# THE EFFECT OF $P_{CO_2}$ ON THE DEPTH OF ANESTHESIA

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Hyperventilation during anesthesia appears to produce sedation somewhat similar to that of additional barbiturate drug. Dundee[1] compared the amount of thiopental required during surgical procedures with and without artificial hyperventilation. In hyperventilated patients about 20 per cent less thiopental was required. Geddes and Gray[2] report that patients were less apt to move with surgical pain during hyperventilation, and the abdominal muscles appeared more relaxed. Gray and Rees[3] believed the abdominal relaxation was due to the removal of the respiratory drive by hypocapnia. Other suggested mechanisms of such a sedative effect during anesthesia include stretch receptor stimulation,[4] cerebral hypoxia,[5] and the central effects of acapnia, particularly on the reticular activating system.[6]

The following experiment was designed to discover whether hyperventilation either with or without fall in $P_{CO_2}$ could be shown to potentiate anesthesia with $N_2O$. We anticipated that with a low $P_{CO_2}$, loss of consciousness and of ability to perform a coordinated task would occur at a lower alveolar $N_2O$ concentration than during normal ventilation. The results do not support this conclusion. In fact, with hypocapnia more $N_2O$ was required to reach the same degree of unconsciousness and loss of coordination. When $P_{CO_2}$ was increased above normal, less $N_2O$ was required to reach the same end point. Hyperventilation with a normal $P_{CO_2}$ had no effect on the end point.

## Method

Twelve healthy young adult volunteers, of both sexes, were exposed to a gradually increasing concentration of $N_2O$ via a face mask. A reproducible, objective end point indicating the depth of anesthesia was found to occur with failure of ability to perform a task requiring visual-manual coordination. This was determined by requiring the subject to squeeze a rubber bulb attached to an aneroid manometer, and maintain a constant 50 mm. of mercury pressure. When the end point was approached, unsteadiness of the recorded pressure became apparent, and at the end point the subject usually relaxed his grasp on the bulb. In most, but not all subjects, coordination failure coincided with loss of consciousness.

$CO_2$ and $N_2O$ concentrations under the face mask were continuously sampled and recorded by two infrared gas analyzers and an ink-writing recorder. An enclosed bellows spirometer was used as a breathing reservoir to facilitate recording of the tidal volume, and the hand-bulb pressure was recorded by including a Statham transducer in the manometer system.

The end point was determined with high, normal, and low $P_{CO_2}$. Low $P_{CO_2}$ was produced by mechanical hyperventilation with either a Bird or a Jefferson ventilator connected to the space surrounding the bellows. Normal $P_{CO_2}$ occurred, of course, during spontaneous respiration. High $P_{CO_2}$ was obtained by the addition of 5 to 10 per cent $CO_2$ to the $O_2$-$N_2O$ breathing mixture, during spontaneous breathing. In order to learn whether the mechanical hyperventilation *per se* had any sedative effect, the end point was also determined during mechanical hyperventilation with sufficient $CO_2$ added to the inspired gases to keep the alveolar $P_{CO_2}$ normal.

## Results

The concentration of $N_2O$ required to reach the coordination end point at various $P_{CO_2}$ levels is displayed in figure 1 for all subjects. The mean of the data is shown in figure 2

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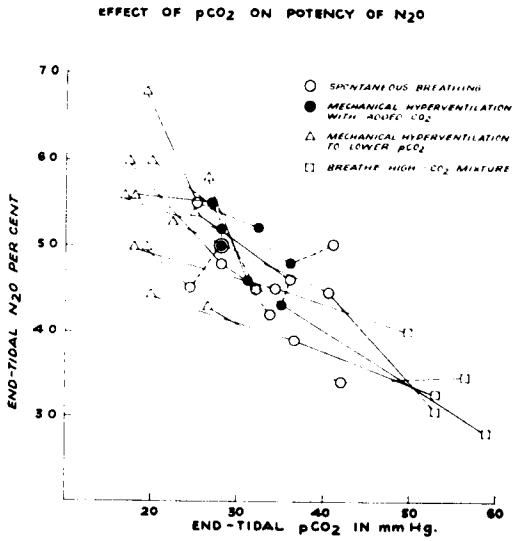


FIG. 1. The concentration of $N_2O$ and $CO_2$ observed in 12 subjects at the end point of failure of coordination.

and table 1. Only 5 of the 12 subjects were tested while breathing added $CO_2$, and only 7 were tested with mechanical hyperventilation while breathing enough inspired $CO_2$ to hold alveolar (end-tidal) $P_{CO_2}$ normal. During mechanical hyperventilation with normal $P_{CO_2}$ the end point was reached at 49.5 per cent $N_2O$, essentially the same as the value of 48 per cent for spontaneous respiration in these 7 subjects. Hyperventilation *per se* therefore had no effect on the end point. The slope of the line in figure 2 indicates that for each 10 mm. rise in $P_{CO_2}$ about 6 per cent

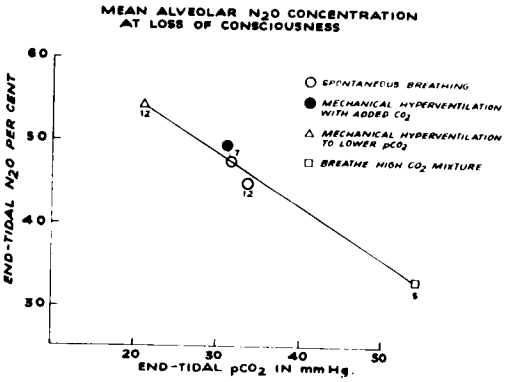


FIG. 2. The effect of altering $P_{CO_2}$ on the mean $N_2O$ concentration required to reach the end point.

TABLE 1

MEAN ALVEOLAR $N_2O$ CONCENTRATION AT LOSS OF CONSCIOUSNESS

| Condition | No. of Cases | Alveolar $P_{CO_2}$ | Alveolar $N_2O$ % |
|---|---|---|---|
| Spontaneous respiration | 12 | 33.4 | 45 |
| Mechanical hyperventilation with added $CO_2$ | 7 | 31 | 49.5 |
| Mechanical hyperventilation to lower $PCO_2$ | 12 | 21 | 54.5 |
| Breathe high-$CO_2$ mixture | 5 | 54 | 33 |

or 40 mm. less $N_2O$ was needed to reach the end point. This suggests that $CO_2$ and $N_2O$ are acting additively in producing anesthesia and that $CO_2$ is about four times as potent an anesthetic as $N_2O$. This agrees well with the known anesthetic effects of 25 per cent $CO_2$.[1, 7-9]

## DISCUSSION

*The Possible Role of Cerebral Blood Flow.* The cerebral vasoconstriction produced by hypocapnia[10] might delay the equilibrium of brain and arterial blood $N_2O$, and permit a higher alveolar $N_2O$ concentration to be observed at the end point during hyperventilation. The fall in central blood flow to be expected in our experiments at a $P_{CO_2}$ of 21 mm. of mercury is about 35 per cent.[10] In order to detect whether equilibration was delayed during hypocapnia, we maintained one subject near the end point as shown in figure 3. He reached the end point 3 times in 6 minutes. If the brain concentration had failed to follow the alveolar concentration closely, we should have expected each successive end point to occur at a lower $N_2O$ concentration. Since this did not occur, it seems unlikely that delay of equilibrium was responsible for our results.

*Cerebral Hypoxia Due to Vasoconstriction.* The low cerebral blood flow with hypocapnia probably produces a relative hypoxia of parts of the brain.[5, 11, 12] One might expect this to reduce rather than rise the resistance to $N_2O$. If this factor plays a role in these experiments then it is probably in the opposite direction, and causes an underestimation of the additive effect of $CO_2$ on depth of anesthesia.

It may well be that hypoxia plays a role

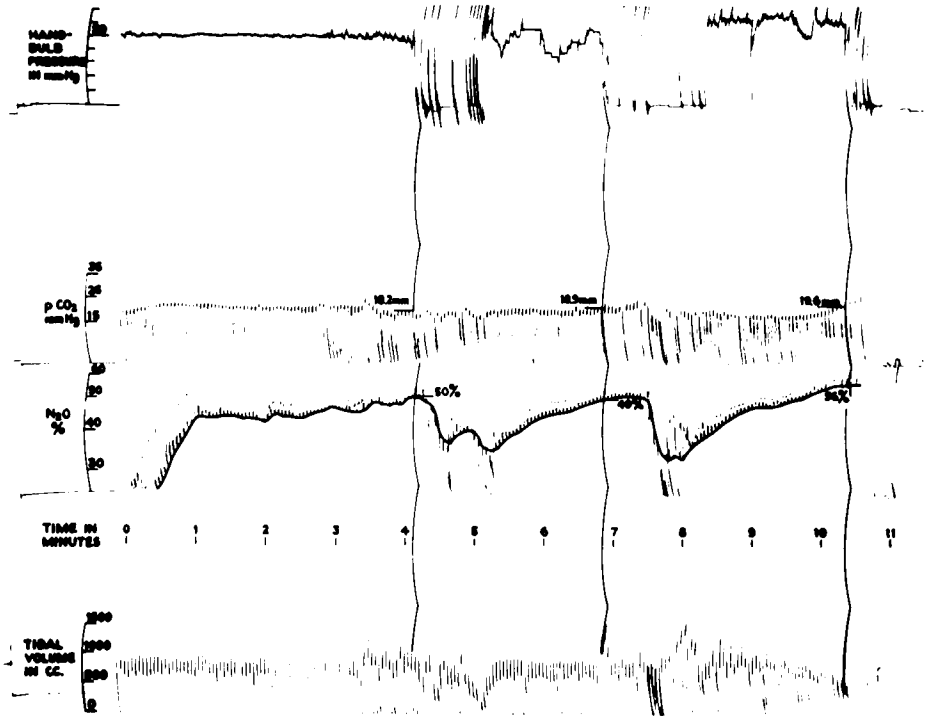


FIG. 3. An experiment done to detect whether or not during hyperventilation a lag of brain $N_2O$ concentration behind alveolar concentration due to cerebral vasoconstriction affected the end point. The subject was hyperventilated mechanically to an end-tidal $P_{CO_2}$ of 18–20 mm. of mercury. The end-tidal $N_2O$ concentration was raised gradually until at 4 minutes the subject's hand released the hand bulb. The $N_2O$ concentration was reduced, the subject awakened, and then returned to the end point twice, at 7 and 10 minutes. If cerebral vasconstriction had resulted in significant delay, the second and third end points should have been at lower $N_2O$ concentrations. They were the same or higher. Therefore, delay in equilibrium resulting from cerebral vasoconstriction could not account for the higher concentration of $N_2O$ needed to reach the end point during hyperventilation.

in the sedative effect of hyperventilation. The $P_{O_2}$ in cortical tissue may fall to 3–5 mm. with hyperventilation.[5]

*The Sedative and Analgetic Role of Acapnia.* When $P_{CO_2}$ falls below about 25 mm. of mercury, central nervous system effects begin to manifest themselves. The EEG shows slow waves similar to sleep[13] and the reticular activating system is depressed.[6]

Clutton-Brock[14] found that the threshold for pain on application of tibial pressure was elevated during voluntary hyperventilation with air. Upon inhalation of 100 per cent $O_2$ the pain threshold fell nearly to normal, while upon inhalation of amyl nitrite the pain threshold returned to normal. He attributed the increase in pain threshold during hyperventilation to cerebral anoxia resulting from cerebral vasoconstriction.

Fenn *et al.*[15] noted unresponsiveness and a condition like sleep in some hyperventilated subjects but were unable to modify any of the actions of acapnia by oxygen breathing.

Balke and Lillehei[16] also noted in some artificially hyperventilated subjects an apathetic state with decreasing responsiveness to external stimuli. The ability of their subjects to perform coordinated tasks decreased progressively with $P_{CO_2}$ values below 30 mm. of mercury, being reduced 30 per cent at 12–15 mm. of mercury. They noted that all the symptoms of hyperventilation except tetany resemble those of hypoxia. In this regard, the subjective sensations associated with artificial hyperventilation and $CO_2$ breathing are of interest. Most subjects find hyperventilation to be relatively pleasant, productive in some of sensations of sleepiness, and

in some of amnesia. They lie quietly, usually with eyes closed. Others report that sensations associated with hyperventilation are not particularly unpleasant or painful. Tetany was not seen in our subjects. Carbon dioxide breathing, on the other hand, called forth the vigorous muscular work of breathing and was associated with extreme restlessness, constant small movements, sweating in some, and a desire to terminate the experience.

The above evidence seems to confirm clearly the clinical impression that hyperventilation during anesthesia has a sedative role. The clinical effect of hyperventilation seems to be a quieting and decrease in restlessness, relaxation and less response to pain. Yet our experimental evidence would seem to indicate the opposite effect on consciousness and coordination. These two effects appear therefore to be different.

It may be that once consciousness has been lost, these other phenomena, of restlessness with high $CO_2$ and relaxation with low, supervene and override the relatively small differences in depth of narcosis. It seems reasonable to state that the sedative effect of hyperventilation is not due to a potentiation of the anesthetic agent.

*The Meaning of the Additive Effect of $N_2O$ and $CO_2$.* The data suggest that the removal of some of the normally present $CO_2$ increases the $N_2O$ concentration required to produce the end point of loss of coordination and unconsciousness. If narcosis is produced when the total concentration of depressants reaches some level, this would imply that the normally present $CO_2$ plays a depressant role. It may be that the $CO_2$ in physical solution acts much as an inert anesthetic gas in this way, and at the same time as an acid and a pharmacologic agent in other areas of the brain such as the reticular activating system. In this respect, $CO_2$ is similar to many inert gases and volatile liquids which are both anesthetic and convulsive or excitatory. On the other hand, these data attribute to $CO_2$, as an anesthetic, about 8 times the potency which its known oil solubility would lead us to predict as compared to all the anesthetic gases and vapors. Carbon dioxide has an oil solubility about half that of nitrous oxide, and water solubility about equal to $N_2O$.

## Summary

Experiments were done to determine whether hyperventilation potentiated $N_2O$ anesthesia. In 12 subjects the concentration of $N_2O$ in alveolar (end-tidal) gas needed to reach the threshold of unconsciousness and incoordination was measured at high, normal and low $P_{CO_2}$ produced by breathing $CO_2$ and air and by mechanical hyperventilation. Contrary to expectation, hypocapnia diminishes the potency of $N_2O$ and hypercapnia enhances it. Carbon dioxide has an anesthetic potency about 4 times that of $N_2O$. Hyperventilation with normal $P_{CO_2}$ had no effect on $N_2O$ potency. The criteria used to judge the depth of anesthesia apparently are unrelated to the clinically apparent sedative effect of hyperventilation.

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**AXILLARY BLOCK** Block of the brachial plexus in the axilla is described as particularly valuable in children. Lidocaine, 1 to 1½ per cent, is used, depositing 3 to 7 cc. in each of four sites. Paresthesias are not purposely elicited. Premedication is omitted frequently to obviate undesirable effects. Under block anesthesia, about 70 per cent of children can be put to sleep easily by suggestion alone. Tourniquets can be used with no further block. (*Dales, J., and others: Axillary Arm Block with Emphasis on Its Use in Children, Canad. M. A. J. 82: 1160 (June 4) 1960.*)

**ALCOHOL-PROCAINE** The course and healing of fractures in response to the application of alcohol-procaine solution (96 per cent alcohol 40 ml., distilled water 60 ml., prociane 2 Gm.) were studied in experiments involving two groups totalling 39 animals: a younger group of one-month-old rabbits and an older group of 4 to 5 month-old rabbits; also, 71 children in the age range from 1 to 15 were clinically observed. One ml. of the solution was given in a single injection into the fracture for the younger group, and 2 ml. for the older group. The solution was also administered to the children in one dose, and the dosage was figured on the basis of one ml. per year of age, but the entire dose never exceeded 10 ml. The experimental as well as the clinical results show that the alcohol-procaine solution injected into the haematoma between the fragments in fractures of long tubular bones in children produces good and prolonged analgesic effects and prevents for long periods painful muscular retraction, eases the reposition and immobilization of splinters, and favorably influences osteogenesis; the healing time of the fractures compared favorably with the cases reported in the literature. (*Topuzov, V. S.: Use of Alcohol-Procaine Solution in Complex Treatment of Fractures in Children, Ortop. Traum. i Protez. 12: 24, 1959.*)