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Resuscitation with Carbon Dioxide: PROFESSOR YANDELL HENDERSON ... 399
Microphotographic Duplication in the Service of Science: WATSON DAVIS ... 402
Obituary:
Arthur J. Weed: DR. N. H. HECK. *Agnes Pockels:* DR. HARRY EAST MILLER. *Recent Deaths* ... 404
Scientific Events:
The Banting Research Foundation; Grants in Aid of Research of the American Academy of Arts and Sciences; Medal Day at the Franklin Institute; The American Philosophical Society ... 405
Scientific Notes and News ... 407
Discussion:
Distribution of Termites: PROFESSOR ALFRED E. EMERSON. *High Altitude Stratosphere Observations:* DR. L. F. CURTISS and DR. A. V. ASTIN. *Flood Injury to Trees:* DR. MALCOLM A. MCKENZIE. *Fish Mortality:* HEM SINGH PRUTHI ... 410
Scientific Books:
Insect Morphology: PROFESSOR CLARENCE HAMILTON KENNEDY. *The Punched Card Method:* DR. DIRK BROUWER ... 413
Reports:
Principal Decisions Concerning Nomenclature Made by the Sixth International Botanical Congress, Amsterdam (1935): DR. T. A. SPRAGUE ... 416
Special Articles:
The Effects of Physiological Agents on Adult Tissues in Vitro: DR. HENRY S. SIMMS. *Bacteriologic Experimentation on the Guinea Pig Fetus:* DR. ORAM C. WOOLPERT and OTHERS. *The Isolation from Cottonseed Oil of an Alcohol Resembling Alpha Tocopherol from Wheat-germ Oil:* DR. OLIVER H. EMERSON, GLADYS A. EMERSON and PROFESSOR HERBERT M. EVANS ... 418
Scientific Apparatus and Laboratory Methods:
A Further Improved Prospecting Pick: DR. I. A. UPDIKE ... 421
Science News ... 10

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RESUSCITATION WITH CARBON DIOXIDE[1]

By Professor YANDELL HENDERSON
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ON the morning of May 9, 1794, in the Place de la Revolution in Paris, Antoine Laurent Lavoisier died under the guillotine.

One hundred and seven years later (1901) Michael Foster in his history of physiology wrote:

> As the sharp stroke of the guillotine severed his neck there passed away from this world, in his fifty-first year, this master mind of science, who had done so much to draw aside from truth the veil of man's ignorance and wrong thought; and there passed away too, the hope of his drawing aside yet other folds of that veil, folds which perhaps wrap us round even to-day.

What I have to say is concerned with one of those "folds of the veil of ignorance and wrong thought" which it has been my good fortune to some extent to draw aside.

A few years before his death Lavoisier had demonstrated the true nature both of combustion and respiration—a fundamental likeness between fire and breathing. It is oxygen, both in combustion and in respiration (in its broadest sense), that unites with carbonaceous matter, liberates heat and produces carbon dioxide.

From this fundamental conception have come far-reaching practical applications and an understanding of the unities of nature that is even more important. We can now measure the energy expenditure of the body by determining the amount of oxygen consumed. We can compare, as Lavoisier suggested, the combustion in the working muscles of a laborer and the reasoning brain of a scientist. We see that respiration

[1] Read before the American Philosophical Society, Philadelphia, April 23, 1936.

is almost life itself; yet not quite, for we find that thought is not merely physical energy.

The lessons of this vast conception are not limited to normal life. They tell us also of the processes involved in dying. As exclusion of oxygen extinguishes a fire, so too in a man or an animal a deficiency of oxygen in the blood and tissues induces death in asphyxia. It is in the tissues and organs that the fundamental process of respiration occurs. Death is the cessation of that process. There are many modes of dying that bring men to their ends; but only one final common cause. Whether the brain is destroyed or the lungs blocked or the heart stopped, death finally occurs but in one way only. When breathing and the heart come to a standstill, the supply of oxygen to the body ceases. Unless a man is burned alive, the tissues of his body always die of asphyxia.

THE PROBLEM OF ASPHYXIA

It is only when we ask the question—"What then is asphyxiation?"—that a "fold of the veil of wrong thinking" hides from us the truth and hides even the nature of our ignorance. Asphyxiation is the process that occurs whenever it becomes difficult for the tissues to obtain their normal supply of oxygen. Any absolute deficit kills quickly. Drowning, strangling or suffocation under a pillow, in a grave or in the uterus all stop both the intake of oxygen and the outgo of carbon dioxide. Therefore, it was inferred, an accumulation of carbon dioxide must be as much the cause of death as a deficiency of oxygen. It even came to be assumed that a deficiency of oxygen kills by producing an excess of carbon dioxide. Two facts were overlooked. One is that without oxygen carbon dioxide can not be produced. The other is that in several of the most important forms of asphyxiation (*e.g.,* carbon monoxide asphyxia), while the supply of oxygen is restricted, the elimination of carbon dioxide is still entirely free or is even abnormally augmented. There is thus a deficiency of oxygen and a deficiency of carbon dioxide also.

Nevertheless, almost down to the present time carbon dioxide has been regarded as par excellence the asphyxiant gas. Only a few years ago nothing would have seemed more improbable or more illogical than that inhalation of carbon dioxide, mixed either with oxygen or air, should ever be employed for the resuscitation of the victims of asphyxia. Yet such inhalation has now become the accepted treatment; and in the light of present knowledge it is entirely logical. It is saving many thousands of lives.

THE INITIAL DISCOVERIES

In the autumn of the year 1900 I received my first appointment to teach. Up to that time I had devoted myself chiefly to the chemical side of physiology. Of respiration and the circulation I knew almost nothing. I taught the old doctrine that respiration is regulated reflexly through the vagus nerves from the lungs. I gave little consideration to the chemical control, and that little was concerned chiefly with oxygen, not with carbon dioxide. But in lecturing on the circulation I had the uncomfortable feeling that such a hydraulic apparatus as I described simply would not work.

I read and reread Tigerstedt's "Lehrbuch des Kreislaufs"; and when it failed to clear up the difficulty, I turned to experiments of my own devising. By means of a child's large rubber ball, I constructed a chamber that could be slipped airtight, but without compression, over the ventricles of the heart of a dog. This simple cardiometer was connected by a wide rubber tube to a large tambour made out of the tin top of a tobacco jar. With this extemporized apparatus, writing on one of the only two revolving drums that my ill-equipped laboratory possessed, I recorded for the first time the volume curve of the heart: a curve that, better than any other form of observation, shows the mechanical action of the pump that keeps the blood circulating.

In order to adjust the cardiometer on the heart it was necessary to open the thorax widely. Under these conditions the lungs collapse; and it was necessary to blow air into them, so as to keep them distended, as well as to maintain artificial respiration. For this purpose I had only a leaky hand bellows; and the janitor who worked it for me was compelled to keep up a rapid succession of pulmonary inflations, the lungs undergoing a considerable deflation between strokes. The over-ventilation was therefore tremendous; and the animals quickly went into collapse and died. And the fact that was most striking was that the more energetic the janitor was with the bellows, the more rapidly the animals collapsed.

ACAPNIA AND THE VENOPRESSOR MECHANISM

The collapse consisted in failure of the circulation. Yet the volume curves of the heart showed that it was not the heart itself that failed. Nor was it the vasomotor mechanism on the arterial side of the circulation. It was the venous return to the heart that failed. Thus it appeared, first, that an acute over-ventilation of the lungs may cause failure of the circulation of the blood; and, second, that the failure lay in a hitherto unrecognized third major mechanical factor in the circulation.

Here were two new facts to be explained. First, as to what happens when the lungs are over-ventilated. Mosso, the Italian physiologist, forty years ago had established a hut on Monte Rosa, the second highest peak in the Alps, where he studied the effects of altitude. He found that in mountain sickness the carbon dioxide of the blood is diminished, and he gave this condition a name. He called it "acapnia," from the Greek word "kapnos," smoke; literally, acapnia means smokelessness—a deficiency of carbon dioxide.

Within a year of my first observations another important piece of collateral evidence came out, this time from England. Haldane and Priestley published their classic demonstration that carbon dioxide, rather than oxygen, is the chief immediate factor in the regulation of respiration. What I had accidentally stumbled upon was the discovery that carbon dioxide is equally potent in the regulation of the circulation.

On the basis of my own observations and those of Haldane and his collaborators, I ventured just thirty years ago to formulate and publish a sweeping hypothesis. It was the so-called acapnia theory of shock: the theory that a deficiency of carbon dioxide is involved in the depression of respiration, circulation and other functions after severe physical injuries and major surgical operations. For fifteen years I campaigned for this theory vigorously, but quite unsuccessfully. It is now, or was until the last few months, generally forgotten, or else referred to only as "one of the disproved and rejected theories."

What I could not achieve by the first fifteen years of direct advocacy has now been won by a maneuver as old as the Trojan horse. This success is the result of another fifteen years in which, avoiding theoretical discussion, I have devoted my efforts mainly along practical lines. I stopped arguing with physiologists and made friends with the anesthetists. We first introduced, as part of the technique of anesthesia, the use of a rebreathing bag to conserve the body's store of carbon dioxide. Then gradually we introduced a mixture of oxygen and carbon dioxide as part of the equipment of the anesthetist. And now cylinders of carbon dioxide, either mixed or pure, are a feature of nearly all operating rooms. And in this way the acapnia theory has captured the citadel of surgery, much as Ulysses and the Greeks captured Troy. They used a wooden horse. The acapnia theory won its entrance in those cylinders of carbon dioxide. And since this almost unnoticed victory, deaths from failure of respiration under anesthesia—once common—have almost ceased to occur.

MUSCLE TONUS AND THE VENOUS RETURN

Yet I do not blame those who so long rejected the acapnia theory. The only cause of acapnia that I had recognized was excessive elimination of carbon dioxide. I now realize that a deficiency of carbon dioxide may equally well be induced by lowered vitality and decreased production. Furthermore, until quite recently, I could offer no adequate explanation as to how deficiency of carbon dioxide affects the circulation; and failure of the circulation is generally regarded as the most significant feature of surgical shock. Now, however, there is an explanation. It is found in the depression of muscle tonus that is the commonest feature of depression of vitality. When a patient is too weak to stand or to sit up in bed or even to lift his head from the pillow, his condition is one of depressed muscle tonus. We have now demonstrated that tonus, the gentle longitudinal pull of the muscles that normally holds us erect, induces also a transverse pressure between the muscle fibers, in the same way that a pull on a rope causes a pressure between its strands. All the tonic tissues of the body have within them this pressure. Normally it causes the blood to flow from the tissues into the veins and on back to the heart. But when tonus is depressed, this intratissue pressure is also lowered; the blood stagnates in the tissues; and the volume flowing back to the heart is so much diminished that the heart appears to fail. Yet it is not the heart itself that fails. Nor is it the vasomotor mechanism. It is this venopressor mechanism: the third major mechanical factor in the circulation that I sought for so many years and find now in muscle tonus.

The depression of muscle tonus after severe physical injuries and major operations is significant also in another relation. Normally the tonus of the thoracic muscles keeps the chest and lungs expanded. But when vitality is depressed and body tonus is low, the muscles of the thorax, and particularly the diaphragm, relax and the lungs are correspondingly deflated. During this deflation, some of the air passages may be occluded or blocked with mucus; the air back of the block is then quickly absorbed; and areas of atelectasis or even a massive collapse of the whole of one lung may result.

Such conditions favor the development of infection in the lungs; a fact which is important in relation to pneumonia.

The effect of inhalation of carbon dioxide that is generally emphasized is the increased volume of breathing that it induces and the rapid elimination from the blood of any volatile substance such as ether or alcohol or carbon monoxide. But carbon dioxide has another and more fundamental effect. It increases muscle tonus, particularly the tonus of the thoracic muscles and the diaphragm. And thereby it increases the expansion of the chest, dilates the lungs and counteracts their collapse. At the same time it increases the intraabdominal pressure and the intratissue pressure generally throughout the body. It thus increases the venous return of the blood to the heart and supports the circulation.

RESUSCITATION FROM ASPHYXIA

While this use of carbon dioxide was developing in surgery, there has been a parallel development in another field. Carbon monoxide is the chief poisonous constituent of illuminating gas and of automobile exhaust gas. It owes its toxicity to the fact that it combines with the hemoglobin of the blood, displacing oxygen and thus inducing asphyxia, even though the victim is breathing vigorously. Haldane had showed that the combination of carbon monoxide with hemoglobin is reversible. The logical treatment appeared therefore to be inhalation of oxygen. Experience showed, however, that this treatment is not very effective and that it is less and less effective the severer the gassing. This was rather a puzzle, until Dr. H. W. Haggard and I found the reason. It is that, during the development of asphyxia, the victims—our victims were dogs—overbreathe excessively and develop an acapnia that depresses both respiration and circulation profoundly. Oxygen is then ineffective, because an inadequate amount is drawn into the lungs. As soon as we knew this, the solution of the problem became clear. We replaced oxygen with a mixture of carbon dioxide and oxygen: at first, 5 per cent. carbon dioxide, and now 7 or 8 per cent. And we devised and introduced a suitable inhalator. As a result this treatment is now so generally used and is so effective in saving life that the mortality from accidental asphyxiation in all our large cities is greatly diminished, and in many communities suicide by means of carbon monoxide is much less popular than formerly.

From the use of carbon dioxide diluted with oxygen for the treatment of carbon monoxide asphyxia another application has now developed. The same treatment has proved effective in the resuscitation of the newborn. The saving of life that can thus be achieved amounts to at least one baby out of every three or four that now die: one in every hundred births: in other words, a saving of more than one per cent. of all human lives. It was by the use of this inhalational treatment that Dr. Dafoe established the respiration of the Dionne quintuplets.

THE FALLACY OF ACIDOSIS[2]

I have here attempted to sketch in twenty minutes the work of more than thirty years. In the early years my proposals met with vigorous opposition, based on a false conception of the function of carbon dioxide in the body. In recent years the administration of carbon dioxide, particularly to the newborn, has been even more vigorously opposed because it contravenes one of the main doctrines of biochemistry—the dogma of acidosis. According to that dogma, all the conditions now treated with carbon dioxide involve an acute acidosis; and inhalation of carbon dioxide should—theoretically—intensify the acidosis. So vigorously have some biochemists urged this objection that they seem almost to think it sinful to save life, if the method of resuscitation involves a violation of the dogma of acidosis.

In answer, I would point out that what is now commonly called acidosis—in the sense of an intoxication by excess of acid—is more correctly conceived as a form of acapnia; for it is relieved by inhalation of carbon dioxide. In my opinion the present conception of acidosis is one of the "veils of ignorance and wrong thought" that still hides from physiology and biochemistry the true nature of the process through which the vast majority of all lives end: the process of asphyxia in its two phases—deficiency of oxygen and deficiency of carbon dioxide.

MICROPHOTOGRAPHIC DUPLICATION IN THE SERVICE OF SCIENCE

By WATSON DAVIS
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As one of its science research aid activities, Science Service has organized a Documentation Division for the development of microphotographic duplication mechanisms, and the experimental operation of two services in scientific documentation: Bibliofilm Service, in cooperation with the Library of the U. S. Department of Agriculture, and the auxiliary Publication Service, operated in cooperation with scientific journals.

Microphotographic duplication consists of making reduced-size photographs, as when a typewritten or printed page is photographed on a frame of 35 mm motion picture film. In 1925 the late Dr. Edwin E. Slosson, first director of Science Service, and the writer became interested in applying microphotographic duplication to scientific literature and publication, following a suggestion from Dr. F. G. Cottrell. Unsuccessful attempts were made at that time to enlist the cooperation of photographic and optical concerns.

[2] For literature, see Y. Henderson: *Bull. N. Y. Acad. Med.*, 11: 11, 639–656, November, 1935; *The Lancet*, July 27, 1935, p. 178; *Am. Jour. Physiol.*, 114: 2, 261–272, January, 1936; SCIENCE, 79: 2057, 508–510, June 1, 1934; *Journal of A.M.A.*, 101: 261–266, July 22, 1933; *ibid.*, 103: 750–754, September 8, 1934, and 103: 834–837, September 15, 1934.