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THE FAILURE TO REGAIN CONSCIOUSNESS AFTER GENERAL ANESTHESIA

FREDERICK P. HAUGEN, M.D.

"AN outstanding feature of anesthesia, as ordinarily seen, is the fact that the removal of the anesthetic from the blood restores the nervous system to its original activity without any appreciable damage." So wrote Henderson and Haggard in their monograph on noxious gases.[1] Although the exact mechanism of action of general anesthetics on the central nervous system has eluded scientists during the more than one hundred years of their widespread employment, all volatile agents in common use have this property of reversibility. If a patient fails to regain the state of awareness he possessed before the anesthetic was administered, the agent is not considered to be the cause unless gross overdosage has occurred. Some other factor, either associated with the administration of the drug, or existing independently of the anesthetic state, is held responsible for the prolongation of the central depression beyond its expected period of action. It will be the purpose of this review to explore these possible causes.

CONSCIOUSNESS AND ITS NEURAL SUBSTRATES

The word "consciousness" has various connotations to investigators in the different clinical and basic sciences.[2] In spite of our problems in semantics and communication, "consciousness" to the anesthesiologist may be assumed to be that state of alertness in which the patient is aware of his relationship in time and space, where he can demonstrate his awareness by communicating with those around him, and where he reveals memory of past events.

There are three propositions relative to the central nervous system that serve to direct thought along a line suitable to the discussion to follow.[3] The first is that mentation is a function of the brain. The second proposition is that the brain is an organ, and as such, is sensitive to alterations of the body's physiology. The third proposition is that whatever disturbs the body's equilibrium, be it mental or physical, chemical or molecular, tends to set in motion a chain reaction of readjustments in which the central nervous system plays an essential part.

There is a growing array of experimental findings to suggest that a fundamental mechanism of the central nervous system, essential in the complex transactions leading to readjustment, lies within that portion of the brain designated as the reticular formation. One of the earliest of the neuroanatomists to direct attention to this region was Allen,[4,5] who accumulated considerable evidence that the core area of the brain stem contained the main pathways for efferent visceral impulses to the spinal cord. He pointed out that its importance persisted in the advance from lower to higher vertebrate forms, having

Dr. Haugen is Professor of Anesthesiology, University of Oregon Medical School, Portland, Oregon.

served in the former as an effective mechanism enabling them to adapt themselves properly to their various inside and outside conditions. The concept upon which much of the present day investigation is based was presented in 1949 by Moruzzi and Magoun.[6] The waking state, up to that time, was thought to be largely due to the arousing influence at the cerebral cortex of afferent impulses evoked from sensory stimulation. This assumption, attributed generally to the writings of J. Hughlings Jackson, was based on the premise that the human nervous system was gradually developed, through evolution, in a series of functional levels.[7] The lowest of these extended from the cauda equina to and including the basal ganglia. The intermediate level was identified with the motor cortex, for Jackson considered the simple reflex as the functional unit from which all action patterns were built. The "highest and most voluntary" was represented by the frontal and occipital lobes. Disease processes attacked the highest level first, and then the lower ones in succession. This doctrine of levels has influenced much of the writing on action of general anesthetics up to the modern period.

Magoun and co-workers chanced upon the observation that direct electrical stimulation of the central portion of the brain stem could change a sleep pattern of an EEG to one of desynchronization seen in wakefulness. Magoun gave this alerting mechanism the name "ascending reticular activating system" (ARAS).[8] It is an interesting sidelight that the reason why the ARAS had been relatively unexplored previously was because the area was largely silent to electrophysiological exploration under conventional laboratory anesthetics. When chloralosane anesthesia or Bremer's *encéphale isolé* preparation was used, the significance of this area to the waking state became apparent.

The midbrain reticular formation is a very old area phylogenetically. To review briefly its development, it should be recalled that the neural tube in vertebrates is formed by an infolding of ectodermal cells along the dorsal aspect of the long axis of the embryo. The cells destined to become neurons are in an undifferentiated reticulum or network extending the entire length of the neural tube. Through a long process of evolution, the phenomenon of neurobiotaxis resulted in an aggregate of neurons at the mouth end of the body. In order that such a creature could correlate the sensory information arriving at this primitive brain from the specialized senses of smell, sight, sound, or touch, the various sensory nuclei had to be interconnected by numerous short chain neurons also developing from the primitive cells of the network. Inasmuch as the entire purpose of a sensory system is to permit an animal to produce a motor action appropriate to the stimulus,[9] it was important that the motor tracts were also interconnected within the reticulum. Such a primitive creature, if we could find a good representative, undoubtedly would have some type of awareness. It is here that there can be the beginnings of an argument as to what constitutes "consciousness." Some would find good cause to carry the phenomenon back to single-celled animals, but to better understand the ARAS it is convenient to begin the concept of awareness at this point of development. Such an animal would not have a thalamus or cerebral hemispheres—these were later evolvements, but it should be borne in mind that as evolution progressed, the thalamus and the cerebrum developed from the primitive brain described above. In the more efficient animals that resulted, connections with the basic brain persisted, and in the scale of evolution this region retained its importance as the mesencephalon or midbrain. It is certain from studies of lesions made in the midbrain structures that their intactness is essential to the maintenance of consciousness. Classical sensory pathways such as the spinothalamic or medial lemniscus send collaterals into the area even though their main "station" is in the thalamus. Descending tracts also send in collaterals. It has been shown that no amount of stimulation of such classical pathways will arouse an animal whose "core area" of the ARAS is destroyed.[10] It was mentioned earlier that this area was not active during deep general anesthesia, yet it has been demonstrated that the impulses traveling rostrally by way of the classical sensory pathways can be recorded at the cortex at that same depth of anesthesia.[11, 12] Such evidence would suggest that former concepts of levels of anesthesia

beginning with cortical depression and progressing downwards to older parts of the brain [13] are not in accord with what is now known.

Though the ARAS is recognized to be important to the maintenance of an awake state, it must not be assumed that the tremendous development of the cerebral hemispheres in man is unassociated with many facets of consciousness beyond a primitive awareness. Jasper's work on the diffuse thalamocortical projection system (DTPS) demonstrates how closely related these systems are.[14] Many studies now in progress on the psychological aspects of memory, motivation, and perception, are based on these two concepts. Further elaboration of this subject is beyond the scope of this review.

In summary, the return to consciousness following general anesthesia is a complex readjustment of central nervous system activity. Fundamental to a restoration of a basic awareness is the reactivation of the ascending reticular activating system, but beyond this much still remains to be learned of those areas important to memory, perception, and other attributes of the mind.

The Role of Hypoxia

The maintenance of a conscious state in man is dependent upon a variety of factors, but essential is a quantity of oxygen sufficient to supply the metabolic demands of the nervous system. In healthy young men, the brain utilizes an average of 3.3 ml./100 g./minute, or about one fifth of the oxygen consumption of the whole body.[15] Interruption of the transport of oxygen to the brain for more than a few seconds will cause alterations in neuronal behavior, and irreversible damage can occur in a matter of a few minutes. One of the earlier accounts of the effects of oxygen deprivation on central nervous system function was Glaisher's report of a balloon ascent in 1862.[16] The symptoms he described were primarily motor weakness, with retention of consciousness to about an altitude of 29,000 feet. Bert [17] in 1878 is credited with first furnishing positive experimental evidence that the effects experienced in such ascents were due to oxygen want alone, unassociated with changes in mechanical pressure or excessive loss of carbon dioxide. Haldane [18] has written an interesting account of his experiences with oxygen deprivation in a steel chamber in which oxygen tensions were changed by lowering barometric pressure. His partner in the experiment described his markedly altered consciousness, lack of awareness of his altered state, and finally evidence of unconsciousness. Such experiences have been repeated innumerable times in the development of aeronautics. Short exposures to oxygen want apparently do not result in persistent central nervous system changes. The seriousness of symptoms depends partly upon the length of time and partly upon the degree of reduced oxygen tension. Haldane also described the effects of a severe degree of hypoxia in men exposed to carbon monoxide or low oxygen tensions in a mine. Their failure to retain consciousness was accompanied by upper motor neuron symptoms of spasticity, convulsions, and opisthotonos. Every function of the central nervous system was concluded to be more or less affected.

The first of the anesthetic agents to become indicted as contributing to the severe central nervous system damage through asphyxia was nitrous oxide.[19] The differences of opinion as to whether nitrous oxide exerted a specific toxic action that limited or arrested normal oxidative processes within the central nervous system or whether it had a specific anesthetic action have served to draw attention to the importance of adequate oxygenation in all general anesthesia. In the modern era, Courville performed a notable service when he compiled a series of cases in which failure to regain or to retain consciousness occurred following nitrous oxide anesthesia. In a monograph on the subject [20] he pointed out that chronic oxygen deprivation, as commonly practiced at that time in the administration of nitrous oxide, followed by an acute episode of respiratory or circulatory failure, was the most common set of factors contributing to a state characterized by failure to regain consciousness, and often times progressing to death. His descriptions of gross and microscopic changes in the cerebral gray matter and basal ganglia are classics. Knowledge of the role of the midbrain in consciousness was lacking at the time of Courville's first studies,

but mention is made of changes in the reticular substance in a similar but smaller series reported by Lowenberg, Waggoner, and Zbinden.[21] The significance of such findings are, of course, open to conjecture. Hoff, Grenell, and Fulton, in a comprehensive review of the pathologic changes that occur in the nervous system as a result of anoxia, point out that the nerve cell damage is the same whatever the cause of the anoxia.[22]

Because of the recognized importance of adequate oxygenation to the safety of general anesthesia, the administration of mixtures of gases containing less oxygen than found in air is no longer considered good practice. There are, however, other factors that may contribute to an hypoxic state. Barcroft, using the term "anoxia," recognized three situations that could pertain to general anesthesia.[23] The first he called the anoxic type in which the arterial blood is insufficiently saturated. The anemic type was present when the oxygen capacity of the blood was abnormally low. The ischemic type resulted when the quantity of circulating blood was less than normal. A fourth type, sometimes in the past thought to be a factor in nitrous oxide anesthesia, was called histotoxic anoxia because the tissues could not utilize the oxygen supplied them. Through the years Barcroft's classification has become standard, but a more usable classification of inadequate oxygenation based on cause has been devised by Comroe and Dripps,[24] and serves to remind the anesthetist of the variety of conditions which may influence the management of the anesthesia period. If a patient fails to regain consciousness when anesthesia is discontinued, the diagnosis of the cause is important to the treatment. Of primary importance in evaluating the situation is the past medical history of the patient, particularly in regard to metabolic and cardiovascular diseases, and the accuracy of the anesthetist's observations of the minute to minute changes in the respiratory and circulatory systems. If uncomplicated hypoxia is the cause of the prolongation of unconsciousness, the attentive anesthetist should be able to point out at what period during the anesthesia the damage to the nervous system occurred. As the hours pass by, the characteristic picture of muscle twitchings or convulsions, hyperthermia, and gradual deterioration of functions makes it apparent that the nervous system has undergone a period of oxygen deprivation.

In the gray zone between very minor manifestations of postoperative depression and the major disasters, predictions as to the outcome may be aided by the use of electroencephalography. Grönqvist, Seldon, and Fauleoner[25] studied six patients who experienced cerebral anoxia. Two patients who survived showed considerable EEG activity in the initial tracings, but the fatal cases showed almost a flat line, or very low amplitude, high frequency sharp waves, which they term "file patterns." Bellville and Howland[26] believe that recovery from hypoxia is unlikely if an encephalographic tracing has continued to be flat for more than four hours. There is, they state, a direct relationship between the time a flat tracing persists and the time required, after correction of the hypoxia, for the electroencephalogram to return to normal.

Treatment of patients who have undergone a significant hypoxic episode, apart from general supportive measures, is aimed at reducing cerebral edema and lowering the oxygen requirements of the brain by hypothermia. Three main methods of treating edema are described in the literature, and consist of using concentrated sucrose solutions, serum albumin,[27] or urea.[28] A more recent adjuvant to therapy has been the use of hypothermia.[29] There seems to be general agreement that cooling to 31–34 C. is optimal. Most patients who recover show some improvement during the first 24–48 hours. Supportive therapy directed towards maintenance of a clear airway, with particular care to avoid accumulation of CO_2, is stressed.

In summary, it is reasonable to assume from the volume of literature on the subject that hypoxia is the most frequent precipitating cause of the failure to regain consciousness after general anesthesia. The hypoxia may occur as an acute or chronic episode, or as a combination of the two. It may have its origin in either an inadequate supply of oxygen to the alveoli, or to a disorder of oxygen transport within the circulatory system. Accurate observation of the patient throughout the anesthesia period constitutes the best

diagnostic tool in differentiating causes of prolonged unconsciousness. The electroencephalograph is useful in evaluating the degree of central damage. Reduction of brain edema and hypothermia are considered to be valuable in treatment.

The Role of Carbon Dioxide Excess

The narcotizing properties of carbon dioxide were demonstrated by Hickman [30] in the early years of the nineteenth century, and later by Snow.[31] Sir James Simpson [32] in 1856 wrote "Carbon dioxide is usually recognized by toxicologists as a very powerful narcotic poison when inhaled in sufficient quantity." Haldane and Smith [33] in brilliant experiments established that when the carbon dioxide content of a rebreathing apparatus reached about 10 per cent they had to stop inhalation because the effect of the mixture was to produce distress and stupefaction, whether oxygen was added or not. Later Haldane states "The effects of excess of carbon dioxide in producing ataxia, stupefaction, and loss of consciousness has become very familiar to me in connection with mine rescue apparatus and diving apparatus. These effects are readily produced in the presence of a large excess of oxygen, and are therefore quite independent of the effects of want of oxygen. The narcotic effect of a large excess of carbon dioxide quiets down the respiration, and this effect in animals led many previous observers to overlook almost entirely the ordinary effects of carbon dioxide in stimulating the breathing." [34] Brown [35] was of the opinion that an individual could not inhale 10 per cent carbon dioxide for longer than ten minutes without losing consciousness. Barcroft states "On occasion on which we were in 10 per cent carbon dioxide I was, when I came out, retaining my grip of things only with an effort. Margaria and I agreed on two things, firstly that we did not want to repeat this experiment unless there was some good reason for doing so, and secondly that our reluctance was due to our unwillingness to expose the higher parts of our brain to the influence of so much carbonic acid." [36]

With such general agreement on the effects of carbon dioxide excess on the nervous system, it is interesting that anesthetists in this country were influenced to use it freely during induction, maintenance, and emergence from anesthesia. Henderson, who wrote and spoke so enthusiastically of the value of inhaling mixtures of carbon dioxide and oxygen, certainly could not have foreseen the extremes to which his ideas were applied.[37] Lundy, who advocated a five per cent carbon dioxide mixture during general anesthesia cautioned that too much carbon dioxide was worse than none, and that care should be exercised not to exceed the recommended percentage.[38] Waters, writing in 1927 on the place of carbon dioxide in anesthesia, showed restraint in saying "Fortunately, and unfortunately, the researches in carbon dioxide of the New Haven school of physiologists have entered the literature of anesthesia in the past decade: fortunately, because researches are brilliant and have taught us many facets of the greatest importance; unfortunately, because the facts have been made use of by practical anesthetists in some quarters to make easy their work without sufficient investigation as to what by-effects may accompany the altered physiology which their methods induce." [39]

It is difficult to trace the origins of the concept that carbon dioxide excess could delay awakening from anesthesia. The carbon dioxide absorption system Waters popularized to combat the misuse of CO_2 in anesthesia probably was responsible for many observations that have led to a general acceptance of the role of hypercarbia in central nervous system dysfunction. The theory of Henderson that most ills from anesthesia could be cured by carbogen mixtures was slow to be discarded. In one of his many papers on the subject, Waters [40] wrote of a case reported to him of obvious carbon dioxide excess, unrecognized by the anesthetist, manifesting itself by severe convulsions which were interpreted to be anoxemic in etiology. The treatment had been to administer a mixture of carbon dioxide and oxygen until shortly before the death of the patient. The anesthetist had commented that in reviewing the treatment of the convulsions, the patient had seemed to be improved when the breathing bag had been emptied and refilled with oxygen a few times!

In the decade or so when the closed system was enjoying widespread popularity much attention was paid to respiratory and circulatory signs that would indicate an accumulation of carbon dioxide. Observations that relaxation was not as marked as that seen in comparable depth of anesthesia with a well-conducted semiclosed or open system of anesthesia pointed to alterations in reflex activity, and indicated that all problems of carbon dioxide excess were not being solved. It was accepted that the apnea technique of administering cyclopropane produced better muscle relaxation at a lighter plane of anesthesia than when it was not employed. The success of Guedel [41] in employing high concentrations of cyclopropane to produce marked abdominal relaxation was undoubtedly due in large measure to hyperventilation, and his claims of freedom from evidence of myocardial irritability could be ascribed partially to a lowered P_{CO_2}.

During this same period, inhalation therapy for respiratory diseases was having a renaissance. In his monograph on the subject, Barach [42] mentioned the possibility of retained carbon dioxide contributing to coma in certain cases of emphysema undergoing oxygen therapy. However, the idea could not have been prevalent at that time (1944) because he considered the primary cause of the coma to be due to the sudden change in oxygen tension in the brain as a result of inhalation of an atmosphere of high oxygen content, and he recommended that a gradual application of the oxygen would obviate the development of unconsciousness.

Dripps and Comroe,[43] studying circulatory and respiratory responses to inhaling 7.6 and 10.4 per cent carbon dioxide, verified earlier studies attesting to narcotic effects. They suggested that it was probable that inhalation of high concentrations of CO_2, in the treatment of individuals with depressed medullary centers due to anesthesia, would produce further narcosis. Baldwin, Cournand, and Richards made the observation that in some cases of emphysema, inhalation of 100 per cent oxygen resulted in further depression of ventilation, with retention of CO_2 (90–100 volumes per cent) and increasing acidosis. Coma might develop as the oxygen tension in arterial blood increased, because as stimulation of the carotid body was reduced, hypoventilation supervened.[44] Donald [45] studied a patient with severe emphysema who lapsed into coma after twelve hours of oxygen therapy, at which time his P_{CO_2} was 120 mm. of mercury. After withdrawal of the oxygen he recovered rapidly with an abrupt fall in his P_{CO_2}, even though he had become intensely cyanotic before consciousness returned. In 1950, Comroe *et al.*,[46] investigating mental changes occurring in chronically anoxemic patients during oxygen therapy, concluded that the causes of the changes were not certain, but carbon dioxide narcosis was a good possibility. They postulated that patients with chronic anoxemia might be more susceptible to the depressant effects of high concentrations of carbon dioxide which might develop as a result of diminished tidal and minute volume when oxygen was administered.

The concept that carbon dioxide narcosis can develop in cases with reduced alveolar ventilation has become well established.[47, 48, 49] It also has become generally recognized that hypoventilation resulting from drugs used in the conduct of anesthesia can produce prolongation of unconsciousness due to the same cause.[50, 51, 52] It would appear that a P_{CO_2} of 90 mm. of mercury or more and a *p*H of 7.25 or less are important findings in establishing such a diagnosis.[53] Recent attempts to treat respiratory acidosis with acetazolamide have not been encouraging.[54] Sodium bicarbonate solutions require large volumes over a long period of time. Trihydroxymethylaminomethane (THAM) shows some promise [55, 56] as an organic carbon dioxide buffer, but the literature does not contain sufficient evidence of its value as yet. Hyperventilation of the patient can be accomplished by several methods, but caution must be used to avoid too rapid a change in the alveolar CO_2 because of the danger of hypotension and arrhythmias.[57, 58, 59]

In summary, carbon dioxide narcosis resulting from hypoventilation is an important cause of failure to regain consciousness after general anesthesia. Its diagnosis depends upon findings of an increased P_{CO_2} and a lowered *p*H. Treatment at present consists mainly in a gradual reduction in the alveolar CO_2 by hyperventilation, although organic buffers may

prove to be helpful in prevention as well as treatment.

The Role of the Anesthetic Agents

The volatile anesthetic agents, even when used to excess, are rarely responsible for alarming delay in the return to consciousness. However, combinations of factors may be present in any given case which will result in an undue prolongation of the anesthesia period. Complete tissue saturation with lipid-soluble agents in patients who have had large dosages of narcotics or barbiturates may be such a circumstance. Surgical shock or hypotension from any cause are significant factors in a delay of recovery. Operations involving the lung, or pathology within its structure, may decrease gaseous exchange to an alarming degree. Dundee has reported cases of prolonged unconsciousness following anesthesia in cases of drug-induced adrenocortical insufficiency,[60] or when replacement therapy had been inadequate in Addison's disease. Morss and Baillie report a case of prolonged unconsciousness and respiratory insufficiency following 500 mg. thiopentone and 35 mg. *d*-tubocurarine in an elderly patient which was reversed following the administration of 100 mg. hydrocortisone.[61] The widespread use of tranquilizers of various molecular derivations has been, and will continue to be, a factor in causing unusual reactions to anesthetic agents. The derivatives and analogues of phenothiazine have been particularly involved in a variety of central nervous system disorders. A case has been reported [62] in which a fatal reaction occurred in a 19 year old in the immediate postanesthetic period following a single intramuscular injection of 5 mg. of perphenazine.

The short acting barbiturates commonly used in intravenous anesthesia constitute a group of agents with problems peculiar to the body's capacity for detoxication. In the early days of their use as the sole anesthetic, excessive dosages resulted in a greatly retarded recovery. In modern anesthesia the anesthetist is less apt to be guilty of flagrant overdosage. However, he will find instances when apparent sensitivity to the drug, or failure of the normal metabolizing processes will be responsible for prolonged unconsciousness. Although the liver is very important in the breakdown of this group of drugs, the paucity of reports of delay in detoxication in known liver disease would indicate that a severe degree of damage must be present to be responsible for retardation of recovery, or an unusual amount of the thiobarbiturate must have been given. The fate and distribution of thiopental is well documented by Price.[63] Dundee [64] considers that interference with the distribution of the drug to non-nervous tissues is the leading cause of a prolonged duration of action. Dean, in discussing the sensitizing properties of the barbiturates in precipitating acute symptoms of porphyria, describes several cases of paralysis brought on by the use of thiopental in the course of anesthesia.[65] In one of the cases described, a young woman was delirious for several days after a small amount of the drug, and later became paralyzed. Two years later an identical episode occurred following a dental extraction under thiopental. Tests for porphyria were positive.

In summary, it would appear that the possibilities of the involvement of anesthetic agents with unusual circumstancees existing in the patient are almost unlimited in their potentialities for interfering with the return of normal central nervous system functions.

Miscellaneous Factors

Cerebrovascular accidents, hypoglycemia, metabolic acidosis, uremia, air embolism, and many of the other causes of coma encountered in medical practice may be associated with the anesthesia period, but as a rule, are only indirectly related to the administration of the anesthetic. Of these, cerebral thrombosis or hemorrhage are encountered most frequently. It is generally conceded that stellate ganglion block is of no value and may be harmful if intracranial bleeding has occurred. Opinion still is divided as to its value in cases of thrombosis. Many cases of at least temporary improvement in awareness have been observed over the years, and the possibilities of gain justify the block, at least in these cases where anesthesia is involved. Cerebral air embolism is rarely encountered apart from open heart surgery, but it must be considered an im-

portant factor in the failure to regain consciousness in this group of patients. The effects are essentially those of hypoxia, and should be treated in the same way.

The effect of marked changes in electrolyte balance on postoperative responsiveness has been recognized in recent years. Bartholomew and Scholz [66] described five cases in which water intoxication and sodium depletion resulted in acute neurological symptoms, including coma, during the postoperative period. All their patients were in the older age group, and although the symptoms did not occur in association with recovery from anesthesia, it is entirely possible that they could develop then. The authors point out that the widespread use of diets containing small amounts of sodium, plus the use of excessive amounts of nonelectrolytic solutions such as 5 per cent dextrose in water, may cause water intoxication to occur. A serum sodium value reduced to less than 120 mEq. per liter was usually found. The treatment in cases of severe degree is a judicious use of hypertonic solutions of sodium chloride (300 ml. of a 3 to 5 per cent concentration).

Infants may show a central depression for a considerable length of time if their body temperature is permitted to fall below 97 F., according to Hackett and Crosby.[67] They believe this is due to the increased solubility of anesthetic gases and vapors as the body temperature falls, resulting in an increased content of the agent in the tissues. It is urged that the body temperature of infants be kept near to normal unless hypothermia is deliberately planned.

Hysteria or a catatonia-like state may be confusing sequelae of anesthesia, particularly likely to be seen after a short, light administration. It should be suspected when all physical findings are normal. Usually painful stimulation will bring a slight change in facial expression or a fluttering of the eyelids.

Conclusion

The mechanism of action of anesthetic agents still is unknown, but evidence is accumulating to indicate that certain areas of the central nervous system are more susceptible to their action than other areas, and that an area in the midbrain is involved in consciousness or awareness. The leading cause of failure to regain consciousness after anesthesia is an episode of hypoxia. This may occur from a variety of causes, and may vary from a slight delay in the return to the awake state to a condition characterized by coma, convulsions, and death.

Considerable space is given to a discussion of carbon dioxide excess because modern methods of administering general anesthesia employing the barbiturates, narcotics, and relaxants tend to make hypoventilation during the emergence period a more likely occurrence than with the older agents and methods.

Other causes of failure to regain consciousness within a reasonable time after anesthesia are discussed briefly. To fulfill his obligation to the patient the modern anesthesiologist must now, more than ever before, be a keen and discerning clinician.

References

1. Henderson, Y., and Haggard, H. W.: Noxious Gases. New York, The Chemical Catalog Co., 1927, p. 146.
2. Abramson, H. A. (editor): Problems of Consciousness. New York, Corlies, Macy & Co., 1950–54 (5 vol.).
3. Livingston, W. K., Haugen, F. P., and Brookhart, J. M.: Functional organization of central nervous system, Neurology 4: 485, 1954.
4. Allen, W. F.: Origin and destination of secondary visceral fibers in guinea-pig, J. Comp. Neurol. 35: 275, 1923.
5. Allen, W. F.: Formatio reticularis and reticulospinal tracts, J. Wash. Acad. Sc. 22: 490, 1932.
6. Moruzzi, G., and Magoun, H. W.: Brain stem reticular formation and activation of EEG, Electroenceph. Clin. Neurophysiol. 1: 455, 1949.
7. Jackson, J. H.: On relations of different divisions of central nervous system to one another and to parts of body, Lancet 1: 79, 1898.
8. Magoun, H. W.: Ascending reticular activating system, Proc. Ass. Res. Nerv. Ment. Dis. 30: 480, 1950.
9. Sperry, R. W.: Neurology and the mid-brain problem, Am. Scientist 40: 291, 1952.
10. Lindsley, D. B., Schreiner, L. H., Knowles, M. S., and Magoun, H. W.: Behavioral and EEG changes following chronic brain stem lesions in cat, Electroenceph. Clin. Neurophysiol. 2: 483, 1950.
11. French, J. D., Verzeano, M., and Magoun, H. W.: Neural basis of anesthetic state,

A. M. A. Arch. Neurol. Psychiat. 69: 519, 1953.
12. King, E. E.: Differential action of anesthetics and interneuron depressant upon EEG arousal and recruitment responses, J. Pharmacol. Exp. Ther. 116: 404, 1956.
13. Etsten, B., and Himwich, H. E.: Stages and signs of Pentothal anesthesia: physiologic basis, ANESTHESIOLOGY 7: 536, 1946.
14. Jasper, H. Diffuse projection systems: Integrative action of thalamic reticular system, Electroenceph. Clin. Neurophysiol. 1: 405, 1949.
15. Kety, S. S., and Schmidt, C. F.: Nitrous Oxide method for quantitative determination of cerebral blood flow in man, J. Clin. Invest. 27: 476, 1948.
16. Glaisher, J.: Notes of effects experienced during recent balloon ascents, Lancet 2: 559, 1862.
17. Bert, P.: La pression barometrique. Recherches de physiologic experimentale Pario: Masson, 1878, 1168.
18. Haldan, J. S.: Respiration. New Haven, Yale University Press, 1922, p. 126.
19. Hewitt, F. W.: Administration of definite mixtures of nitrous oxide and oxygen, Lancet 1: 444, 1899.
20. Courville, C. B. Untoward Effects of Nitrous Oxide Anesthesia. Mountain View, Calif. Pacific Press, 1939.
21. Lowenberg, K., Waggoner, R., and Zbinden, T.: Destruction of cerebral cortex following nitrous oxide anesthesia, Ann. Surg. 105: 801, 1936.
22. Hoff, D. C., Grenell, R. G., and Fulton, J. F.: Histopathology of central nervous system after exposure to high altitudes, hypoglycemia, and other conditions associated with central anoxia, Medicine 24: 161, 1945.
23. Barcroft, J.: Features in the Architecture of Physiological Function. New York, The Macmillan Co., 1934, p. 216.
24. Comroe, J. H., Jr., and Dripps, R. D.: The Physiological Basis for Oxygen Therapy. Springfield, Illinois, Charles C Thomas, Publisher, 1950, pp. 19–22.
25. Grönqvist, Y. K. J., Seldon, T. H., and Faulconer, A. J., Jr.: Cerebral anoxia during anesthesia, Ann. chir. gynaec. Fenn. 41: 149, 1952.
26. Bellville, J. W., and Howland, W. S.: Prognosis after severe hypoxia in man, ANESTHESIOLOGY 18: 389, 1957.
27. Seldon, T. H., Faulconer, A., Jr., Courtin, R. F., and Pino, D. M.: Postanesthetic encephalopathy: postulation of cerebral edema as a basis for rational treatment, Proc. Mayo Clin. 24: 370, 1949.
28. Javid, M.: Urea—new use of an old agent, Surg. Clin. N. Amer. 38: 907, 1958.
29. Sedzimir, C. B.: Therapeutic hypothermia in cases of head injury, J. Neurosurg. 16: 407, 1959.
30. Keys, T. E.: Development of anesthesia, ANESTHESIOLOGY 2: 552, 1941.
31. Foregger, R.: John Snow's early research on carbon dioxide, ANESTHESIOLOGY 21: 20, 1960.
32. Simpson, J.: Quoted by Waters, R. M.: Toxic effects of carbon dioxide, New Orleans Med. Surg. J. 90: 219, 1937.
33. Haldane, J. S., and Smith, J. L.: Physiological effects of air effects of air vitiated by respiration, J. Path. Bact. 1: 168, 1892.
34. Haldane, J. S.: Respiration. New Haven, Yale University Press, 1922, p. 16.
35. Brown, E. W.: Physiological effects of high concentrations of carbon dioxide, U. S. Naval Med. Bull. 28: 523, 1930.
36. Barcroft, J.: Features in the Architecture of Physiological Function. New York, Macmillan Co., 1934, p. 84.
37. Henderson, Y.: Adventures in Respiration. Baltimore, Williams & Wilkins Co., 1938, p. 25.
38. Lundy, J. S.: Carbon dioxide as aid in general anesthesia, J. A. M. A. 85: 1953, 1925.
39. Waters, R. M.: Carbon dioxide, its place in anesthesia, Canad. Med. J. 17: 1510, 1927.
40. Waters, R. M.: Toxic effects of carbon dioxide, New Orleans Med. Surg. J. 90: 219, 1937.
41. Guedel, A. E.: Cyclopropane anesthesia, ANESTHESIOLOGY 1: 13, 1940.
42. Barach, A. L.: Inhalational Therapy. Philadelphia, J. B. Lippincott Co., 1944, pp. 128–129.
43. Dripps, R. D., and Comroe, J. H., Jr.: Respiratory and circulatory response of normal man to inhalation of 7.6 and 10.4 per cent CO_2, Amer. J. Physiol. 149: 43, 1947.
44. Baldwin, E. deF., Cournand, A., and Richards, D. W., Jr.: Pulmonary insufficiency: study of 122 cases of chronic pulmonary emphysema, Medicine 28: 201, 1949.
45. Donald, K.: Neurological effects of oxygen, Lancet 2: 1056, 1949.
46. Comroe, J. H., Jr., Bahnson, E. R., and Coates, E. O., Jr.: Mental changes occurring in chronically anoxemic patients during oxygen therapy, J. A. M. A. 143: 1045, 1950.
47. Westlake, E. K., Simpson, T., and Kaye, M.: Carbon dioxide narcosis in emphysema, Quart. J. Med. 24: 155, 1955.
48. Motley, H. L.: Oxygen in comatose states, Bull. N. Y. Acad. Med. 26: 479, 1950.
49. Sieker, H. O., and Hickham, J. B.: Carbon dioxide intoxication: clinical syndrome, its etiology and management with particular reference to use of mechanical respirators, Medicine 35: 389, 1956.

50. Scurr, C. F.: Carbondioxide retention simulating curarization, Brit. Med. J. 1: 565, 1954.
51. Campbell, D.: Carbon dioxide narcosis following thoracoplasty. Case report, Anaesthesia 14: 331, 1959.
52. Young, T. M., and Mendel, D.: Acidotic coma, Anaesthesia 14: 366, 1959.
53. Sieker, H. O., and Hickham, J. B.: Acidotic coma. Medicine 35: 389, 1956.
54. Galdston, M.: Respiratory and renal effects of carbonic anhydrase inhibitor (Diamox) on acid-base balance in normal man and in patients with respiratory acidosis, Amer. J. Med. 19: 516, 1955.
55. Nahas, G. G.: Use of organic carbon dioxide buffer in vivo, Science 129: 782, 1959.
56. Manfredi, F., Sieker, H. O., Spoto, A. P., and Saltzman, H. A.: Severe carbon dioxide intoxication: treatment with organic buffer (trihydroxymethylaminomethane), J. A. M. A. 173: 999, 1960.
57. Dripps, R. D.: Immediate decrease in blood pressure seen at conclusion of cyclopropane anesthesia: "cyclopropane shock," ANESTHESIOLOGY 8: 15, 1947.
58. Schultz, M. D., Buckley, J. J., Oswald, A. J., and Van Bergen, F. H.: Profound acidosis in anesthetized human: report of case, ANESTHESIOLOGY 21: 285, 1960.
59. Brown, E. B., Jr., and Miller, F. A.: Ventricular fibrillation following rapid fall of alveolar carbon dioxide concentration, Amer. J. Physiol. 169: 56, 1952.
60. Dundee, J. W.: Anesthesia and surgery in adrenocortical insufficiency, Brit. J. Anaesth. 29: 166, 1958.
61. Morss, H. L., and Baillie, T. W.: Case of postoperative respiratory insufficiency and prolonged unconsciousness, Brit. J. Anaesth. 30: 19, 1959.
62. Questions and Answers: Severe and fatal reactions to tranquilizers, J. A. M. A. 172: 1872, 1960.
63. Price, H. L.: Dynamic concept of distribution of thiopental in the human body, ANESTHESIOLOGY 21: 40, 1960.
64. Dundee, J. W.: Thiopentone and other Thiobarbiturates. Edinburgh and London, E. & S. Livingston Ltd., 1956, p. 125.
65. Dean, G.: Porphyria, Brit. Med. J. 2: 1291, 1953.
66. Bartholomew, L. G., and Scholz, D. A.: Reversible postoperative neurological symptoms. (Report of five cases secondary to water intoxication and sodium depletion.) J. A. M. A. 162: 22, 1956.
67. Hackett, P. R., and Crosby, R. M.: Some effects of inadvertent hypothermia in infant neurosurgery, ANESTHESIOLOGY 21: 356, 1960.

PULMONARY EDEMA The effects of positive pressure breathing, intravenous aminophylline, and intravenous morphine have been assessed in six patients with acute pulmonary edema. Pulmonary compliance rose acutely by an average of 36 per cent during positive pressure breathing. Positive pressure produced no consistent change in pulmonary resistance. Intravenous aminophylline produced significant acute increases in pulmonary compliance and prompt decreases in pulmonary resistance. Intravenous morphine had no significant effect on either pulmonary compliance or pulmonary resistance in patients with acute pulmonary edema. (*Sharp, J. T., and others: Effect of Therapy on Pulmonary Mechanics in Human Pulmonary Edema, J. Clin. Invest. 40: 665 (Apr.) 1961.*)

THORACIC SCOLIOSIS In 14 patients with severe thoracic scoliosis the maximum breathing capacity was found to be below normal, but the arterial oxygen saturation was lower than would be expected from alveolar hypoventilation alone. Total lung capacity was also reduced. Those with chronic bronchitis had a marked increase in airway resistance. All had abnormalities in the distribution of blood and gas flow throughout the lungs and to this the hypoxemia was ascribed. (*Shaw, D. B., and Read, J.: Hypoxia and Thoracic Scoliosis, Brit. Med. J. 2: 1487 (Nov. 19) 1960.*)