The Role of Preliminary Oxygenation Prior to Induction With High Nitrous Oxide Mixtures:

Polarographic PaO_2 Study

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With the recent development of the polarograph,[1,2] direct arterial oxygen tension measurements in the presence of inhalation anesthetic agents may now be made with accuracy. This is important during nitrous oxide studies where the inspired oxygen concentration may vary over a wide range. With the polarograph, arterial oxygen tension values can be obtained for all concentrations of oxygen irrespective of the other gases administered simultaneously.[3]

In 1953 Clark[1] showed that when the oxygen electrode was inserted into the aorta of a dog inhaling 100 per cent nitrous oxide, the polarographic curve was almost identical with that following nitrogen breathing. We have obtained similar polarographic results *in vitro* by equilibrating blood with pure nitrous oxide and helium (fig. 1). To carry this investigation further, blood and saline were equilibrated with known calibrated mixtures of nitrogen and oxygen. Subsequently, identical percentage mixtures of nitrous oxide and oxygen were prepared, and equilibration with blood and saline was carried out. Identical tracings were obtained at the same oxygen concentrations, showing that the oxygen electrode at 0.6 volts is indifferent to gases other than oxygen (fig. 1).

More accurate knowledge of arterial oxygenation during nitrous oxide anesthesia is desirable. Nitrous oxide is a gas of low potency, and it is often difficult to achieve in the cerebral circulation an adequate partial pressure necessary for a suitable anesthetic level. In order to accomplish a rapid and smooth induction with this weak gas, varying concentrations greater than 80 per cent have been utilized. On occasion pure nitrous oxide is administered for various periods of time resulting in an encroachment on the alveolar oxygen tension. To prevent a decreasing P_{O_2} preliminary oxygenation may be carried out by breathing pure oxygen for a few minutes.[4] Denitrogenation thus occurs prior to the inhalation of high concentrations of nitrous oxide. Near peak levels of arterial oxygen tension are achieved in two to three minutes of oxygen inhalation (figs. 4–8).

We have previously recorded with the polarograph the rapid changes in arterial P_{O_2} in the well oxygenated subject during apnea and during the transition from 100 per cent oxygen to air breathing.[6] In the present study we determined the rate of fall of arterial oxygen tension when high concentrations of nitrous oxide (including 100 per cent) were administered. In one group the administration of nitrous oxide followed air breathing, and in another group we evaluated the role of preliminary 100 per cent oxygen breathing prior to the inhalation of high nitrous oxide mixtures. Five patients in the latter category breathed pure nitrous oxide. One subject was studied for 30 seconds during the transition from room air to pure nitrous oxide.

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Material and Method

The polarographic studies were carried out on surgical patients during anesthesia in preparation for operation. Their ages ranged from 21 to 74 years. No attempt was made

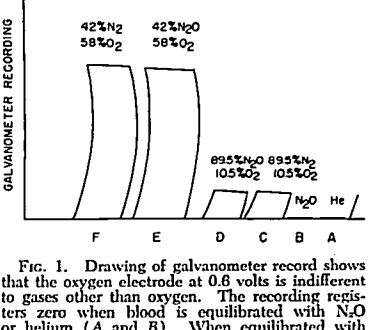

FIG. 1. Drawing of galvanometer record shows that the oxygen electrode at 0.6 volts is indifferent to gases other than oxygen. The recording registers zero when blood is equilibrated with N_2O or helium (*A* and *B*). When equilibrated with blood, oxygen-nitrous oxide or oxygen-nitrogen mixtures containing the same oxygen concentration show identical galvanometer values (*C* and *D*; *E* and *F*).

to select individuals with perfect pulmonary systems. However, no patient was chosen who had an obvious gross pulmonary disability.

We studied 8 patients during the transition from air to high nitrous oxide mixtures. Eleven patients were oxygenated prior to inhaling high concentrations of nitrous oxide. Of this group, 5 breathed pure nitrous oxide.

A nonrebreathing system was used in the majority of patients, so that a constant, accurate oxygen percentage was maintained during the period of study. For comparison, in a few patients, a semiclosed technique with high flows was utilized because this method is in common clinical use. With the nonrebreathing system, both spontaneous and fixed minute volume breathing were used. With the semiclosed technique, only spontaneous respiration was studied.

The oxygen in the varying mixtures of oxygen and nitrous oxide was calibrated with a laboratory Beckman oxygen analyzer with an accuracy of plus or minus one per cent.

A 20 gauge needle was previously inserted into the brachial artery, and 7 ml. arterial blood samples were taken. Subsequent withdrawals were made at one half to one minute intervals. In some instances, the period was slightly longer.

In 1957, Kreuzer and Watson [7] incorporated the oxygen electrode of Clark into a reliable arrangement for measuring blood oxygen tension through all ranges of P_{O_2}. The electrode consists of a platinum cathode and a silver anode which are connected by an electrolyte bridge (0.9 per cent KCl). Clark [1] made a significant contribution to clinical polarography by using a polyethylene membrane to separate the whole electrode system from the blood, thereby preventing the blood from coming in contact with the electrode. The membrane is permeable to oxygen, but impermeable to water, cells, and electrolytes. At a constant voltage of 0.6 volts, the dissolved oxygen (the reducible substance) is reduced by H^+ ions at the cathode, according to the equation, $O_2 + 4H^+ + 4e = 2H_2O$. The tiny current generated as a result of this electrolysis is measured through a suitable circuit by a galvanometer. The amount of current generated is a linear function of the oxygen tension (P_{O_2}).

We have previously emphasized the advantages of measuring direct blood oxygen tensions with the polarograph.[5] Oxygen saturation studies are inadequate when high oxygen mixtures are inhaled. The microbubble tech-

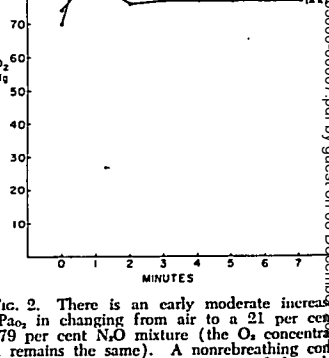

FIG. 2. There is an early moderate increase in Pa_{O_2} in changing from air to a 21 per cent O_2–79 per cent N_2O mixture (the O_2 concentration remains the same). A nonrebreathing constant minute volume technique was used throughout.

niques are inaccurate in the presence of anesthetic gases and are unreliable outside of the physiological range of P_{O_2}. The polarograph has none of these limitations.[3]

The average barometric pressure where these studies were performed was 745–750 mm. of mercury.

Results

Arterial oxygenation during induction of anesthesia with 21 per cent O_2–79 per cent N_2O (following air breathing) is depicted in figure 2. Constant minute volume ventilation was used here. The Pa_{O_2} increased during the first minute, then decreased somewhat but remained greater than the control level for a few more minutes. During polarographic monitoring, we have often noted this early increase in oxygen tension when a change is made from air to a nitrous oxide mixture containing 21 per cent oxygen. This is explained by the fact that nitrous oxide is 30 times more soluble than nitrogen in blood. Since alveolar nitrous oxide is readily absorbed by the pulmonary circulation and only a small volume of nitrogen is eliminated from the blood into the alveoli, the alveolar P_{O_2} rises.[8] The converse effect occurs at the end of nitrous oxide anesthesia when nitrous oxide pours out of the blood into the alveoli, and the alveolar P_{O_2} falls, since the lung oxygen is diluted by the outward diffusion of nitrous oxide. This situation at the conclusion of a nitrous oxide anesthesia was studied by Fink who labeled this process "diffusion hypoxia."[9]

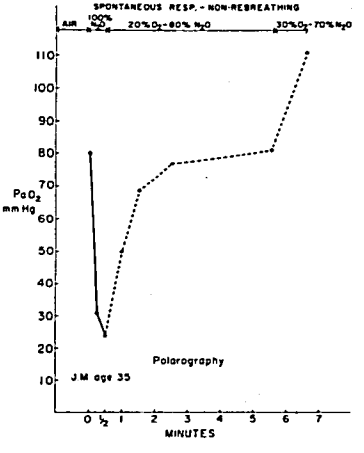

FIG. 3. Shows a very rapid decline in Pa_{O_2} to a low level when changing from air to 100 per cent N_2O for 30 seconds, utilizing a nonrebreathing gas machine. The hypoxia is quickly compensated when 20 per cent O_2 is added to the inhaled mixture.

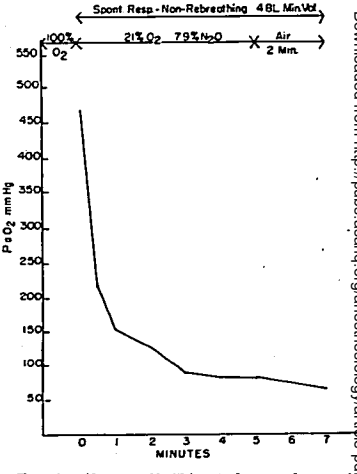

FIG. 4. (Patient Y. T.). Polarographic study showing effect on Pa_{O_2} when 100 per cent O_2 was breathed for 3 minutes reaching 465 mm. of mercury. With a change to 21 per cent O_2–79 per cent N_2O, the excess arterial oxygenation disappeared within 3 minutes. With a substitution of air for the N_2O mixture, the rate of fall of the P_{O_2} increased, probably due to the outpouring of the N_2O from pulmonary blood to the alveoli.

Induction of anesthesia with 14 per cent O_2–86 per cent N_2O resulted in a moderate drop in the arterial P_{O_2}. This was compensated rapidly when the oxygen concentration was increased to 20 per cent (table 1).

There was a precipitous fall in arterial oxygen tension when a healthy premedicated patient breathing air had anesthesia induced with 100 per cent nitrous oxide for a period of 30 seconds (fig. 3). Spontaneous ventila-

TABLE 1. Change in Pa_{O_2} (mm. Hg) During Induction (After Air) with Varying Concentrations of O_2 with N_2O

Pt.	Pa_{O_2} Control-Room Air	21% O_2–79% N_2O													
		15 sec.	½ min.	1 min.	2 min.	3 min.	4 min.	5 min.							
CN	70 mm. Hg	—	87	87	82	81	—	81	Nonrebreathing-Constant Min. Vol.						
AK	74 mm. Hg	—	(45 sec.) 82	82	76	77	77	77	Nonrebreathing-Constant Min. Vol.						
		19% O_2–81% N_2O													
JM	107 mm. Hg	—	101	101	94	90	87	85	Hyperventilation throughout 9 l./min.						
		14% O_2–86% N_2O							20% O_2						
									1 min.						
EG	75 mm. Hg	—	63	59	61	61	56	—	68						
		(1½ min.) (2½ min.)							20% O_2			25% O_2			
									2 min.			1 min.			
RW	77 mm. Hg	—	74	74	70	68	—	59	77			87			
									19% O_2		24% O_2		30% O_2		
									1 min.		1 min.		1 min.		
FK	68 mm. Hg	—	65	67	53	51	—	49	60		72		91		
									20% O_2						
									1 min.						
LD	64 mm. Hg	—	57	57	59	59	—	56	66						
		100% N_2O							20% O_2						
									½ min.		1 min.		2 min.		5 min.
JM	80 mm. Hg	31	24	—	—	—	—	—	50		68		77		81

tion and a nonrebreathing system were used. The Pa_{O_2} showed a prompt large decrease from 80 to 31 mm. of mercury in 15 seconds. At 30 seconds the P_{O_2} reached a low level of 24 mm. of mercury, or one third of the original value. By adding 20 per cent oxygen to the nitrous oxide, the arterial hypoxia was quickly compensated. There was a progressive return to the control level within two minutes.

The following observations were carried out

TABLE 2. Pa_{O_2} (mm. Hg) During Induction with Varying Concentrations of O_2 with N_2O after Preliminary Oxygenation

Pt.	Pa_{O_2} after Preliminary Oxygenation	O_2–N_2O Mixtures								
		15 sec.	30 sec.	45 sec.	1 min.	2 min.	3 min.	4 min.	5 min.	
		21% O_2–79% N_2O								
YT	465 mm. Hg	—	219	—	154	131	92	87	83	Nonrebreathing
		15% O_2–85% N_2O								
BH	484 mm. Hg	—	358	—	145	88	69	58	—	Nonrebreathing
		12% O_2–88% N_2O								30% O_2
										1 min. | 2 min.
FR	371 mm. Hg	—	229	—	112	69	58	—	—	76 | 91 Nonrebreathing
		10% O_2–90% N_2O								30% O_2
		(1¼ min.)								1 min.
RD	531 mm. Hg	—	—	—	97	78	62	55	47	78 Semiclosed
		9% O_2–91% N_2O								
PB	370 mm. Hg	—	176	—	100	60	47	—	—	Nonrebreathing
		5% O_2–95% N_2O								30% O_2
										1 min.
FC	333 mm. Hg	—	176	—	112	72	49	—	—	69 Semiclosed

in patients who inhaled 100 per cent oxygen for three or more minutes prior to induction with the high nitrous oxide mixtures.

Patient Y. T. had anesthesia induced with 21 per cent O_2–79 per cent N_2O following a three minute preliminary period of oxygen breathing (fig. 4). There was a relatively rapid decline in the arterial oxygenation to ordinary air values within two to three minutes. We have previously reported similar findings in a polarographic study during the transition from 100 per cent oxygen to air (21 per cent oxygen).[6]

Fifteen per cent O_2–85 per cent N_2O was administered to patient B. H. (table 2). The rate of fall of Pa_{O_2} was rapid and within two minutes the P_{O_2} was slightly less than the control value.

Figure 5 (patient F. R.) shows the salutary effect on the Pa_{O_2} when the minute volume ventilation was increased. Subsequently pure oxygen produced a rapid rise in the arterial tension. With the administration of 12 per cent O_2–88 per cent N_2O there was a rapid decrease to the control level in approximately 90 seconds. Increasing the oxygen concentra-

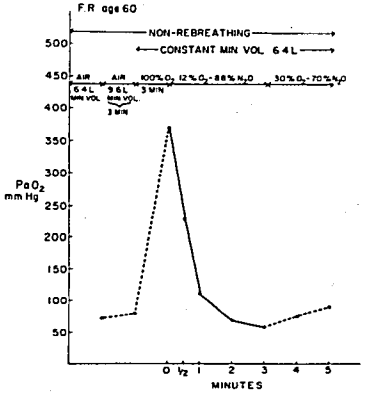

FIG. 5. Polarographic study showing moderate increase in Pa_{O_2} with increase in minute volume ventilation prior to oxygenation. After preliminary oxygenation the inhalation of 12 per cent O_2–88 per cent N_2O resulted in a fall in P_{O_2} to air levels within 2 minutes. With an increase in O_2 concentration to 30 per cent, the P_{O_2} increased rapidly.

tion to 30 per cent for two minutes more than compensated for the slight hypoxia.

The normal lung showed a rapid rise in P_{O_2} with oxygen breathing. Figure 6 depicts a high Pa_{O_2} achieved within two minutes (456 mm. of mercury). A one liter O_2–9 liters N_2O mixture in a semiclosed system was then administered (the oxygen concentration measured 10 per cent). In two minutes the P_{O_2} decreased from 531 to 78 mm. of mercury. In the case of patient P. B. (table 2), a similar period of time was required for the oxygen tension to reach the control level. The induction mixture was 9 per cent O_2–91 per cent N_2O administered by a nonrebreathing fixed minute volume technique.

One subject (patient F. C.) breathed 5 per cent O_2–95 per cent N_2O from a high flow semiclosed system, after previous oxygenation. The arterial oxygen tension dropped from 333 to 72 mm. of mercury in two minutes (table 2).

Figure 7 is a composite graph of 5 patients who breathed pure nitrous oxide after preliminary oxygenation for three minutes. High oxygen tension values were obtained during the oxygen breathing. With a sudden change to pure nitrous oxide there was a precipitous fall in Pa_{O_2}. Within one to one and a half minutes, the elevated tensions fell to the original control air levels. One of the patients (E. C.) (fig. 8) showed a decline in Pa_{O_2} from 420 to 66 mm. of mercury in 90 seconds. With the addition of 20 per cent oxygen there was a rapid improvement to 89 mm. of mercury. With 30 per cent oxygen, the P_{O_2} rose to 97 mm. of mercury in two minutes. A similar pattern in the arterial oxygen tension was noted in patient N. M. (table 3).

Discussion

Much emphasis has been placed on arterial oxygenation during nitrous oxide anesthesia. Often, in order to achieve a smooth induction the inspired oxygen is diminished by increasing the nitrous oxide concentration above 80 per cent. In a mixture of the two gases, the percentage of one is the reciprocal of the other. It is unfortunate that at ambient pressure the potency of an 80 per cent mixture is not equal to that of the pure gas. Faulconer and his associates have shown conclusively that nitrous oxide is a true anesthetic drug and does not depend on hypoxia for its anesthetic properties.[10]

The work of Kety has been extremely valuable in explaining the various factors controlling the uptake of inert gases in the body.[11,12] The depth of anesthesia with nitrous oxide

TABLE 3. Pa_{O_2} (mm. Hg) During 100 Per Cent Nitrous-Oxide Induction-Nonrebreathing—Spontaneous Respiration (After Preliminary Oxygen)

Pt.	Preliminary Oxygenation	100 Per Cent Nitrous Oxide				
	Pa_{O_2} after 3 min. O_2	15 sec.	¼ min.	½ min.	1 min.	1½ min.
EC	420 mm. Hg	—	229	—	118	66
NM	421 mm. Hg	—	237	—	142	56
LB	411 mm. Hg	—	132	—	41	—
RJ	497 mm. Hg	193	83	—	60	48
AB	319 mm. Hg	—	—	127	65	42

depends primarily on the partial pressure of that agent in the brain, and the rate of induction is governed by its rate of change. The tension of an inert gas like nitrous oxide depends, among other factors, on the partial pressure of the gas in arterial blood which is approximately equal to the alveolar tension.

It should be emphasized that there is a slow process of total body saturation with nitrous oxide, requiring several hours for complete saturation.[8] This is different from the rapid arterial saturation upon which depends the depth of anesthesia. Because the solubility, or partition coefficient, of nitrous oxide is relatively slight, the alveolar tension is built up rather rapidly. Equilibrium between alveoli and arterial blood is quickly established. The arterial uptake curve for nitrous oxide shows that the rate of induction is rapid. Three minutes is required for approximately 70 per cent saturation at the inspired tension of the gas. Ninety per cent of complete saturation requires 20 minutes.[11] The greater the inspired concentration of nitrous oxide the more quickly is the high alveolar tension or driving force achieved. Thus, unconsciousness and a rapid smooth induction without excitement are accomplished more readily with pure nitrous oxide than with lesser percentages of the gas. However, there is a precipitous drop in arterial P_{O_2} when 100 per cent nitrous oxide is administered for 15 to 30 seconds (fig. 3). When the patient has been breathing air prior to the administration of the pure gas, deoxygenation of the arterial blood starts at a relatively low level.

TABLE 4. Percentage of Original Pa_{O_2} During Administration of 100 Per Cent N_2O (After Preliminary Oxygenation)

Pt.	Per Cent Pa_{O_2} after 3 min. O_2	100 Per Cent Nitrous Oxide				
		15 sec.	30 sec.	45 sec.	1 min.	1½ min.
EC	100% (420 mm. Hg)	—	54.5%	—	28.1%	15.7%
NM	100% (421 mm. Hg)	—	56.3%	—	33.7%	13.3%
LB	100% (411 mm. Hg)	—	32.1%	—	10.0%	—
RJ	100% (497 mm. Hg)	38.6%	16.7%	—	12.1%	9.7%
AB	100% (319 mm. Hg)	—	—	39.8%	21.8%	13.2%

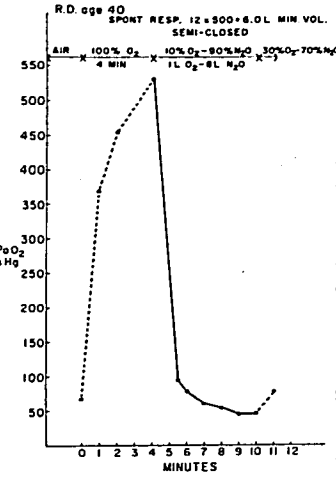

FIG. 6. A high flow semiclosed CO_2-absorption technique was used in this study. Although a very high Pa_{O_2} was reached in 4 minutes, there was an abrupt fall to the control level in approximately two minutes of breathing a 10 per cent O_2–90 per cent N_2O mixture. By increasing the O_2 to 30 per cent for one minute, the Po_2 increased from 47 to 78 mm. of mercury.

Preliminary inhalation of oxygen for two to three minutes results in approximately 90 per cent elimination of alveolar nitrogen in the normal patient.[13] Two or more liters of oxygen are added in the functional residual capacity of the lung, and the arterial Po_2 rises to a high level.[5,6] When pure nitrous oxide is now administered, deoxygenation starts at an elevated arterial tension. In spite of this, the fall in P_{O_2} is still very rapid (figs. 7 and 8). Approximately one minute is required for the arterial oxygen tension to fall to control levels. Thus, 100 per cent nitrous oxide may be inhaled with safety for one minute following a short period of preliminary oxygenation. It is interesting to note that, in each case, at the end of 90 seconds the arterial blood shows a similar percentage (10–15 per cent) of the original high oxygen tension, irrespective of the absolute level reached with oxygen breathing (table 4).

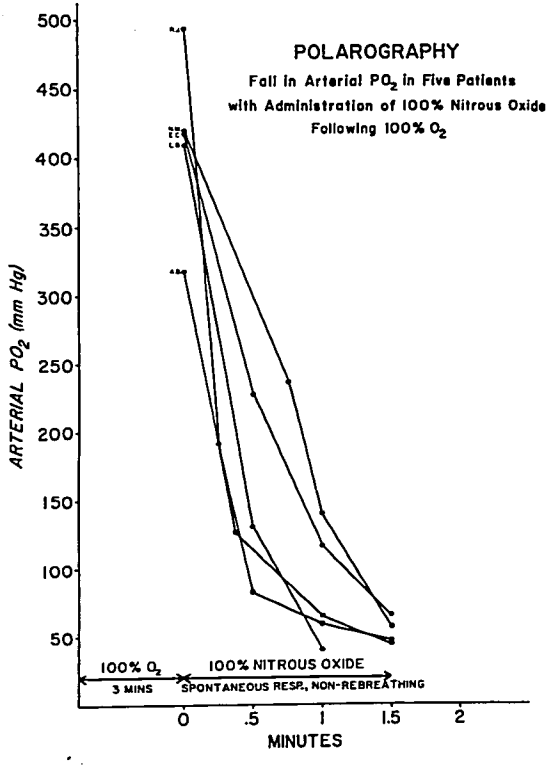

FIG. 7. Composite graph of 5 patients who received preliminary oxygen ventilation for 3 minutes prior to a 100 per cent nitrous oxide induction. The hyperoxygenation reverts to the normal value in less than 1½ minutes. Spontaneous respiration with a nonrebreathing type of gas machine was utilized in all subjects.

Low concentrations of oxygen (5 to 12 per cent) added to the nitrous oxide after preliminary oxygenation contribute somewhat to a higher oxygen tension. The excess oxygen in the lungs plus a very small amount in the blood allows the use of these relatively high nitrous oxide concentrations (95, 90 and 88 per cent) for approximately two minutes. At this point the Pa_{O_2} reaches control levels, and the oxygen advantage of the preliminary oxygenation disappears (figs. 5 and 6, and table 2). With a 15 per cent oxygen mixture there is a similar response with slightly higher values of the P_{O_2} (table 2).

We have previously described the rate of fall of the arterial oxygen tension during transition from 100 per cent oxygen to a 21 per cent mixture with air breathing.[6] A similar curve is noted with a 21–79 mixture of oxygen and nitrous oxide (fig. 4). Near peak arterial P_{O_2} levels are reached with the inhalation of oxygen for three minutes. Excellent preliminary arterial oxygenation is achieved in this period of time, provided that the minute volume is adequate and the rebreathing is kept at a minimum. Longer periods of preoxygenation are clinically impractical. With a change to a gas mixture containing 21 per cent oxygen

there is a return to the pre-exisiting level in two to three minutes.

What then are the advantages of preliminary oxygenation prior to induction of anesthesia with high nitrous oxide concentrations?

Minor surgical procedures including simple dental extractions may be carried out in non-premedicated patients who have had preliminary denitrogenation and subsequent administration of pure nitrous oxide for a one minute period.[4] The patient should be told that he will not become sleepy during the oxygenation period. The induction with 100 per cent nitrous oxide is usually rapid and pleasant, but after this interval, if further anesthesia is necessary, 15 to 20 per cent oxygen should be added to the nitrous oxide. At this point, the anesthetic level in some non-premedicated patients may become too light for prolonged complicated procedures. However, many individuals will be kept adequately anesthetized for several more minutes on a 20 to 80 oxygen-nitrous oxide mixture. In the more robust subject, a small amount of an oxybarbiturate plus 50 mg. meperidine will contribute to the smooth course of the rapid induction. We have found that the change from 100 per cent oxygen to pure nitrous oxide is facilitated by using a demand flow nonrebreathing gas machine such as the McKesson 'Nargraf.' The transfer from one gas to the other is rapidly accomplished. Furthermore, dilution of the oxygen or nitrous oxide by air leaks under the face mask is prevented by increasing the inhalation pressure a few millimeters of mercury. These outpatients are able to leave the hospital shortly after the minor surgical procedure is finished.

The preliminary oxygenation technique is of value in the parturient female in strong labor. Between pains 100 per cent oxygen is administered, and when the uterine contraction starts, 100 per cent nitrous oxide is administered for 30 or more seconds up to one minute with rapid complete pain relief. The maternal arterial oxygen tension does not drop below the usual normal level and thus the umbilical venous blood will remain adequately oxygenated.

Ventilation with 100 per cent oxygen prior to induction of anesthesia is recommended for the patient who has a fixed cardiac output. This individual cannot compensate for hypoxia with an increased cardiac output. Preliminary oxygenation is beneficial by ensuring an adequate arterial oxygen tension throughout the induction period, with an elevated P_{O_2} during the first few minutes. Proper premedication is essential here as it is for every complete induction with nitrous oxide.

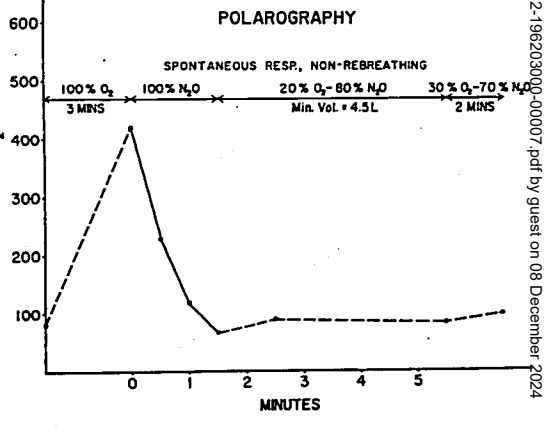

FIG. 8. Polarographic study of a healthy 27 year old patient (E. C.) who showed a Pa_{O_2} of 420 mm. of mercury with preliminary O_2 breathing for 3 minutes. After inhaling pure N_2O for 90 seconds the P_{O_2} dropped precipitously to 66 mm. of mercury. The addition of 20 per cent oxygen to the N_2O improved the arterial oxygenation, reaching 89 mm. of mercury in a one minute period. With an increase in the O_2 to 30 per cent there was further improvement in the Pa_{O_2}.

After preliminary oxygenation, a high nitrous oxide mixture (10 per cent O_2 and 90 per cent N_2O) may be used to induce a gas-oxygen-ether anesthesia in the premedicated patient (fig. 6). Oxygen is given for two or more minutes, and the nitrous oxide-oxygen is then started. After a minute, ether is added more rapidly than usual. Within three minutes the oxygen is gradually increased to 20 per cent or more. A rapid, smooth induction of ether anesthesia can be carried out in this manner.

In the average patient, when nitrous oxide anesthesia is selected for more prolonged procedures and a full five to ten minute induction period is contemplated, it is preferable to start with a 20–80 mixture of oxygen and nitrous oxide rather than to subject the wakeful patient to a preliminary period of oxygen breathing. The polarographic studies have shown that the excess oxygenation disappears within a few minutes. The exact length of time depends on the concentration of the oxygen in the inspired anesthetic mixture. The oxygen advantage gained by preliminary denitrogenation is short-lived. In a healthy patient without previous oxygenation, we do not hesitate to administer a 10–90 or a 15–85 mixture of oxygen and nitrous oxide for a few breaths at the start of the induction. The oxygen percentage is then gradually increased to 20 per cent. There are no unpleasant sensations noted by the patient. With proper premedication the induction is rapid and smooth. We have observed previously that with a 20–80 mixture there is an actual rise in Pa_{O_2} during the early phase due to the rapid uptake of nitrous oxide and the relatively slower elimination of nitrogen from the pulmonary blood to the alveoli (fig. 2). The arterial oxygenation at the end of five or ten minutes is usually somewhat greater than the control value. Many patients may now be adequately anesthetized with greater than 20 per cent oxygen in the inspired mixture, and the P_{O_2} range will often exceed 100 mm. of mercury. Succinylcholine prior to tracheal intubation is administered only when the induction of anesthesia is complete.[14] After the relaxant is injected the patient's lungs are hyperventilated with 35 or more per cent oxygen. P_{O_2} studies made by us during the actual intubation have shown values in the 100 to 150 mm. of mercury range. After intubation is accomplished and relaxants are continued, a change is made to a semiclosed system with moderately high flows of oxygen and nitrous oxide.

We can learn much from the clinical observations of anesthesiologists who have anesthetized thousands of patients with nitrous oxide, and correlate their impressions with the more recent laboratory studies. Waters[15,16] and Clement[17] have emphasized that during a nitrous oxide induction of anesthesia higher concentrations of this gas are allowable. As the anesthesia progresses, the oxygen in the inspired mixture is increased and the nitrous oxide is lowered. These observations coincide with the theoretical equations of Kety[11] and the laboratory studies of Severinghaus[8] who demonstrated the rapid arterial uptake of nitrous oxide during early induction. Previously some of these aspects were recognized clinically, and effective techniques were worked out to obtain smoother anesthesia with this weak anesthetic drug. Clement[17] has stressed the advantages of a demand flow nonrebreathing gas machine which produces rapid denitrogenation. The less nitrogen there is in the functional residual capacity of the lung, the higher the P_{O_2} and P_{N_2O} for a given inspired mixture. A semiclosed system with flows greater than 4 to 6 liters per minute is also effective,[18] but with this technique one does not have the rapid control of changing the mixture instantaneously in the more resistant individual where it is desirable to increase the nitrous oxide concentration for a few breaths. There is also less disturbance to the patient during the early part of the induction by using an increased inhalation pressure (5 to 10 mm. of mercury) from the demand flow machine. The face mask need not be secured to the face of the patient until he is asleep—a smoother induction is thus attained. With the semiclosed system the mask must be fitted snugly with the first breath, otherwise the gas mixture is diluted with nitrogen and the induction is thereby prolonged and more difficult. With the demand flow system, a sufficient quantity of new gas is supplied as the body continues to absorb large quantities of the gas. A low flow 500 ml. oxygen–500 ml. nitrous oxide mixture is permissible in associa-

tion with thiopental, but is not adequate to supply the uptake requirements of a true nitrous oxide-oxygen anesthesia. If a semi-closed system is used, a moderately high flow should be supplied.

There is always the possibility of a lowered arterial oxygen tension when high nitrous oxide mixtures are administered. The problem of hypoxia should be thoroughly understood by the anesthesiologist. It should be emphasized also that oxygen deprivation in the tissues is often due to several factors other than the inspired concentration of oxygen. Amongst them, there may be included depressed respiratory exchange, an obstructed airway, laryngospasm or bronchospasm, and circulatory collapse with inadequate blood perfusion of the vital organs. Waters, in his classic paper, has defined hypoxia as a "reduction in the tension of oxygen which produces disturbances of function only while the reduction persists."[15] It is important to differentiate between transient short periods of reduced oxygen tension and the more prolonged profound degrees of oxygen deprivation. Our studies emphasize the rapidity of interchange of oxygen and nitrous oxide between the atmosphere inhaled and the arterial blood. By utilizing a demand flow gas machine whereby the mixture of the two gases can be changed in either direction, a transient period of oxygen slightly less than 20 per cent during the early induction is permissible in the average, well medicated patient without preliminary oxygenation. The rapid uptake of nitrous oxide compensates for the initially lowered oxygen content (15 per cent, for example). After a few breaths of this mixture, the oxygen concentration is increased. Pulmonary exchange is usually excellent with nitrous oxide where the problems of breath-holding and depressed minute volume are minimal. An inadvertent or intentional temporary lowering of the arterial oxygen tension returns quickly to normal levels as the inhaled mixture is enriched with oxygen (figs. 3, 5, 6 and 8). We are not implying that prolonged hypoxia is to be condoned; however, neither should we have an unwarranted fear during induction of a transient lowering of the oxygen tension which is readily compensated.[15] Once the early induction period is completed, higher concentrations of oxygen should be the rule. Although oxygenation of the arterial blood changes rapidly with alteration of the inspired mixture of gases, the venous oxygen content responds in a somewhat different manner. Kinch administered 100 per cent nitrous oxide for one half minute to female patients in labor.[19] He found that the oxygen content in arterial blood declined, but that the venous blood showed no appreciable degree of hypoxia in conjunction with the inhalation of pure nitrous oxide for this short period. In some cases there was even a slight rise in venous oxygen content. This may have been due to an increased cardiac output associated with the fall in arterial P_{O_2}. However, if the lowered arterial oxygen content continues and is not soon compensated, both venous and arterial oxygen tensions will change, assuming that the arterial–venous difference remains constant. In the past, research studies of blood gases have not emphasized sufficiently the role of the venous system, which, after all, reflects more accurately the actual state of tissue oxygenation. More attention should be paid to the simultaneous investigation of arterial and venous blood oxygen.

Summary and Conclusions

The polarograph has been used to measure the arterial oxygen tension before and during induction with high nitrous oxide concentrations (80 to 100 per cent nitrous oxide). Eight patients were observed following air breathing and 11 patients were studied with preliminary oxygenation before induction with the nitrous oxide mixtures.

The role of preliminary oxygenation was evaluated. (1) The polarograph showed rapid elevations of arterial oxygen tension when oxygenation was carried out for two to three minutes. (2) When 100 per cent nitrous oxide was inhaled after oxygen, the Pa_{O_2} fell precipitously to the control level in one minute. (3) With the addition of 5 to 15 per cent oxygen to the nitrous oxide, the extra oxygen in arterial blood showed a decline to previous levels within approximately two minutes. When a 20–80 mixture of oxygen and nitrous oxide was administered, the time interval was found to be slightly over two minutes.

There is a definite clinical role for preliminary oxygenation prior to high nitrous oxide

mixtures. (1) This technique is of value in the non-premedicated outpatient for whom a minimal period of anesthesia is desired for short minor procedures. Pure nitrous oxide may be administered with safety for one minute. (2) This method may be used for the pregnant female in strong labor. (3) Preliminary oxygenation followed by high nitrous oxide mixtures will facilitate induction with the gas-oxygen-ether sequence. (4) The subnormal patient with a fixed cardiac output will benefit from the increased oxygen tension during induction with nitrous oxide.

Polarographic studies demonstrate that with a change from air to the same oxygen mixture with nitrous oxide (21–79 per cent) there is an early moderate increase in the Pa_{O_2}. This is a laboratory corroboration of previous concepts of nitrous oxide uptake—that because of the greater solubility of nitrous oxide as compared with nitrogen, the alveolar oxygen concentration rises. A gas mixture with slightly less than 20 per cent oxygen is permissible for a few breaths during early induction with nitrous oxide.

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