EDITORIAL

Breathing in Anesthesia

τὸ πρῶτον οὐ σπέρμα ἐστὶν ἀλλὰ τὸ τέλειον· *

Aristotle, Metaphysics, 1072 b.

In the proud realization of Self, one may be reluctant to admit the inborn propensity to *mimesis,* although repeatedly throughout the ages this attribute has been commended. Longinus in his treatise *On the Sublime,* at considerable length, points out that zealous emulation leads to sublimity; and Robert Bridges in *The Testament of Beauty* eulogizes well-directed mimicry. Thus at the risk of seeming unduly imitative, I have borrowed from Irving Babbitt the epigraph to his work *On Being Creative,* which he took from Aristotle. Such borrowing is no conceit, it is rather like taking an impression from fine characters as one does from moulded figures or other works of art. Thus in speaking of breathing in the broader sense, I shall consider chiefly the achievements of others more particularly as they are of interest to the anesthetist.

The essential end in breathing is characterized by metabolism; indeed, this end might be given the high epithet of *quintessential*—having to do with the mystery of life. All other processes, although vital, whether of internal respiration or of external respiration, belong to the category of means to that perfect (τέλειον) end. Although, as Pascal has it, "the end of things and their beginnings are invincibly hidden from man in impenetrable secrecy," yet we may expose somewhat the middle of things, may disclose in part the influences exercised in the *means* presently before us. Physiology has addressed itself to these problems with pertinacity, and clearly with remarkable success. The success, however, is due not to the physiologist's omniscience, but to his discretion. Recently, so-called internal respiration has been reviewed by Barron (1), and the problems of external respiration were made more clear by Gesell (2). This deals with breathing and its adjustments, while that has to do with cellular oxidation-reductions.

As long ago as 1770, Lavoisier (3) declared his conception of respiration to be the combustion of foodstuffs through oxygen. Barron now states that this is still our conception and so retains the term *oxidation* in his review. Since Lavoisier's time, it has been shown that there are intermediate steps between foodstuff and oxygen. "Foodstuffs, which *in vitro* are oxidized only by powerful oxidants or under conditions which do not exist in biological systems, are oxidized in living

* Translation: That which is first is not the seed but the perfect creature.

cells at relatively low temperatures, at neutrality, through the action of mild oxidizing agents, the oxidizing enzymes. Thus cellular respiration, the consumption of oxygen accompanied by the production of CO_2 and H_2O, represents the integral of a number of partial oxidation-reductions, each of which has its peculiar mechanism." Even in the case of the simplest solid food, dextrose, its fate in supplying energy may be along four separate paths. 1. This carbohydrate is directly oxidized by some cells. 2. In other cells glucose is split by glycolysis, the products being partially oxidized in irreversible steps. 3. In others again, through the action of enzymes, the split products of glycolysis are oxidized in thermodynamically reversible steps. 4. Lastly, in some cells dextrose is oxidized to completion by the aid of a series of reversible oxidation-reduction systems. In all this, respiration takes place by a transfer of electrons from the foodstuff through the oxidation catalysts to molecular oxygen. In the simplest cases the transfer is made by only one reversible system; in the more complicated cases the electron transfer is carried on step by step through a series of reversible oxidation-reduction systems, which *regulate the release of energy, like locks in a canal, and prevent its sudden wasteful liberation.* Thus we may conceive of cellular respiration as the process by which the cell extracts energy from foodstuffs. There used to be fruitless discussions over the question whether biological oxidations are characterized by the addition of oxygen or the withdrawal of hydrogen until 1923 when Clark (4) explained matters and gave the definition of oxidation as "the withdrawal of electrons from a substance with or without the addition of oxygen or elements analogous to oxygen; or, as the withdrawal of electrons with or without the withdrawal of hydrogen or elements analogous to hydrogen." Barron gives an account of the three groups of reversible oxidation-reduction systems which are found in cells, namely, the sluggish, the enzymatic sluggish, and the electroactive system. Their meanings are rather cryptic, at least from an anesthetist's point of view; therefore, I shall not attempt a parody of the author's elucidation. Suffice it to say that the energy required for the maintenance of cell activities comes from nutriment. The cell either splits it or burns it. The splitting process is that of Pasteur's fermentation and is the simpler, although the less economical because the largest part of the energy of the carbohydrate molecule remains in the lactic acid. The greater energy requirements of complex organisms introduced the oxygen of the all-ambient air into metabolism and hence the genesis of breathing. In all of the many reactions implied there is a variety of factors which are beyond the scope and magnitude of this paper; however, it can be said that the reactions may be oriented toward either the oxidation or the synthesis of carbohydrates, proteins, and fats. In all there is, as it were, control of the plucking of brands from the burning.

At this juncture it is apposite to take some facts from a survey by Quastel (5), entitled *Respiration in the Central Nervous System,* and to give them, so to speak, as aphorisms for the simple reasons that they possess the latest information and are of particular interest in anesthesia: There appears to be a close association between oxidation processes in the brain and cerebral activity. The gray matter of the brain has a high rate of oxygen consumption and a continuous supply of blood to the brain is essential for the normal functioning of this organ. From six to eight seconds of interruption of cerebral circulation produces loss of consciousness. Unconsciousness supervenes if oxygen to the brain is reduced to the extent that the O_2 saturation of the blood of the internal jugular vein is 24 per cent or less. Thirty per cent or more will suffice for consciousness. Pressure on the carotid sinus causes unconsciousness without preliminary cerebral anemia or fall in cerebral blood flow. Although the unconscious state may be the result of lowering of oxygen supply, it may also occur when oxygen is as freely available as in the conscious condition, as during sleep and in epileptic seizures. The number of capillaries of the gray matter is small compared with that of muscle, yet the residual O_2 saturation of the blood in the internal jugular vein in conscious humans is approximately 60 per cent, whereas for the arm it is 72 per cent. A constant supply of oxygen to the brain is of greater importance than an interrupted rich supply. This seems related to the fact that the brain is very restricted in its choice of metabolites for respiratory purposes. It demands, at the least, a minimum concentration of dextrose and a constant supply of oxygen. After thirty minutes without access to fresh oxygen, neurones in the brain can partially regain their function; that is, respiration, vasomotor and pupillary reflexes. Oxygen lack longer than five minutes results in cessation of cerebral function but within this interval full recovery, except for blindness, can take place. Various parts of the nervous system differ in their sensitivities to O_2 lack and ability to recover. Under certain conditions of respiratory depression the administration of oxygen may further depress respiration, probably by removal of an anoxemic stimulus (e.g., CO_2) to respiration. There is a greater difference between the amounts of glucose of arterial and cerebral venous blood (9 mg. per cent) than between those of arterial and muscle venous blood for arm (5 mg. per cent) and for leg (4 mg. per cent). In lowering blood glucose, insulin robs the central nervous system of its most important substrate for respiratory purposes, and may produce an anoxia even though oxygen is freely available. However, this does not forbid the addition of insulin to a glucose-Ringer solution. Slices of guinea-pig's brain cortex treated with chloretone show diminished oxygen consumption, which effect is reversible as respiration is recovered on washing. This whole set of ponderous information is nothing if it is not entirely appropriate to breathing in anesthesia.

Quastel suggests that a narcotic is adsorbed from the blood at a specific area or center of the nervous system. Here it brings about a diminution of the ability of the cells constituting the nervous center to oxidize pyruvic acid, lactic acid and glucose. The specific effects of narcotics will depend on the specificities of adsorption in various parts of the nervous system. Jowett (6) finds that a definite inhibition of respiration is produced by concentrations of the order producing deep narcosis, and states that inhibition of glucose oxidation may be the cause of narcosis. Quastel goes on to say that narcotics appear to bring about a local anoxia in those parts of the nervous system where they are adsorbed, owing to their interfering with the oxidation of glucose at the nervous center in question. The access of oxygen, however, is quite unimpaired. Sellei and Mayer (7) have shown decreased respiration in the cerebral cortex of rats after ether, chloroform and ethyl chloride; these substances had no effect on the thalamus, or on the white matter. Oppositely, evipal decreased respiration of the white matter and the thalamus, but had no effect on the respiration of cerebral cortex. With such reduced metabolism is associated release of water by the cells (8).

Such, then, is my review of reviews on internal respiration, even though it be as a ghost of a ghost, in the words of John Drinkwater, articulated in the echo of an echo. And now it may be seen, the relevancy, the essential influences of those manifold oxidation-reduction processes upon the various effects of anesthetics as these tend to interfere with normal function in the blood (9), the brain (10), the liver (11), and the kidney (9, 12), which effects every anesthetist knows.

Numerous organisms, such as the firefly, have solved the problem of transforming chemical energy directly to that of light. As this phenomenon is evidently an oxidation, it seems a pity it does not occur in human cerebral cortex, so to "lighten" the darkness that we might perhaps be able more easily to understand the recondite teachings of the profound Robert Gesell, and more readily to follow the intricate and subtle discoveries of that Nobel prizeman, the erudite Charles Heymans (13). Gesell, in his account of *Respiration and its Adjustments* (2), states that the principles of chemical control apply to the central as well as the peripheral parts of the respiratory mechanism. The latter were shown by Heymans and his co-workers when they produced hyperpnea by lack of oxygen, or by excess of carbon dioxide, confined to the aortic, or to the carotid chemoceptors. While the control of energy, comprehensively, is through conjunctive physical and chemical means, rapid adjustments in the exchange of carbon dioxide for oxygen depend upon pulmonary ventilation and the circulation of the blood. These two systems function in harmony under similar influences at and from the respiratory and the circulatory centers, and their outlying chemoceptors. By themselves, the chemical mechanisms, central and peripheral, are capable of acting efficiently. Complementary control obtains through the physical forces of stretchings of the carotid sinus, the aortic arch, and the proprioceptive endings in the lungs. "Unable directly to sense changing oxidations, but quick to feel a drop in pressure which would curtail oxidations, the vascular proprioceptors forewarn and forestall a chemical change, which through delays of direct chemical control might assume much larger proportions. Quick to feel a volume change of the lungs, the pulmonary proprioceptors are as prompt to modify circulation and ventilation in their own way." Stimulation of breathing at the chemosensitive structures is brought about either through oxygen lack, leading to decreased oxidation and a consequent increase in intracellular H-ions; or, through carbon dioxide excess, leading to decreased intracellular alkalinity and a consequent decrease in oxidation. In other words, whether caused by anoxia or hypercapnia, hyperpnea signifies impaired oxidation or increased H-ion concentration, or both, at those chemosensitive elements. By virtue of the three sets of control, each possessed of almost imperceptible tenuities of delicate sensitivity in their secret penetralia, there is evidently a very finely adjusted interaction, so that "the type of breathing which prevails at any time may then be looked upon as a resultant of highly variable chemical and physical drives." Gesell concludes that there are two immediate threats to a smooth supply of usable energy: *oxygen lack,* and *acid excess.* Of the two the first is by far the more serious, for without oxygen, oxidations cannot continue and the mechanism for the renewal of oxygen and removal of carbon dioxide is deranged. At this time, it may be mentioned, from a most recent review, that Schmidt and Comroe (14) emphasize the part played by reflex factors in physiological adjustments of pulmonary ventilation, and give the observations of Harrison (15) and his collaborators on anesthetized animals in which hyperpnea occurred when a limb was moved passively, even though all vascular communications were interrupted and the leg was connected with the body only by the sciatic nerve; when the latter was cut, movements of the leg no longer affected breathing even though vascular communications were reestablished.

Thinking of the epigraph from Aristotle, wherein he gives primacy to ends over origins, teleologically, the object of breathing is to provide energy for the activities of life; indeed its accomplishment is the supreme biological exigency. Cannon (16) states that we exist in a fluid matrix. Just in so far as this internal environment or fluid matrix is kept from noteworthy variations, there are no internal adjustments to be made; the internal organs can perform their functions undisturbed by the ups and downs of external circumstance or by possible consequences of our own strenuous activity. Regulatory processes preserve in the fluid matrix a relatively constant state. "So characteristic is this constancy, and so peculiar are the processes which maintain it, that it has been given a special name, *homoeostasis.*" Ordinarily, the oscillations on either side of the homoeostatic norm are slight. Every anesthetist knows that anesthesia is apt to be accompanied by interferences with external respiration, as well as by disturbances to internal respiration; indeed, such derangements may be extensive and quite serious. Every anesthetist knows the significant changes which may occur in the blood as a result of anesthesia, for instance in its fluid state and in its acid-base balance; in the liver, its functions and structure; in the kidney, its activities and appearance. Every anesthetist knows well the necessity of maintaining good oxygenation during anesthesia, as well as he knows how to lessen the deleterious effects of anesthetics and to alleviate them when they occur. In Aristotelian high seriousness, it is axiomatic that there is nothing in anesthesia that is of any consideration in comparison with breathing.

As there is so little time, and as our subject so often enters into the region of imponderables, I have been forced, in the language of Dr. Johnson, to indulge in "the grandeur of generality." It seems suitable to close with some lines from *The Testament of Beauty:*

> And yet hath pleasure truly its main stronghold in Self,
> because the greatest pleasure that man knoweth, is aye
> the pleasur of life, even as his chief displeasur is death.
> This Life-joy, like the breath-kiss of the all-ambient air
> unnoticed til the lack of it bring pain and death,
> is coefficient with the untrammel'd energy
> of nativ faculty, and the autometric scale
> of all functions and motions, which in the animal
> struggle for Self persistently against all hindrance:
> it is the lordly heraldry of the banner'd flower,
> in brutes the vaunt of vigour and the pose of pride,
> their wild impersonation of majesty; and in man
> the grace and ease of health alike in body and mind,
> thatt right congruity of his parts, for lack whereof
> his sanity is disabled maim'd and compromised.

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COMBINED MEETING OF THE OHIO SOCIETY OF ANESTHETISTS AND THE AMERICAN SOCIETY OF ANESTHETISTS, INC.

DESHLER-WALLICK HOTEL, COLUMBUS, OHIO

APRIL 30, 1942—2:30 P.M.

1. Shock.
   By H. D. Green, M.D., Associate Professor of Physiology, Western Reserve Medical School, Cleveland, Ohio.
2. Intravenous Anesthesia.
   By Norris E. Lenahan, M.D., Anesthetist to White Cross Hospital; Clinical Assistant, Ohio State University, Columbus, Ohio.
3. The Anesthetic Management for Drainage of Abscess of the Submandibular Space.
   By James A. Bennett, M.D., Assistant Professor of Surgery in Charge of Anesthesia, University of Cincinnati, Cincinnati, Ohio.
4. Casualty Anesthesia in England.
   By K. C. McCarthy, M.D., Anesthetist to Toledo, Mercy, Flower and Lucas County Hospitals, Toledo, Ohio.
5. Anesthesia in Thyroid Surgery.
   By J. K. Potter, M.D. and R. M. Crane, M.D., Department of Anesthesia, Huron Road Hospital, East Cleveland, Ohio.
6. The Use of Picrotoxin in Barbiturate Poisoning—A Case Report.
   By A. L. Schwartz, M.D., Director of the Department of Anesthesia, Jewish Hospital, Cincinnati, Ohio.