NITROUS OXIDE-OXYGEN ANESTHESIA

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As a result of research, experimentation and clinical interpretation, our knowledge of anesthesia has steadily expanded. Formerly accepted theories and teachings have in many cases been altered or discarded, to be replaced by newer concepts. Change is an inevitable accompaniment of progress. A perusal of anesthetic literature, however, must always be tempered by the fact that we are still ignorant of the most important and basic principle of “How is anesthesia produced, or how does it act?” The very multiplicity of theories advanced to explain this action is, in itself, evidence of this fact (1). If, and when, this puzzle is solved, doubtless our present day theories and conceptions of anesthesia will undergo very radical alterations. Theories and deductions may then be replaced by facts.

Nitrous oxide and ether are our oldest anesthetic agents. They have been in use over 100 years. The continuous use for so long a period implies that the advantages or benefits of these agents must exceed or outweigh their disadvantages or drawbacks.

TERMINOLOGY

Anoxemia, anoxia, asphyxia and cyanosis are familiar terms in the annals of anesthesia. While they stem from a common causation, namely, oxygen deficiency, too frequently these terms are confused or loosely applied. For instance, the term asphyxia is frequently employed in connection with nitrous oxide-oxygen anesthesia. Asphyxia, however, implies a restriction of the oxygen intake plus obstruction to the normal elimination of carbon dioxide from the lungs. In nitrous oxide-oxygen anesthesia, restriction of the oxygen intake may occur, but the elimination of the carbon dioxide from the lungs is unhampered.

Similarly, the terms anoxemia and anoxia are often confusing or inaccurate. Waters states (2), “By derivation the meaning of anoxia is ‘without oxygen’—a condition incompatible with life, and therefore scarcely a suitable word in clinical discussions. For want of such a word as hypo-oxia, or hypoxia, anesthetists are in the habit of using the clumsy expressions—oxygen want, oxygen lack or oxygen deficit.”

The term hypoxemia implies a reduction of the oxygen in the circulating blood. Hypoxia implies a reduction of the tissue oxygen, resulting, as a rule, from the hypoxemia. The degree and duration of the hypoxia may vary from slight and transient to severe, prolonged or even fatal. Ordinarily, during anesthesia, the condition of hypoxia
is rapidly reversible following oxygen administration. Should a severe prolonged degree of hypoxia be allowed to develop, however, the condition may become irreversible, in which case a true state of anoxia results. Such a condition may be evidenced by cerebral damage with accompanying typical neurologic symptoms.

Anoxia is not confined to the administration of nitrous oxide alone, but may, and does, occur with any and all of the anesthetic agents at our disposal today. If a nearly fatal state of anoxia occurs under anesthesia the patient presents a characteristic train of symptoms. The patient fails to react after the anesthesia and may remain for hours in a stupor or semicomatose state. This may be followed by irrational states, delirium, convulsions, paralysis, hyperpyrexia, coma and finally death. At necropsy, damage to the cerebral cortex is evidenced by petechial hemorrhages. Less severe degrees of anoxia may result in mental confusion—amnesia, and similar changes. The recovery period is variable and the prognosis uncertain. The condition may be transient or persistent.

The neurologic changes resulting from fatal degrees of anoxia as described may result from anesthesia, carbon monoxide poisoning, trauma, or in fact from any condition which imposes upon the organism prolonged severe degrees of hypoxia. With the lesser degrees of mental disturbance, the possibility of other etiologic factors must be considered. Consideration of these factors would indicate that anesthesia has doubtless been unjustly blamed in many cases of postoperative psychosis. Regarding these psychotic states Kaye (3) in Practical Anesthesia writes:

"Persistent, as opposed to transient, mental changes following anesthesia or operation are occasionally encountered. The probable etiologic factors include (a) cardiac decompensation, (b) septic and toxic states, (c) prolonged anoxemia, (d) the effect of premedication, (e) the individual mentality of the patient.

"The symptoms fall into the following three groups:

"1. Confusional, with or without excitement, and probably dependent upon cardiac decompensation, toxic states, sepsis and prolonged hypoxemia.

"2. Hysterical, a varied group of mental and physical symptoms being presented. They probably depend upon the individual psychology of the patient, the anesthesia or operation acting merely as a trigger for the release of latent complexes.

"3. Psychotic, the anesthesia or operation merely releasing a preoperative psychosis. The resulting symptoms are usually those of primary dementia or the manic-depressive syndrome."

Also Batten and Courville (4) state:

"No case of post surgical psychosis can be correctly evaluated until hereditary and environment factors, habits, and pre-existing diseased states as well as the lesion at hand, have been considered as possible etiological factors."

Insanity, in all its forms and degrees of severity, existed before the art of anesthesia was dreamed of. However, if the present day investi-
gator can show that the mental patient had ever been given an anesthetic (especially nitrous oxide), then he is assured of an etiologic basis for the existing condition. A consideration of the many complex factors involved in every mental case shows that seldom is one factor alone directly responsible for the condition.

Theory of Anesthesia

Nitrous oxide possesses such properties as low boiling point, stability in living tissues and great solubility in body fluids. It is one hundred times more soluble in the blood plasma than is oxygen (2.4) and fifteen times more soluble than is nitrogen (1.7). It is known that the various body tissues vary in their oxygen requirements. The most highly specialized tissue, such as the brain, requires more oxygen than any of the other tissues, and is the first to be affected by a decreased oxygen supply. Thus for many years the "oxygen exclusion" theory, whereby the saturation of the body fluids with nitrous oxide excluded oxygen, was accepted to explain the action of nitrous oxide in producing anesthesia. If this mechanical exclusion of the oxygen were the only factor involved, then the upper limit of oxygen administration during nitrous oxide-oxygen anesthesia should be around 20 per cent. Above this limit we would expect the patient to awaken since normal air contains roughly 20 per cent oxygen. Every anesthetist of experience has encountered cases in which the oxygen percentage in the mixture could be increased considerably above that present in normal air, while still maintaining anesthesia. In fact, not infrequently, this increase is imperative if deep narcosis is to be avoided. Other factors involved are the physical condition of the patient, the effect of the preanesthetic sedation and the duration of the operation.

The commonly accepted theory of today is that nitrous oxide of itself possesses weak anesthetic properties. The fact that the analgesic state may be produced with a mixture containing 90 per cent oxygen and 10 per cent nitrous oxide supports this view. In order to produce surgical anesthesia, this weak action may have to be enhanced by some restriction of the oxygen intake, or by varying degrees of hypoxia. The degree of hypoxia imposed upon the patient is controlled by the anesthetist, guided as always by the true signs of anesthesia, and upon him rests the responsibility to see that such degrees are never allowed to become unduly depressing or prolonged.

The factors that retard the use of nitrous oxide-oxygen anesthesia are the fear of (1) cyanosis and (2) anoxia.

Cyanosis

The mechanism of the production of cyanosis during nitrous oxide-oxygen anesthesia is too well known to be repeated in detail here. Its causation, significance and importance as a true sign of such anesthesia have been discussed in detail elsewhere (5). Briefly, it may be stated
that "the presence of cyanosis is not necessarily a sign of danger, nor is its absence any indication of safety."

**Anoxia**

The danger of anoxia during nitrous oxide-oxygen administration has been emphasized by various writers during the past decade, so much so that many anesthetists and students consider anoxia an inevitable accompaniment of all nitrous oxide administrations. Many are thereby deterred from its use, thus depriving themselves of a very valuable anesthetic agent. It is necessary and fitting that all anesthetists be familiar with the possible dangers of nitrous oxide-oxygen anesthesia, but it should also be stressed that such dangers arise, not from the action of the gas itself, but from its maladministration.

The possible danger of anoxia during nitrous oxide-oxygen anesthesia has been widely publicized. It would seem that the fact that a similar hazard exists with the use of other anesthetic agents should be equally stressed. Courville has described the effects of anoxia upon the brain in fatalities occurring under nitrous oxide-oxygen anesthesia (6). He also wrote of cerebral anoxia during ether anesthesia (7). Numerous cases are reported of similar mishaps occurring with cyclopropane and spinal anesthesia. The erroneous selection of the agent to be employed, or its maladministration is the commonest cause of anoxia occurring during anesthesia. Prolonged deep anesthesia and obstruction of the airway are contributing factors. Danger signals are either unrecognized or unheeded. In addition to the anesthesia, of course, other factors are involved, such as surgical trauma, hemorrhage, shock, and so forth. Thus, with the barbiturates, anoxia may result from depression of the respiration (anoxic anoxia) or of the circulation (stagnant anoxia). Similar effects may occur with avertin. Anoxia may result with cyclopropane from respiratory depression and laryngospasm. Chloroform, because of its depressant cardiac effect, may cause stagnant anoxia as well as the histotoxic type from direct effect on the tissues. Spinal anesthesia may produce anoxia by vasodilatation (stagnant anoxia), by paralysis of the muscles of respiration or of the respiratory center itself. With ether, anoxic anoxia may develop from an obstruction to the airway, and histotoxic anoxia from depression of cellular oxidative processes.

Van Liere (8), in "Anoxia," stated "The following produce histotoxic type of anoxia;—barbiturates, bromides, urethane, chloral, ether, chloroform, urethane, ethylene, cyclopropane and to a lesser extent carbon monoxide. Nitrous oxide produces the anoxic type and carbon monoxide the anemic type plus histotoxic to a lesser degree."

**Personal Factor**

We have no perfect anesthetic method or agent—none is absolutely safe. Admittedly, the anoxic state may be more readily produced with
nitrous oxide-oxygen anesthesia than with other agents as restriction of the oxygen intake is used to enhance the normally weak anesthetic action of the nitrous oxide. Further, the margin of anesthesia is narrow—the transition from the light to the deep plane may be very rapid (during the induction) or the development of the deep plane may be slow and insidious (during prolonged anesthesia). This latter phase presents much the greater danger as the marked muscular reactions commonly indicative of oxygen want are no longer exhibited. In fact, muscular spasticity is often replaced by flaccidity. Hence it becomes imperative that the anesthetist be thoroughly familiar with the true signs of such anesthesia. This requires training and experience. Many anesthetists are not willing to expend this time and effort in order to achieve proficiency. It is much easier to use some other anesthetic agent either as a supplement or a substitute. The success of administration of nitrous oxide-oxygen is determined by the degree of proficiency of the administrator. In all anesthesias the most vital single factor concerned is the ability of the anesthetist.

An anesthetic agent, ordinarily considered safe, may become a deadly agent when improperly administered. The old adage still holds true, "No anesthetic is any safer than the one who gives it."

**Importance of Respiration**

Respiration is by far the most important single sign during nitrous oxide-oxygen anesthesia. The exact condition of the patient is accurately portrayed at all times by the character of the respiration. Every shift toward the lighter or deeper level of narcosis can be anticipated by variations in the respiratory rate or rhythm. The control of respiration is extremely flexible and sensitive; alterations of even 1 or 2 per cent of the oxygen in the mixture are rapidly reflected in the character of the breathing. As long as an efficient type of breathing is maintained, the patient is in no danger. By efficient breathing is meant respirations machine-like in character, inspiration and expiration about equal, the rate somewhat faster than normal, continuous or uninterrupted with adequate volume. Any change or variation of this respiratory rhythm must at once be noted by the anesthetist and its cause determined.

**Cause of Anoxia**

During nitrous oxide-oxygen anesthesia the greatest single hazard is the failure, once anesthesia has been established, to effect a gradual increase in the oxygen percentage of the mixture employed. This applies particularly to all prolonged anesthesias, and to the subnormal risk type of patient.

During the induction and early stages of anesthesia, overdosage may result in the rapid production of the deep or even profound plane. However, in such cases, the muscular responses of the patient are usu-
ally so marked or violent that the need for oxygen to correct the situation is very apparent. It should be remembered that when dealing with the weak, anemic, or debilitated patient, the production of deep anesthesia is not necessarily heralded by muscle spasm; in fact the opposite, flaccidity, may occur. In such cases the danger signals are largely respiratory in character. In either case the administration of a few breaths of 100 per cent oxygen rapidly restores the patient to his former normal—the hypoxic condition is still rapidly reversible.

Most beginners with nitrous oxide-oxygen administer too much oxygen during the induction and early stages of anesthesia, and too little during prolonged narcoses. It is a common misconception that low oxygen concentrations are maintained throughout all nitrous oxide-oxygen anesthesias. Once the desired level of anesthesia is attained, then it becomes imperative that the oxygen concentration in the mixture be increased as rapidly as is possible without disturbing the level of narcosis—that is, allowing the level of anesthesia to become sufficiently light that reflex movements occur. Every patient's reaction to anesthesia is determined by his degree of tolerance or resistance. This tolerance factor varies with each patient and with the same patient from day to day. It is modified by numerous factors such as disease, trauma, preanesthetic sedation, and so forth. Those with a high degree of tolerance constitute the normal and resistant group of patients. Those with low tolerance fall into the subnormal risk classification.

This tolerance level of each patient determines how rapidly and to what extent the oxygen percentage in the mixture may, or must, be increased as anesthesia progresses. The increase is usually effected gradually, 1 or 2 per cent at a time, while the effect of each increase on the level of anesthesia is noted. Should an increase of the oxygen from 8 to 10 per cent produce the reflex signs of lightening anesthesia, then it is evident that no depressing level or degree of hypoxia existed at the former percentage. Later on anesthesia may be found satisfactory with 10 per cent oxygen but 12 per cent or higher is too much. In this manner the oxygen percentage in the mixture is gradually increased. Should adequate anesthesia be obtainable with a 15 per cent oxygen mixture, then it is obvious that any less percentage is unjustifiable. Failure to increase the oxygen supply as anesthesia progresses may well lead to fatal, or near fatal, degrees of anoxia. It is the insidious onset of this condition that makes it so dangerous. The danger signals, though present, are not marked or violent as they are during the induction period. Just the opposite occurs. Muscular rigidity may be replaced by flaccidity. The blood pressure gradually falls, the pulse becomes fast, of poor volume, thin or thready in character, finally slower and irregular; the pupils slowly dilate; and the breathing becomes slow, quiet, shallow, irregular and always inefficient up to the point of final arrest. Hypoxia has been allowed to progress to the point where it becomes irreversible and a true state of anoxia is then
established. Just how long is required to reach this point of irreversibility depends upon the degree and the duration of the hypoxia, the patient’s physical condition, or his degree of tolerance or resistance, plus other factors such as an obstructed airway and surgical trauma, hemorrhage, and so forth. The development of anoxia is heralded by definite danger signals. Failure to recognize such signs is the result of either ignorance or carelessness.

**Oxygen Apnea Test**

During nitrous oxide-oxygen anesthesia the application of a simple and accurate test will reveal whether or not anesthesia is being maintained at a depressing level. This test is respiratory in nature, and is based upon the fact that whenever a patient in need of oxygen is given an abrupt and abundant supply, slowing of the respiratory rate or even temporary cessation of breathing (apnea) occurs. The duration of the apneic period is in direct ratio to the degree of oxygen deficiency. During periods of lowered oxygen intake, respiration is maintained by an hypoxic stimulus, by way of the chemoreceptors of the carotid and aortic bodies (peripheral action) plus carbon dioxide effect (central effect). Inhalation of a high oxygen concentration quickly abolishes the hypoxic stimulus to respiration and a period of apnea follows. Thus, if at any time the anesthetist is in doubt regarding the efficiency of the respiration or the depth of narcosis, he should administer one or two breaths of 100 per cent oxygen and observe the effect (if any) on the respiration. An interval of three to ten seconds or an average of seven seconds elapses before the oxygen increase reaches the brain. If this is followed by a definite slowing of the respiratory rate, or a period of apnea, it is a definite indication that the anesthesia is being maintained at an unnecessarily deep level and the oxygen percentage in the mixture must at once be increased. The respiratory rate is largely controlled by oxygen and the depth by carbon dioxide. At times during anesthesia the respiratory rate may quicken. This variation may be due to light anesthesia (painful reflexes) or it may be caused by deepening narcosis (oxygen want). When in doubt the anesthetist administers oxygen. A slowing of the respiratory rate, or apnea, would be indicative of oxygen want; no effect on the respiratory rate, or a further increase, indicates light anesthesia. The mixture is then altered accordingly.

The test is simple and may be applied at any time throughout the narcosis. It affords an effective method of detecting and preventing the gradual development of a depressing level of anesthesia which if uncorrected may well lead to serious results.

**Criticisms of Nitrous Oxide-Oxygen Anesthesia**

Nitrous oxide-oxygen anesthesia has been assailed upon the grounds that it is not physiologic, that anoxia must be an inevitable accompani-
ment of its use, that never less than 20 per cent oxygen should be administered in the mixture; in short, that its administration is so fraught with danger that its use should be abandoned or that it should be used only in conjunction with other more potent agents.

The administration of nitrous oxide anesthesia, no doubt, is not physiologic, but the same applies to ether, cyclopropane or any other of the anesthetic agents. The state of anesthesia is itself unphysiologic. We "asphyxiate with nitrous oxide, drown with ether, poison with cyclopropane or paralyze with spinal." Our anesthetic methods are crude—in that we administer a drug to paralyze the higher centers and keep a patient relaxed while hoping its action will stop short of a fatal issue. Doubtless, anesthesia will be continued in this manner until the perfect agent or method is discovered.

Over a century of use has shown that nitrous oxide is too valuable and useful an anesthetic agent to be summarily discarded because there are dangers associated with its use. Every anesthesia is fraught with hazards. Safety is contingent upon the recognition of such hazards and proper administration of the agent employed. Anoxia (as opposed to hypoxia) is by no means the inevitable sequela of every nitrous oxide-oxygen anesthesia. Safety is not necessarily synonymous with oxygen. Patients die under ether, cyclopropane and chloroform given with an excess of oxygen. (Carbon monoxide is only slightly less deadly in the presence of high oxygen concentrations.) Anesthesia is only one factor involved in surgical procedures. People drop dead on the street, they die suddenly in bed and under all sorts of conditions. The wonder is, not that some die under the combined insult of surgery plus anesthesia, but that more do not do so.

Twenty Per Cent Oxygen

Cullen and his associates (9) following the administration of nitrous oxide-oxygen anesthesia to patients (carbon dioxide absorption technic) have assumed that never less than 20 per cent oxygen should be administered in the mixture. It is stated that "any appreciable reduction below 20 per cent oxygen may become extremely dangerous to the patient. Mixtures of 15 to 13 per cent oxygen and nitrous oxide are credited with producing evidences of 'extreme asphyxia.'"

The percentage of oxygen in the air varies directly with the altitude above sea level, as shown by table 1 from Van Liere (8).

At 10,000 feet the oxygen percentage in the inspired air is 14.25. The airlines fly passengers for long periods at levels up to 10,000 feet without the use of oxygen. (At 10,000 feet breathing air, the arterial oxygen saturation is 90 per cent. See table 2.) In the Army Air Forces the use of oxygen is not mandatory until above the 10,000 foot level. Cases are on record of pilots engaging in active combat at altitudes well above 10,000 feet without the aid of the oxygen apparatus. Yet a patient, premedicated, asleep and quiet in anesthesia, is pre-
TABLE 1

RELATION OF ALTITUDE, PRESSURE, AND OXYGEN

<table>
<thead>
<tr>
<th>Mm. Hg</th>
<th>Elevation (Feet)</th>
<th>O₂ (Per cent)</th>
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</thead>
<tbody>
<tr>
<td>760</td>
<td>0</td>
<td>20.95</td>
</tr>
<tr>
<td>732</td>
<td>1,000</td>
<td>20.15</td>
</tr>
<tr>
<td>704</td>
<td>2,000</td>
<td>19.38</td>
</tr>
<tr>
<td>677</td>
<td>3,000</td>
<td>18.54</td>
</tr>
<tr>
<td>651</td>
<td>4,000</td>
<td>17.93</td>
</tr>
<tr>
<td>626</td>
<td>5,000</td>
<td>17.25</td>
</tr>
<tr>
<td>602</td>
<td>6,000</td>
<td>16.60</td>
</tr>
<tr>
<td>579</td>
<td>7,000</td>
<td>15.97</td>
</tr>
<tr>
<td>557</td>
<td>8,000</td>
<td>15.37</td>
</tr>
<tr>
<td>536</td>
<td>9,000</td>
<td>14.80</td>
</tr>
<tr>
<td>518</td>
<td>10,000</td>
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<tr>
<td>497</td>
<td>11,000</td>
<td>13.73</td>
</tr>
<tr>
<td>478</td>
<td>12,000</td>
<td>13.23</td>
</tr>
<tr>
<td>461</td>
<td>13,000</td>
<td>12.75</td>
</tr>
<tr>
<td>444</td>
<td>14,000</td>
<td>12.28</td>
</tr>
<tr>
<td>428</td>
<td>15,000</td>
<td>11.83</td>
</tr>
</tbody>
</table>

Assumed not to be able to tolerate (without danger of serious anoxia) a decrease of oxygen in the inspired air below 20 per cent. It is claimed that the administration of nitrous oxide-oxygen mixtures under increased pressures (up to 15 mm.) produces no significant increase of the concentration of either gas in the blood. As shown in table 2, however, the Army Air Forces found that the altitude ceiling could be raised 4,000 to 5,000 feet by the employment of pressure breathing.

TABLE 2

ALTITUDES FOR EQUIVALENT ARTERIAL OXYGEN SATURATION WHEN BREATHING AIR, OXYGEN, AND OXYGEN UNDER PRESSURE*

*(Air Surgeons Journal, Sept. 1944)*

<table>
<thead>
<tr>
<th>Arterial O₂ Saturation, per cent</th>
<th>Breathing Air, feet</th>
<th>Breathing O₂ (10 per cent mask leak), feet</th>
<th>Breathing O₂ (no leak), feet</th>
<th>Pressure Breathing O₂, feet</th>
<th>Pressure (inches water)</th>
</tr>
</thead>
<tbody>
<tr>
<td>95</td>
<td>3,000</td>
<td>33,000</td>
<td>35,000</td>
<td>38,000</td>
<td>2</td>
</tr>
<tr>
<td>90</td>
<td>10,000</td>
<td>37,500</td>
<td>40,000</td>
<td>42,000</td>
<td>4</td>
</tr>
<tr>
<td>85</td>
<td>13,000</td>
<td>39,000</td>
<td>41,500</td>
<td>44,500</td>
<td>8</td>
</tr>
<tr>
<td>80</td>
<td>15,000</td>
<td>40,000</td>
<td>42,500</td>
<td>45,500</td>
<td>8</td>
</tr>
<tr>
<td>75</td>
<td>17,000</td>
<td>41,000</td>
<td>43,500</td>
<td>46,000</td>
<td>8</td>
</tr>
<tr>
<td>70</td>
<td>18,000</td>
<td>41,500</td>
<td>44,000</td>
<td>49,000</td>
<td>12</td>
</tr>
</tbody>
</table>

* The figures in this table are combined from calculated and observed data.
† Assuming that leaks up to 10 per cent are to be expected with the simple demand system, the use of pressure breathing raises the ceiling from 4,000 or 5,000 feet before serious anoxia begins to set in. In producing this result, the elimination of the effects of mask leakage is at least as important as the increase in alveolar oxygen tension.

Apparently there are factors involved other than the mere reduction of the oxygen intake. One such factor may be the method of administration of the gases. In our experience the positive pressure, semiclosed, fractional rebreathing method has proved to be by far the
most efficient. The administration of nitrous oxide-oxygen by the closed or carbon dioxide absorption method (without ether) has left much to be desired. One method employs pressure plus partial carbon dioxide retention; the other, no pressure and elimination of the carbon dioxide. This loss of carbon dioxide is apparently the important factor.

Carbon dioxide plays a vital role in the physiology of respiration and circulation. The sensitivity of its influence on respiration is shown by the fact a variation of either plus or minus 0.1 per cent in the alveolar carbon dioxide will produce a 5 per cent increase or decrease in pulmonary ventilation; an increase of 0.2 per cent alveolar carbon dioxide will double the ventilation, while a decrease of 0.2 per cent causes apnea. Gellhorn (10) has pointed out the importance of the carbon dioxide in the compensatory reflex mechanism which protects the body in cases of lowered oxygen intake. He describes carbon dioxide as "a potent antagonist of anoxia." The influence of adequate carbon dioxide tension on brain function has been outlined by Gibbs (11).

"Normal brain function can be maintained with low percentages of oxygen even as low as 2 per cent in the inspired air provided the carbon dioxide tension is maintained. The addition of carbon dioxide to a mixture of gas low in oxygen increases the amount of available oxygen to the brain because it (a) increases pulmonary ventilation, (b) causes peripheral vascular constriction and cerebral dilation, (c) shifts the hemoglobin dissociation curve so that the blood unloads a greater portion of oxygen in the tissues.

"Improved oxygenation of the brain is not the only function of carbon dioxide. It was demonstrated that even when sufficient oxygen was present, normal brain function could not be maintained unless there was an adequate tension of carbon dioxide. Consequently there is a direct action on the brain by carbon dioxide, an effect which is apparently necessary for normal brain function."

A recent issue of this Journal (12) contained a review of the writings of Courville, Cullen and others, pertaining to the dangers of anoxia associated with nitrous oxide-oxygen anesthesia. The suggestion is made that, in the interests of safety, gas cylinders should contain mixtures of 20 per cent oxygen and 80 per cent nitrous oxide, so that never less than 20 per cent oxygen may be administered during the anesthesia.

Safety cannot be prescribed or written into anesthesia. The pilot in the "restricted control" airplane can still kill himself. Pilot error accounts for most of the crashes. Training and experience are necessary in anesthesia as elsewhere.* Fixed mixtures may readily give the inexperienced a false sense of security. Human beings are not standardized. Induction with 20 per cent oxygen with some patients may produce an excitement stage requiring considerable restraint. In the majority of cases production of the anesthesia level will be unduly prolonged. With subnormal risk patients, the rapid production of the profound plane is possible on even a 20 per cent oxygen mixture. A mixture of 20 per cent oxygen and 80 per cent nitrous oxide, if admin-
istered continuously, will eventually produce the anesthetic stage. So will a 50/50 mixture. In fact it is possible to kill a patient (by anoxia) with either mixture;—it is simply a question of time. If the anesthetist is unable to recognize or interpret the signs and danger signals on a 10 per cent oxygen and 90 per cent nitrous oxide mixture, will he be any more competent when employing a mixture of 20 per cent oxygen and 80 per cent nitrous oxide, or even a 50/50 mixture?

Before anesthesia is established with any inhalation anesthetic agent, saturation of the blood and tissues with that agent must be accomplished. Induction with 100 per cent nitrous oxide (for normal risk patients) accomplishes this saturation rapidly. Induction with a mixture of 20 per cent oxygen and 80 per cent nitrous oxide will do the same more gradually, plus possible disadvantages. The end result is the same. For subnormal risk patients and children, a mixture of oxygen-nitrous oxide is advocated in order to decrease the possibility of inadvertent rapid production of the profound plane. Such patients have a narrower margin of anesthesia than has the normal group, and so respond more rapidly to overdosage. As a matter of fact, induction with 100 per cent nitrous oxide could be employed for any case, provided the anesthetist is sufficiently experienced and alert to interpret the finer variations of the respiratory signs as they occur.

**Acclimatization**

The body possesses remarkable powers of adaptation or acclimatization to both acute and chronic states of hypoxia, or reduced oxygen intake. Without such, man could not long survive. Resistance to acute hypoxia is shown by the fact that if 100 per cent nitrous oxide is administered to a patient to the point of respiratory arrest, followed by inhalations of 100 per cent oxygen, within less than two minutes this patient will be awake, oriented and answering questions coherently. Rapid recovery following near death from drowning, strangulation, and suffocation, is another example. Varying degrees of hypoxia exist in many diseases, both acute and chronic, such as pneumonia, emphysema, asthma, cardiac disease, blood dyscrasias, patent foramen ovale, and so forth. Many workers in industrial plants and mines spend years of their lives in an atmosphere containing less than the normal percentage of oxygen. This power of adaptation has made possible the scaling of high mountain peaks and continuous existence at high altitudes. The mechanism which protects the human organism against hypoxia (or anoxia) during the (unphysiologic) vicissitudes of normal life also functions during the (unphysiologic) state of anesthesia. The degree of protection afforded varies with the individual. Some succumb readily; others are more resistant. During anesthesia, it is the responsibility of the anesthetist to estimate, from the reactions of the patient, this variable factor of resistance, and to adjust or vary the anesthetic accordingly.
Nitrous Oxide-Oxygen Anesthesia

Safety

The question of safety of any anesthetic agent is always relative. Figures regarding mortality or morbidity with any one agent become truly indicative only if the total number of administrations of that agent is known. A report from one section of the country may show a high rate of morbidity or mortality while from another section the opposite may hold true. Numerous factors complicate the tabulation of anesthetic mortality or morbidity rates, such as the ability or experience of the anesthetist, the physical condition of the patient, the nature and duration of the operation, the skill of the operator, the effect of surgical trauma, and so forth. In many instances anesthesia has been unjustly blamed for a fatal outcome; in other instances the anesthesia has doubtless been responsible for death occurring perhaps hours after the patient has left the operating room. Fatalities, if reported at all, are usually done so reluctantly; morbidity figures are too frequently inaccurate. As a result, the reputation any anesthetic agent has acquired regarding its safety is the result of general impressions from all over the country rather than from specific scientific data. Important factors concerned are how widespread and over how many years has the particular agent been employed.

During the past forty years the annual world-wide administrations of nitrous oxide-oxygen have been estimated at 6,600,000 (13). As we yet have no perfect anesthetic agent, it would be difficult to conceive of this number of administrations of any agent occurring without fatalities or near fatalities. The ratio of anesthetic fatalities has been variously estimated at 1:4 to 20,000. The author has knowledge of several deaths occurring under nitrous oxide-oxygen during the past several years. During the same interval, to his knowledge, there occurred a number of fatalities with cyclopropane, spinal and ether anesthesia. Of the cyclopropane fatalities, several were of the delayed type with typical neurologic symptoms of anoxia. In other cases, death occurred suddenly, probably due to cardiac failure. Fatal cerebral anoxia occurred with both open drop ether and spinal anesthesia.

If it were possible to accumulate all the facts and figures regarding the mortality and morbidity of all anesthetic agents, it is felt that nitrous oxide-oxygen would compare most favorably of any in the list.

Dental Anesthesia

By far the greater number of nitrous oxide-oxygen anesthesias are administered in dental offices and various clinics. Because of its rapid action, absorption and elimination, nitrous oxide is an ideal agent for use in the dental office. It is obviously impossible for every patient requiring the extraction of a tooth, or several teeth, to go to a hospital for this procedure. (The present day tendency of many exodontists is
to hospitalize patients requiring complete extractions or extensive oral surgery.) The mere admission to a hospital does not, in itself, ensure the best in anesthesia. In many hospitals throughout the country, anesthesia methods are still rather haphazard.

Unfortunately, too many dentists employing general anesthesia in their offices know little or nothing about the action of the agent or its proper method of administration. This important function is usually relegated to an office nurse or technician, often with little or no previous training or experience. It is little wonder that under such circumstances anesthesia may often prove unsatisfactory from the viewpoint of both the patient and operator. The relative safety of nitrous oxide-oxygen anesthesia is stressed by the fact that in spite of its frequent maladministration, postanesthetic complications are comparatively few.

The dentist wishing to employ general anesthesia in his office practice thus finds himself in a quandary. He had had no training in this subject; professional or medical anesthetists are not available (many of them are none too proficient in the administration of anesthesia for open mouth operations); and it is impractical to refer every case to a hospital. Thus he is forced to rely upon nurse or technician services, or confine his efforts to local anesthesia only.

To ensure a greater degree of efficiency and safety in the administration of general anesthesia in the dental offices the following suggestions are offered:

(1) Anesthesia should be taught in the dental schools. All dental students, sometime during their course, should be given a series of lectures dealing with the various anesthetic agents and methods of administration. (Local anesthesia is taught in dental schools but usually not general or inhalation methods.) With each agent should be stressed its mode of action, advantages and disadvantages, indications and contraindications, danger signals and methods of resuscitation, etc. In addition, each student should have the opportunity to administer as many anesthetics as is possible, under supervision, in order to obtain the essential practical experience.

(2) Pending the adequate teaching of general anesthesia in the dental schools, all dentists desirous of employing general anesthesia in their offices should be required to undertake postgraduate study in this subject and possess a certificate of proficiency in the same. This would apply particularly to those limiting their practice to exodontia and oral surgery.

(3) Under existing conditions, nurses or technicians can designate themselves as qualified anesthetists, and assume such duties in dental offices or clinics. No previous training or evidence of proficiency is required. As long as the administration of anesthesia by nurses continues to receive legal sanction, each one should be required to possess a certificate of proficiency in this art.
Nitrous oxide is truly a remarkable gas. While it is inert, it apparently does have some anesthetic action. No other agent equals it in its speed of absorption and elimination from the body. It is free from the hazard of explosion. It produces the minimum of postanesthetic complications or discomfort. It fulfills the majority of the attributes of the perfect anesthetic agent. It is the only gas which may be administered in safety with low concentrations of oxygen, as it does not interfere with the protective mechanism whereby respiration and circulation are maintained during hypoxic states. Its greatest drawback is its lack of potency or inability to produce muscular relaxation. The margin of anesthesia with nitrous oxide is narrow, and transition through the various stages of anesthesia may occur very rapidly. Thus, proficiency in its administration comes only with training and experience, and when improperly administered it may well become both unsatisfactory and dangerous.

My associates and I during the past twenty years have administered nitrous oxide-oxygen to many thousands of patients and for every sort of surgical procedure. The patients varied in age from two days to 95 years and the duration of the anesthesias from a few moments to nine and a half hours. From our experience it is felt that nitrous oxide-oxygen (unsupplemented) is not a suitable agent for routine use for major abdominal procedures, nor is its use so advocated. In certain selected cases (subnormal risk types), it may be employed satisfactorily, but not for robust or muscular individuals. The recent introduction of intocostrin (Squibb) has greatly increased its usefulness in this particular field.

With this exception, however, our experience has shown that there is no reason why nitrous oxide-oxygen may not be administered for the vast majority of operative procedures with safety to the patient and satisfaction to the operator.

Summary

The danger of anoxia is not confined to nitrous oxide-oxygen anesthesia, but may, and does, occur with any anesthetic agent in present use.

When anoxia occurs with nitrous oxide-oxygen anesthesia, it is the result of maladministration, and not of any direct effect of the gas itself.

The most vital factor in any anesthetic is the ability of the anesthetist.

All psychotic states occurring postoperatively are not attributable to anesthesia.

Safety cannot be prescribed or legislated into anesthesia.
REFERENCES


RESOLUTIONS ON MORTON CENTENARY, FROM SECTION ON ANESTHESIOLOGY (AMERICAN MEDICAL ASSOCIATION)

Dr. Henry S. Ruth, Section on Anesthesiology, presented the following resolutions:

WHEREAS, The year 1946 marks the one hundredth anniversary of the first public demonstration of the use of ether as an anesthetic agent by W. T. G. Morton on October 16, 1846, in the Massachusetts General Hospital in Boston; and

WHEREAS, This event represents one of the most important steps in medical history; therefore be it

Resolved, That, in recognition of this great contribution to the relief of human suffering, the American Medical Association give public recognition of this historical event by publication in The Journal of the American Medical Association; and further be it

Resolved, That the American Medical Association cooperate with the American Society of Anesthesiologists and other acceptable medical organizations in programs celebrating this centenary.

It was moved by Dr. Ruth that the resolutions be adopted and the motion was seconded by Dr. Arthur J. Bedell, Section on Ophthalmology. After discussion, the resolutions were laid on the table on motion of Dr. H. A. Luce, Michigan, seconded by Dr. Walter E. Vest, West Virginia, and carried.

(From Journal of the American Medical Association, Organization Section, 131: 1001–1002, July 20, 1946.)