Nitrous Oxide and Oxygen Anesthesia With Curare Relaxation*

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NITROUS oxide anesthesia has been the subject of bitter controversy ever since its first public demonstration by Horace Wells in 1844. Not until Andrews showed that the admixture of oxygen with nitrous oxide increased its safety was it considered sufficiently flexible for use in general surgery. Profound differences of opinion have been very much in evidence among anesthetists, physiologists and pharmacologists regarding the status of nitrous oxide anesthesia. The extremes of viewpoint range from those who believe that nitrous oxide is sufficiently potent to afford adequate anesthesia for all kinds of abdominal operations to those who feel that nitrous oxide is incapable of producing anesthesia independent of oxygen lack. At present the consensus appears to favor the contention that nitrous oxide with oxygen in atmospheric proportions will produce light surgical anesthesia, but only slight muscular relaxation.

The practice of producing greater depth of narcosis by restriction of oxygen in nitrous oxide-oxygen mixtures has been properly discredited but frequently resorted to in order to avoid the addition of ether. Many recently trained anesthetists have had little experience with nitrous oxide anesthesia. The popularity of cyclopropane anesthesia, wherein any degree of narcosis might be maintained without danger of oxygen lack, has been a strong reason for the failure to use nitrous oxide to its fullest extent.

One has only to review briefly the physical and physiological advantages of nitrous oxide and oxygen anesthesia to understand the desirability of a re-investigation of its present status in the light of recent advances in the clinical use of curare.

Nitrous oxide and oxygen provide us with a general anesthetic which is neither inflammable nor explosive and which is relatively non-toxic. Its inability to produce adequate muscular relaxation in the majority of abdominal operations is well recognized. Pre-anesthetic medication with narcotic drugs increases, markedly, the field of usefulness of nitrous oxide and this field may be broadened further by the use of nerve blocks with solutions of local anesthetics.

The introduction of clinically adequate curare into anesthesia offered the possibility of the greatest advance in gas anesthesia since Andrews suggested the combination of oxygen with nitrous oxide.

When Griffith first decided to use curare to secure muscular relaxation during light surgical anesthesia, it was only natural for him to select cyclopropane, of which he is a leading exponent, for the trial. Nevertheless, curare appeared to the authors of this paper to offer a means whereby muscular relaxation or even flaccidity might be obtained during the course of anesthesia with nitrous oxide. Decision to study it was motivated by a desire to extend the physiological advantages of nitrous oxide anesthesia, rather than a wish to veer away from cyclopropane or ether solely because of their inflammable nature. Observations herein are based on experience with the use of nitrous oxide anesthesia with curare relaxation in a wide variety of cases, 160 in number, during the last two years.

ADEQUATE PAIN RELIEF AND REFLEX OBTUNDATION

Very early in the study the observation was made that the attainment of adequate muscular relaxation might not be the only obstacle to be overcome in this effort to widen the scope of nitrous oxide anesthesia. Even when curare was administered in doses sufficiently large to provide good muscular relaxation, there was evidence of insufficient pain relief during the period of manipulation of the abdominal viscera. The patient will usually respond to such stimulation by contracting, however, feebly, the musculature which the curare has not completely paralyzed, such as the muscles of the face. A grimace is observed and the pulse and blood pressure will usually rise simultaneously. The intravenous administration of morphine will cause the grimace to disappear and the blood pressure and pulse may assume their pre-manipulative level.

The well-known respiratory embarrassment consequent upon the intravenous administration of morphine led us to try Demerol. Clinically, Demerol given intravenously in doses of 50 to 100 mg. will fortify the pain-relieving qualities of nitrous oxide and oxygen with less respiratory depression than that observed following equivalent doses of morphine. Not only will the degree of respiratory depression be less profound, but it will be of much shorter duration, ranging in the neighborhood of one-half hour in the average case. Curare relaxation should, in our opinion, never be considered a substitute for adequate pain relief, even though the patient may, by reason of certain hypnotic drug action, have a complete amnesia for the horrible experience. The administration of curare should be reserved until complete freedom from the effects of painful stimuli can be guaranteed. This having been done, curare may then be administered in amounts sufficient to obtain the required relaxation of the skeletal musculature.

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EFFECTS OF NARCOSIS AND CURARIZATION ON VENTILATION

Regardless of the drugs used for narcosis, anesthesia, or muscular relaxation, the primary concern should be the maintenance of optimum pulmonary ventilation. All anesthetics and narcotics employed to produce general depression of the central nervous system are respiratory depressants. The narcotic drugs such as morphine afford good pain relief with only moderate respiratory depression, in contrast to the hypnotic drugs, including the barbiturates of all classes, which produce marked respiratory depression with only slight pain relieving qualities. The so-called intravenous anesthetics, pentothal and evipal, fall into this category and might better be regarded as "super-hypnotics" than anesthetics.

Nitrous oxide and oxygen, plus intravenous Demerol, plus curarization, afford good anesthesia and excellent muscular relaxation. On the other hand, one must be prepared to deal with the additive depressant action of each of these drugs on respiration.

When the patient has been given enough of the aforementioned drugs to produce good surgical anesthesia, it has been our practice to supplement the patient's feeble respiratory efforts by rhythmically inflating his lungs. This may most efficiently be accomplished by using the "to and fro" carbon dioxide absorption system and exerting gentle intermittent pressure on the breathing bag. The airway should be perfectly free. To insure this, endotracheal intubation is highly desirable. This has been our practice in most intra-abdominal procedures. Under circumstances wherein the patient has been intubated, one may be assured that the compression of the breathing bag will result solely in the inflation of his lungs. In some cases, where the control of ventilation was attempted without endotracheal intubation, there was a marked distention of the stomach and intestines simultaneous with the inflation of the lungs. Indeed, this has been demonstrated in a cinema intended to illustrate the use of curare in anesthesia! In some instances where the anesthetist fortifies the patient's spontaneous respiratory movements to insure adequate ventilation, it will be observed that the respiration has become completely under his control. Adequate ventilation may be guaranteed by the rhythmic, intermittent inflation of the lungs, allowing expiration to proceed passively against only atmospheric pressure. When spontaneous respiratory movements of sufficient amplitude have returned, the mechanical assistance may be discontinued.

Under-ventilation will be noticed much more quickly during nitrous oxide anesthesia than when agents such as cyclopropane or ether, which carry a much higher complement of oxygen, are employed. It has been our practice to combine nitrous oxide with 20 per cent or more of oxygen checked by actual gas analysis. Frequent gas samples were taken for analysis during the course of many operations. The residents are instructed to feel free to make these determinations at any time, in any case. This procedure tends to make all the anesthetists avoid oxygen deprivation.

The respiratory depression consequent upon the administration of curare is different in character from that which is produced by increasing the depth of narcosis with the various general anesthetics. Curare and the potent anesthetics, such as ether, both produce inactivity of thoracic respiratory movements before diaphragmatic paralysis, but here the similarity ceases. When ether anesthesia is pushed to the point where the intercostal musculature becomes paralyzed, the diaphragmatic movements appear to be very little affected. This phenomena offers a marked contrast to the combined paralysis of the intercostal musculature and paresis of the diaphragm observed following the administration of curare. Spontaneous respiratory movements which result in little more than the displacement of the dead space air back and forth are not satisfactory for the purpose of ventilation.

When the administration of curare is superimposed on anesthesia with cyclopropane, combined with very high proportions of oxygen, cyanosis will naturally be more slow in appearing than during nitrous oxide anesthesia when atmospheric proportions of oxygen are employed. Regardless of the degree of oxygenation of the blood, its carbon dioxide tension may be dangerously elevated by depressed respiration. When carbon dioxide is permitted to accumulate in the patient who has received curare, the usual increased blood pressure response may not occur until the curare action has partially or totally worn off. It would appear that the reason for this has to do with the decreased peripheral resistance of the vascular bed consequent upon the general relaxation of the skeletal musculature. The pulse rate increase which follows an elevated carbon dioxide tension in the blood will be observed in the under-ventilated patient who has received curare. When the effect of curare has worn off, under-ventilation will cause the blood pressure to rise. It is important to note at this point that insufficient pain relief in the patient who is adequately ventilated will cause the blood pressure to rise when the curare action has become dissipated. The differentiation is important and is a matter for the physician familiar with respiratory physiology to decide. The treatment for the former is supplemental ventilation; for the latter, supplemental anesthesia. Perhaps by reason of our concern with the problems of ventilation during the course of anesthesia for intrathoracic operations, we have not experienced any untoward effects of over-ventilation, although conceivably this might occur. Here again, emphasis must be placed on the qualifications of the individual conducting the anesthesia and the ventilation rather than the person administering the curare. We believe that the former should never be delegated to anyone except a properly qualified physician anesthetist, while the latter may be performed by anybody who is able to insert a needle into a vein. These matters are stressed because of the all too frequent experience of witnessing the reverse. This, too, was recently demonstrated in a cinema intended to show the technique of controlling ventilation during cyclo-

propane anesthesia in a patient who had been given curare.

PROPER TIME OF CURARE ADMINISTRATION

When curare is employed as a means of obtaining satisfactory muscular relaxation during nitrous oxide anesthesia, it should only be given after adequate pain relief has been assured. After nitrous oxide anesthesia has been induced by the carbon dioxide absorption technique, Demerol, given intravenously and slowly enough so that respiration is not too greatly depressed (usually 50 to 100 mg.), is injected over a period of three to four minutes. Adequate pain relief thus having been achieved, curare in the amount of 80 or 100 mg. may be administered intravenously to insure sufficient relaxation for endotracheal intubation. Subsequent doses of curare may then be given as needed to secure the necessary muscular relaxation. The dose required for the subsequent injections has ranged betwen 40 and 60 mg. of curare. During the course of operations lasting four hours or longer, it will usually be necessary to give additional doses of Demerol. We usually administer 25 to 50 mg. intravenously for this purpose. The largest total amount of curare which we have employed in one case was 260 mg. for a bowel resection lasting six and a half hours. The largest amount of Demerol was 225 mg. during a gastric resection lasting four hours.

REVERSAL OF ANESTHETIC, NARCOTIC AND CURARE EFFECTS

The anesthetist should try to conduct every anesthetic in such a manner as to provide the surgeon with the approximation of ideal operating conditions and still guard against any action which will delay the return of the patient's reflexes upon completion of the operation. The reversal of the effects of nitrous oxide is almost immediate. Recovery from the respiratory depressant action of intravenous Demerol takes approximately one-half hour, while the return of the cough reflex may require an additional hour or an hour and a half. The hypnotic action of Demerol is of short duration and patients may readily be awakened 15 to 20 minutes after the intravenous administration of 50 mg. of the drug.

Curare is effective for approximately one-half hour after its intravenous injection. The length of time during which it is effective clinically appears to be affected very little by the size of the dose when it is administered in the amounts which we have employed for obtaining muscular relaxation during nitrous oxide anesthesia. An initial 100 mg. dose appears to last no longer than an 80 mg. dose, although the result of the former may be muscular flaccidity and of the latter muscular relaxation.

CUMULATIVE EFFECTS OF DEMEROL AND CURARE

There is a certain amount of cumulative effect after the administration of repeated doses of Demerol so that the duration of action of the subsequent doses becomes progressively longer.

Curare, also, shows a cumulative action and when large amounts of the drug are required, as in the case of prolonged operations, a sensation of muscular weakness may persist for some hours after the termination of anesthesia.

SUMMARY

1. A method of rendering nitrous oxide anesthesia more flexible by the use of curare for obtaining muscular relaxation has been outlined based on experience in 160 clinical cases.

2. The importance of first securing adequate pain relief before the administration of curare has been stressed. The intravenous injection of Demerol to fortify the anesthetic properties of nitrous oxide has been suggested.

3. The problems of altered respiratory physiology consequent upon the employment of the nitrous oxide-Demerol-curare combination have been discussed.

4. Satisfactory anesthesia for major abdominal operations may be provided by nitrous oxide and oxygen when the skeletal musculature has been relaxed with curare.

5. The toxicity of nitrous oxide and curare are low and the safety of the method depends on the ability of the anesthetist to apply his physiological knowledge to a clinical procedure.