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THE HAZARD OF ANOXIA DURING NITROUS OXIDE ANESTHESIA * †

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IN THE following discussion, it is proposed (1) to review the extent to which asphyxia has been used and advocated as an adjunct to nitrous oxide anesthesia, (2) to establish that death and psychotic disease have resulted from anoxic nitrous oxide anesthesia, and (3) to criticize the deliberate use of anoxia as unphysiological, dangerous to life and mental health, without justification in anesthetic practices and, finally, to remonstrate against its continued recognition in clinical practice or student instruction.

Historical

When Joseph Priestley, more than 170 years ago, heated iron filings that had been treated with nitrous air, he obtained nitrous oxide, a gas destined to play a unique role in medicine. Humphry Davy used the gas to inaugurate his brilliant investigations in pharmacology. He pointed out that "the gas (nitrous oxide) may probably be used with advantage during surgical operation" (1). The provincialism of the medical profession of that time (1800) allowed more than forty years to pass before nitrous oxide again played a dominant role in medical history when Horace Wells introduced it as an anesthetic agent for exodontia. For more than a century thereafter, nitrous oxide has main-

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† The term anoxia as used in this manuscript is interpreted as it is generally used now. Waters (17) has pointed out properly that by derivation anoxia means without oxygen and has suggested "hypoxia" a better word for oxygen want or oxygen deficit.

tained an important place in clinical anesthesia and today is administered probably to more individuals each year than any other inhalation agent. Throughout its long story are many incidents that highlight its present prominence. Although Wells was not successful with it, Colton, the itinerant chemist who introduced it to him, was responsible for many thousands of administrations without a death in his "painless dental parlors" (2). Through the American dentist, Evans, who maintained a large practice in Paris, Colton brought nitrous oxide to Europe. It soon became the favorite dental anesthetic agent and was given to many thousands of patients.

At the beginning of the next century, it was hailed by Hewitt, the recognized European leader in this field, as "the safest anesthetic agent known" (3). This record was established without the advantage of refined apparatus and often without the use of oxygen. Oxygen mixtures were first recommended by the Chicago surgeon Andrews in 1868 (4). His advice, long since forgotten, was founded on experiments with rats and clinical observations on his own patients as well as those of friends in the dental profession. The mixtures most successfully used were one-fifth oxygen and four-fifths nitrous oxide. Before Andrews, it was generally believed that the body could in some way split off and utilize the oxygen of the nitrous oxide molecule. Paul Bert, who also added oxygen to nitrous oxide, gave mixtures "containing five-sixths nitrous oxide and one-sixth oxygen under pressure of one-fifth above atmospheric" to patients in a closed chamber (5). Bert's work served to confirm the argument in favor of the positive anesthetic property of the gas, but the method was costly and cumbersome and gained no place in practical anesthesia.

In 1886, Hewitt, experimenting with definite proportions of nitrous oxide and oxygen, found that anesthesia could be maintained with nitrous oxide when given with a concentration of oxygen equal to that in atmospheric air (3). The time required for induction was increased but the period of available anesthesia was proportionately prolonged. Finally, he recommended a 7 per cent oxygen mixture which gave a rapid induction and an available anesthesia for fifty seconds. It is unlikely that Hewitt made this recommendation of a 7 per cent oxygen mixture for a dental anesthesia of less than one minute with the remotest idea that it would be adopted for operations lasting more than an hour.

From the time of its first use, procedures for the convenient administration of nitrous oxide have developed progressively. Preparation of the gas compressed in metal cylinders, construction of ingenious apparatus for its administration, the introduction of rebreathing and the carbon dioxide absorption technic, together with many safety accessory appliances have been a part of the nitrous oxide story.

The Advocacy and Teaching of Anoxia in Nitrous Oxide Anesthesia

A great impetus to nitrous oxide-oxygen anesthesia in this country was the work of Teter, who developed a very popular gas-oxygen apparatus. Working with Crile in Cleveland, and enthusiastically endorsed by him, Teter was soon able to influence the trend of nitrous oxide-oxygen anesthesia and to be responsible for the sale of a thousand gas machines by 1915, although there were fewer than one hundred professional anesthetists in this country at that time. Every machine carried instructions which recommended a 5 to 10 per cent oxygen mixture, disregarded cyanosis, and endorsed a state of anoxemia as essential to gas anesthesia (6).

In 1911, McKesson introduced the principle of fractional rebreathing into gas anesthesia. He developed and manufactured apparatus which provided conveniences not previously available with earlier machines for gas administration. More significantly, he proposed, practiced, and taught new but potentially hazardous technic for using nitrous oxide in major as well as minor surgery. McKesson's most radical departures from the recommendations of Hewitt, Andrews and others were firstly, induction of anesthesia with undiluted nitrous oxide, and secondly, the saturation technic.

In inducing anesthesia with 100 per cent nitrous oxide, McKesson and his followers admit that asphyxia is produced but insist it is of little consequence, since the appearance of signs of severe oxygen want would indicate the need for oxygen, and then a low concentration of oxygen (5 to 10 per cent) was to be added. Thereafter, the patient is given all the oxygen that can be administered without permitting anesthesia to become ineffective for completion of the surgical procedure. In practically all instances, except for the aged, those with reduced resistance from disease, and those given generous amounts of sedative drugs before induction, anesthesia is maintained with considerably less than 20 per cent oxygen in the respired mixtures.

When saturation is practiced, 100 per cent nitrous oxide is continued to the point of profound asphyxia and finally, respiratory arrest. At this point or immediately before, if the pulse becomes irregular or very slow, oxygen is given under pressure sufficient to inflate the lungs. This prevents the immediate resumption of breathing, and before spontaneous respirations recur, muscles become relaxed. After the single inflation of the lungs with oxygen, an anesthetic mixture is provided which, experience suggests, may be needed, depending upon the operation and the patient. When this mixture is inadequate to maintain relaxation, the asphyxial procedure is repeated as a secondary saturation.

Many anesthetists, and others who administer anesthesia without physiological training, have accepted McKesson's teaching. The saturation and secondary saturation technics are not practiced extensively but the rapid induction with 100 per cent nitrous oxide is popular. The

fear of serious consequences from asphyxia during nitrous oxide anesthesia has been minimized, since temporary bouts of severe asphyxia or the presence of moderate or severe anoxia has not been generally understood as representing an extremely grave hazard.

Clinical Results from the Use of Anoxia during Nitrous Oxide Anesthesia

The morbidity and mortality following the use of nitrous oxide for surgical anesthesia have increased despite the refinements of administration and the more modern technics; in fact, such morbidity and mortality probably are of higher incidence today than at any time during the century of its use. The "safest of all anesthetic agents" in 1900 has become one of the most, if not the most, dangerous today. Although anesthetic mortality statistics are regularly reported for the various agents in use, anesthetists will admit readily that the deaths following anesthesia are most often due to technical errors during the administration or to improper use of the drug in question. This is unreservedly true when nitrous oxide is employed, since the gas itself has not been found to produce a toxic reaction for any tissue. In fact, this singular property of nitrous oxide, together with its commanding appeal because it is a simple, inorganic chemical with a low boiling point that does not explode or ignite, has been a strong indorsement for its continued use. Furthermore, convenience of administration and lack of discomfort for the patient are strong factors in favoring its frequent selection for clinical anesthesia. No drug, except those given by vein produces its effects more rapidly or pleasantly, or leaves the body more quickly than nitrous oxide.

The single serious imperfection of nitrous oxide is its lack of potency. When given with a concentration of oxygen found in air, nitrous oxide will not produce a degree of narcosis in many individuals that could be identified as surgical anesthesia. Some degree of muscular flaccidity is regularly regarded as essential to surgical anesthesia as well as insensibility to pain stimuli. Furthermore, surgical anesthesia is always predicated on the basis that freedom from pain and muscle relaxation are secured without oxygen want. It follows, then, that if nitrous oxide is to fulfill the requirements for surgical anesthesia in a patient who has not received previous depressant drug medication, some degree of anoxia may be an accompaniment. This is suggested by extensive clinical observation and abundant experimental data.

Early efforts to analyze the blood gases during nitrous oxide anesthesia were without benefit of the refined apparatus for blood analysis now available. However, from the first reports, it was obvious that anoxemia was always a factor. Kemp (7), Leake and Hertzman (8), Green et al. (9) agree with Brown, Lucas and Henderson (10), who, following experimental work on animals, insisted that "patients anes-

thetized with nitrous oxide will always suffer from a *severe* degree of anoxemia." McQuiston, Cullen and Cook recently reviewed the evidence supporting the contention that a mixture of 20 per cent oxygen and 80 per cent nitrous oxide may be used without causing serious anoxemia (12). They also completed significant studies on human beings and concluded that the administration of nitrous oxide-oxygen mixtures under pressures of 10 to 15 mm. mercury above atmospheric produced no significant increase in the concentration of nitrous oxide or oxygen of the blood. They emphasized the fact, after analyses of blood gases, that "any appreciable reduction in oxygen below 20 per cent may become extremely dangerous to the patient." In all their experiments, when the percentage of oxygen in the inspired gases was below 13 per cent, the arterial oxygen tensions were in the range of *extreme asphyxia, 30 mm. of mercury.* It is obvious, then, that the administration of nitrous oxide is often accompanied by anoxemia, and that the degree of anesthesia is more dependent upon the reduction of oxygen than upon an increased concentration of nitrous oxide.

It may be argued that in the modern practice of anesthesia, it is uncommon to anesthetize patients who have not received some depressant drug, usually one of the opiates or a basal anesthetic agent such as tribromethanol or a barbiturate. This is true certainly for hospitalized surgical patients. It is also true that in the hospital a vast array of drugs and equipment is available to permit changing agents or technics as the individual requirements demand. However, this is unusual in the office of physician or dentist, or in out-patient hospital clinics. It follows, also, that when patients are properly prepared with sedative and hypnotic drugs, it is often not necessary to administer a mixture of nitrous oxide and oxygen which contains less than 20 per cent oxygen. There are numerous reports attesting to the truth of this statement. Cullen and his associates use mixtures that never contain more than 80 per cent nitrous oxide (usually 60–70) during the operation for thoracoplasty (13). Raginsky and Bourne found blood oxygen content with safe limits when not more than 80 per cent nitrous oxide was given for satisfactory anesthesia in man (14).

The mortality and morbidity following nitrous oxide anesthesia in hospital practice is apparently not high when determined from reported statistics. This may be true but there is much misleading information accumulated, since it is frequently the practice to consider as anesthetic deaths only those that occur in the operating room or soon thereafter. Moreover, in hospital practice, if there is evidence of asphyxia during nitrous oxide anesthesia, the usual procedure is to add another agent which may then be held responsible for any untoward results.

The mortality and morbidity statistics for nitrous oxide-oxygen anesthesia in office and clinic practice are difficult to obtain, since reports from these sources are infrequent and inadequate. If statistics are collected from the files of daily newspapers, the representatives of insur-

ance companies and the personal reports from confreres, anesthetists must admit it is not negligible. The authors have knowledge of 11 sudden deaths during anesthesia in New York City offices during the past five years. This is not a large number but one must not lose sight of the fact that all of these deaths were preventable; in no instance was the surgical procedure of such magnitude as to require hospitalization or done for a patient whose physical condition merited hospitalization. It should be noted further that newspaper reports are written only when the subject has sufficient prominence to merit "a story." Since deaths do occur not infrequently during and as a result of nitrous oxide anesthesia, one must assume that *technical errors are often committed* or *the present approved principles for administering nitrous oxide are themselves at fault.* That the former is often true is readily admitted since many individuals, not trained or with little experience in physiological anesthesia, are using nitrous oxide daily. The latter fault, namely, the grave hazard of currently approved technics, is now being critically scrutinized, since recent investigations have revealed that widespread degeneration of the brain may result from nitrous oxide-oxygen anesthesia.

Lesions Produced by Anoxia during Nitrous Oxide Anesthesia

One of the most significant of such investigations was the report by Courville in 1936 (15), followed by a more elaborate monograph three years later (16). These extensive studies left little room for disagreeing with his conclusion that serious as well as fatal results may follow nitrous oxide-oxygen anesthesia, even though it is administered without gross error and by accepted technics. Courville classified the cases studied into several groups. The first of these included patients who died during anesthesia with nitrous oxide. Death in these instances could be attributed to a pre-existing lethal lesion, to an inter-current lesion independent of the surgical one, to a combination of disease and asphyxia, or, finally, as directly due to the effect of the anesthetic agent itself. In the last group, no pathologic lesion is found at autopsy to account for sudden death. Reviewing similar published case reports, the cause of death may be ascribed to status thymicolymphaticus, idiosyncrasy or anoxemic depression of the respiratory center. The latter cause is more widely accepted. There are case reports, however, that suggest a specific depressant action of nitrous oxide in some individuals. At the present writing sufficient evidence has not accumulated to support this suggestion.

Delayed exitus after nitrous oxide-oxygen anesthesia constitutes a second group. These patients may survive for hours or months, and from them valuable pathological studies have been made. The anoxia produced in these individuals during anesthesia "initiates a process that progresses until a situation is reached that is incompatible with life." Cases corresponding to this classification are numerous, and

most anesthetists with wide experience are familiar with one or more in their own or in the practices of their confreres. A typical case report is epitomized from Courville's monograph. A male, aged 42, had 18 teeth extracted during one half hour of nitrous oxide-oxygen anesthesia. He failed to regain consciousness and soon developed generalized convulsions. He remained in coma and exhibited typical decerebrate rigidity with extensor convulsions until death sixty-four hours after anesthesia, at which time there was a temperature of 105.2 F. and pulmonary edema. No gross evidence of disease in any of the body organs was found at autopsy. Tissue from the grossly normal brain revealed the characteristic changes to account for the clinical manifestations.

Instead of hours, the survival period may be greatly prolonged. Typical among these are patients who have transient respiratory failure, followed by a period of several hours of convulsions and coma, temporary improvement of the mental state for a day or even weeks, and finally death. The typical degenerative changes in brain tissue are present. One such instance is that of a 13 year old school boy who had had no previous illness of any consequence. While playing vigorously he sustained a fractured femur. Nitrous oxide-oxygen anesthesia was administered during closed reduction with the aid of the fluoroscope. Anesthesia was uneventful from the standpoint of pulse rate and respiration during twenty-five to thirty minutes of darkness. (The fluoroscope did not function properly.) When the light in the room permitted, marked cyanosis was noted. Oxygen was administered, and the color quickly became normal. Convulsions were not present during or after anesthesia. The child failed to regain consciousness and died with terminal hyperthermia after five days' existence completely decerebrate.

Another group in the classification of Courville with serious morbidity due to the anesthetic agent includes cases with recovery but with residual mental symptoms indicating cortical nervous system damage. These patients may present few clinical manifestations of anoxemia during anesthesia. Recovery from narcosis is usually delayed, and mild to severe convulsions may be noted during the prolonged coma. The residual symptoms may be indicative of cortical or lenticular damage or both. The following cases are illustrative.

A girl, aged 19, submitted to appendectomy during nitrous oxide-oxygen anesthesia. She regained consciousness three days later and learned that she had had several convulsions. She was blind for three months and was unable to make herself understood for six months. Eight years later, her mental reactions were those of a 10 year old, but without evidence of disordered mental activity. Characteristic athetoid movements were noted in the arms and legs; hyperactive deep reflexes, moderate atrophy of muscles of the hand and spastic extremities added to the clinical picture of serious damage to the lenticular nucleus (15). A 30 year old patient was operated upon for ectopic pregnancy during

nitrous oxide-oxygen anesthesia. As the abdomen was being opened, respirations ceased but were restored after ten or twelve minutes' artificial respiration. When a neurological examination was done eight hours later, the patient was stupid and apathetic. The extremities became spastic, and mental and emotional disturbances persisted. Eight months later, because of an advanced degree of dementia, she was committed to a hospital for the insane. Her condition was but slightly improved seven years later (15).

Another tragic case was reported by McClure: "A student at the University of Michigan was leading her class in the particular group. She came to Detroit and had an impacted molar extracted. She went alone to the dentist. When she reached home that afternoon, her vision was blurred. She was later taken to an ophthalmologist, and glasses were prescribed. In school her companions noticed no change in her, but the teachers did. Her work began to fall off, and before many months had passed, this girl had failed completely in her school work. She returned home and visited the same dentist to have an impacted molar on the other side removed. He said, 'Don't let anybody give you gas again, for you can't take it.' She had become blue; artificial respiration had been given" (17).

The final group from Courville includes those who have transitory mental and emotional manifestations but apparently recover completely. Visual and auditory disturbances, aphasia, convulsive states and delirium are among the complications from which complete recovery has been reported.

The consequences of nitrous oxide anesthesia which have been reviewed above are due to the accompanying anoxia. One group only, Lowenberg, Waggoner and Zbinden, support the contention that a specific action of nitrous oxide in some measure at least may be responsible (18). Granting that anoxia is the pathogenic factor in cerebral damage during nitrous oxide-oxygen anesthesia, the existence of predisposing factors, if any, assumes major importance. There are numerous reports of prolonged severe anoxia with complete recovery. Ward and Olson describe "the most severe case with recovery that has ever been reported" (19). A member of the crew of a bomber flying at 25,000 feet was found, after being without oxygen for fifty-five minutes, "unconscious, apneic and markedly cyanotic with ice in mouth and nostrils." The patient was unconscious for eight hours and semi-comatose for eleven more. After this, there were no subjective symptoms, and psychological changes lasted only six days. Recovery was considered to be complete. Many other reports provide evidence that some individuals may survive, without serious residual manifestations, prolonged stagnant anoxia (shock) and anemic anoxia (hemorrhage).

In the clinical literature, observers have frequently suggested that some predisposing factor or factors may account for the apparent disparity in the tolerance of individuals to low oxygen concentrations. The rather loose term, idiosyncrasy, has been used to explain a minimal

tolerance to anoxia. Other more or less vague explanations have associated untoward effects of anoxia with status thymicus, chronic alcoholism and other disease processes. It has been regularly recognized that the contributory effect of certain disease states in the production of anoxemia may be significant. Pulmonary lesions that interfere with the transport of gases to aerate the blood, anemias that result in one type of anoxia, diminished cardiac reserve and hyperthermia are unanimously acknowledged as predisposing factors in low tolerance for anoxic anoxia. It may be generally stated that an individual who suffers from chronic anoxia will quickly react severely to an imposed acute anoxemic state. However, except in the presence of the specific conditions enumerated above, no method is available for the selection of individuals who may suffer very severely from brief bouts of anoxia from those who will recover fully after prolonged oxygen want. Even the physiologically trained anesthetist who deals with anoxia constantly will avoid such prognosis, although extensive, intelligent experience improves his judgment and provides an alert defense against complications in individuals who, before or during induction of anesthesia, arouse the suspicion that they have little resistance to anoxia.

In order to protect the patient-public against death or permanent impairment in mental functioning, asphyxia of very short duration must be regarded as a grave hazard to the great majority of individuals. Experimental investigations point strongly to this assumption. The earlier studies on the histological changes in nerve cells were made by ligating the blood supply for varying periods, with and without recovery. Gildea and Cobb reviewed and added morphological studies on the effects of cerebral anoxia (anemic) (20). Non-specific cortical lesions were found, such as focal areas of necrosis (devastation areas) if several hours elapsed after an anemic period of a few minutes had been suffered by cats. Weinberger and the Gibbons produced temporary occlusion of the pulmonary artery of the cat and found permanent, severe, pathologic changes in the cerebral cortex after an anemic period of three minutes and ten seconds (21). Thorner and Lewy immersed guinea pigs and cats in nitrogen for varying sublethal periods (22). They conclude that anoxia of no more than sixty seconds "is followed by metabolic changes and by morphological changes in the cortical nerve cells" even though the recovery period was only thirty minutes. If it was longer (ten hours), "the cortex was markedly damaged." The results from anoxic anoxia studied by Armstrong and Heim were similar (23).

Morrison, in a recent significant pathological study of dogs and monkeys, found that a single, sudden exposure to asphyxia with an atmosphere containing 7 per cent oxygen for twenty-five minutes was "capable of producing extensive laminar necrosis in the cortex of the monkey" (24). With repeated exposures of mild hypoxia (12 to 13 volumes per cent oxygen in the blood), histological changes occurred, first, in the cell bodies of the cortical gray matter and often in the cortex of the

frontal lobe when the temporal and occipital lobes were normal (24). Studies on human beings have been made on patients who have been exposed to asphyxia from some cause and whose central nervous tissues have been available later for examination. Such studies by Courville (16), Schreiber (25), McClure and associates (26), Hartman (27), O'Brien and Steegman (28), Stewart (29), Schnedorf, Lorhan and Orr (30) leave little doubt that the lesions in the brain in man after anoxemia resemble closely those demonstrated in animals. There is essential agreement with Courville that such lesions most often include (a) sclerosis of scattered pyramidal nerve cells, (b) patchy necrosis, (c) degeneration of various cortical layers, (d) sub-total destruction of limited portions of the cortex and (e) similar lesions in the lenticular nucleus.

It has long been known that the brain is the organ most sensitive to anoxia. The recent findings of Morrison, indicating that the cortex of the frontal lobe may show pathological changes during exposure to moderate degrees of oxygen-want when the parietal and temporal lobes are normal, are of special interest (24). Alteration in the function of the frontal lobe cortex may not be detected by psychological tests. Earlier reports of the change in mental functioning produced by altitude anoxia mention characteristic insidious cerebral disturbance. Heber, in discussing the symptoms of the average European at Ledak, Cashmir (11,500 feet), says: "Mental deterioration is not as serious, however, as the change in temperament and/or subjective functions. It is astonishing how the most decisive of men will slowly and insidiously lose the power of decision and become unwilling to bear responsibility" (31). Barcroft also remarked that any prolonged mental effort in Cerro de Pasco, at an altitude of 14,200 feet, involved a degree of effort at times which necessitated a trip to the Coast to prevent a nervous breakdown (32). Barach concluded that impairment in emotional control was a more consistent response to anoxia at a simulated altitude of 15,000 feet than the results of psychometric and physiological testing (33, 34). In a study of 16 subjects exposed to this altitude for one and three-quarter hours, overconfidence and euphoria with exaggerated self-esteem took place in the majority, whereas dullness, irritability and lethargy were observed in the remainder as consequences of exposure to this degree of anoxia. It seems, therefore, quite possible that permanent damage in the frontal lobe cortex as well as in other areas of the brain may take place with little obvious personality change, although subtle disturbance in emotional response may nevertheless have been produced.

Next to the brain the heart is the organ most sensitive to anoxia. The inhalation of 12 per cent oxygen as a test for coronary insufficiency must be carefully administered since pulmonary edema and shock have been encountered as a consequence of this degree of anoxia (11). Under conditions of anesthesia, patients with coronary sclerosis or unrecognized myocardial disease may develop acute coronary insufficiency as a result of anoxic nitrous oxide anesthesia without the warning signal of pectoral pain.

The Proposal of 80 Per cent Nitrous Oxide, 20 Per Cent Oxygen Mixtures in a Single Cylinder

After the introduction of helium as a therapeutic gas, the advisability of dispensing this therapeutic agent combined with a minimum percentage of oxygen was apparent (35). Mixtures of 20 to 25 per cent oxygen with the remainder helium were used in the clinical administration of helium and have been adopted in practice. The conspicuous danger of administering a low concentration of oxygen by inadvertently increasing the flow of helium made helium-oxygen mixtures appear to the authors as a clinical necessity. It is the purpose of this paper to lay a sound physiological corner-stone for the conviction that nitrous oxide-oxygen anesthesia should not be administered with an oxygen percentage of less than 20 per cent. Even with this safeguard, the dangers of asphyxia during nitrous oxide-oxygen anesthesia are not abolished. Respiratory obstruction remains a principal cause for asphyxia. It is most certain, however, that transient bouts of obstruction, as from laryngospasm, will be tolerated without damage more often if the patient is breathing 20 per cent oxygen when they occur. It is, furthermore, our conviction that this cannot be assured unless such mixtures are prepared and delivered from a single cylinder. It is proposed that such mixtures be made available.

An investigation by Mr. Parker Francis * led to the conclusion that a mixture of 80 per cent nitrous oxide and 20 per cent oxygen could be supplied in cylinders now in use, providing that the cylinder is filled to one-third its normal content. The cost of the gases and the transportation charges obviously would be increased. However, the E cylinder which holds 165 gallons of oxygen at 2,000 pounds pressure or 420 gallons of nitrous oxide at about 800 pounds pressure could be filled with 150 gallons of the mixture at 700 pounds pressure. If this amount was not exceeded, the mixture would come out uniformly from start to finish with a concentration of 20 per cent oxygen and 80 per cent nitrous oxide.

Unfortunately, there is at the moment no device other than that of a mixture of nitrous oxide and oxygen which will ensure the provision of 20 per cent oxygen. Even among the better anesthetic appliances on the market today, the accuracy of flow meters may vary as much as 5 per cent, and anesthetists are constantly exposed to the temptation to decrease oxygen to aid the induction or to produce more profound anesthesia.

First of all, it is important to recognize that inducing anesthesia with pure nitrous oxide or using a concentration of oxygen lower than 20 per cent to produce profound anesthesia has been the cause of serious central nervous system damage as well as death itself. Since severe anoxia has now been established as the primary factor in the pathogenesis of psychoses, degenerative changes in the central nervous system and death itself, the only tenable conclusion must be an unqualified avoidance of asphyxia as an adjunct to nitrous oxide-oxygen anesthesia.

* Results of observations made by the Puritan Compressed Gas Corporation.

After an extensive consideration of the factors that have been discussed, the authors can find no possible justification for a continuance of such an unphysiological practice as is carried on by anoxic nitrous oxide-oxygen anesthesia. It is evident that a considerable proportion of the population will not become anesthetized sufficiently to permit painless surgery or exodontia with the proposed mixture of 80 per cent nitrous oxide and 20 per cent oxygen when preanesthetic sedation has not been provided. Modern anesthesia must decree emphatically that the patient is not to be fitted to the anesthetic technic, but new technics must be devised to meet the circumstances. If anesthesia with a 20 per cent oxygen–80 per cent nitrous oxide mixture is not sufficiently profound, other anesthetic gases must be employed or pre-anesthetic sedation used which does not force the individual to breathe a mixture containing a deficient concentration of oxygen.

SUMMARY

The current use of anoxia as an adjunct to nitrous oxide-oxygen anesthesia has been the cause of (A) death from asphyxia, (B) psychoses from permanent brain damage, (C) personality defects which may or may not be recognized, (D) impairment in circulatory and respiratory function which may contribute to pulmonary atelectasis, pulmonary edema, or cardiac failure.

Nitrous oxide-oxygen anesthesia is an alarming hazard at the present time, since oxygen-want is advocated deliberately to aid anesthesia. The available evidence indicates that nitrous oxide should never be administered with an oxygen concentration below 20 per cent. If sufficiently profound anesthesia is not then obtained, other technics should be used rather than resort to asphyxia or even so-called moderate anoxia.

Cylinders containing 80 per cent nitrous oxide and 20 per cent oxygen will provide an unvarying concentration of these gases with a cylinder pressure of 700 pounds. The increased cost of such mixtures should not be made the basis of permitting a practice that is dangerous as well as unphysiological, e.g., the use of sub-normal oxygen concentrations in anesthesia.*

Finally, the medical profession should be widely informed that so-called "gas oxygen" anesthesia is in many instances a procedure that deliberately exposes the patient to severe anoxia, the results of which may be psychotic invalidism, personality defects, or death from circulatory or respiratory failure.

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* The use of 80 per cent helium–20 per cent oxygen mixed in tanks has been made mandatory in clinical medicine despite the high charges for mixing these gases which, when added to freight expense, results in cylinders that sell for $17.00 to $25.00 for approximately 200 cubic feet. Avoidance of asphyxia is as important in anesthesia as it is in clinical medicine.

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