conditions which precede and follow this experimental period. (*b*) On increasing the endosinusal pressure in a dog whose contralateral carotid sinus has been denervated it is found that the blood pressure falls less during anoxia than in the control period. (*c*) On tilting into the 'feet down' position the blood pressure in the carotid artery falls more in a dog after denervation of both carotid sinuses than was observed prior to this operation in the same animal during inhalation of oxygen deficient gas mixtures. This indicates that anoxia does not eliminate these reflexes completely.

"Under conditions in which carbon dioxide and oxygen deficiency cause a rise in blood pressure, i.e., in the normal dog with and without artificial respiration, and further after vagotomy *or* removal of both carotid sinus areas with artificial respiration, the effect of carbon dioxide plus low oxygen tension is greater than corresponds to the algebraic sum of the individual effects. In the dog deprived completely of its buffer nerves and artificially ventilated, it is found that carbon dioxide completely offsets the fall of blood pressure produced by the inhalation of a gas with a low oxygen tension. The experiments indicate that the cause of this potentiation lies in the fact that the effect of carbon dioxide is increased in anoxia. This is in part due to the weakening of the carotid sinus pressor reflexes. In addition to that it is assumed that the intracellular metabolites formed during short periods of anoxia may interact with the effects of carbon dioxide and thereby cause the potentiating effect described above."

J. C. M. C.

REID, L. C.: *Cellular Respiration.* Brit. J. Anesth. **17**: 41–56 (July) 1940.

"Cellular respiration may be defined as those biological processes and chemical mechanisms by which the cell converts the bound, radiant energy of the sun, stored in foodstuff molecules, to free utilizable biotic energy, thereby making possible cellular activity and even cellular existence. . . . The cell . . . has two methods for liberating the energy present in the foodstuff molecules: (1) fermentation; (2) oxidation. . . . Fermentation is the term used to cover those processes by which glucose is converted into simpler substances in the absence of oxygen with the liberation of energy. . . . Glycogenolysis . . . represents the conversion of glycogen to glucose and, strictly speaking, does not form a part of cellular respiration, but is added for the purpose of rounding out the picture with some degree of continuity and completeness. . . . It is well known that hydrogen and oxygen do not combine with a measurable velocity at ordinary temperatures but will do so under special conditions, such as the presence of inorganic catalysts, for example, palladium or platinum or enzymes, so-called organic catalysts. . . . The enzymes, dehydrogenases, were first described by Wieland and have since been extensively investigated by Thunberg, who has recently published an extensive review. These dehydrogenases are responsible for the activation of the hydrogen of the foodstuff molecules, which is transferred to a suitable acceptor or carrier substance. They are highly specific in their actions; that is, some will only transfer hydrogen to cytochrome, others to flavoprotein, and it is interesting in this connection to note that this specificity is due to the variability of the bearer portion of the molecule. Their prosthetic groups are all the same. The peculiar specificity of reaction depending on changes in the bearer portion rather than the active prosthetic group seems, at first sight, to be unusual, but the well-known substance, hemoglo-

Downloaded from http://pubs.asahq.org/anesthesiology/article-pdf/2/1/93/279726/0000542-194101000-00012.pdf by guest on 25 January 2021

bin, is an example of a similar action. . . .

"Fumarase is a very powerful enzyme present in all tissues, having the unique quality of maintaining the ratio of malic acid to fumaric acid in the proportion of three to one. . . . The enzyme, oxidase—or as it is sometimes called, the respiratory enzyme, or the Atmungsferment of Warburg—is unusually widely distributed and has apparently a specific relationship to reduced cytochrome to activate its hydrogen, and in the presence of molecular oxygen to form water. . . . The role of the four carbon dicarboxylic acids are very important. These are unique substances. It is a simple rule of biological chemistry that the first and second molecules next the COOH group are the most reactive, and, therefore, these substances having the central CH_2 groups in both the alpha and beta positions possess unusual chemical affinities, and as Szent Gyorgyi says, gives these substances their peculiar reactivity. . . . Respiratory carriers are substances which can be hydrogen acceptors and, under certain conditions, hydrogen donators. These play an essential role in all oxidation reduction systems. The better known ones are: Cytochrome, Flavoprotein, Coenzyme I, Coenzyme II [and] Glutathione. . . . Cytochrome is a mixture of three hemochromogen compounds, hemochromogen being a combination of a hematin and a nitrogenous base like nicotine or pyridine. . . . There is a definite parallelism between the amount of this substance present in any tissue and its respiratory activity. . . . Cytochrome does not lose its oxygen in a vacuum like hemoglobin. The heart, according to Keilin and Hartree, in mammals is the best source of cytochrome. Cytochrome goes through an oxidation reduction cycle 3,000 times per minute in vivo, while in vitro this is reduced to about 300 times. . . . Flavoprotein is another widely distributed pigment, and is also known as the yellow enzyme of Warburg. . . . This is a hydrogen carrier, but differs from cytochrome in containing no iron. It bears a very specific relationship to certain dehydrogenases, and under some conditions it joins the chain as a second carrier to cytochrome. . . . It has been known for some years that some dehydrogenases could only reduce particular dyes in the presence of certain specific cellular constituents which received the name of coenzymes. However, as a result of the work of Warburg and his group, these coenzymes have been found to be true carriers and play an important part in the transfer of hydrogen to flavoprotein. According to Szent Gyorgyi their role as respiratory carriers with the action of the dhydrogenases account for the changes occurring in the four carbon dicarboxylic acids. This transference is accompanied through their nicotinic acid amide ring. . . . Gluathione . . . represents one of the earliest carriers found, and at first was considered to play a dominant role in oxidation reduction systems. However, its exact position is not evident, and in any event it seems to be decreasing in importance. Another respiratory carrier is the recently discovered adrenochrome . . . but at the moment its exact significance in the scheme of things is not at all clear. . . .

"An important question arises as to how one is going to utilize practically these conceptions of cellular oxidation reduction systems. . . . The post-operative supplemental supply of oxygen becomes a very logical procedure in the light of this scheme, and under many conditions an imperative necessity. For example, it is well known that in high mountain altitudes the decreased oxygen tension is compensated for by increased blood volume, increased red cell count, increased per-

Downloaded from http://pubs.asahq.org/anesthesiology/article-pdf/2/1/93/279726/0000542-194101000-00012.pdf by guest on 25 January 2021

centage of hemoglobin, and increased respiratory activity. Therefore, it would seem a perfectly logical procedure to compensate for a decreased efficiency of cellular oxidation reduction systems as a result of anesthetic agents by an increased oxygen tension through a supplemental oxygen supply. This, of course, is most important in the immediate post-operative period although it is still of value whenever the cellular oxidation reduction systems are under strain as in anesthesias, anemias, shock, etc. This would seem to provide an excellent basis for the wider application of the use of a post-operative supplemental oxygen supply.

"If one speculates on this scheme, some otherwise imperfectly understood phenomena become more susceptible of understanding. For example, it is well known that anesthetic agents such as ether, etc., give rise to a pronounced hyperglycemia which is not fundamentally an autonomic nervous system effect as it is uninfluenced by adrenalectomy, atropine, or ergotomine. . . . The genesis of this hyperglycemia is, therefore, not clear, but if one considers that these anesthetic agents inhibit the dehydrogenases with a consequent decreased tissue utilization of triose and its parent, glucose, which accumulates in the blood particularly if the enzymes responsible for the conversion of glycogen to glucose are not inhibited, then a ready explanation is available. Another interesting phenomenon is that of the use of morphine in cyanosis and dyspnea. It is well known that morphine is very beneficial in cases with cyanosis and dyspnea as a result of cardiac decompensation, but on the other hand was positively harmful when these symptoms were due to pulmonary lesions such as bronchitis, emphysema, asthma, etc. The explanation given has been entirely founded on the depression of the respiratory center, but if this were the whole story an accumulated CO_2 should stimulate even a depressed center. Therefore, if one turns to this scheme it shows at once that morphine, being an alkaloid, depresses the dehydrogenases, the cellular use of oxygen is inhibited, less carbon dioxide is formed, and eventually less chemical stimulation of the respiratory center takes place from accumulated carbon dioxide. Therefore, in severe inhibition of the dehydrogenases the respiratory center is only stimulated by the action of oxygen deficiency on the specific nerve endings in the aorta. This, of course, gives a shallow gasping respiration which is not efficient enough under such conditions, and that respiration sometimes abruptly fails is not surprising. Not infrequently, in other cases of a lack of carbon dioxide build up where the classical explanation has been the insufficiency of oxygen intake, an inhibition of the dehydrogenases probably plays a very important role."

J. C. M. C.

BUTLER, T. C., AND DICKINSON, H. L.: *The Anesthetic Activity of Optical Antipodes. I. The Secondary Butyl Alcohols.* J. Pharmacol. & Exper. Therap. **69**: 225–228 (July) 1940.

"Because of the peculiar structural relationship of optical antipodes, the pharmacological comparison of antipodal pairs has attracted the attention of many investigators. Such a comparison gives an indication of the importance of asymmetric processes in the pharmacological action and may thus throw some light on the mechanism of action not only of the compounds tested but of the whole pharmacological group to which they belong. Despite the great amount of thought which has been devoted to the explanation of the mechanism of narcosis, only a few pairs of antipodal narcotics have been compared and the reports of some of these experiments are not thor-

Downloaded from http://pubs.asahq.org/anesthesiology/article-pdf/2/1/93/279726/0000542-194101000-00012.pdf by guest on 25 January 2021