Great tendency to decubitus (q. v.), also due to vascular paresis, requires special precautionary measures.

Constant nursing care is imperative to give these desperately sick and helpless patients their best chance for survival.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY OF THE AMERICAN MEDICAL ASSOCIATION HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE.
H. A. CARTER, Secretary.

RESUSCITATION

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The art of resuscitation [1] has made great advances during the past twenty years both in theory and in practice. These advances will be briefly reviewed here. There are also some developments to report, so recent that they have not yet reached practical application, and some further developments are indicated as probable during the next few years. Such developments deserve encouragement, for there are still large possibilities of improvement in the field of resuscitation. The chief objects of this article are three:

1. To promote the widest possible use of those measures and devices that have been proved by experience to be safe and effective.
2. To give warning against the use of drugs and apparatus that, instead of benefiting, may injure patients or may even result in loss of life.
3. To show that the facts of resuscitation largely refute the theory of asphyxia that is now generally accepted, and to promote the development of sound theory as a basis for further progress in the art of resuscitation.

FORMS AND DEGREES OF ASPHYXIA

Resuscitation is the therapeutics of acute asphyxia. The causes and forms of asphyxia, both acute and chronic, are many, and their treatment should vary to correspond with their differences. They include drowning, electric shock, carbon monoxide poisoning, neonatal apnea and atelectasis, anesthetic and postoperative depression, mountain sickness, aviators' collapse, and the impairment of the lungs by irritant gases and by pneumonia. Indeed, the terminal stages of most of the various ways of dying—the stages when the circulation and respiration are failing—are largely asphyxial.

Short of death there are also three degrees of asphyxia. They differ in the duration and intensity of the asphyxia. According to their outstanding features they are apneic asphyxia, acarbic asphyxia and chronic asphyxia.

Apneic Asphyxia.—Brief but intense asphyxia, under complete deprivation of oxygen, is exemplified in drowning. Its outstanding feature for treatment is apnea: cessation of breathing. The vital machine is little damaged. It is merely stopped. It is restarted mainly by means of artificial respiration. Inhalational treatment is secondary, although it is often of critical value for the saving of life. If recovery occurs at all, it is generally rapid and complete.

Acarbic Asphyxia.—More prolonged but less intense asphyxia is exemplified in those cases in which sublethal atmospheres of carbon monoxide have been breathed for several hours. The patients are often still breathing, although in profound coma, when removed from the poisonous atmosphere. The vital machine has been so deranged by asphyxia that, without treatment, recovery is slow and painful. There may be sequelae of mental or physical incapacity, indicating profound tissue damage especially in the nervous system, or even subsequent death. In such cases artificial respiration is often not needed, as breathing has not stopped. But if further damage is to be prevented and recovery is to be rapid, inhalational treatment is essential. Prolonged acute deprivation of oxygen through any agent or process induces this type of asphyxia. But restoration of oxygen alone does not cure it or cures it only very slowly. Experience has shown that for rapid restoration of normal conditions the effective means, along with oxygen, is inhalation of carbon dioxide in proper dilution. In the benefits of this inhalation the stimulation of respiration is important, but the deeper effects of carbon dioxide on the conditions in the blood and tissues, particularly the relief of acarbia (defined below), are equally or even more important.

Chronic Asphyxia.—In addition to these two forms of acute asphyxia there is also a third or chronic asphyxia due to a partial deprivation of oxygen. It occurs in anemia and in heart disease and is characterized by shortness of breath and continual oxygen debt. Restoration of red corpuscles and prolonged inhalation of oxygen [2] are the logical treatments.

The fundamental processes occurring in all forms of asphyxia are as yet but incompletely understood or, rather, they have been generally misinterpreted. They have been variously termed acapnia, acidosis and acarbia: deficiency of carbon dioxide, excess of acid and diminution of the amount of alkali bicarbonates in the blood. This much only is clear: Deficiency of oxygen induces a profound disturbance of the state in which carbon dioxide is normally held in the body and in its amount. I shall call this state "acarbia." It is the state generally called "acidosis" and mistakenly regarded as an intoxication by acid.[3] Restoration of the supply of oxygen overcomes this state but slowly. If injury to the tissues has not gone too far, restoration of carbon dioxide by inhalation, together with adequate oxygen, rapidly and completely restores normal conditions in the body.

ARTIFICIAL RESPIRATION AND INHALATIONAL APPARATUS

In such states as the complete apnea induced by submersion in water or by electric shock, even seconds are precious. Death will quickly result unless the supply of air to the lungs is immediately renewed. The prompt application of artificial respiration is therefore the measure of primary importance and for this purpose the

From the Laboratory of Applied Physiology, Yale University.

1. Henderson, Yandell: Resuscitation from Carbon Monoxide Asphyxia, from Ether or Alcohol Intoxication, and from Respiratory Failure Due to Other Causes; with Some Remarks also on the Use of Oxygen in Pneumonia, and Inhalational Therapy in General, J. A. M. A. **83:** 758-763 (Sept.) 1924.

2. Kroetz, C.: Formen der Dyspnoe: 1. Cardiac Dyspnoe, Deutsches Arch. f. klin. Med. **169:** 257, 1930. Uhlenbruck, P.: Ueber die Wirksamkeit der Sauerstoffatmung, Ztschr. f. d. ges. exper. med. **74:** 1, 1930. Jansen, K.; Knipping, H. W., and Stromberger, K.: Klinische Untersuchungen über Atmung and Blutgasen, Beitr. z. Klin. d. Tuberk. **80:** 305, 1932. Barach, A. L., and Richards, D. W. Jr.: Effects of Treatment with Oxygen in Cardiac Failure, Arch. Int. Med. **48:** 325-347 (Aug.) 1931. Barach, A. L.: The Treatment of Asphyxia in Clinical Diseases with Especial Reference to Recent Developments in the Use of Oxygen in Heart Failure, New York State J. Med., to be published.

3. Henderson, Yandell: Fundamentals of Asphyxia, J. A. M. A. **101:** 261 (July 22) 1933. This and the following paper contain references to all papers on asphyxia referred to but not specifically cited here. Henderson, Yandell, and Greenberg, L. A.: Acidosis: Acid Intoxication or Acarbia? Am. J. Physiol. **107:** 37 (Jan.) 1934.

prone pressure method introduced by Schafer [4] is the procedure of choice. It should always be continued until natural breathing returns or rigor mortis sets in. Lives have been lost by physicians interfering with the policeman, fireman or boy scout who was performing artificial respiration. It is easy to order a nonbreathing victim of drowning or electric shock or other acute asphyxia into an ambulance, but he will be dead before he reaches the hospital.

In using the Schafer method or any other form of artificial respiration, on a victim of drowning, the question of removing water from the lungs may be disregarded. If the body has been in fresh water, the water that reaches the lungs is quickly absorbed into the blood. If salt water is involved, the absorption is slower. But in either case there is really no way to get the water out of the finer tubes and chambers of the lungs by manipulation. If all of them are occluded, the circulation of the blood through the lungs is believed to be obstructed in a manner similar to Valsalva's experiment and death is immediate by so-called immersion shock. Fortunately there are generally enough spaces in the lungs still free from water to permit sufficient ventilation under artificial respiration to supply that minimum amount of oxygen which is necessary to maintain life. If life is thus maintained the victim is generally resuscitated, provided of course that the heart is still beating and the blood circulating.

Artificial respiration is also the measure of primary importance in electric shock, although it is effective only in cases in which respiration, but not the heart, has been stopped. If the heart has been thrown into fibrillation, no means now available can restore a coordinated pulsation and resuscitate the victim. There is distinct experimental progress toward restoration of coordinated heart action after electric shock,[5] but there is as yet no practical application of such laboratory observations requiring discussion here. If the heart has not been thrown into fibrillation, but only respiration is stopped, recovery under artificial respiration is brought about essentially as in cases of immersion.

In connection with artificial respiration, three recent practical developments deserve mention. One is the tilting board developed by Eve [6] in England and by Cornish [7] in California. This device is in principle a seesaw on which the victim is laid and rocked slowly through an angle of 30 degrees or more from the horizontal each way. Adjustable pegs are placed in holes in the board at the shoulders and feet to keep the body from sliding. When the head is lowered and the feet are raised, the weight of the abdominal viscera acts on the diaphragm to induce expiration. When the head is raised, the movement of the viscera and diaphragm feetward induces inspiration. If the body is completely flaccid, the victim should be laid on his face, so that the tongue will fall forward; otherwise on his back. The device is quite easily constructed by any carpenter and would probably prove useful at bathing places and in the accident rooms of hospitals for use in cases of concussion, morphine poisoning and other conditions of hypopnea and apnea. An apneic baby has been revived with it. It is also particularly adapted to use by laymen.

An apparatus for prolonged artificial respiration by compression of the chest has recently been described by Kerridge.[8]

The other development is of a different type; it is for use by physicians only. It is the device, recently developed by Flagg,[9] to facilitate the introduction of a sound into the trachea for the administration of intratracheal insufflation. It consists of an electrically lighted laryngoscope. Because of the flaccidity of the muscles of the mouth and throat in the victims of drowning and in asphyxial new-born babies, the larynx is readily made visible with this device and a tracheal sound is easily introduced. Through this sound a mixture of oxygen and carbon dioxide may be blown directly into the lungs. The principle involved is essentially that of artificial respiration by intermittent insufflation, as introduced by the late Dr. Meltzer.[10] There can be no doubt that some victims of submersion, of neonatal apnea and of collapse under surgical operations, particularly in the thorax, who can be resuscitated in no other way can be saved by this means. The apparatus will be useful as an attachment of the inhalator at large bathing places, such as Coney Island, where enough drowning and other accidents occur to justify regular medical attendants. The number of cases of drowning and of asphyxia of the new-born needing insufflation is, however, small compared to those needing only inhalation. The capacity of the apparatus to induce dilatation of the atelectatic lungs, especially in cases of birth shock and asphyxia pallida, contributes a marked advantage over simple inhalation; but it should be used with precautions against excessive intrapulmonary pressure. These precautions consist in setting the blow-off valve at not more than 25 mm. of mercury pressure. For the adult, 40 mm. is allowable.

The report of a referee of the Council on Physical Therapy indicates that in its present form the Flagg laryngoscope is somewhat too large for convenient use on infants and that the metal cannulae will also need some modification to prevent trauma. These are however details that can be easily improved. The revival of intratracheal insufflation for clinical use is a valuable contribution to the art of resuscitation.

During surgical operations in the thorax there is sometimes urgent need for artificial respiration. Apparatus of the general type used in physiologic laboratories would meet this need, if combined with intratracheal insufflation. Such an apparatus has recently been devised by Coryllos.[10a]

Reports based on the practical experience of obstetricians indicate that, in the mixtures of oxygen and carbon dioxide used for resuscitation of the new-born, high percentages of carbon dioxide—up to 20 or even 30—are found most effective for the initiation of spontaneous breathing in difficult cases but that, after spontaneous breathing has been established, percentages of 7 or 8, or even as low as 5 are sufficient. Such is the testimony of the referees to whom the Council on Physical Therapy has referred the infant resuscitation apparatus recently submitted for testing. It is probable

4. Schafer, E. A.: Harvey Society Lectures for 1907-1908, New York, 1909, p. 223.

5. Hooker, D. R.; Kouwenhoven, W. B., and Langworthy, O. R.: The Effect of Alternating Electric Currents on the Heart, Am. J. Physiol. **103**: 444 (Feb.) 1933. Williams, H. B.: Personal communication to the author on Resuscitation by Electric Countershock.

6. Eve, F. C.: Actuation of the Inert Diaphragm by a Gravity Method, Lancet **2**: 995 (Nov. 5) 1932. Killick, E. M., and Eve, F. C.: Physiologic Investigation of Rocking Method of Artificial Respiration, Lancet **2**: 740 (Sept. 30) 1933.

7. Cornish, R. E., cited in Lazarus, Dead and Alive, Time **23**: 49 (March 26) 1934.

8. Kerridge, P. M. T.: Artificial Respiration for Two Years, Lancet **1**: 786 (April 14) 1934.

9. Flagg, P. J.: Resuscitation, New York State J. Med. **33**: 395 (March 15) 1933.

10. Meltzer, S. J.: Simple Devices for Effective Artificial Respiration in Emergencies, J. A. M. A. **60**: 1407 (May 10) 1913.

10a. Coryllos, P. N.: Etiology, Prevention and Treatment of Postoperative Hemorespiratory Complications, J. Thoracic Surg. **2**: 384 (April) 1933.

that a high initial carbon dioxide mixture followed by a lower mixture would also be the most effective agents for resuscitation in cases of drowning. On theoretical grounds it would seem to me that both for the newborn and for the drowned 20 per cent of carbon dioxide in the stronger mixture and 7 per cent in the weaker should be enough. But, of course, practical experience, not theory, must determine the final decision.

For administering inhalation in all varieties of cases of asphyxia, the H-H Inhalator,[11] with the recent addition of a Flagg device, affords in general the best means of stimulating respiration after submersion, electric shock and carbon monoxide asphyxia. Several thousand of these inhalators are now in use with a very large saving of life. The Davis Inhalator[12] also has been approved by the Council on Physical Therapy. The infant resuscitators of the Ohio Chemical and Manufacturing Company[13] and of the Foregger Company[14] have both been found efficient and have recently received the approval of the Council on Physical Therapy. Both of these companies supply also excellent inhalators for administering carbon dioxide (from cylinders of liquid carbon dioxide) mixed with air in an open mask. The first, third, fourth, fifth and sixth of these appliances are made according to my designs.

The Sparklet Resuscitator, now advertised in medical journals, has possibilities of usefulness that have not as yet been developed to a point deserving of approval by the Council. The amount of the oxygen carbon dioxide mixture that one of the Sparklets affords is so small that it can be used effectively only for total rebreathing. But, used in this way, it should be valuable for the treatment of asphyxial new-born babies delivered in private homes. The amount of liquid carbon dioxide contained in a sparklet would be sufficient to stimulate respiration for a few minutes if the control apparatus regulated the flow effectively. But such is not now the case.

The Pulmotor[15] has been condemned so frequently in reports by committees of high scientific competence that, except for its name, it would long since have passed, as it should, into the limbo of things forgotten. Unfortunately the word "pulmotor" has become in popular speech a generic term for any and all respiratory and resuscitative devices and particularly for an inhalator. Because of this confusion of terms, the newspapers often report the resuscitations effected by means of inhalators as cases of "victims restored to life by the Pulmotor." Then some ill informed community buys one of these discredited devices for its fire department.

Recently another device has been brought out and vigorously promoted by sales agents, which is in all essentials, simply another pulmotor. As it is intended for use by laymen, it applies mechanical artificial respiration by means of a mask. It has, therefore, the same disadvantages as the original pulmotor; namely, leakage from the mask, inflation of the stomach, possibility of injury to the lungs by overdistention, and rapid and inefficient reversal of inspiration and expiration. If set to produce low pressures, such apparatus is ineffective; if set to high pressures, it is likely to injure the lungs. The apparatus has an inhalation attachment, but the airways are too small for full efficiency in supplying oxygen and carbon dioxide for natural breathing. This defect could be corrected; the pulmotor feature should be eliminated. The name of this device is the E and J Resuscitator. The inventors of apparatus of this type should learn that mechanical artificial respiration apparatus employing pressure and suction with a mask cannot be made effective with a mask or safe for use outside a laboratory or a hospital. Pressure and suction require intubation of the trachea, an operation that properly and legally can be performed only by physicians. The administration of pressure and suction with a mask sometimes works; but it is liable to fail when most needed. In the hands of laymen, such apparatus cannot be made free from serious danger of injury to the lungs.

A device for artificial respiration of a quite different order is the Drinker apparatus[16] and one of the same type offered by Emerson.[17] In such apparatus the entire person of the patient is enclosed in a steel chamber with the exception of the head. A rubber collar fits airtight, but comfortably, around the neck and intermittent suction, or alternating suction and pressure with precautions against excessive forces, are applied to the body within the chamber. The device finds its usefulness in maintaining artificial respiration for periods of days or weeks in cases of poliomyelitis with severe respiratory involvement. It has been used successfully in cases of neonatal apnea and atelectasis but appears to offer no considerable advantages over simple inhalation of oxygen and carbon dioxide in the easier cases of asphyxia of the new-born or over the Flagg technic in extreme cases. In the new-born the object is not, as in poliomyelitis, to supply prolonged artificial breathing but rather to get the child to breathing for itself.

The oxygen tents, now used in cases of pneumonia, have also possibilities of value, as yet undeveloped, as resuscitation apparatus, particularly in cases of extreme hemorrhage.

The lack of apparatus for measuring respiration is now one of the greatest deficiencies in medical technic. Measurement of respiration—in the sense of the volume of air breathed in liters per minute—is quite as important as a guide to prognosis and treatment in many disorders as is measurement of arterial pressure. The apparatus now used for determining basal metabolism could easily be modified to serve also as respirometers.

All subcutaneous, intravenous or intracardiac medication is harmful rather than beneficial in asphyxia.[18] Oxygen administered subcutaneously is absorbed too slowly to be helpful.[19]

CONFLICTING THEORIES OF ASPHYXIA[20]

In the development of resuscitation, practice has outrun theory. Resuscitation by means of carbon dioxide

11. The Mine Safety Appliances Company, Pittsburgh.
12. Davis Emergency Equipment Corporation, New York.
13. Ohio Chemical & Manufacturing Company, Cleveland.
14. Foregger Company, New York.
15. Report of the Commission on Resuscitation from Electric Shock, New York, National Electric Light Association, 1913. Report of the Committee on Resuscitation from Mine Gases, Technical Paper 77, U. S. Bureau of Mines, Washington, D. C., 1914. Work of the Commission on Electric Shock, editorial, J. A. M. A. **61**: 1637 (Nov. 1) 1913. Proceedings and Resolutions of the Third Resuscitation Commission, Science **48**: 563 (Dec. 6) 1918. Drinker, K. R.; Drinker, C. K., and Redfield, A. C.: J. Indust. Hyg. **6**: 109 (Aug.) 1923. Final Report of the Commission on Resuscitation from Carbon Monoxide Asphyxia, ibid. **6**: 125 (Aug.) 1923.
16. Warren E. Collins Company, Boston.
17. J. H. Emerson, Cambridge, Mass.
18. Henderson, Yandell: False Remedies for Carbon Monoxide Asphyxia, Science **78**: 408 (Nov. 3) 1933; Treatment of Carbon Monoxide Asphyxia, Current Comment, J. A. M. A. **102**: 217 (Jan. 20) 1934. Trautman, J. A.: Methylene Blue in the Treatment of HCN Gas Poisoning, Pub. Health Rep. **48**: 1443 (Dec. 1) 1933.
19. Singh, I.: Absorption of Oxygen from Subcutaneous Tissues, Quart. J. Exper. Med. **20**: 193, 1932.
20. A more detailed discussion and references to the extensive literature of the topics dealt with in this section are given in the papers quoted under reference 3.

is now justified mainly by the incontrovertible fact that in many forms of asphyxia this treatment is highly effective in saving life. But this fact is not greatly reinforced by theory. On the contrary, it has had to meet an extraordinary succession of obstacles in the form of adverse theories. Plausible theories are not easily refuted by facts unless the facts are reinforced by equally plausible alternative theories. In this case the principal obstructive theory is very plausible and very firmly intrenched; it is one of the foundations of modern biochemistry. The alternative theory is as yet crude and incomplete: a mere beginning for a sound conception of asphyxia.

When I [21] first proposed inhalation of carbon dioxide twenty-five or thirty years ago, the gaseous excretion, carbon dioxide, was still regarded as the physiologic opposite of oxygen. Its use in asphyxia or in any condition related to asphyxia, such as postoperative depression, was directly contraindicated. Asphyxia was considered to involve not only lack of oxygen but also excess of carbon dioxide and obstruction or stoppage of breathing. Investigations in this laboratory showed, on the contrary, that in carbon monoxide asphyxia there is excessive breathing and decrease of carbon dioxide. Low oxygen, low carbon dioxide and hypernea are concomitants in mountain sickness, in anesthetic depression and in other states related to asphyxia. In all such states, overbreathing and the development of a deficiency of carbon dioxide are among the conditions inducing the final depression and failure of respiration.

The demonstration by Haldane [22] and his collaborators of the preeminent part that carbon dioxide plays in the regulation of respiration in man facilitated the introduction of carbon dioxide as an agent by which anesthetists may control the breathing of patients under operation. But my advocacy of this use of carbon dioxide was based not merely on the control of breathing but to a greater extent on certain experimental observations on animals in this laboratory. These observations were that after anesthesia and operation the amount of carbon dioxide in the blood is diminished and that, contrariwise, conservation of the body's store of carbon dioxide largely counteracts postoperative depression of the circulation. The low carbon dioxide content of the blood was regarded as a form of acapnia.

Almost simultaneously, another theory [23] based on quite different grounds developed in biochemistry. Under that theory, as commonly interpreted and applied, inhalation of carbon dioxide after asphyxia or in any related condition would have been absolutely prohibited. It would intensify the acidosis that even a slight degree of asphyxia was supposed to induce.

This biochemical theory was beautifully clear and complete. It was based on the principles of physical chemistry. It afforded an apparently perfect theory of asphyxia and of acidosis. According to that theory, asphyxia develops as follows: Combustion in the tissues of the living body is first anaerobic; sugar breaks up into lactic acid. Under normal conditions, part of this lactic acid undergoes combustion; the remainder was supposed to be reconverted into sugar. Under oxygen deficiency, however, some of this lactic acid failed to be either burned or converted back to sugar. This acid then reacted with the alkali bicarbonates of the blood, neutralized them and thus decreased the carbon dioxide content and alkalinity of the blood. Asphyxia led to acidosis, and acidosis was acid poisoning.

In close accord with the requirements of this theory, it was demonstrated that a low p_H, low alkali bicarbonates and a considerable increase of lactic acid in the blood do occur in the terminal stage of asphyxia and of all related conditions. Biochemists therefore gave warning that inhalation of carbon dioxide, which is the anhydrous form of carbonic acid, must intensify asphyxial acidosis dangerously, perhaps even fatally.[20]

Faced with such opposition—then theoretically insurmountable—resuscitation by inhalation of carbon dioxide could be introduced only clinically, and lives thus saved by avoidance of theory. My discussions of practical means of resuscitation dealt strictly with facts. No well rounded alternative theory was—or is even now—available. With this suppression, inhalation of carbon dioxide was successfully introduced into the surgical field, where it soon proved its usefulness. Its success was complete in the nonmedical field of carbon monoxide asphyxia, where treatment is administered by the rescue crews of city fire departments and theory offered no obstacle.

The justification for such unconventional disregard of theory and the authorities lay strictly in facts. It was found in experiments on animals in this laboratory that so-called asphyxial acidosis differs profoundly from a true acid intoxication. The alkali of the blood is not lost from the body in asphyxia, nor is it permanently neutralized; it is merely rendered occult. Dogs that had been made truly acidotic by intravenous injection of dilute hydrochloric acid were quickly overwhelmed, or even killed, by inhalation of carbon dioxide. On the other hand, animals rendered pseudo-acidotic, or acarbic, by asphyxia were quickly restored to a normal condition by such inhalation. And at this point a fact was discovered that may afford a beginning for a sound theory of asphyxia. This fact is that inhalation of carbon dioxide, instead of intensifying "acidosis" in an acarbic animal or man, quickly recalls the alkali bicarbonates in the blood to their normal amount.[20] In this respect carbonic acid (i. e. carbon dioxide) differs from such acids as hydrochloric. The latter would kill at, or above, a point (p_H 7.0) to which the blood of an asphyxiated man, animal or new-born baby may be acidified with carbonic acid with no harm whatever during resuscitation.

This mobilization of alkali under the influence of carbon dioxide in the presence of oxygen is a vital reaction occurring not only in animals but even in plants, such as the potato. The contrary reaction occurs in men and animals during the development of asphyxia. Under deficiency of oxygen the carbon dioxide in the blood is also diminished; and following this diminution a considerable part of the blood alkali is somehow neutralized or immobilized. It is highly significant that this sequence occurs not only during the development of asphyxia under carbon monoxide but equally in the asphyxia of a baby before birth. The

21. Henderson, Yandell: Acapnia as a Factor in Shock, Brit. M. J. **2**: 1812, 1906; Fatal Apnea and the Shock Problem, Bull. Johns Hopkins Hosp. **21**: 235 (Aug.) 1910; Acapnia and Shock, Am. J. Physiol. **21**: 126 (Feb.) 1908; **23**: 345 (Feb.) 1909; **24**: 66 (April) 1909; **25**: 310, 385 (Feb.) 1910; **26**: 260 (June) 1910; **27**: 152 (Nov.) 1910. Henderson, Yandell, and Harvey, S. C. P., ibid. **46**: 533 (Aug.) 1918.

22. Haldane, J. S.: Respiration, New Haven, Conn., Yale University Press, 1922.

23. Henderson, L. J.: Blood, a Study in General Physiology, New Haven, Conn., Yale University Press, 1928. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company **1**: 868-1018, 1931.

former can lose carbon dioxide through the lungs; the latter cannot. The orthodox theory, which fails in respect to these matters, has failed also, it may be noted, in others. It has failed particularly in respect to the value of alkaline therapy in diabetic acidosis; and extensive revision has been needed in respect to the part supposedly played by lactic acid in muscular contraction. So fallible a theory should not be allowed longer to interfere with the saving of human life.

CONTRASTING INFLUENCES OF OXYGEN AND CARBON DIOXIDE [20]

Even when the obstacle of "acidosis" had been in practice largely surmounted, or at least circumvented, a third theoretical obstacle remained. Until quite recent years this imaginary "lion in the path" has blocked the application of carbon dioxide to what should be its most important field: resuscitation of the asphyxiated newborn. Surely—so it was argued—an asphyxiated baby or drowned adult must have already a supernormal respiratory stimulus in its blood. Because of the accumulated carbon dioxide, lowered p_H and increased lactic acid in its blood, it should not need any additional stimulus. How, then, could one justify administration of carbon dioxide in cases of asphyxia neonatorum?

It happened however that, in cities where inhalators were available, many babies were resuscitated by the rescue crews of the fire departments, called in by physicians after all the ancient procedures—slapping, swinging, and dipping in cold water—had failed. For a time even the hospitals invoked this aid. Now the large majority of hospitals are equipped with inhalational apparatus and cylinders of carbon dioxide diluted to various percentages in oxygen.

These facts forced a reconstruction of theory with the result that, in this laboratory at least, a conception that has been recently widely current in physiology was rejected. That conception was that the p_H of the respiratory center itself was the dominant factor in the control of breathing and that it is through this factor that both oxygen and carbon dioxide act.[23a] Instead, it was seen that the most practical conception of respiration requires a sharp distinction between the influences of oxygen and of carbon dioxide in the control of breathing. Neither oxygen nor oxygen deficiency acts as a stimulus. Instead, oxygen largely determines the sensitivity of the neurorespiratory system to its specific stimulus, which is carbon dioxide. Slight oxygen deficiency increases the sensitivity, so that even the normal amount of carbon dioxide affords an excessive stimulus, and hyperpnea results. On the other hand, extreme deficiency of oxygen diminishes the sensitivity and finally paralyzes the system. And the greater the depression of sensitivity, the stronger the stimulus required to excite respiration to activity. This is not a theoretical explanation; that is still to be developed. It is a practical statement of the unique effectiveness of high concentrations of carbon dioxide, up to 20 or even 30 per cent, in extreme cases of asphyxia neonatorum, while lower percentages are sufficient in all moderate cases.

After the presentation of these conceptions, the more important forms of asphyxia, and their characteristics in relation to resuscitation, may now be considered in some detail.

(To be continued)

23a. Gesell, R.: The Chemical Regulation of Respiration, Physiol. Rev. **5**: 551 (Oct.) 1925.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

DEXTROSE (See New and Nonofficial Remedies, 1934, p. 270).

The following dosage form has been accepted:

Ampoules Dextrose (d-Glucose) 50 Gm., 100 cc.: Each ampule contains dextrose (*d*-glucose) 50 Gm., in distilled water, to make 100 cc.

Prepared by the Lakeside Laboratories, Inc., Milwaukee. No U. S. patent or trademark.

DIPHTHERIA TOXOID, ALUM PRECIPITATED (REFINED) (See New and Nonofficial Remedies, 1934, p. 393).

United States Standard Products Company, Woodworth, Wis.

Diphtheria Toxoid, Alum Precipitated, Refined.—Prepared by treating diphtheria toxin with 0.3 to 0.4 per cent formaldehyde at temperatures of from 35 to 40 C. until its toxicity is reduced to the point where five human doses, injected into a guinea-pig, produce no symptoms of diphtheria poisoning. The toxoid is treated with a 4 per cent solution of potassium aluminum sulphate, the total amount of which is not to exceed 20 mg. per human dose of the finished product. The resulting precipitate is washed with sterile physiologic solution of sodium chloride and resuspended in physiologic solution of sodium chloride to which merthiolate (1: 10,000) has been added. The product is tested for antigenic potency according to the method prescribed by the National Institute of Health: guinea-pigs, weighing 500 Gm., given one human dose, must produce at the end of six weeks at least two units of diphtheria antitoxin in each cubic centimeter of blood.

Marketed in packages of one 1 cc. vial (one immunizing dose); in packages of ten 1 cc. vials (ten immunizing doses); and in packages of one 10 cc. vial (ten immunizing doses).

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

SQUIBB ADEX TABLETS 10-D NOT ACCEPTABLE FOR N. N. R. (II)

In 1932 the Council published a report on this product declaring it unacceptable because the application of a proprietary name to a cod liver oil concentrate with viosterol is not in the interest of the medical profession or the public (THE JOURNAL, March 19, 1932, p. 982). Subsequently the firm expressed a desire to meet the wishes of the Council in the matter of the name for this product and proposed the name "Squibb A and D EXT. Tablets 10-D." The product was then declared to be "a concentrated extract of the vitamins of Cod and Halibut Liver Oils with Viosterol." The firm was informed that the proposed name was not acceptable, since it is essentially a proprietary name differing from "Adex" only in spelling. The firm later proposed the name "Squibb Vitamin A and D Tablets." The Council could not recognize this name, because the product is not pure vitamins A and D; this name does not indicate whether the product is an extract or a concentrate. The firm has been informed, however, that the Council has voted to accept such products under the nonproprietary name "Tablets Vitamins A and D Concentrate" with the understanding that the label state the genesis of vitamins as well as the number of units from each source. Although the most recent available labels for Adex Tablets as well as the firm's proposed label for "A and D EXT. Tablets" declare the sources of the vitamins contained, none give the amount taken from each source.

After considerable correspondence, the firm informed the Council that since it would mean considerable loss to change the name "Adex" and to adopt a longer name in conformance with the Council's desire for a more informative designation, it had reluctantly decided to continue the name "Adex." The firm expressed the desire to adhere "in every other respect" to the rules of the Council concerning the marketing of this