FACTORS AFFECTING THE RAPIDITY OF ALTERATION OF NITROUS OXIDE CONCENTRATION IN A CIRCLE SYSTEM

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THE rapidity of alteration of the concentration of an anesthetic agent breathed by a patient from an anesthetic system is dependent on many factors. These include the flow rate of the gas entering the system, the volume of that system, the volume contained within the patient's respiratory system, the effective minute volume, and the uptake of gas by the circulatory system and other tissues. Other factors such as changes in inflowing gas concentration, oxygen consumption, carbon dioxide elimination from the patient and absorption by the absorbent within the system are also important. The individual and combined effects of these factors have been determined for several gases under various conditions.[1-27]

The majority of the work published on anesthetic (and nitrogen) gas concentrations in anesthetic systems, in the lungs, or in arterial blood may be divided into two groups. The first concerns itself with constant concentrations and the effects achieved.[11, 15, 16, 21-23, 25-27] The second deals with the dynamic alteration of concentration that occurs on introduction or excretion of gases. In the majority of this latter group a nonrebreathing system or it's equivalent was used.[1, 2, 4-10, 12-13, 15, 21-23] Two exceptions are noteworthy: the work of Hamilton [3] and of Crowley [11] involved the changes in conventional anesthetic systems, with oxygen and nitrogen being used in both cases.

No data have been presented which illustrate the rate of change of concentration of nitrous oxide in a circle system which ocurrs on induction, although such a system is the one most frequently used for its administration. One possible exception consists of a single graph in Crowley's work.[11] Several theoretical equations have been set forth which might be used to graph the above changes,[28-30] but none are accompanied by substantiating data for the circle system. The present study was undertaken to provide such data and to evaluate the influence of factors that vary or can be altered clinically.

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METHOD

Young patients (average age 31, range 20 to 47) who were to undergo various operative procedures were given morphine (16 to 35 mg.) or meperidine (100 to 200 mg.) with scopolamine (0.5 to 0.8 mg.) subcutaneously. These amounts were given to provide a moderate degree of basal hypnosis and amnesia which when combined with thiopental allowed for a period of 20 to 30 minutes after induction where further anesthetic agent was not needed. No patient was asleep on arriving in the operating room (1½ hours later); all moved from cart to table without assistance and no reduction in blood pressure greater than 25 per cent of that obtained on the ward was noted prior to induction of anesthesia. Both stability and amnesia were obtained as evidenced by the little variation in vital signs during the latter portion of the 20 to 30-minute post-induction period, and by the fact that no patient volunteered recollection of this period in the postoperative visits.

About one and one-half hours after the preanesthetic drugs had been given, induction of anesthesia was begun with thiopental and continued to the point of loss of the corneal reflex. The average amount was 300 mg. with a range of 200 to 450 mg. Succinylcholine 40 to 60 mg. was administered intravenously; the trachea was intubated and the endotracheal tube was connected to a conventional anesthetic circle system (Heidbrink Kinet-o-meter with 9-B absorber—figure 1-A). Additional thiopental was given when indicated by patient movement or after a steady state had been obtained when the effect of barbiturate on oxygen consumption was to be observed. An intravenous infusion of succinylcholine was given throughout the study at as constant a rate as possible in order to provide immobility and adequate relaxation.

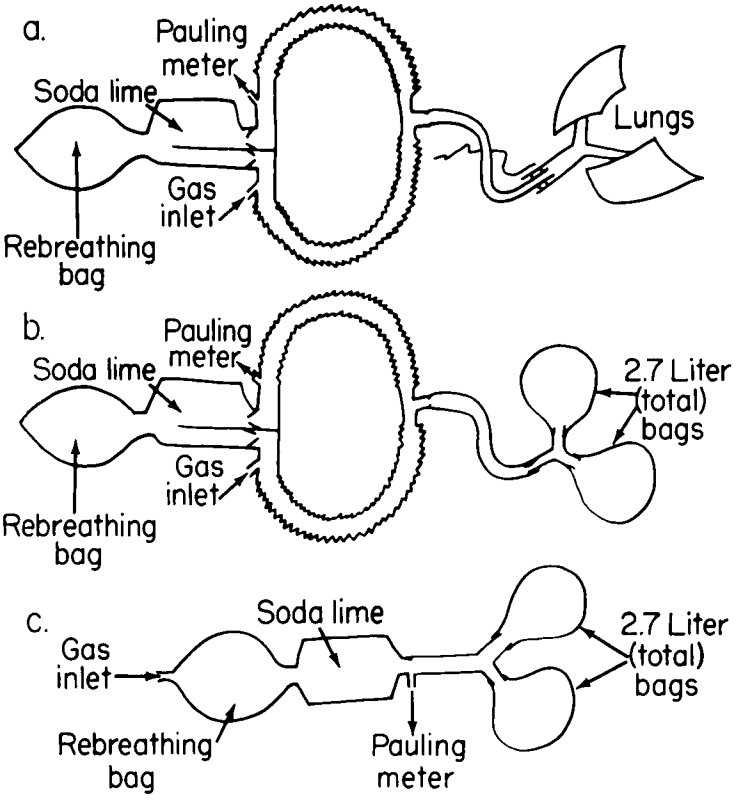

FIG. 1. A. Diagrammatic representation of the combined circle system and patient showing the physical arrangement, the points of gas inflow and of gas exit for sampling. The gas exit for overflow (not shown) is at the usual point just before the experiatory valve. B. The same system with the substitution of a 2.7-liter "lung" composed of two rubber bags for the patient's lungs. C. A to-and-fro system is substituted for the circle system, the 2.7-liter "lung" being retained. The gas exit for overflow (not shown) lies at the same point as the exit for the Pauling meter.

The lungs of all patients were manually hyperventilated throughout the study. After ten or more minutes of denitrogenation by hyperventilation with 10 liters per minute (LPM) or greater flows of oxygen,[3] the oxygen inflow was decreased to the flow rate to be used as the total flow rate (nitrous oxide and oxygen) for an additional ten minutes. This resulted, in every case, in an oxygen tension in the circuit of between 95 and 100 per cent (room air measured at 20 per cent). Following this, various mixtures of nitrous oxide and oxygen (constant for any one patient) were admitted at a constant flow rate and the changes in oxygen concentration in the expiratory side of the circle (fig. 1-A) at frequent intervals. A Pauling-type meter (A. O. Beckman, Model D Oxygen Analyzer) was used for all oxygen determinations. It was tested for accuracy with measured combinations of nitrous oxide and oxygen and was found to vary less than two per cent over the 0 to 100 per cent range. The nitrous oxide-oxygen flow was continued until stability (no variation of more than one to two per cent for one hour) of the oxygen concentration was reached. For 1 LPM this took three or more hours whereas with 10 LPM it could be done in one and one-half hours.

The values obtained were tabulated as percentages of the total range through which the nitrous oxide concentration moved (assuming oxygen decrease is an accurate reflection of nitrous oxide increase). Thus if the concentration of oxygen began at 100 per cent and the final value was 20 per cent the range was 100 minus 20 or 80. A value of 40 per cent oxygen for this range would be (100 minus 40)/80 or 75 per cent change of nitrous oxide. These data were then plotted in relation to time.

Flow rates totaling 1, 2, 3, 5, and 10 LPM of the nitrous oxide-oxygen mixtures were used. An amount of oxygen beyond the flow rates quoted and varying from 150 to 300 ml. per minute depending on patient size and body type was also admitted at a constant rate to account for oxygen uptake. Thus a 1 LPM flow rate really represents 1.15 to 1.30 LPM.

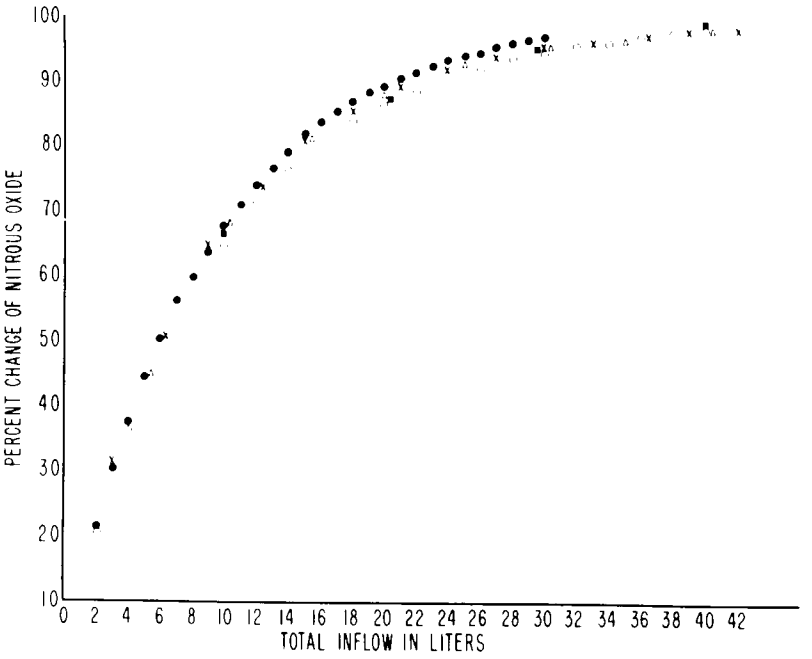

FIG. 2. A composite graph of the total inflow in the model illustrated in figure 1-B related to concentration attained. Flow rates of 1 (●), 2 (○), 3 (×), 5 (△), and 10 (■) LPM.

Displacement studies of the flow meters indicated an error of no more than ten per cent for the meters used.

A model was constructed in an attempt to account for all the changes found excluding tissue uptake. The same machine (bag, canister, valve system, and corrugated tubes) was connected to two rubber bags containing a total of 2.7 liters at a pressure of four to five cm. of water (fig. 1-B); 2.7 liters approximates the functional residual capacity in the supine patient whose trachea had been intubated given a compliance of 40–50 ml. per cm. water.[31, 32] After thorough denitrogenation with oxygen, various flow rates of nitrous oxide were introduced into the system and the rebreathing bag intermittantly compressed as in the clinical situation. The percentage change in oxygen was measured and tabulated as before. Another model was also constructed using the same "lung" (the two bags containing 2.7 liters), but in which a to-and-fro system was substituted for the circle system (fig. 1-C). This system had a smaller volume than that of the circle. Change in nitrous oxide concentration was measured as before. At all times during each study the rebreathing bag was maintained at a point near fullness without appreciable tension.

There are several sources of error in this study. However, consistency of the data obtained would indicate that the errors are not great or at least are consistant. Some of the possible incorrect assumptions and rationale behind them are noted below.

The volume of the circuit obviously was subject to some variation, but because the curves for a specific flow rate in the models were consistently reproducible (within a range of 2 to 3 per cent) and showed little deviation from a smooth logarithmic shape as would be expected if the volume remained constant [11, 28] it would appear that this variation is minor. The volume of patient's respiratory systems varied, but since these were all young, healthy patients (without known cardiorespiratory disease) in the same weight ranges (except where noted) this variation may also be assumed to be minor.

Hyperventilation was done manually and obviously is subject to considerable variation. Controlled ventilation was chosen because the depressants used would not safely allow spontaneous respiration. In addition, it is believed that hyperventilation produced readings which reflected the most rapid rise in concentration in the lungs. Thirdly, hyperventilation provided the most thorough mixing of entering

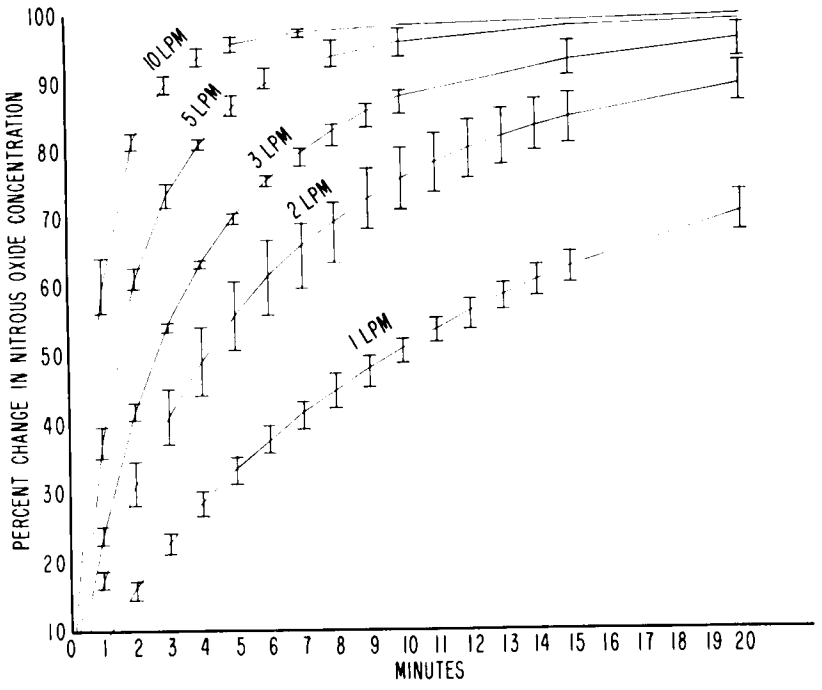

FIG. 3. These graphs relate the change in nitrous oxide concentration in the circuit of a Heidbrink Kinet-o-meter with 9-B absorber with time at the flow rates noted. The anesthetic circuit was connected to 60–80-kg. subjects who were hyperventilated throughout each determination. The 0 time point marks the point of induction with nitrous oxide. Each graph follows the arithmetic mean of an average of four cases for each flow rate. The bars represent the concentration ranges for the flow rates noted.

gas with that in the circuit and lungs, and as far as the study was concerned this was most important as it would give the least variable results since then no portion of the system would lag behind the other to distort the "tail" of the concentration curves obtained. For this last purpose, beyond a certain point it does not matter how much the patients lungs are ventilated, this will not add to the mixing. Evidence that this point was passed is provided by the concentration curves obtained from the models. In a given model, the percentage of change was closely related (a range of 3 to 4 per cent) to the total inflow. Thus a flow of 1 LPM for ten minutes produced the same percentage change as a flow of 10 LPM for one minute (fig. 2). This is in agreement with Carré's equations.[28] Any variation in mixing would have more effect at the higher flows (since there would be lesser time or a lesser number of ventilations) than at the lower flows and the two graphs obtained should not coincide if this is the case. Since they do coincide it may be concluded that mixing is adequate, at least in the models. This also may be assumed for the clinical situation since the only alteration there was the substitution of the patient's lungs for the 2.7-liter rubber bags.

Oxygen uptake will vary with metabolic requirements. Increase in uptake was noted by decreased concentration in the circle on movement by the patient. The decrease in oxygen concentration under these circumstances rarely exceeded two per cent even at the 1 LPM flow rates. Return to previous levels occurred on return to immobility. Surgical stimulation unaccompanied by movement did not alter the oxygen levels. Operation of course, did not commence until well after the introduction of nitrous oxide. The administration of one-half or more of the induction dose of thiopental to patients who had reached a constant oxygen tension occasionally caused that tension to rise one percentage point.

Carbon dioxide elimination also varies with metabolic requirements. An attempt was made to account for the effect of the basal output by decreasing the oxygen flow rate for ten additional minutes after denitrogenation to the level of the total flow rate to be used during the remainder of the study. The oxygen concentration obtained after this time was that used as the upper baseline (zero point) for

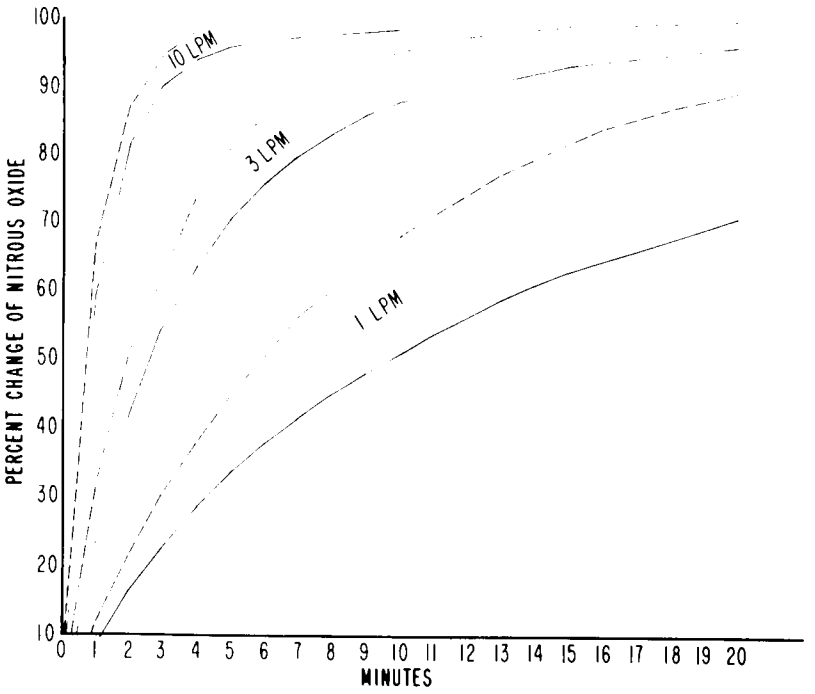

FIG. 4. A comparison of the time-concentration curves obtained in the clinical situation (solid lines) using the circle system illustrated in figure 1-A and those obtained from the model circle system (broken lines) noted in figure 1-B. Flow rates as noted. 60–80 kg. subjects.

the study. Usually, this represented a decrease of less than one percentage point from that obtained immediately following hyperventilation with higher flow rates. The absorbing system appeared to function well (no direct measurement was made of carbon dioxide levels), cases taking six to seven hours being carried on 1 LPM flow rates without appreciable rises in blood pressure, flushing, sweating, attempts to breath, or postoperative blood pressure fall attributable to carbon dioxide excess.

RESULTS

Figure 3 shows the relationship of change in nitrous oxide concentration with time at various flow rates. These graphs are representative of the results obtained in subjects weighing 60 to 80 kg., each graph being an average of four cases. It was found in this group that in order to achieve a 90 per cent change within three minutes, a flow rate of at least 10 LPM was necessary. A 5 LPM rate caused the same change in six to seven minutes while a 1 LPM rate required 35 to 60 minutes.

Figure 4 represents the difference between the results shown in figure 3 and the results obtained in the model for flow rates of 1, 3, and 10 LPM. As can be seen, the concentration changes in the model occurred more rapidly than those in the clinical situation, the

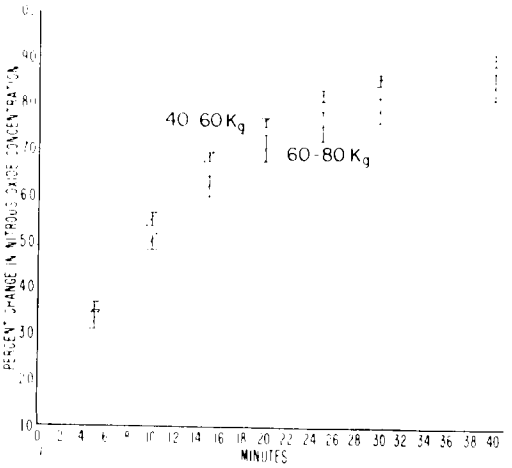

FIG. 5. A comparison of the time-concentration curves obtained in the clinical situation with two groups of subjects. The flow rate in all cases was 1 LPM. The graph of the 40–60 kg. group represents the arithmetic mean of 3 cases. The graph of the 60–80 kg. group represents the arithmetic mean of 4 cases. The bars indicate the concentration ranges in each group.

difference between the two systems decreasing as the flow rates increased.

The rate of change was altered by weight and body type: the heavier, more muscular patients usually having the slower rate of change. This is illustrated on a weight basis in figure 5. The lighter subjects attained any concentration more rapidly than the heavier. This agrees with the theoretical work of Kety [29] and of Harris.[30] Comparison of the data obtained from the models indicated that the system holding the lesser volume (the to-and-fro) gave the most rapid change in concentration at similar flow rates. This agrees with the work of Hamilton.[3]

Discussion

If 90 per cent of final concentration of nitrous oxide is accepted as the desirable figure to obtain in a short space of time, then in this system (the one used clinically) flow rates of 10 LPM or more are necessary. The lower flow rates (1 to 3 LPM) result in a slow approach to the final concentration. Supplementation with intravenous or inhalation agents will necessarily be increased during this period.

The volume of this system is less than that seen in those circles having larger carbon dioxide absorbers or larger rebreathing bags (the one used was a 5-liter bag). The volume of the system is greater than that or most to-and-fro systems. From the results obtained in the models it is apparent that a lower rate is required to reach a desired concentration in the same space of time in the system containing the lesser volume (i.e., the to-and-fro). Conversely, in systems with larger volumes a larger flow rate would be required.

Larger respiratory system volume and greater tissue uptake, both to blood flowing through the pulmonary bed and to the peripheral tissues, will be found in larger patients, and these then require higher flow rates to attain the same concentration in the same space of time as smaller subjects (fig. 5). It appears (fig. 4) that the effect of tissue uptake decreases as flow rates increase. It is quite marked at 1 LPM but small at 10 LPM.

These results were obtained with hyperventilation as part of the conditions of the study. This is not always the case in clinical practice. Without hyperventilation, the anesthetic concentration in the anesthetic circuit will rise more rapidly (being in effect a smaller volume without the full influence of the patient's respiratory system volume, and without being as greatly affected by circulatory and tissue uptake) while the concentration in the lungs and blood will rise more slowly. Under these conditions a lower flow rate will cause the same rise in concentration in the anesthetic system in the same time as a higher rate with hyperventilation. However, if blood gas concentration may be equated to anesthesia, the patient who is hyperventilated will be anesthetized more rapidly.

These findings are relevant to all anesthetics in which nitrous oxide is to be used. They apply primarily at induction and recovery (i.e., the times of greatest alteration of concentration of nitrous oxide) and are especially pertinent in short procedures where the induction may be the longest portion of the case. These findings also imply that the interests of rapid induction and of economy would both be best met in the case of nitrous oxide by commencing anesthesia with high flows (10 LPM or greater) and then reducing them, after an interval of five to ten minutes, to low flows (1 to 3 LPM).

Summary

The rate of change of nitrous oxide concentration in a conventional anesthetic circuit during induction of anesthesia was determined. Various flow rates were used with various sizes of patients as subjects. All patients were hyperventilated during the determinations. Model systems were constructed to differentiate the effect of tissue uptake and of differences in the volumes of anesthetic systems.

It was found that high inflow rates (10 LPM or more) of nitrous oxide were necessary to achieve a rapid change of concentration. This was believed to be especially applicable in cases where induction might be the longest portion of the anesthetic procedure. It was believed that after induction had been completed, the anesthetic level due to nitrous oxide might be well and economically maintained with low (1 to 3 LPM) flows.

It was found that the larger, more muscular patients usually were associated with a less rapid rise in concentration. Decreasing the

volume of the anesthetic system was found to increase the rapidity with which a particular concentration would be reached.

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NUCLEIC ACIDS The influence of narcotics on the content of RNA and DNA in the motor neurons of the spinal cord of rats, to whom barbamyl (0.07 mg./Gm.) or urethan (1 mg./Gm.) was administered intraperitoneally, was studied by the method of photometry of microphotograms prepared by means of UV microscopy in the 265 mu spectral band. No pathological changes in the structure of motor neurons could be detected. The quantity of DNA in nuclei is not changed under narcosis. The quantity of RNA is changed; with use of barbamyl it is somewhat reduced, while with use of urethan it is somewhat increased. (*Brodskii, V. Ya.: Nucleic Acids in Motor Neurons of the Spinal Cord Under Influence of Barbamyl and Urethan, Doklady Akad. Nauk SSSR 112: 753 1957.*)

PSYCHIC TRAUMA The psychotraumatic aspects of pediatric surgery and anesthesia have been studied in a series of 155 children admitted for tonsillectomy and adenoidectomy. Ages ranged from three to 12 years. The children were seen in groups preoperatively, were given only atropine by hypodermic injection for preanesthetic medication, and anesthesia was induced with thiopental intravenously. Anesthesia was maintained with endothracheal nitrous oxide and oxygen and suxamethonium as required. The postoperative course was carefully followed and the parents questioned by means of a questionnaire after the discharge of the patient from the hospital. Only three patients (2 per cent) showed psychic trauma that could be ascribed to the anesthesia. (*Hodges, R. J. H.: Induction of Anesthesia in Young Children, Lancet 1: 82 (Jan. 9) 1960.*)