FACTORS INFLUENCING THE ELIMINATION OF NITROGEN USING SEMICLOSED INHALERS

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The necessity and importance of the elimination of nitrogen when inducing and maintaining anesthesia with drugs of low potency, such as nitrous oxide or ethylene, has been emphasized by many anesthesiologists. Failure to obtain satisfactory anesthesia with gases which require high alveolar tensions is ascribed to dilution of the anesthetic by nitrogen. It has been assumed that the nitrogen which is displaced from the tissues accumulates in a closed inhaler and results in inadequate anesthesia during maintenance. How rapidly and effectively the elimination of nitrogen is accomplished in anesthesia apparatus has not been studied.

Considerable data are available on the replacement of nitrogen in the lungs by oxygen in pulmonary function studies using nonrebreathing techniques (1, 2, 3). In fact, the emptying time is used as a measure of the degree of pulmonary insufficiency due to emphysema, fibrosis and other pathologic states. These data are not applicable to anesthesia apparatus because semiclosed inhalers for anesthesia permit rebreathing and recirculation of gases. Seldom is the nonrebreathing technique supplying anesthetic mixtures on demand used for adults. In a recent report from this department it was shown that the effective elimination of carbon dioxide from semiclosed inhalers is not accomplished unless gases are used at flow rates corresponding to the minute volume exchange of the subject (4). Whether or not this applies to nitrogen was not determined. We felt that a study of the role nitrogen plays during the induction and maintenance of anesthesia with agents of low potency and the manner and the rapidity of its elimination from anesthetic apparatus was indicated.

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Method of Study

It is known from the studies of Benkhe (5), Courmand (6) and others that the rate of nitrogen washout is influenced by variations in tidal exchange, functional residual air volume, dead space, and respiratory rate. It is obvious, then, that such factors as premedication, size of dead space in masks and fittings, and stimulation during operation, all of which cause changes in the ventilatory pattern, would introduce variables which might invalidate data obtained from anesthetized patients.

In order to eliminate as many variables as possible and to have data on nitrogen elimination from appliances used for inhalation anesthesia, a study was first done on 40 healthy young male and female volunteers using oxygen as the washout gas. The minute volume exchange of each subject was first determined at rest with a spirometer. The subjects then breathed oxygen from a circle system (Foregger) composed of a Connell type mask, two corrugated 30 by 1/4 inch tubes, unidirectional valves and their housings, an 8 by 13 centimeter canister charged with fresh soda lime, and a 5 liter breathing bag and fittings. The total capacity of the system was computed to be 6.5 liters. Elimination of nitrogen was determined using flow rates at 1/4, 1/2, 3/4 and at the minute volume exchange of the subject being studied. Excess gases escaped through an exhalation valve. When the flow rate was at the minute volume exchange, the expired tidal volume was eliminated in toto through the exhalation valve with no rebreathing. When the flow rate was less than the minute volume exchange, rebreathing, obviously, was necessary. Samples for analysis were drawn from a nipple on the expiratory limb of the circle system into a Beckman oxygen analyzer in which carbon dioxide was removed with soda lime and water vapor with silica gel. The difference between the determined oxygen tension and the existing barometric pressure was assumed to be the residual nitrogen tension. After nitrogen was completely washed out, as was assumed to be the case when none but a trace was present in the exhalations, the filling time was determined by allowing the subject to breathe room air with the mask still in situ but with the tube on the inspiratory limb disconnected.

In order to observe the effect of varying the capacity of the inhaler, studies were also performed using a to-and-fro system composed of a Connell type mask, a 7 by 12 centimeter canister, and a 5 liter breathing bag. An exhalation valve was placed on the obturator connecting the mask with the canister. Samples for analysis were withdrawn from a nipple in the mask at the expiratory phase of respiration.

After this phase of the problem was completed, the study was extended to surgical patients anesthetized with ethylene. Ethylene was selected for a number of reasons: (1) It is impotent compared to other volatile anesthetics and requires a high alveolar partial pressure to be effective. Nitrogen, therefore, would play a role in reducing its ef-
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fectiveness. (2) It is more potent than nitrous oxide and difficulties due to incomplete anesthesia are lessened. (3) The concentration is easily determined by absorption with sulfuric acid in the Orsat apparatus. (4) Ethylene must be administered by the semiclosed technique.

In order to minimize the number of variable factors which obviously creep into such a study, such as variations in functional residual gas volume, tidal volume, dead space volume, rate of respiration, and so on, patients were selected who were free from pulmonary and cardiovascular disease. The majority were young subjects undergoing superficial operations, usually of a minor nature. All received a narcotic, usually morphine, together with scopolamine or atropine for premedication. An 80 to 20 ethylene-oxygen mixture was admitted into a circle type inhaler at flow rates and under circumstances to be described later. Samples for analysis were withdrawn from the expiratory limb of the system and the concentration of ethylene was determined by absorption with fuming sulfuric acid. Carbon dioxide was absorbed with alkali, water vapor with silica gel, and the oxygen tension was measured with the Beckman analyzer. The residual gas was presumed to be nitrogen. The carbon dioxide absorber was used whenever rebreathing was utilized.

Results

Elimination of Nitrogen from Semiclosed Inhalers Using Oxygen. When oxygen was admitted into the inhaler upon demand, that is, at the minute volume exchange of the subject, with no rebreathing, the nitrogen tension fell to the zero level in an average of 2½ minutes in the majority of subjects (fig. 1). The minute volume exchange varied between 5 and 14 liters in all the volunteers. Elimination of nitrogen was the same for each subject regardless of his minute volume exchange if oxygen was supplied at his minute volume exchange. In a recent study from this department, heretofore mentioned, it was observed that a mixture composed of 20 per cent oxygen and other gases must be admitted into semiclosed inhalers at flow rates approximating the minute volume exchange of the subject to maintain oxygen tensions of inspired gases at the physiological norm of 152 mm. of mercury. Since tensions of carbon dioxide and oxygen in such an inhaler depend upon flow rates, then it should follow that nitrogen tensions should be influenced likewise. Accordingly, after determining the average minute volume exchange of the subject, oxygen was admitted at a flow rate of 3/4 of the minute volume exchange. Elimination of nitrogen, as one would expect, was prolonged and required four to six minutes. At 3/4 the minute volume exchange, elimination required eight to ten minutes; at 3/4 the minute volume exchange, elimination was prolonged still more, requiring fifteen to eighteen minutes (fig. 1).

Rate of Pulmonary Filling with Nitrogen After Pulmonary Emptying. After nitrogen had been completely eliminated the subject
breathed room air through the inspiratory limb of the filter, from which the corrugated tubing had been disconnected, in order to determine refill time. Samples for analysis were drawn from the expiratory tube. As one would expect, nitrogen tensions in the exhaled gas rose quickly during the first minute. However, they required a total of five and one-half to six minutes to return to the control level (fig. 2). This lag is due to the presence of the corrugated tubing. If the obturator is opened to room air, the return to the control level requires two to three minutes.

![Diagram](image)

Fig. 1. Typical curve showing the rapidity and completeness of the elimination of nitrogen from the lungs of a healthy young volunteer breathing pure oxygen from a circle filter at his minute volume exchange and with no rebreathing and at \( \frac{1}{4} \), \( \frac{1}{2} \), and \( \frac{2}{3} \) of the minute volume exchange with rebreathing.

**Elimination of Nitrogen from the Tissue.** It has been assumed that nitrogen which is immediately eliminated is alveolar and plasma nitrogen. As the pressure gradient is altered, nitrogen passes from the tissues into the blood and thence into the alveoli. This tissue desaturation occurs after the pulmonary depletion of nitrogen. The premise of primary and secondary saturation is based upon this behavior of nitrogen. The former occurs when alveolar and plasma nitrogen are replaced by another gas, such as nitrous oxide or ethylene, whereas the latter occurs when nitrogen in the tissues is replaced by a
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Gas. It has been assumed, particularly during nitrous oxide or ethylene anesthesia, that nitrogen from the tissues dilutes the gases in a closed system and reduces the effectiveness of the agent.

Data on the accumulation of tissue nitrogen in closed anesthesia inhalers after pulmonary emptying are not available. To study this, the minute oxygen consumption of resting volunteers was first determined. Pure oxygen was then administered at the demand flow with no rebreathing until nitrogen was completely eliminated. The system was then closed to permit rebreathing and the flow meter was set to deliver

![Graph](image)

**Fig. 2.** Typical curve showing nitrogen filling time of a healthy volunteer breathing air after desaturation by inhaling oxygen using the nonrebreathing technique in a semiclosed inhaler. The curve is almost the mirror image of the one for desaturation in figure 1.

the predetermined metabolic requirement of oxygen. Accumulation of nitrogen in the inhaler was gradual. After thirty minutes the concentration in the inhaler ranged from 2 to 14 volumes per cent, averaging 9 volumes per cent in ten subjects (fig. 3). This amounted to an average of 0.5 to 0.6 liters inasmuch as the total capacity of the inhaler was 6.5 liters. These data are in agreement with those of others on nitrogen excretion using different types of apparatus.

**Effects of Varying the Size of the Inhaler.** The washout of nitrogen from the to-and-fro inhaler occurred in a similar manner and as
rapidly as in the circle filter, at flow rates corresponding to $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ and at the minute volume exchange of the subject. Size of the inhaler is not of clinical significance. This is in agreement with data of the recent report on semiclosed inhalers.

Elimination of Nitrogen During Ethylene Anesthesia. Determinations of minute volume exchange of patients prior to anesthesia were not satisfactory. Wide variations were noted between successive readings and a base line was difficult to establish. However, volumes above 10 liters were not encountered. Accordingly, a flow rate of 10 liters was adopted in the nonrebreathing experiments. Using an 80 per cent ethylene and 20 per cent oxygen mixture at a 10 liter flow, a 60 to 65

![N_2 Tissue Desaturation](image)

**Fig. 3.** The rate of "excretion" of nitrogen from the tissues after complete pulmonary emptying by using pure oxygen in a semiclosed inhaler with the nonrebreathing technique. The system was closed after the emptying and the metabolic oxygen was admitted. The fine lines indicate the ratio for ten volunteers. The heavy line is the mean.

per cent concentration of ethylene was attained in the expiratory limb of the inhaler within thirty seconds and a 75 to 78 per cent concentration within two minutes. The curve which represents pulmonary filling with ethylene (fig. 4) is similar to that obtained for nitrogen filling in the volunteers (fig. 2).

Loss of lid reflex was used as the criterion for loss of consciousness and attainment of third stage anesthesia. This reflex consistently disappeared when the expired ethylene concentration ranged between 60 and 70 volumes per cent. The oxygen concentration was consistently above 20 per cent. At a flow rate of 5 liters, using an 80 to 20 per cent mixture, an average of sixty seconds elapsed before the 60 to 70 volumes per cent concentration was obtained. A still greater lag was ob-
served at the 3½ liter flow rate, the time ranging from 90 to 120 seconds.

At the 10 liter flow rate, using 75 to 80 per cent concentrations of ethylene, complete elimination of nitrogen and oxygen concentrations of 20–25 per cent were obtained in less than three minutes and were maintained in several cases at constant levels for over two hours. When lower flow rates were studied, the time for nitrogen washout increased progressively (fig. 4). Oxygen concentrations using flow rates less than 8 to 10 liters per minute (using 80 to 20 per cent mix-

![Graph](image)

**Fig. 4.** The rates of filling of the lungs with ethylene after an 80 to 20 per cent mixture is admitted into a semiclosed inhaler at 3.5, 5 and 10 liters per minute.

tures) invariably fell below 20 per cent. In many instances they were as low as 12 per cent within five minutes. The residual gas was nitrogen. Third stage anesthesia was not attained unless the exhaled ethylene concentration was over 60 per cent regardless of the composition of the remaining gases. Induction time at the 5 liter flow rate did not differ significantly from the 10 liter flow rate.

**Influence of Leaks.** The influence of leaks in the system was striking both during anesthesia and during studies in conscious subjects using oxygen. Even at 10 liter flow rates, rarely were ethylene con-
centrations greater than 50 per cent if face pieces were not properly adjusted. Complete elimination of nitrogen was more difficult to achieve using the to-and-fro inhaler because of difficulty in obtaining a snug fit of the face piece.

**Discussion**

The foregoing data indicate that the rate of nitrogen washout from semiclosed inhalers used for anesthesia with no rebreathing is as rapid as that observed using techniques for study of pulmonary function. There is a striking agreement between data on nitrogen elimination using oxygen and that using ethylene at all flow rates, including flow rates less than the minute volume exchange. This is noteworthy since all variable factors were not necessarily excluded in studies on anesthetized patients.

These data suggest that nitrogen elimination is of limited importance for anesthesia with gases which are effective at high partial pressures. After a 60 to 70 per cent exhaled concentration is attained, nitrogen plays an insignificant role in influencing either induction time or maintenance of anesthesia. Presumably the tension at this concentration is necessary for an adequate uptake of drug to establish equilibrium between blood and brain. When ethylene is diluted below this concentration by a gas such as nitrogen or oxygen, the uptake is insufficient for surgical anesthesia.

These data also indicate that the effective tension for adequate uptake is attained almost as rapidly at the 5 liter flow rate as at the 10. Exceeding this tension does not significantly shorten induction time. It must be emphasized, though, that higher flow rates are necessary to maintain adequate oxygen tensions in the inhaler when 80 to 20 per cent mixtures are used. Nitrogen which is in the inhaler at a lower flow rate does not appreciably influence induction time if the pulmonary anesthetic gas tension is sufficient for adequate uptake. However, nitrogen which is not eliminated dilutes the oxygen below physiological limits. Enriching the mixture with oxygen does not correct the situation at low flow rates, because the anesthetic gas is then diluted below the tension necessary for adequate uptake of anesthetic gas. These data suggest, then, that an initially high flow rate be used for several minutes to eliminate the nitrogen completely. The flow rate may then be reduced. However, the mixture must be enriched with oxygen above 20 per cent to prevent anoxia.

Inasmuch as the elimination of nitrogen is the same when oxygen or ethylene-oxygen mixtures are used, it is not unreasonable to assume that the same principles apply when nitrous oxide is used.

**Summary**

1. The elimination of nitrogen from the lungs of healthy volunteers, breathing oxygen from semiclosed inhalers used for anesthesia, has
been studied. At flow rates equal to the minute volume exchange of
the subject, with no rebreathing, elimination occurred at an average
of two and one-half minutes. When flow rates lower than the minute
volume exchange were used, rebreathing became necessary, and the
elimination was prolonged in proportion to the reduction in flow rate.
After nitrogen was completely washed out by oxygen and the subject
breathed room air, the refilling time equalled desaturation time.

2. With the subject desaturated, using a closed circle system with
rebreathing and supplying the metabolic flow of oxygen, excretion of
tissue nitrogen was slow, requiring thirty minutes or more to eliminate
0.5–0.6 liters of nitrogen.

3. The size of the inhaler does not appreciably alter nitrogen elimi-
nation time. Elimination curves for the to-and-fro inhaler differed
little from those of the circle filter. The rate of elimination of nitrogen
from anesthesia appliances corresponds closely to figures for nitrogen
elimination obtained in pulmonary function studies using apparatus
which differs in design from anesthesia apparatus.

4. The nitrogen elimination curves in patients anesthetized with
ethylene corresponded closely to those obtained using oxygen in volun-
teers. When flow rates less than the minute volume exchange are
used, the oxygen tension in the inhaler is reduced below the physiologic
limit using 80 per cent ethylene and 20 per cent oxygen mixtures.
If the oxygen concentration is increased, the ethylene tension is re-
duced below that necessary to induce and maintain anesthesia. These
data suggest that initially high flow rates be used to eliminate nitrogen.
The flow rate may then be reduced using an oxygen enriched mixture.

5. The similarity between displacement of nitrogen by oxygen and
ethylene-oxygen mixtures suggests that this pattern of behavior applies
to other gases such as helium and nitrous oxide.*

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* Since preparing this report we have had a communication from Drs. Wm. K. Hamilton
and Douglas W. Eastwood stating they have studied this phase of the problem using nitrous
oxide. Their results agree with our statement, and their report has been submitted to
ANESTHESIOLOGY for publication.