Hazards of Nitrous Oxide Anesthesia in Bowel Obstruction and Pneumothorax

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An enclosed gas-filled space in the body will expand if gas within it is less soluble than the gas respired. Blood arriving at such a space can discharge a greater quantity of the soluble gas into the space than that blood can take up, assuming the tension gradient of each gas is equal. This results from the greater capacity of blood for the more soluble agent. When air was placed in the intestinal lumens of 3 dogs and nitrous oxide respired, intestinal gas volume increased 75 to 100 per cent in two hours and 100–200 per cent in four hours. Similarly, 300 ml. of air placed in the pleural space doubled in volume in 10 minutes, tripled in 45 minutes, and in one dog quadrupled in two hours. Nitrous oxide concentrations rose concomitantly in both the intestinal and pleural spaces. With either gas in the intestine or in the pleural space, no volume changes were seen when the animal respired oxygen and halothane alone. These results suggest that nitrous oxide is relatively contraindicated in cases of intestinal obstruction or pneumothorax.

In 1953, Tenney and his associates found that a closed pocket in the body containing an insoluble gas would expand with time.[1] The blood arriving at this pocket releases whatever gas it contains (mainly nitrogen, if atmospheric air is respired) into the pocket until the tensions of nitrogen in blood and in the pocket are equal. Since the original gas within the pocket is insoluble none of this gas can be removed as nitrogen enters. The pocket, therefore, must expand or the pressure within it must increase. Gas within the pocket need not be totally insoluble for expansion to occur: It need only be less soluble than the gas respired. Tenney *et al.* used sulfur hexafluoride to produce pneumoperitoneum in cats while air was respired. Gas volume within the peritoneal cavity increased to a peak twice the initial volume because nitrogen is roughly 14 times as soluble in blood as sulfur hexafluoride. This required about nine days. Tenney and his coauthors mathematically described the factors which govern the rate at which changes in volume take place. There are two main factors: (1) rate is increased when blood flow to the pocket is increased (or the pocket is small), and (2) rate is also increased as the solubility of the respired gas in blood increases.

In 1955, Hunter [2] found that patients with artificial pneumothorax, pneumoperitoneum or pneumopericardium, often developed tachycardia and hypotension when anesthetized with nitrous oxide. He measured gas pressures within these cavities and found a significant pressure rise during anesthesia. Analysis of the gas suggested the presence of nitrous oxide in concentrations of 20 per cent or less. Hunter surmised that the pressure increase resulted from a more rapid entrance of nitrous oxide than exit of nitrogen from the gas space. His reasoning was essentially similar to Tenney's and was based on the 34-fold difference in blood solubility between nitrous oxide and nitrogen.

We have speculated on the extremes in volume changes that might be achieved under the above circumstances. Let us assume that a pocket with highly compliant walls is initially filled with a totally insoluble gas (*i.e.*, none of the original gas can leave the pocket). At equilibrium, the tension of a second inert gas administered via the lungs must be equal to that in the gas pocket. Thus, if 50 per cent nitrous oxide is present in the alveoli, then 50 per cent will be found in the pocket at equilibrium. Since the original gas cannot escape, this means the total gas pocket

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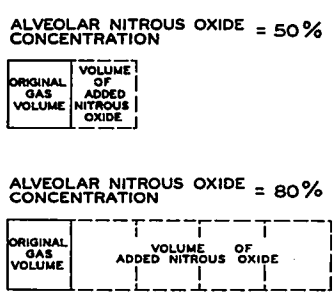

FIG. 1. Volume changes in a gas pocket when the alveolar nitrous oxide is 50 per cent (A) or 80 per cent (B).

volume must be doubled (fig. 1A). Similarly, if 80 per cent nitrous oxide is present in the lungs, 80 per cent must exist in the pocket at equilibrium. The total gas pocket volume must, therefore, be increased five-fold (fig. 1B). A curve may be drawn relating alveolar nitrous oxide concentration to maximum increase in pocket volume (fig. 2). Actually, these maxima would not be attained since the original gas within the pocket must be somewhat soluble and some must escape as nitrous oxide enters. However, this reciprocal loss could be offset by the concomitant entrance of approximately 5–10 per cent oxygen and 5 per cent carbon dioxide. At any rate, the maxima are far in excess (at the 80 per cent alveolar nitrous oxide concentration) of those found by Tenney or suggested by Hunter's finding of 20 per cent or less nitrous oxide in the pneumothorax patients.

In this study, we have attempted to quantitate the volume changes and the rate at which changes occur in gas pockets filled with air when nitrous oxide, 70–80 per cent in oxygen is inhaled.

Method

Mongrel dogs were anesthetized with intravenous thiopental followed by inhalation of halothane and oxygen via a cuffed endotracheal tube. Arterial blood pressure was monitored via an indwelling catheter with a Statham strain gauge.

In 3 dogs 30–40 cm. segments of various portions of the bowel (stomach, ileum, and colon) were isolated by purse string ties of umbilical tape. A catheter with multiple perforations was inserted into one end of the intestinal segment and secured with the intestinal tie. Care was taken not to injure the vascular arcades leading to the segment. The lumen of the bowel was repeatedly flushed with saline through the catheter until returns were clear. This required only 1–2 flushes for stomach and ileum, but 10–20 in the case of the colon. At this time the colon often looked somewhat inflamed and edematous while the ileum and stomach appeared reasonably normal. Air was injected into each segment and then withdrawn to determine if leakage or clogging were present. In all cases, the air injected could easily be recovered. The bowel was returned to the abdominal cavity and the skin over the cavity brought together with towel clips. A measured volume of air (varying from 20–120 ml.) was then injected. Subsequently the volume remaining within the segment was withdrawn, measured, and returned to the segment. This air was withdrawn after 60–80 minutes and a second

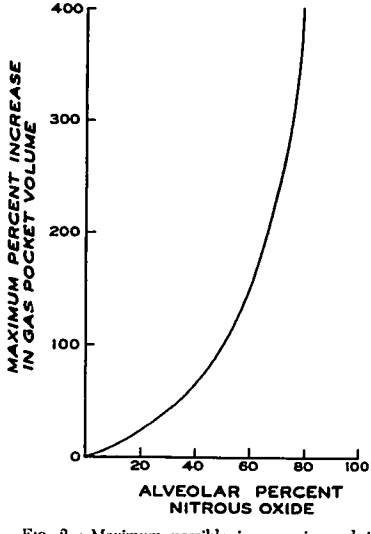

FIG. 2. Maximum possible increase in pocket volume at various alveolar concentrations of nitrous oxide.

aliquot of air was injected. The animal was then given 70–80 per cent nitrous oxide to breathe as measured by end-tidal infrared gas analysis. Again at intervals, gas was withdrawn, volume measured, analyzed with the infrared analyzer, and returned to the intestine. Pressures within the intestine were measured before and after gas volume determinations.

Three other dogs were anesthetized with thiopental. After endotracheal insertion of a cuffed catheter, ventilation was controlled while anesthesia was maintained with halothane and oxygen. A small incision was made in the chest wall through parietal pleura. A catheter with multiple perforations was inserted into the pleural space and tied in place with a purse-string suture. Following evacuation of air from the pleural space, 300 ml. of air was injected. After 10 to 20 minutes this was withdrawn and the volume remeasured. The dog was then given 68 to 78 per cent nitrous oxide to breathe. Again 300 ml. of air was injected into the pleural space. At repeated intervals, the gas in the pleural space

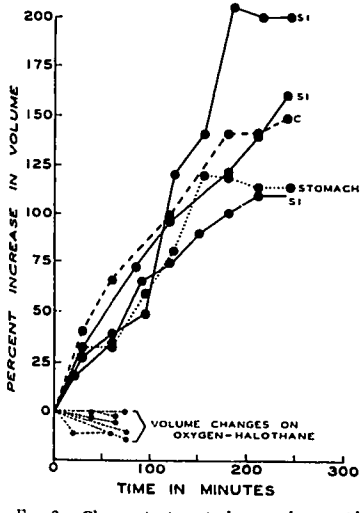

FIG. 3. Change in intestinal gas volume with administration of nitrous oxide (large dots) as opposed to halothane and oxygen (small dots). SI signifies small intestine, C signifies colon.

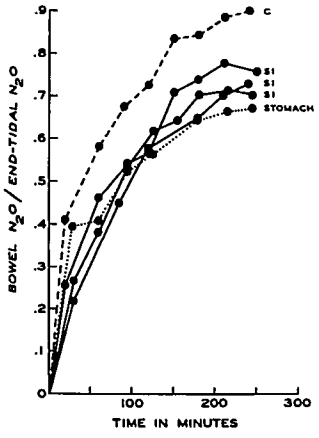

FIG. 4. Rate at which the nitrous oxide concentration within various parts of the intestine approached that in the end-tidal gas. SI signifies small intestine, C signifies colon.

was withdrawn, the volume measured, nitrous oxide content analyzed, and the entire gas sample returned to the pleural space.

Results

Figure 3 gives the changes in intestinal gas volume as per cent change from the original volume. When the animal respired only halothane and oxygen the volume remained constant or slightly decreased. When nitrous oxide was subsequently administered volume increased with time. At two hours the volume had risen by 80 to 100 per cent and at four hours increased still further, from 100 to 200 per cent. The rate of change did not appear to depend on whether a small (20–50 ml.) or large (90–100 ml.) initial gas (air) volume had been injected. A graded series of injections might be expected to show a slower change with larger initial gas volumes. The type of bowel selected for injection (stomach, ileum, or colon) appeared to make little difference. Figure 4 shows the rate at which nitrous oxide concentration in the bowel approached that in end-tidal pulmonary gas. Even after four hours of nitrous oxide inhalation, equilibrium was only 75 per cent complete and a continuing but slow rise in both

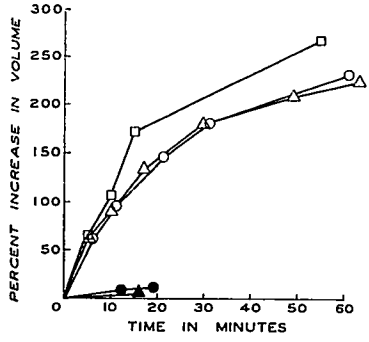

FIG. 5. Increase in intrapleural gas volume on administration of nitrous oxide (open squares, circles and triangles) as opposed to change in volume on administration of oxygen, plus halothane (filled triangles and circles).

nitrous oxide concentration and intestinal gas volume could be anticipated.

Intestinal pressure recordings taken during this time initially showed a slight but irregular tendency to rise. However, as distension increased pressures returned to normal or near normal levels. Considerable rises in pressure were seen on reintroduction of gas into the intestine. In one case, pressure before removal of gas was 6.5 mm. of mercury and after reinjection reached 70 mm. of mercury. Such rises, however, are not representative of pressure changes occurring during the course of anesthesia where volume changes take place gradually.

Figure 5 illustrates changes in intrapleural gas volume with and without nitrous oxide administration. When oxygen and halothane were respired little change in volume occurred. However, when the lungs were ventilated with nitrous oxide, the volume doubled within 10 minutes and tripled in half to three quarters of an hour. The concomitant rate of change of nitrous concentration relative to end-tidal concentration is shown in figure 6. After a rapid initial rise to 50 per cent in the first 5 minutes, there was a continuing but slower rise to about 80 per cent at the end of an hour. A further slow increase in volume and concentration was to be expected and actually was seen in one dog observed after two hours. By this time the gas volume had quadrupled and intrapleural nitrous concentration had risen to 85 per cent of the end-tidal concentration.

Discussion

Our findings are in general in agreement with the work of Tenney and his co-workers[1] and with that of Hunter.[2] The rates of change are more rapid than those seen by Tenney *et al.* but this may be explained by the difference in the gas systems used. Tenney employed two relatively insoluble gases (SF_6 and N_2) whose total volume transport by blood to and from any gas cavity would be extremely limited. In comparison, nitrous oxide is a relatively soluble gas which may be transported in sizeable quantities. We also found a greater increase in volume than found by Tenney despite a slightly lower alveolar concentration of the respired gas (80 per cent or greater nitrogen concentration in his case and 70 to 80 per cent nitrous oxide concentration in this study). This probably can be explained by the difference in solubilities between the respired gas and that present initially in the gas pocket; the greater the difference, the greater the input of the respired gas relative to the loss of the initial pocket gas. In Tenney's work the respired gas, nitrogen, is roughly 14 times as soluble as the sulfur hexafluoride injected into the peritoneal cavity while in our study the respired gas, nitrous oxide, is about 34 times as soluble as the nitrogen (the main constituent of the injected air) introduced into either intestinal or pleural space.

Although our findings support the clinical observations of Hunter, we found far greater concentrations of nitrous oxide in both pleural and intestinal gas spaces. The reason for this probably lies in the different techniques used for analysis. We attempted to absorb nitrous oxide with concentrated sulfuric acid as he described but were able to dissolve only a small amount of nitrous oxide. It would appear that this technique is inadequate for quantitative nitrous oxide analysis.

The rate at which the pleural gas space expanded was far greater (at least 15 times more rapid) than the rate at which the bowel gas space increased. In part, this is probably

due to the greater blood flow to pleura. It probably also results from direct diffusion of nitrous oxide from the alveoli beneath the pleural surfaces. Since nitrous oxide is more soluble than nitrogen the rate of diffusion is greater.

In prolonged operations in which the peritoneal cavity is entered we have observed that closure is often difficult because of distension of the bowel. This may be explained by the increase in intestinal gas volume if nitrous oxide is used. Once present, such distension may be reversed by the administration of oxygen. However, though this technique will eventually eliminate nitrous oxide from the bowel, it will not do so rapidly (in less than an hour) because of the relatively low blood flow to the gas space within the bowel.

Gaseous distension of the bowel prior to anesthesia increases the hazard introduced by nitrous oxide. Thus, in intestinal obstruction, not only may it be difficult to close the peritoneal cavity but in addition the increase in intestinal volume may compromise the blood supply to the bowel or possibly cause rupture. Limitation of blood flow in intestinal mucosa may accompany intra-intestinal pressure increases. Fortunately, at least this would also reduce the rate at which nitrous oxide could be brought to the bowel and hence reduce the chance of rupture. Although some of the above is speculation, it would seem prudent to consider bowel obstruction as a relative contraindication to nitrous oxide anesthesia at inspired concentrations exceeding 50 per cent, particularly if it is anticipated that anesthesia will be prolonged.

Hunter has already demonstrated the hazard of nitrous oxide anesthesia in the presence of pneumoperitoneum, pneumothorax or pneumopericardium. Both his and our studies would suggest 70–80 per cent nitrous oxide is contraindicated if these states exist. Other diseases may be added to the above list of pathologic states which contraindicate the use of nitrous oxide. Any pulmonary disease in which air is trapped throughout the respiratory cycle might be so considered. In particular the existence of noncommunicating blebs and bullae [3, 4, 5] makes the use of nitrous oxide hazardous. Such spaces actually need not be

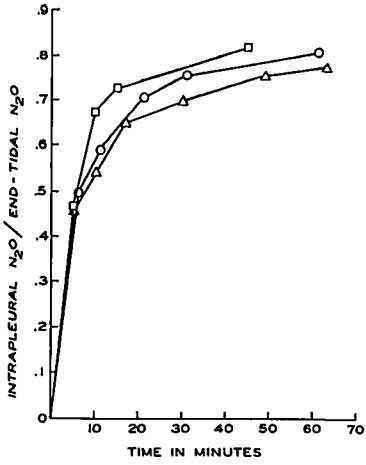

FIG. 6. Rate at which intrapleural nitrous oxide concentration approached that in the end-tidal gas.

noncommunicating: a ball-valve-like opening into such a space allowing the entry of air enhances the hazard. Such air pockets must expand just as those in the intrapleural space. With increase in size, they may compress adjacent lung tissue and at some point of distension may rupture. In addition, as Hunter pointed out, an increase in air volume in pneumothorax may be accompanied by an increase in intrathoracic pressure. This increase in pressure may impair venous return and cardiac output.

Although our comments have been directed mainly to nitrous oxide, it is obvious from figure 2 that they apply to any relatively soluble gas used in concentrations exceeding 40 to 50 per cent. Thus, ethylene or xenon should produce the above phenomena while the more potent anesthetics requiring lesser concentrations such as halothane, fluroxene, methoxyfluorane, diethyl ether, and to a lesser extent cyclopropane, should not. It also may be predicted according to figure 2 that at concentrations exceeding 80 per cent the phenomenon of gas pocket expansion is markedly exaggerated. In pressure chamber work where such concentrations of nitrous oxide have been

obtained in otherwise normal dogs, we have seen gross abdominal distension.

We have assumed that the gas space enlarged by the nitrous oxide is surrounded by compliant walls. That is, as the nitrous oxide enters and the volume expands there is essentially no change in the pressure within the space. However, if the walls are inexpansible, expansion cannot occur; instead of volume, pressure rises. In a separate study, this has been examined and found to be the case. There are relatively few naturally occurring gas spaces within the body. The cranial sinuses or the middle ear may become such spaces in pathological conditions where their ostia are occluded. Another space is that present during pneumoencephalography. In dogs, we have found [6] that following the injection of air into the cisternal space there is a fall in cisternal pressure if the dog breathes air or oxygen. However, if the dog respires 70–80 per cent nitrous oxide following the air injection, a pressure rise of 40–70 mm. of mercury occurs. Pressures of 90–110 mm. of mercury are commonly obtained. Qualitatively similar results have been obtained in man.

Summary

Administration of 70–80 per cent nitrous oxide in dogs caused the expansion of an air-containing pocket either within the bowel (stomach, ilium, or colon) or the pleural space. Expansion of the gas space occurred slowly in the bowel, increasing approximately 70 per cent in two hours and 150 per cent in four hours. Expansion of the gas in the pleural space took place more rapidly. The volume was doubled in 10 minutes and quadrupled in two hours. These findings indicate that it may be hazardous to administer high concentrations of nitrous oxide in the presence of intestinal obstruction, pneumothorax, pneumoperitoneum, pneumopericardium, or bulbous disease of the lungs.

Halothane (Fluothane) for this study was supplied by Ayerst Laboratories.

References

1. Tenney, S. M., Carpenter, F. G., and Rahn, H.: Gas transfers in a sulfur hexafluoride pneumoperitoneum, J. Appl. Physiol. 6: 201, 1953.
2. Hunter, A. R.: Problems of anaesthesia in artificial pneumothorax, Proc. Roy. Soc. Med. 48: 765, 1955.
3. Fischer, C. C., Tropeaa, F., Jr., and Bailey, C. P.: Congenital pulmonary cysts, J. Pediat. 23: 219, 1943.
4. De Sant'Agnese, P. A.: Bronchial obstruction with lobar atelectasis and emphysema in cystic fibrosis of the pancreas, Pediatrics 12: 178, 1953.
5. Ting, E. Y., Klopstoch, R., and Lyons, H. A.: Mechanical properties of pulmonary cysts and bullae, Amer. Rev. Resp. Dis. 87: 538, 1963.
6. Saidman, L. J., and Eger, E. I., II: Change in cerebrospinal fluid pressure during pneumoencephalography under nitrous oxide anesthesia, ANESTHESIOLOGY 26: 67, 1965.

BLOOD VISCOSITY In the dog heart-lung preparation reduction of blood viscosity led to increased cardiac output. Exchange transfusion of 1 liter of dextran resulted in a reduction of hematocrit from 53 to 13 per cent, a 33 per cent drop in blood viscosity and an associated 38 per cent increase in cardiac output while left atrial pressure fell. The results were similar when Krebs' solution-suspended red cells were substituted for dextran, indicating that anemia per se was not responsible. An additional observation was that in the face of anemic heart failure induced by serial dextran exchanges until hematocrits reached the range of 2–7 per cent, ouabain in 0.3–0.5 mg. doses led to marked improvement, as did restoration of a normal hematocrit. Digitalis preparations might therefore be expected to be useful in clinical situations in which severe anemia is a factor in the production of congestive heart failure. (*Fowler, N. O., and Holmes, J. C.: Dextran-Exchange Anemia and Reduction in Blood Viscosity in the Heart-Lung Preparation, Am. Heart J. 68: 204 (Aug.) 1964.*)