

# Nitrous Oxide and Low Inflow Circle Systems

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Concentrations of oxygen and nitrous oxide delivered at low flow rates to a circle system and concentrations expired by the patient were studied over a range of clinical conditions. No useful relation was found between the delivered and mixed expired oxygen concentrations. Expired concentrations were also compared with those predicted by two different equations. No reliable agreement between observed and predicted concentrations was found below total fresh gas inflows of 1.2 liters per minute. A major factor in the lack of agreement was a variation in gas exchange. Oxygen uptake ranged from 125 to 230 ml./minute/sq. meter. Nitrous oxide exchange after one hour of inhalation varied more than 200 ml./minute uptake to 100 ml./minute excreted. One, therefore, cannot rely on the oxygen concentrations delivered to the circuit or on predictions based on average uptake values. The convenience of low inflow nitrous oxide anesthesia can be achieved only when oxygen concentration within the breathing circuit is monitored.

THE CLOSED system technique for nitrous oxide anesthesia was originally developed by Waters to conserve the gas which was relatively expensive at that time.<sup>1</sup> There is still a logistic requirement for conservation of nitrous oxide in military campaigns and in many geographical areas. In addition, the closed system for nitrous oxide anesthesia offers advantages other than logistic; the estimation of tidal volume is easier as the flow decreases, and the danger of excessive airway pressure from distention of the reservoir bag is lessened.

The paramount disadvantage to closed system anesthesia lies in the difficulty of predicting the inspired oxygen concentration. This study indicates that with inflows of oxygen and nitrous oxide totaling less than 1.2 liters/minute, reliable prediction is not possible.

## Methods

Fifty-eight patients, A.S.A. physical status 1 or 2, undergoing a range of operations were

studied during low inflow nitrous oxide anesthesia. Ages varied from 8 to 52 years, and weight from 65 to 210 pounds. Operative sites included 22 head, neck or spine, 5 intra-thoracic, 8 intra-abdominal and 25 extremities. All patients were given meperidine and promethazine in equal doses (0.2–0.5 mg./pound) and either scopolamine or atropine (0.003 mg./pound) 45 minutes before induction of anesthesia.

In 43 patients induction of anesthesia was accomplished with the intravenous administration of 2–3 mg./pound of thiopental followed by succinylcholine (0.5 mg./pound). The trachea was intubated and nitrous oxide inhalation started. Intravenous supplementation with thiopental or meperidine was used to control muscular movement, tachypnea, tachycardia, or hypertension; intravenous lidocaine was used to control coughing.<sup>2, 3</sup> In the remaining 15 patients muscular relaxation was first established by means of epidural or spinal block (eighth thoracic or lower). Nitrous oxide anesthesia was then induced. In all patients 25–30 minutes of breathing through an Ohio circle no. 20 system with inflows of 8 liters of nitrous oxide and 2 liters of oxygen was used for denitrogenation and to avoid the rapid changes in uptake found by Severinghaus<sup>7</sup> to occur during the first half hour. Total gas flows were then reduced to less than 1.2 liters per minute. The oxygen flow meter was set to deliver one to three times the predicted metabolic demand.<sup>4</sup> Sufficient nitrous oxide was delivered to keep the mixed expired concentration of oxygen between 15 and 35 per cent.

The sampling site for oxygen was at the pop-off valve, which was in the expiratory limb between the rebreathing bag and the canister. Inspired oxygen concentration when measured was found to be 3–4 per cent higher than the expired. Continuous measurement of CO<sub>2</sub> at this site by means of an infrared analyzer yielded a straight line indicating that mixing of expired gas was complete. This site was chosen because of the requirement

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for use of pop-off gas concentrations in calculating gas uptake (see below).

Oxygen concentration was measured with a Beckman Oxygen Analyzer Model D after absorption of water and CO<sub>2</sub>. The oxygen analyzer was linear within one-half per cent and was calibrated daily. Nitrous oxide was assumed to represent the balance of gases except for 1 per cent attributable to prolonged excretion of nitrogen by the patient<sup>6</sup> and the presence of nitrogen as an impurity in the gas supply.

A 13-liter spirometer was used for volume measurements. Flow meters of an Ohio 2,000 series kinetometer were calibrated by displacement of water. The meters were within 2 per cent of the scale readings in the range used. Gas volumes were expressed at ambient temperature and pressure dry as delivered from the gas machine. Studies were carried out in an air-conditioned room (75 ± 2° F.) with 60 per cent relative humidity.

A study period consisted of one half hour or longer of unchanged gas inflows. The period ended when at least ten minutes of unchanging oxygen measurements indicated a steady state. A new study period was begun when the inflow of both gases was changed.

### Calculations

The observed values were compared with predictions made from two equations:

$$\overline{F_{O_2}} = (\dot{R}_{O_2} - \dot{V}_{O_2}) / (\dot{R}_{O_2} + \dot{R}_{N_2O} - \dot{V}_{O_2}) \quad (1)$$

$$\overline{F_{N_2O}} = (\dot{R}_{N_2O} - \dot{V}_{N_2O}) / (\dot{R}_{O_2} + \dot{R}_{N_2O} - \dot{V}_{O_2} - \dot{V}_{N_2O}) \quad (2)$$

Definition of symbols:

|                       |                                                                                               |
|-----------------------|-----------------------------------------------------------------------------------------------|
| $\dot{V}_{O_2}$       | Rate of metabolic uptake of oxygen.                                                           |
| $\dot{V}_{N_2O}$      | Rate of absorptive uptake of nitrous oxide.                                                   |
| $\dot{R}_{N_2O}$      | Rotameter setting for nitrous oxide.                                                          |
| $\dot{R}_{O_2}$       | Rotameter setting for oxygen.                                                                 |
| $\overline{F_{O_2}}$  | Fractional concentration of oxygen in dry mixed expired gas after CO <sub>2</sub> absorption. |
| $\overline{F_{N_2O}}$ | Fractional concentration of nitrous oxide in mixed expired gas.                               |
| $t$                   | Time in minutes after beginning inspiration of nitrous oxide.                                 |

The first equation was suggested by Foldes *et al.*<sup>6</sup> who assumed no nitrous oxide uptake after a short time and a metabolic rate 15 per cent in excess of basal. The second equation is a modification of the first, assuming basal oxygen consumption, and the nitrous oxide uptake described by Severinghaus at various times after beginning inhalation,<sup>7</sup> with appropriate linear corrections for differences in inspired concentration and body weight. The equation for calculating nitrous oxide uptake is:

$$\dot{V}_{N_2O} = \frac{1,000 t^{-0.5} \times (1 - \overline{F_{O_2}}) \times \text{patient weight}}{0.8 \times 145} \quad (3)$$

In 11 of the 58 patients the exchange of nitrous oxide and oxygen was measured at five to ten minute intervals during a study period by a minor modification of the pop-off valve so that excess gas,  $V_{\text{excess}}$ , was collected in a continually recording spirometer. End-expiratory volume of the system was kept constant by permitting expiration to distend the re-breathing bag with pressures of one half to one millimeter of mercury at which point the excess went into the spirometer. The uptakes were calculated by solution of two simultaneous equations:

$$\dot{R}_{O_2} + \dot{R}_{N_2O} = \dot{V}_{N_2O} + \dot{V}_{O_2} + \dot{V}_{\text{excess}} \quad (4)$$

$$\frac{(\overline{F_{O_2}}) / (0.99 - \overline{F_{O_2}})}{=} = (\dot{R}_{O_2} - \dot{V}_{O_2}) / (\dot{R}_{N_2O} - \dot{V}_{N_2O}). \quad (5)$$

Equation 4 states that, in a constant volume system, the input must be equal to the gas lost by uptake and pop-off. Equation 5 is a description of the concentration of gases in the pop-off, stating that the ratio of oxygen concentration to nitrous oxide concentration is equal to the ratio of volumes delivered in excess of the volumes absorbed. During the uptake measurements, respiration was spontaneous, and was never below 90 per cent of that predicted by the Radford nomogram.<sup>8</sup>

### Results

The results of 201 measurement periods representing 108 hours of low inflow anesthesia were analyzed. Twenty-eight per cent of these representing 17 hours included total gas inflows of 600 ml. per minute or less.

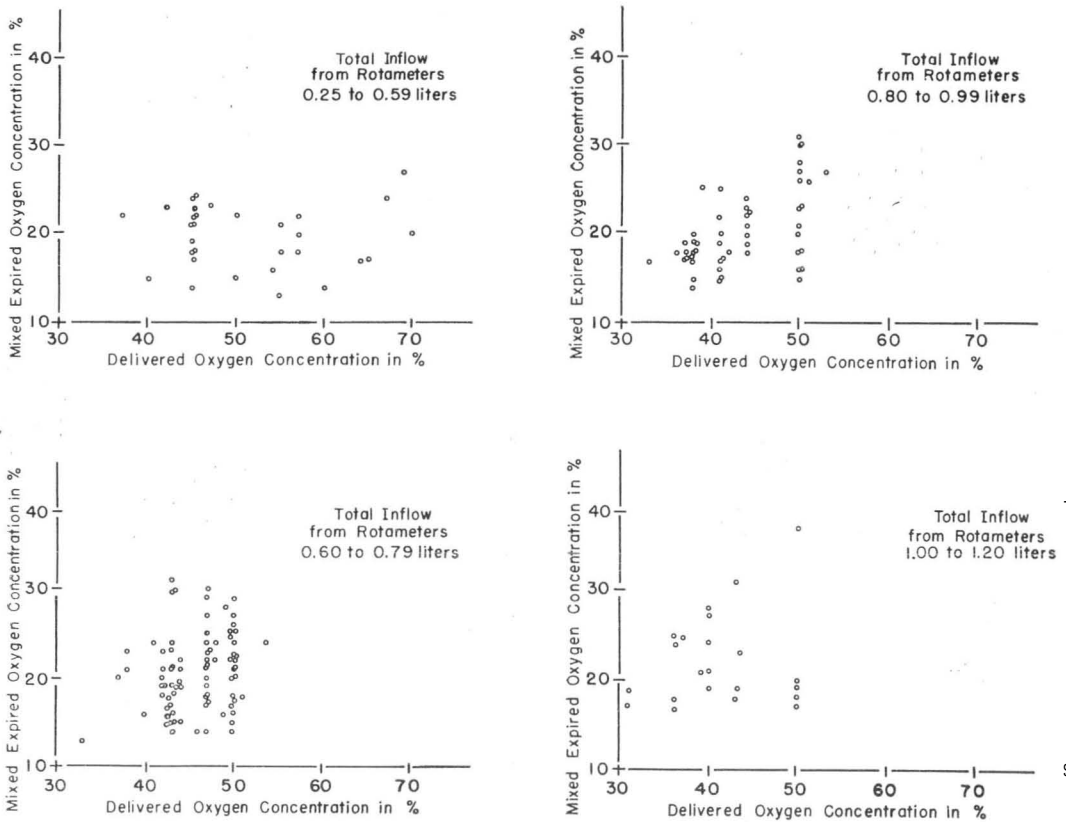


FIG. 1. The mixed expired oxygen concentrations are plotted against the oxygen concentrations delivered from the flow meters. The data have been subdivided on the basis of the total inflow from the gas machine to the breathing circuit. Over the range of total inflow of 0.250 to 1.200 liters per minute there is no correlation of delivered and expired oxygen concentration. Generally, 20-30 per cent higher oxygen must be delivered from the machine than is found in the circle. The design of the experiment excludes measured expired concentrations below 12 per cent and above 40 per cent.

*Comparison of Delivered and Measured Expired Oxygen Concentration.* The lack of correlation between delivered and mixed expired concentration of oxygen in four ranges of total inflow is shown in figure 1. Below total flows of 600 ml. per minute it was necessary to deliver from 40 to 70 per cent oxygen to maintain 20 per cent in the mixed expired gas. As total delivery rates were increased toward 1.2 liters, the data suggest some correlation between inflow and expired oxygen, but wide scatter was still apparent. The average oxygen concentration delivered from the flow meters was  $45.7 \pm 5.0$  per cent, while that measured in the mixed expired gas was  $20.6 \pm 4.3$  per cent. However, this average

difference of 25 per cent was clearly not constant.

*Reliability of the Two Predicting Equations.* Comparison of the expired oxygen concentrations with predicted concentrations after one half hour or longer of low inflow technique are shown in figure 2, which illustrates the large variation between measured and predicted values. Using equation 1 for the predicted oxygen concentration (left hand illustration) most of the points fell below the 45 degree line of identity. This could have been caused either by a lower oxygen consumption than was assumed or a greater nitrous oxide uptake. Both factors are likely. The difference between observed and predicted values

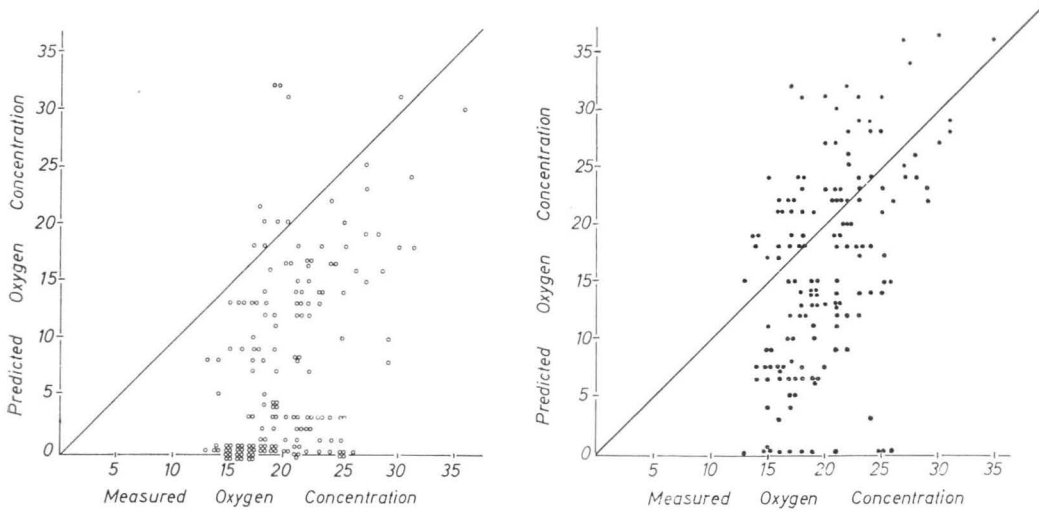


FIG. 2. Comparison of measured and predicted mixed expired oxygen concentrations by the simple equation of Foldes plotted as circles and a modified equation plotted as dots. The diagonal line is the line of identity. Measured values below 12 per cent are excluded by the protocol. Neither equation closely predicts the observed concentration, but allowance for basal oxygen demand and continued nitrous oxide uptake improves the prediction. Both equations predict zero oxygen in some instances which is obviously impossible. This occurred 51 times with the simple equation, and 12 times with the modified equation.

ranged from predictions of 15 per cent higher to 26 per cent lower than observed. On the average the predicted value was 13 per cent below the observed value. Only one-sixth of all the observations were within 5 per cent of the predicted value. In eight instances involving 3 patients, less than the room air equivalent of oxygen was observed despite predictions of higher concentrations. Nearly one-third of the observations were paired with predictions of zero oxygen tension illustrated by the cluster of points about the abscissa. After two hours of anesthesia the deviation of predicted from observed values decreased slightly, but not enough to justify use of equation 1.

Computations from equation 2 are plotted in the right hand illustration. The scatter was still large, ranging from predictions of more than 15 per cent above to 26 per cent below that observed. If reliance had been placed upon this equation, 17 patients would have been breathing less than 20 per cent oxygen when 20–31 per cent oxygen was predicted by the equation. Forty per cent of the observations were within 5 per cent of the predicted

value. No trend toward improvement with the passage of time was evident.

When the differences between observed and predicted values were examined as a function of the inflow, it was apparent that the greatest discrepancies arose with lower inflows. Above 900 ml./minute total inflow, all predictions from equation 2 were within 5 per cent of the observed value in each of 25 instances. Equation 1 led to the same small range of deviations if the flow exceeded 1 liter per minute. Thus, as larger flows are provided, variation in gas uptake represents a progressively smaller fraction of the excess gas.

The data from 15 patients who had spinal or epidural block were examined separately. In comparison with the other patients there was no significant difference in the average concentration delivered, measured, nor in the differences between those observed or predicted by either equation.

All of the patients were grouped in increments of 50 pounds of body weight. No significant difference was found in the average values nor in the range of differences between observed and predicted. Similar examination

of the results according to age, sex, and extent of the operative wound was unrewarding also.

*Variation in Oxygen and Nitrous Oxide Uptake in Individual Patients.* Equation 2 assumes a constant inspired nitrous oxide concentration. In this study no attempt was made to keep the inspired mixture constant, and it was expected that fluctuations in the concentrations in oxygen and nitrous oxide would occur. Measurements in 11 adults illustrated the effect of these fluctuations during maintenance of closed system anesthesia.

Oxygen consumption during light nitrous oxide thiopental lidocaine anesthesia varied from 125 to 230 ml./minute/sq. meter compared with the predicted basal value of 160. In most patients, the consumption of oxygen varied less than  $\pm 30$  ml./minute during extended periods. However, in 3 individuals the earliest values were considerably higher than later, and in 6 patients there was marked rise in oxygen consumption in the last one half hour. This variation was thought to represent an unstable balance of anesthesia and stimulus during various surgical conditions such as exploration, wound closure, and application of the dressings.

Nitrous oxide exchange was even less constant than oxygen uptake. Although the average values showed a steadily decreasing uptake of nitrous oxide with time, periods of excretion of nitrous oxide during maintenance were occasionally observed. After 60 minutes of anesthesia the average was 75 ml./minute uptake, and after 170 minutes the average was 20 ml./minute. The greatest maintenance value measured was 245 ml./minute uptake in a large male after 50 minutes of anesthesia. There were considerable variation from one interval to another in a given patient and marked variation among the patients. Excretion of nitrous oxide from the patient into the breathing circuit at the rate of 75 to 100 ml./minute was observed in 6 patients during periods of adjustment to lower nitrous oxide concentration. After three hours of anesthesia in 9 patients, nitrous oxide exchange varied from 110 ml./minute uptake to 90 ml./minute excretion.

## Discussion

Reliable prediction of oxygen concentration in a closed or nearly closed system could be made if there were a relation between the delivered oxygen and the inspired oxygen, or if there were a constant, predictable oxygen consumption and anesthetic uptake. Both possibilities were examined in this paper.<sup>9</sup>

Crowley *et al.* have shown a relationship between delivered and inspired oxygen when total inflows exceed two liters per minute. The present observations clearly indicate that below total inflows of 1.2 liters per minute such a relationship does not exist.

*Oxygen Consumption During General Anesthesia.* Data from several groups<sup>10, 11, 12</sup> suggest that general anesthesia reduces the metabolic demand for oxygen. The finding in this study that the expired oxygen concentration in expired gas was 4 per cent above that predicted in equation 2 is consistent with such a reduction. The data are of greater interest, however, in indicating that one cannot predict values for oxygen consumption at a given time for a particular patient during an operation.

*Nitrous Oxide Exchange.* Even greater variations in nitrous oxide exchange were found by us, and have been suggested by others.<sup>7, 13</sup> Three factors contribute to this:

- (1) Initial uptake of the gas is rapid, and the rate of uptake changes rapidly during the first 20–30 minutes of inhalation of a constant inspired tension.<sup>7, 13</sup>
- (2) Uptake of nitrous oxide continues for hours during inhalation of a constant inspired tension.<sup>7, 13</sup>
- (3) A change in inspired concentration causes a change in uptake of nitrous oxide. There are sufficient data in the report of Frumin *et al.*<sup>13</sup> to estimate the change in nitrous oxide exchange with a sudden change in inspired concentration, by integration of excretion curves with an assumed alveolar ventilation. After fifteen to twenty minutes of breathing an 80 per cent nitrous oxide mixture with an inflow of 10 liters per minute, the change of input to 3 liters per minute of 67 per cent nitrous oxide will cause the inspired concentration to fall 10 per cent. In less than one minute there will be an ex-

cretion of approximately 100 ml. of nitrous oxide. Indeed, whenever the alveolar concentration changes, a change in rate of uptake will occur. Since there is a difference between inspired and alveolar concentration, even a change in the pattern of respiration (the institution of assisted respiration) would affect a change in uptake.

It is difficult enough to predict nitrous oxide uptake during inhalation of a constant inspired tension. It becomes more difficult under clinical conditions when various factors combine to change alveolar concentration.

### Conclusions

When total inflow into a nearly closed system is less than 1.2 liters per minute there is no reliable relationship between oxygen concentration delivered and that in the circuit. Neither can one rely on average values for oxygen consumption and uptake of anesthetic agent in attempting the calculation of oxygen concentrations in the system. The variation in oxygen demand and anesthetic uptake from time to time in a given patient, or from one patient to another, is too large to permit such a calculation.

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## July–August 1966 Symposium

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