NITROUS OXIDE ANAESTHESIA WITHOUT HARM

BY

J. W. MOSTERT, M.B., Ch.B., D.A., F.F.A.R.C.S.
Anaesthetic Registrar, Worthing Group of Hospitals

Although evidence has been presented showing that the anaesthetic effect of nitrous oxide is not produced by and need not be accompanied by anoxia, it is equally certain that 85 to 90% of this gas is required in the inhaled atmosphere to produce anaesthesia. It follows that the 20.93% oxygen present in the surrounding air cannot be allowed if the anaesthesia is to be of short duration. The fact, perhaps not so well known, that anaesthesia produced solely by nitrous oxide is possible and practical without hypoxia is the subject of this paper.

The Physiological Basis

Normally the effective tidal volume is of the order of 300 ml., while the total effective lung volume after normal inspiration is equal to this volume plus the functional residual capacity, some 2.8 litres in all. Respiration, being a cyclical process, thus causes the anaesthetic gas inhaled in the first breath to be diluted in a considerable lung volume containing no anaesthetic gas, but only 14.2% oxygen and 80% nitrogen. It is therefore apparent that after the administration of pure nitrous oxide begins a precipitous drop in this 14.2% oxygen must occur, with anoxic anoxia. If, however, the nitrogen is replaced by oxygen before induction of anaesthesia, the same precipitous decline in oxygen concentration must occur, but at least the gradient then begins at 100% instead of 14.2%. Ninety-eight per cent. of "washing out" of nitrogen can actually be accomplished by administration of pure oxygen for merely two minutes, except in cases of grossly uneven distribution of the inspired gas, such as obtains in advanced pulmonary emphysema (Comroe *et al.*, 1955).

More precisely, oxygen diffuses across the pulmonary epithelium normally under a partial pressure of about 60 mm. Hg. After breathing pure oxygen for a few breaths the gradient will be around 600 mm. Hg. On the basis of a functional capacity of 2,500 ml. some 1,800 ml. of oxygen could then be absorbed or eliminated via the tidal air before the oxygen tension in the alveoli would fall to the normal level of 100 mm. Hg.

Miles, Martin, and Adriani (1956) and Hamilton and Eastwood (1955) studied the elimination of nitrogen from the lungs of healthy volunteers breathing oxygen from semi-closed inhalers used in anaesthesia. The former group of workers confirmed that at flow rates equal to the minute-volume exchange of the subject, with no rebreathing, elimination occurred at an average of two and a half minutes. Hamilton and Eastwood found, as expected, that the rate of nitrogen elimination is affected by the rate of flow of gases more than by the system used, and concluded that there appeared to be no clinical advantage in the use of gas flows above 4 litres per minute for the purpose of nitrogen elimination.

Another advantage of preliminary oxygenation is suggested by a comparison of the speed of diffusion of the relevant gases. An isolated lung lobule filled with nitrogen whose bronchus is occluded requires some 16 hours for the nitrogen to diffuse into the blood and for complete deflation of the lobule. Under similar circumstances oxygen disappears in 15 minutes and nitrous oxide in 17 to 35 minutes (Adriani, 1946). This may account for my experience that anaesthesia induced with pure nitrous oxide after preliminary oxygenation is more prompt and profound than in the absence of preliminary oxygen breathing. Again, these considerations apply only to the healthy, Comroe *et al.* (1955) listing various diseases of the lungs which secondarily or specifically impair diffusion.

Finally, a change from the inhalation of 20.93% oxygen to 100% increases the oxygen content of normal blood by a total of 2.2 volumes% or 11% of the total (Comroe and Dripps, 1950). Firstly, the saturation of haemoglobin is increased from 97.5 to 100%, adding 0.5 volume% of oxygen in combination with haemoglobin. Secondly, an additional 1.7 volumes% of oxygen is dissolved in the blood.

Under these conditions, despite the administration of pure anaesthetic gas, perfect oxygenation is assured for 30 to 45 seconds, 6 to 10 respirations, by virtue of the reservoir of oxygen present in the lungs and blood.

Pure nitrous oxide administered for 40 to 60 seconds, or 16 to 20 breaths, is ample for the production of the state of anaesthesia in the healthy. This view can be verified without harm in as many seconds by anyone who wishes to do so. Kety (1951) discussed in great detail the theory and applications of the exchange of inert gas at the lungs and tissues, and the physiological factors more simply elsewhere (Kety, 1950). With every anaesthetic agent the various stages of anaesthesia are associated with definite concentrations of the anaesthetic agent in the brain, and, provided equilibrium has been attained, with definite concentrations in the blood. With a number of gases, including nitrous oxide, the concentrations in blood and in whole brain have been found to be approximately equal. The problem of the rate of induction is thus reduced to the solubility, or rate of uptake, of the anaesthetic gas by the blood. As already indicated, the relatively small and lipid-soluble molecules of nitrous oxide diffuse very rapidly across cell membranes. Thus, gas in the alveoli equilibrates practically instantaneously with blood passing through the pulmonary capillary bed. This has been established by careful physiological studies, most recently by the use of radioactive gases.

The solubility of nitrous oxide, or the ratio of the concentration of dissolved gas to the concentration in the gas phase, at equilibrium is quite low—namely, 0.47. Therefore the major physiological factor limiting equilibration is the cardiac output rather than the respiration, as is the case with high-solubility agents like ether (15.0). The blood is already carrying all the anaesthetic it can for a given partial pressure of gas, and only a small fraction is removed by the blood at each breath, while at the next breath even this is replenished. And this is the only site where the anaesthetist can exert control by providing maximal "driving force," or "pressure head," of gas. For nitrous oxide is such a mild anaesthetic agent that it must be given in high concentration during induction if the excitement stage is to be avoided and smooth anaesthesia is to be produced.

The word "saturation" is often incorrectly used in this connexion, the word "equilibrating" being more satisfactory in describing approximation of body and fat anaesthetic concentration to a given alveolar anaesthetic concentration. It is said that if the blood carries a fixed and safe concentration of nitrous oxide away from the lungs, the cardiac output being 5 litres per minute and the total body water about 45 litres, it follows that the latter can be brought to equilibrium only in a minimum of nine minutes; and in view of the asymptotic nature of the process (blood returning to the lungs will soon contain some anaesthetic, diminishing the net transfer) the calculated time for 90% equilibrium of the whole body must be much more—approximately 21 minutes (Kety, 1951).

Organs such as the heart and brain are, however, richly supplied with blood. Thus the blood supply to the brain has been found to be about 350 ml. per kg. per minute, while the mean figure for the rest of the body water is approximately 100 ml. per litre per minute. Equilibration in the brain can therefore be expected to occur about 3.5 times faster for brain than for body water as a whole, the observed time of about seven minutes for 90% equilibration being in accord with the theory. Gray (1954) provided experimental evidence that this may be more rapid, and in practice I find that the inhalation of pure nitrous oxide for

one minute invariably provides adequate anaesthesia within the next half-minute. While the rate of equilibration can be expected to be most rapid early on, confirmation of an adequate approximation to equilibrium in the brain after one minute of nitrous oxide inhalation is nevertheless clearly desirable; for on it probably depends the whole future of nitrous oxide anaesthesia in dentistry and out-patient surgery.

It is certainly not necessary for equilibration of the whole body mass to be aimed at. Such a state inevitably occurs with anaesthetics of a high solubility resulting in prolonged induction and recovery, and Fink (1955) has shown this to result in one of the main hazards of prolonged nitrous oxide anaesthesia—the rapid elimination of some 28 litres of anaesthetic gas ensuing at the termination of anaesthesia, providing the necessity, once more, of oxygen therapy to remedy the “diffusion” or dilution variety of anoxic anoxia.

Technical Considerations

As a first step pure oxygen is administered at a flow rate of 10 litres or more per minute for two minutes. The patient is previously instructed to breathe normally via a tight-fitting nose- or face-piece. Pure nitrous oxide subsequently administered for one minute, at a flow rate similarly well in excess of the minute-volume and without rebreathing, will produce surgical anaesthesia in all healthy patients. Breath-holding is very rare with nitrous oxide as opposed to cyclopropane. At least 20% oxygen is then added as well as supplementary agents if the surgeon requires more than two to three minutes for the operation. If supplementary agents are not used anaesthesia will lighten during this period. It is interesting that Tom (1956) regards this stage, resulting after breathing 20% oxygen with nitrous oxide, still suitable for dental surgery in older children and adults. Certainly, less than 20% oxygen cannot safeguard against harmful anoxia if it is remembered that the average administrator of nitrous oxide is not an expert.

I have used this technique for over two years. Dental surgeons and casualty officers have appreciated the apparent lack of anoxia, nausea, and delirium. No premedication is used, but emptiness of stomach, bowel, and bladder is desirable.

The technique is useful in allowing time for patients to become accustomed to the apparatus while the anaesthetist carries on a monologue keeping the patient informed that he is not expected to feel any effect during the prelude of oxygen therapy. A few patients who had previous experience of nitrous oxide anaesthesia suggested that this technique removed the unpleasant sensations associated with increasing anoxia, and personal experimentation confirmed this admittedly biased impression.

My attention has been drawn to three facts which, if not mentioned, may allow the method to fall into disrepute. They are: (1) After administering pure nitrous oxide for one minute I habitually allow (except in obstetrics) merely 10–15% oxygen for 15–30 seconds, during which time the surgeon is generally able to embark on his operation without having to contend with a moving patient. Only then do I very carefully administer at least 20% of oxygen. (2) A single breath of air early on, such as during the switchover to anaesthetic gas, may vitiate the advantage gained by this method to a remarkable extent. This point cannot be overemphasized. (3) The astute may economize by using merely 4 litres of oxygen per minute for the purpose of nitrogen elimination. This will, however, result in some carbon dioxide accumulation.

Conclusions and Summary

A technique of nitrous oxide anaesthesia for brief operations in healthy subjects is described. It depends simply on routine nitrogen “washout” by administration of pure oxygen for two to two and a half minutes prior to the administration of pure nitrous oxide. Further reasons are advanced why this technique may avoid anoxia and, incidentally, nausea and delirium,

provided that the inherent limitations of nitrous oxide as a sole anaesthetic agent are observed. Except in expert hands, there must be strict limitation of the time spent on surgery, unless recourse is made to supplementary agents or a state of amnesia and analgesia such as results after the inhalation of 20% oxygen in nitrous oxide.

The idea of nitrogen elimination and its replacement by oxygen prior to nitrous oxide anaesthesia is not new (Neff *et al.*, 1950), but its overall importance appears to be overlooked in practice.

I am indebted to Dr. F. R. Gusterson for advice and encouragement.

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ACUTE RENAL FAILURE IN SALICYLATE POISONING

BY

E. J. M. CAMPBELL, M.D., M.R.C.P.

Assistant

AND

R. E. MACLAURIN, M.B., B.S.

Late House-physician

Medical Unit, the Middlesex Hospital, London

Salicylate poisoning causes complex acid-base and metabolic disturbances. If serious renal damage is present in addition, as in the following case, the management demands careful biochemical control.

Methods.—The plasma sodium and potassium concentrations were measured by flame photometry, the chloride by the method of Van Slyke and Hiller (1947), the bicarbonate by the method of Van Slyke and Neill (1924), and the salicylate by the method of Smith and Talbot (1950). The arterial carbon dioxide and oxygen tensions were measured by the Riley method (Riley, Campbell, and Shepard, 1957) and the pH calculated from the nomogram of Singer and Hastings (1948).

Case History

On February 13, 1957, a spinster of 52 swallowed 75 aspirin tablets—total dose approximately 375 gr. (25 g.). Throughout February 13 and 14 she became increasingly drowsy, but remained rousable and was drinking adequately but passing little or no urine. She did not vomit. She was referred to hospital at midday on February 15. There was no previous history suggestive of renal disease.

On admission she was drowsy and confused but responded to simple questions. Her oral temperature was 98° F. (36.6° C.), pulse 105. She was breathing deeply at a rate of 32 a minute. The blood pressure was 100/70; all her extremities were warm and she was sweating. There were bilateral subconjunctival haemorrhages and a purpuric rash on the trunk and arms. During the first six hours in hospital she passed 26 oz. (740 ml.) of urine which was acid and contained protein, hyaline and granular casts, and large amounts of salicylates. Gastric washings contained no salicylates. The blood Hb concentration was 13.9 g./100 ml. Results of other measurements are given in the