 decades of the 20th century, and from its theoretical results is now making valuable contributions to clinical medicine and surgery, and particularly to therapeutics.

Contrast Between Life and Fire

The most important advance in the physiology of respiration as presented by Foster, beyond the conception left by Lavoiseir, was that the oxidation in living matter, although like a fire in materials and products, is profoundly different in its process and control. If a fire is supplied with pure oxygen instead of air, it burns with enormously augmented intensity. But when a man or animal breathes oxygen, or enriched with oxygen, no more of that gas is consumed, no more heat is produced and no more carbon dioxide is exhaled than when air alone is breathed. Although clinicians still find it hard to believe, oxygen is in no sense a stimulant to living creatures. It is merely en essential food; it is a food of which the body cannot be induce to take more, or to get along on appreciably less, than its own interior regulation determines according to its needs. Even in rarefied air, or in cases of heart disease - conditions in which a man may suffer severely from the deficient supply of oxygen - the body actually consumes practically a normal amount. The asphyxial symptoms are the expression of the strain on the body to obtain this amount. It gets it, or it dies.

Lavoiser had supposed that the vital combustion must occur in the lungs where the inspired air comes in contact with the blood. Spalanzani, the Italian physiologist, soon recognized, however, that in fact the oxidation does not occur in the lungs: it is in the tissues, to which oxygen is transported by the blood. That such is the fact was proved by Magnus, a German physiologist, who first extracted the gases from blood by means of the vacuum pump and showed that arterial blood contains more oxygen and less carbon dioxide than does venous blood. Then Hoppe-Seyler, one of the first of the biochemists, separated hemoglobin, the coloring matter of the red blood corpuscles, in the form of pure crystals, and showed that this substance forms a loose chemical compound with oxygen. Hemoglobin is the means by which the blood transports oxygen.

Blood Alkali as Carrier of Carbon Dioxide

Later, in the 19th century, Zuntz, in Berlin, recognized that carbon dioxide, unlike oxygen, is not carried by hemoglobin, but that hemoglobin is nevertheless an essential factor in the transportation of this gas but the blood. He showed that in the blood carbon dioxide is combined with bases, chiefly as sodium bicarbonate. He thus demonstrated, for the first time, what is now generally, but rather unwisely, called the "alkaline reseve". It were better to call the bicarbonates of the plasma the "alkali in use" - the true reserve alkali is combined with hemoglobin and is given off to unite with carbonic acid, or to neutralize stronger acids. As carbon dioxide is given off in the lungs, the amount of alkali thus set free recombines with hemoglobin.

This mode of transportation of carbon dioxide is one of the most extraordinary features of the blood and respiration. The evidence for it rests upon 2 facts demonstrated by Pfluger and others during the great epoch of German physiology in the second half of the 19th century. One of these facts is that the blood plasma, if separated from its corpuscles, will part with little of its carbon dioxide even in the presence of a vacuum. The other fact is that all the carbon dioxide in the plasma, both that in simple solution and that combined with alkali into the bicarbonates, comes off readily if the red corpuscles of the blood are present. Thus, the hemoglobin of the red corpuscles, by supplying or recombining with alkali, dominates the capacity of the plasma to transport carbon dioxide; it thus enables the blood to take up this gas in the tissues and to give it off in the lungs under very slight differences of pressure. Meanwhile, another problem of primary importance was attracting the attention of investigators: the problems not only of how we breathe, and why, in the sense of the need, by also why, in the sense of the cause and stimuli. It is one of the commonest observations of life that physical exertion, owing to its increased consumption of oxygen and production of carbon dioxide, is accompanied by the breathing of an increased volume of air. The need is evident. But what is the nature of the stimulus and what is the controlling mechanism which together induce this adjustment of the ventilation of the lungs to the respiratory needs of the body? This matter was long debated. Nearly every champion of every shade of opinion for more than 50 years contributed some particle of truth on one phase or another. But every contributor was in error who claimed for any one factor an exclusive control; for breathing is the resultant of many factors.

Nervous and Chemical Regulation of Breathing

The factors thus revealed were 2 main classes: nervous and chemical. Throw a bucket of cold water over a man and he draws one or more deep breaths. Irritate an afferent nerve, causing pain, and he cries out. Tickle his nose or throat and he sneezes or coughs. These are all respiratory reflexes excited by nervous impulses coming to the respiratory center. But more important than any other nervous element in breathing are the vagus nerves whose may fibers there are some which have endings in the lungs and convey impulses from them to the respiratory center in the medulla oblongata. Through these pathways, as Hering and Breuer showed, each expiratory deflation of the lungs stimulates the center to discharge a reflex to the diaphragm and other respiratory muscles inducing inspiration; and contrariwise, each inspiration induces reflexly an expiration. To this mechanism breathing owes its rhythmic character; or, as an engineer would express it, breathing is a reciprocating mechanism.

Over against this explanation, based upon nervous factors, evidence gradually accumulated indicating a chemical control of respiration. The blood flowing to and through the respiratory center was found to exert a dominating influence upon the activity of breathing. Whenever the blood was rendered venous, the center was stimulated to produce a counteracting increase of the volume of breathing. If, on the contrary, the blood were overventilated in the lungs, the activity of the center ceased for a time and apnea resulted. In this state, the subject neither breathes nor feels any desire to do so.

As this conception of the chemical control of breathing developed, its advocates separated into 2 groups. One held that it is primarily the degree to which the blood is oxygenated which influences the respiratory center and controls its activity. The other presented evidence indicating that is rather the amount of carbon dioxide in the blood which is the determining factor. In this matter also both sides of the controversy contributed experimental facts of value and each was in part correct. Respiration is, indeed, influenced fundamentally by the oxygen pressure to which the individual is acclimatized: a pressure which depends upon the elevation of his home above sea level. But acclimatization to altitude is very slow, requiring days or weeks. It is only under conditions of sudden extreme oxygen deficiency, verging on asphyxia, or after intense muscular exertion, that respiration is stimulated - in fact, as we shall see later, over stimulated - by an urgent demand for oxygen.

On the other hand, nature provides that in a healthy man or animal, except under intense exertion, the oxygen supply is always ample and its influence upon breathing is therefore, under normal conditions relatively slight. It is the variations in the amount of carbon dioxide produced n bodily rest and exercise that afford the stimulus inducing the adjustments of breathing to the varying energy needs of the body. Foster, in his book above referred to held that the evidence then available indicated that oxygen is a more important control than carbon dioxide. But even as early as 1885, Miescher, a Swiss physiologist, in a paper that is one of the masterpieces of physiology, had summarized all the evidence then available and reached the conclusion that it is the variations in the amount of carbon dioxide which principally induce the immediate adjustments of respiration. In a classic phrase inspired by the insight of genius he wrote: "Over the oxygen supply of the body carbon dioxide spreads its protecting wings". He died before he could complete his work and his death may be said to have closed the second chapter in the history of respiration and the functions of carbon dioxide in the body.

The Breath of Life

The first 3 decades of the present century have witnessed an extraordinary reversal of standpoint and increase of interest in regard to the functional importance of carbon dioxide in the animal body. Moreover, discoveries in this field, which were initially purely scientific and theoretical, are now finding a wide range of clinical applications for the alleviation of suffering and the saving of life.

Before considering these matters, it will be best that the mind be cleared of certain deep rooted misconceptions that have long opposed the truth and impeded its applications. It will be seen that carbon dioxide is truly the breath of life.

The human mind is inherently inclined to take moralistic view of nature. Prior to the modern scientific era, which only goes back a generation or two, if indeed it can be said as yet even to have begun in popular thought, nearly every problem was viewed as an alternative between good and evil, righteousness and sin, God and the Devil. This superstitious slant still distorts the conceptions of health and disease; indeed, it is mainly derived from the experience of physical suffering. Lavoisier contributed unintentionally to this conception when he defined the life supporting character of oxygen and the suffocating power of carbon dioxide. Accordingly, for more than a century after his death, and even now in the field of respiration and related functions, oxygen typifies the Good and carbon dioxide is still regarded as a spirit of Evil. There could scarcely be a greater misconception of the true biological relations of these gases.

Physiology

Relations of Carbon Dioxide and Oxygen in the Body

Carbon dioxide is, in fact, a more fundamental component of living matter than is oxygen. Life probably existed on earth for millions of years prior to the carboniferous era, in an atmosphere containing a much larger amount of carbon dioxide than at present. There may even have been a time when there was no free oxygen available in the air. Even now, such animals as ascaris will live and be active in an atmosphere of hydrogen and entirely without oxygen. In vertebrates, the process of muscular contraction is fundamentally anaerobic.

A frog's muscle will contract effectively and repeatedly under suitable stimulation in an atmosphere of pure nitrogen. In contraction, a muscle produces lactic acid, partly by reconversion into sugar. In other words, oxygen is not one of the primary factors in muscular work. The reserve store of oxygen in the body is small. Vigorous breathing does not take place before an exertion; the exertion is first made and then the oxygen needed to clear the system in preparation for another exertion is absorbed. The demand for oxygen for this scavenging of waste and restoration of power is termed by A.V. Hill the "oxygen deficit" of exercise.

On the other hand, present knowledge indicates that carbon dioxide is an absolutely essential component of protoplasm. It is one of the factors in the balance of alkali and acid for the maintenance of the normal pH of the tissues. Acapnia, that is diminution of the normal content of carbon dioxide, involves therefore, a disturbance of one of the fundamental conditions of life.

Another natural, but very obstructive misconception is that oxygen and carbon dioxide are so far antagonistic that in blood a gain of one necessarily involves a corresponding loss of the other. On the contrary, although each tends to raise the pressure and thus promote the diffusion of the other, the 2 gases are held and transported in the blood by different means; oxygen is carried by the hemoglobin in the corpuscles, while carbon dioxide is combined with alkali in the plasma. A sample of blood may be high both gases, or low in both gases. Moreover, under clinical conditions low oxygen and low carbon dioxide - anoxemia and acapnia - generally occur together. Each of these abnormal states tends to induce and intensify the other. Therapeutic increase of carbon dioxide, by inhalation of this gas diluted in air, if often the effective means of improving the oxygenation of the blood and tissues. Under such conditions of acute deprivation of oxygen as those in carbon monoxide asphyxia, the body suffers from an excessive elimination of carbon dioxide: and the restoration of carbon dioxide is in itself helpful. In a drowned man or a non-breathing newborn child, the deprivation of oxygen does not cause and excess of carbon dioxide. On the contrary, in the absence of oxygen, lactic acid and other primary decomposition products of the tissues acannot be converted into carbon dioxide; for that conversion oxygen is necessary. The saying of Miescher, quoted at the end of a previous section, has therefore, a depth of truth and breadth of application greater than he could possibly have realized.

As a factor in the Acid-base Balance of the Blood.

Modern physiology has shown that, in addition to the control and regulation exerted by the nervous system, there are many chemical substances produced in the body that influence function and form. To these active principles Starling gave the name of "hormones". Among the hormones are epinephrine (often called adrenaline), pituitrin, thyroxin, insulin and many other products of the glands of internal secretion and other organs. Carbon dioxide is the chief hormone of the entire body; it is the only one that is produced by every tissue and that probably acts on every organ. In the regulation of the functions of the body, carbon dioxide exerts at least 3 well defined influences:

- (1) It is one of the prime factors in the acid-base balance of the blood.
- (2) It is the principal control of respiration.
- (3) It exerts an essential tonic influence upon the heart and peripheral circulation.

In recent years, an extensive literature has grown up on the subject of the so-called "alkaline reserve", the acid-base balance, and the pH or hydrogen ion concentration of the plasma. There have also appeared many investigations and discussions of the real or assumed relations of these features of the blood to clinical acidosis and alkalosis. In the complicated adjustments of the physico-chemical equilibrium in the blood, carbon dioxide is, more than any other factor, subject to disturbance by every variation in bodily activity or heat production; but it is also that factor which is most immediately readjusted. The automatic reactions which effect this readjustment are the increase or decrease of the volume of breathing. This volume depends upon the depth more that the rate of respiration; or rather, it is the product of depth and rate. It determines the degree of the ventilation of the blood as its passes through the lungs. Normally, it is so adjusted that the carbon dioxide in the alveolar air of the lungs is maintained at a partial pressure of a little more that 5% of an atmosphere. This amount of carbon dioxide gas in the alveolar air produces exactly that amount of carbonic acid in solution in the blood needed to balance the normal amount of alkali and thus to induce and maintain normal pH. This is the principle expressed by the equation of L.J. Henderson:

$pH = K \times [H_2CO_3] / [NaHCO_3]$

If, however, because of some disturbance of the function of the kidneys or other organs, the blood alkali in use is not of normal amount, the pH of the blood would also be rendered abnormal, except for the counteracting control of respiration over the carbon dioxide in the alveolar air and thus over the carbonic acid in solution in the blood. Whenever the blood alkali is lower than normal, respiration increases and maintains a more vigorous pulmonary ventilation. The object and effect of its augmentation are that alveolar carbon dioxide is mixed with more fresh air and diluted. Consequently, the carbonic acid of arterial blood-pressure is decreased proportionally. This is the explanation of the increased respiration occurring in the acidosis of acute nephritis and in diabetic coma, and developing into air hunger as death approaches: an increase of respiration is the natural compensation for a decrease of blood alkali. On the other hand, if the amount of carbon dioxide is deficient simultaneously with a normal or excessive blood alkali, respiration is decreased or fails entirely. These respiratory reactions depend upon the relating influence of carbon dioxide in its chemical balance with the blood alkali; for, if the carbon dioxide and alkali are even slightly out of balance, the respiratory center is powerfully stimulated or depressed.

Whether the physiological reactions to carbon dioxide are due directly to a specific effect of this substance, or rather to the pH of the blood and of other humors in which carbon dioxide is an important factor, is still under active investigation. It is, however, noteworthy that the existence of these reactions renders invalid much of the now prevalent conception of the chemistry of clinical acidosis and alkalosis. It is not correct chemistry or physiology to infer that, because the amount of the alkali in use is high or low, the pH of the blood must be correspondingly affected. A high or low blood alkali needs merely a corresponding affected. A high or low blood alkali needs merely a corresponding decrease or increase of the volume of breathing for its compensation to afford an normal pH. If, therefore, in nephritis or diabetes or other disorders, the pH is really abnormal and the blood actually becomes even slightly more acid or more alkaline than normal. There must be some disturbance of the respiratory regulation of the alveolar carbon dioxide as yet not understood. A normal regulation of the carbon dioxide pressure is adequate to compensate either a high or a low blood alkali in practically all conditions compatible with the continuance of life.

The part normally played by the kidneys and the influences of abnormal conditions and processes in them in other organs in determining the amount of alkali in use in the blood, both in health and in such disorders as diabetes and clinical acidosis and alkalosis, are beyond the scope of this article. The problems which these matters present are, indeed, as yet only incompletely analyzed.

In the Control of Respiration and the Circulation.

The modern development of the knowledge of the part played by carbon dioxide in the control of respiration began with a classic paper by Haldane and Priestly, entitled "The Regulation of the Lung Ventilation", and was followed by other important papers by Haldane and Douglas. In these papers it was shown by observations on normal men that breathing quite unaffected either by inhalation of oxygen-rich air by such a moderate decrease of oxygen as occurs on first going to an altitude. On the other hand the breathing changes its volume automatically in such close adjustment to the amount of carbon dioxide produced in the body that the alveolar air is kept nearly constant in this respect. Carbon dioxide is the chief immediate respiratory hormone.

A few months after the first paper by Haldane and his collaborators showed the influence of carbon dioxide upon respiration, Henderson had his collaborators began the publication of a long series of papers dealing with the influence of carbon dioxide upon the circulation. They showed that acapnia may induce acute disturbance of the heart and failure of the peripheral circulation. These conditions resemble the functional depression of shock in patients after prolonged anesthesia and major operations. On the other hand it was found that if the carbon dioxide content of the body is conserved by partial rebreathing, the vitality of an animal, even under prolonged and extensive operation and trauma, is but little depressed.

These observations upon the circulation showed also that in animals reduced to a state of shock the carbon dioxide of the blood, or as it now be generally termed, the "alkaline reserve", is greatly reduced. This experimental result was later confirmed by the observations of Cannon upon wounded soldiers during the war.

The observations upon the respiration of animals under a mode of anesthesia that was intentionally made to imitate inexpert administration showed that the failure of breathing which was formerly one of the principal hazards of the operating room is largely due to excessive breathing during the stage of excitement. If, during the initial stage of anesthesia, an excessive elimination of carbon dioxide is induced and then the sensitivity of the respiratory center is depressed by a sight excess of anesthetic, respiration ceases. It does not return until the chemical stimulus of the blood gases and the sensitivity of the respiratory center are sufficiently restored to induce again the natural activity of breathing.

Therapeutics

In Anesthesia

In 1920, Henderson, Haggard and Coburn carried their observations to the clinic and found that when inhalations of carbon dioxide (8%) in air were administered to patients after major surgical operations under open ether anesthesia, the effects were strikingly beneficial. With the return of deep breathing, the cyanosis then common after anesthesia disappeared. The cutaneous circulation improved. The skin changed in color and temperature, from blue- gray and cold to pink and warm. The volume of the pulse, previously thready, rapidly became full; and arterial pressure was restored to normal. Owing to the increased volume of breathing, the anesthetic (ether) was rapidly ventilated out of the blood and consciousness returned within a few minutes, even after profound anesthesia. Nausea and vomiting were either greatly reduced or entirely absent and after the inhalation the patient dropped off to sleep.

In continuation of these observations, White found that when slow hemorrhage occurs after operations upon the brain, the rate of breathing gradually decreases until death is imminent. In several of such cases life was saved by stimulation of respiration with inhalation of carbon dioxide.

The use of this inhalation has now become general in connection with anesthesia. Nearly every American anesthetic apparatus now has an attachment for a cylinder of carbon dioxide, or of a mixture of carbon dioxide and oxygen. By this means any tendency to failure of breathing on the operating table is counteracted. At the close of the operation, an inhalation of carbon dioxide is given to stimulate respiration and induce rapid elimination of a large part of the anesthetic. By this inhalation a vigorous heart action and the tonus of the peripheral circulation are also restored.

Postoperative Atelectasis and Pneumonia - Prophylaxis

From the use of carbon dioxide for the purposes just described, another even more important application has developed, i.e., the prevention of postoperative atelectasis and pneumonia. Many observers have noted that after major surgical operations, the vital capacity of the lungs is often reduced to as little as one-third of the preoperative volume. The diaphragm may be elevated toward the thorax by several centimeters. In x-ray pictures, this condition of partial collapse of the chest is found to continue to some extent for several days. The position of the thorax is essentially like that which occurs in a normal man for a few minutes after vigorous forced breathing. It is, therefore, a phenomenon of acapnia.

This acapnial position of the thorax may leave considerable parts of the lungs unventilated. The airways to these parts may become obstructed and the occluded air is then absorbed into the blood.

As a result, atelectasis of a lobe, or even a massive collapse of an entire lung, may develop. From this condition, as Coryllos and Birnbaum have demonstrated experimentally, pneumonia may develop, for if pathogenic organisms happen to be present, they find in an atelectatic lung conditions favorable to their growth.

The essential correctness of this conception of the origin of postoperative atelectasis and pneumonia is attest by the prophylactic and therapeutic means that have been found effective to counteract or prevent them. In many surgical clinics in America and Germany, results have been obtained which show that when the inhalation of carbon dioxide is administered to all cases after anesthesia and operation, the lungs are reexpanded, the tonus of the respiratory muscles is restored, atelectasis is prevented, and the risk of postoperative pneumonia is virtually eliminated.

Pneumonia

The possible benefits of a similar inhalational treatment of medical pneumonia, for example after influenza, are just now under active investigation. Henderson, Haggard, Coryllos and Birnbaum have shown that in dogs, in which pneumonia has been experimentally induced, the lungs may be cleared and the pneumonia cured by placing the animals in an atmosphere of about 8% carbon dioxide for 12 to 24 hours. In support of the claim that these are real cures is the fact that pneumococci are inhibited in growth or even killed by a lowering of pH no greater than carbon dioxide may induce. A lowering of the pH by carbon dioxide contributes also to the autolysis and liquefaction of the exudate responsible for the consolidation of the lungs in pneumonia. Many cases of pneumonia have now been treated with inhalation of carbon dioxide in oxygen; and a special tent for this treatment is being introduced by Henderson and Haggard. It is believed by those who have used it that this treatment is decidedly superior to that with oxygen alone.

Asphyxia

Very similar to the use of carbon dioxide inhalation after anesthesia is the modern treatment of carbon monoxide asphyxia. This form of asphyxia is the cause of many thousands of deaths annually. Its commonest causes are city manufactured gas, which usually contains 20 to 30 % of carbon monoxide, and the exhaust from automobiles. Carbon monoxide forms a combination with hemoglobin which displaces oxygen. The compound is not so firm, however, as was once believed, for the carbon monoxide may be, in turn, displaced. The oxygen-carrying power of the blood is thus restored. The critical feature of carbon monoxide poisoning is the asphyxia, especially of the nervous system, because of the diminished capacity of the blood to transport oxygen. It seemed, therefore, at first that inhalation of oxygen would be the logical treatment. In practice, however, oxygen alone was found to be much less beneficial than was expected.

Investigating this problem, Henderson and Haggard found that in the development of carbon monoxide asphyxia the victim overbreathes and blows off an excessive amount of carbon dioxide. He thus develops acapnia, as well as anoxemia. On removal from the noxious atmosphere, the victim may exhibit a marked depression of breathing. The administration of oxygen is therefore, only slightly effective; for it is not adequately inhaled.

In experiments on asphyxiated animals these investigators showed that by administering a mixture of oxygen and carbon dioxide the respiration could be so stimulated, and the elimination of carbon monoxide so accelerated, that rapid recovery was induced. In the beneficial results, the relief of acapnia is almost as important as the elimination of carbon monoxide and the restoration of an ample supply of oxygen.

A special form of apparatus, the H-H Inhalator, for the administration of a mixture of oxygen and carbon dioxide to asphyxiated patients was, therefore, devised and has been widely introduced. This treatment has been so successful that many thousands of these inhalators are now in use: several hundred, for instance, in metropolitan New York, and a number corresponding to the population in Chicago and other cities. The rescue crews of the fire and police departments, the gas and electric companies, and now also the hospital ambulances generally have them. At first a mixture of 5% carbon dioxide in oxygen was used, but 7% has proved even more beneficial.

The value of this treatment is not merely for the saving of life, but also for the prevention of such postasphyxial sequelae as pneumonia, injury to the heart, and permanent nervous impairment. In many cases of brief but intense asphyxiation the patient is completely restored within an hour; he may then voluntarily and safely go back to work.

The same treatment is effectively used for resuscitation from a wide range of other noxious gases occurring in industry.

Asphyxia of the Newborn

Out of this treatment of carbon monoxide poisoning has developed the use of inhalation for the relief of a far more common form of asphyxia: that of the newborn. The story of this development is interesting. In it the men of the rescue crews of the Chicago Fire Department have played somewhat the same part that the milkmaids immune to smallpox did in the discovery of vaccination.

Many times it happened that a physician in Chicago who had seen a resuscitation of a case of carbon monoxide asphyxia had occasion soon after to deliver a baby that would not breathe. After swinging, spanking, and dipping the child in cold and hot water, the accoucheur, unable to induce active, natural breathing, thought to telephone for one of the rescue crews and their inhalator. The ministrations of these men were in many cases so successful that within a couple of years the fire department had developed a considerable practice in this field. With justifiable pride, it claimed the saving of several hundred babies.

When this information came to the attention of the writer it occurred to him that on theoretical grounds inhalation of oxygen and carbon dioxide is exactly the method that should be most effective in combating asphyxia of the newborn. As a result of this discovery, chemical stimulation and support for the depressed respiratory center of the newborn child by inhalation of carbon dioxide is now rapidly replacing the older, and often ineffective, methods of resuscitation depending upon cutaneous stimulation.

Neonatal Pneumonia - Prophylaxis

The lungs at birth are atelectatic. The first cry effects a partial dilation. Later breaths should dilate them further; but the dilation is often incomplete for several days, or even for some weeks. If during this time, pathogenic organisms happen to be present, they find conditions favorable for their growth in any part of the lungs that are still atelectatic. The number of deaths from this cause during the neonatal period is often as high as 4 for each of 100 live births. To forestall this hazard, it has long been the custom to stimulate the child to cry at least once daily. For this purpose some painful stimulus, such as stinging of the soles of its feet with an elastic rubber band, is applied. Experience demonstrates, however, that a premature or weak child may not be adequately stimulated and pneumonia may develop. A more humane, scientific and effective method of inducing dilation of the lungs is the routine administration to all babies during the first week or two of life of 5 or 10 minute inhalations of oxygen and 7 or 8 % carbon dioxide. The mixture is entirely safe for general use by nurses and midwives. Higher concentrations can be used effectively on difficult cases, but preferably only by those who have experience in the use of such concentrations in connection with anesthesia.

Angina Pectoris and Intermittent Claudication

In most of the applications of inhalational treatment discussed in the foregoing pages the influence of carbon dioxide upon respiration is chiefly involved. The equally important influences of carbon dioxide upon the hear and the peripheral blood- vessels have not as yet been exploited to an equal degree. Henderson and his collaborators showed many years ago that under certain experimental conditions the heart tends to develop a partial tetanus or cramp, and that this condition may be overcome by means of carbon dioxide. They showed also that, owing to the loss of muscular tonus in animals under prolonged anesthesia and operation, the blood stagnates in the peripheral vessels, the venous return to the right heart decreases progressively, and the circulation finally comes to a standstill.

With these considerations as a physiological background, the influence of carbon dioxide inhalation has recently been tried on several cases of angina pectoris. This is not an emergency treatment, but a therapy for prolonged application. It is administered for 10 to 15 minutes at a time 2 or 3 times a day. The method of inhalation is essentially like that applied by Henderson, Haggard and Coburn, and by White, after anesthesia and operation. As the inhalation consists of carbon dioxide in air, instead of in oxygen, its cost, aside from the control apparatus, is small.

The effects of this treatment are a distinct improvement in the color and temperature of the lips and skin, indicating an effect upon the peripheral circulation somewhat like that of amyl nitrate. Arterial pressure and the pulse rate are not increased, although a markedly fuller circulation is evident. The sense of oppression in the chest and the pain referred to the shoulder and arm is considerably decreased; it may cease altogether for some hours after the inhalation. After some weeks of daily inhalations, the capacity to take moderate exercise is markedly increased.

This inhalation has also been used upon a few cases of intermittent claudication. A marked improvement in the local circulation resulted both under the inhalational and as a cumulative effect of the treatment for some weeks. When it was discontinued , the patients soon relapsed into their previous condition.

Drowning and Electric Shock

The accepted treatment of the victims of drowning and electric shock is the Shafer prone pressure method of artificial respiration. Experience has demonstrated that the return of natural breathing is considerably aided and accelerated by the administration oxygen and carbon dioxide from an inhalator, while artificial respiration is being applied. Not only are the lungs thus supplied with a high concentration of oxygen, but the depressed respiratory center is also stimulated by the carbon dioxide to an earlier renewal of neural activity than would otherwise occur.

Catatonia

Finally, mention may be made of the extraordinary observations reported by the late A.S. Lovenhart, in which he found that inhalation of carbon dioxide to cases of catatonia induced a temporary restoration of intelligence and mental responsiveness. The simplest explanation of the results in these cases is attained by postulating an habitual contraction of blood-vessels in the brain of the catatonic patient, similar to that in the heart and limbs of the cases discussed in the previous section. If this view is correct, the beneficial effects of the inhalation are due to improvement in the circulation in the brain under the influence of carbon dioxide upon the finer blood vessels.

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References
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