

## THE ROLE OF ANOXIA IN GASTROINTESTINAL EFFECTS OF ANESTHESIA \* †

EDWARD J. VAN LIERE, PH.D., M.D.

*Morgantown, W. Va.*

Four types of anoxia are commonly recognized: (1) anoxic (or anoxemic), (2) anemic, (3) histotoxic and (4) stagnant. The anesthetist presumably is mainly interested in the first three of these. Some anesthetists might logically contend that if anesthetic agents were properly administered, anoxic anoxia would not obtain. This, in a measure, would be true if anesthetics were given only by experienced and skillful individuals. If we grant, however, that any agent which depresses respiration is capable of producing anoxic anoxia, then anesthetics would fall into this category.

There is still some question whether anesthetic agents produce an histotoxic anoxia under ordinary conditions of usage.

Although there may be a divergence of opinion as to whether or not anesthetic agents are capable of producing an anoxic or histotoxic anoxia, a severe hemorrhage under almost any condition will produce a certain amount of anemic anoxia.

Studies on the effect of anesthetic agents on the gastrointestinal tract have not been as exhaustive as those made, for example, on the heart and lungs. It would seem that the problems of postoperative distention and of paralytic ileus alone would have produced a greater interest in such studies.

My own interest in this subject was aroused by my work in the field of anoxia. During the past eighteen years or so my colleagues and I have devoted the major part of our research time to studies in anoxia. We have studied the effect of anoxia on nearly all the organs of the body. Recently I have reviewed the literature in this field (1). In this paper it is my plan to present some of the results of our researches as far as they might apply to the effects of anesthesia on the gastrointestinal tract.

### THE EFFECT OF ANOXIA ON THE MOTILITY OF THE ALIMENTARY TRACT EFFECT OF ANOXIC ANOXIA

It has been shown in our laboratory that anoxic anoxia depresses hunger contractions (2) and digestive peristalsis of the stomach (3).

\* From the West Virginia University School of Medicine, Morgantown, West Virginia.

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Anoxemia, too, retards gastric emptying in both man (4) and dog (5). The threshold lies about at an oxygen percentage of 15 (which corresponds to an approximate altitude of 8,000 feet) as far as the effect on gastric emptying is concerned. There is, however, considerable individual variation both in man and dogs.

It was found that the motility of the small intestine of the dog is not appreciably altered by anoxic anoxia. (It is altered, however, in the mouse.) It is difficult to understand why the small intestine of the dog is unaffected by anoxic anoxia. Further work is needed on this point.

Colonic motility (6) is definitely affected by anoxic anoxia. The threshold is about the same as mentioned previously for the gastric emptying time, namely about an oxygen percentage of 15. In view of the fact that the activity of both the stomach and the colon are depressed by anoxemia, it would be expected that the small intestine would be likewise affected.

#### EFFECT OF ANEMIC ANOXIA

Carlson (7) in 1918 reported that dogs, which had been bled 30 per cent of their calculated blood volume, showed an increase in the tone of the stomach and intensified hunger contractions. This augmented effect lasted for twenty-four hours. Van Liere and his coworkers (8) found, however, that four human beings, who had had one-tenth of their calculated blood volume withdrawn, showed on the average a prolongation of gastric emptying time of 41 per cent. There was still some delay in three of the four individuals twenty-four hours after the hemorrhage. At the end of forty-eight hours the delay had disappeared.

It has been reported by Peterson *et al.* (9) that carbon monoxide, which produces an anemic type of anoxia, also inhibits gastrointestinal peristalsis.

#### THE EFFECT OF ANOXIA ON GASTRIC AND INTESTINAL SECRETION

##### EFFECT OF ANOXIC ANOXIA

It was reported by Bayeux (10) in 1911, working with dogs, that at an altitude of 14,000 feet there was a diminution in the volume of gastric juice, but the amount of total acid secreted was unaffected. Delrue (11) in 1934, however, also working with dogs, observed that at an altitude of 8,000 feet the gastric juice showed a decrease in hydrogen ion concentration and in total acid. In my laboratory (12) it has been shown that dogs with either a Pavlov or a Heidenhain pouch showed a diminution in the volume of gastric juice and in the total acid when subjected to an effective degree of anoxemia. The threshold lay at a simulated altitude of approximately 14,000 feet (which corresponds to about 12 per cent oxygen). Anoxemia has no appreciable influence on the chloride, acid or hydrogen ion concentration of the basal secretion of dogs

with a Pavlov pouch (13). Intestinal secretion, too, is relatively resistant to anoxia (14).

#### EFFECT OF ANEMIC ANOXIA

Interesting observations have been made on the effect of hemorrhage on gastric secretion. Alvarez and Van Zant (15) reported that the mean gastric acidity fell off sharply when the hemoglobin fell below 12 Gm. or 72 per cent. Goldhamer (16) observed a direct relation between the erythrocyte count and the amount of gastric juice secreted. Experimentally it has been shown by Apperly and Cary (17) that when the red cell count of the blood fell below a critical level, free acid disappeared from the stomach.

In summary, it may be said that the gastric and intestinal glands are relatively resistant to oxygen want. The secretory mechanism of the stomach appears to be less resistant to anemic than to anoxic anoxia. A partial explanation of this may be that chlorides are lost during hemorrhage.

#### THE EFFECT OF ANOXIA ON ABSORPTION FROM THE SMALL INTESTINE

##### THE EFFECT OF ANOXIC ANOXIA

It is of interest to consider the effect of anoxic anoxia on absorption from the small intestine. Studies thus far in our laboratories have been made only on simple substances such as water, sodium chloride, glucose, glycine and magnesium sulfate.

The absorption of water from the small intestine is practically unchanged until a simulated altitude of 14,000 feet (which is approximately that of Pike's Peak) is reached. At this altitude, absorption is somewhat decreased, but not significantly. At a simulated altitude of 18,000 feet, which is approximately equal to a pressure of half an atmosphere (which corresponds to about 10 per cent oxygen), absorption of water from the small intestine in the mammal is significantly decreased. The cause for this is not known. It should be remarked here that water, as such, is not a normal constituent of the lower ileum, from which portion of the small intestine these absorption studies were made.

The absorption of physiologic saline solution is practically unchanged by anoxemic conditions. There is an apparent increase at a simulated altitude of 18,000 feet, but it is not statistically significant.

The absorption of isotonic glucose or of glycine is not influenced until a simulated altitude of 24,000 feet is reached (which corresponds to about 8.4 per cent oxygen). At this altitude the absorption of glucose is increased while that of glycine is decreased (18).

Isotonic magnesium sulfate (6.66 per cent) is uninfluenced by anoxic anoxia (19)). This is of more than academic interest, since this agent is widely used in conditions associated with anoxia, for example, in cardiac failure. If the velocity of absorption of magnesium sulfate

were increased in these conditions, respiration might be dangerously depressed.

In summary, it may be noted that the rate of absorption of simple crystalloids is more resistant to anoxic conditions than that of substances absorbed by so-called vital processes.

#### THE EFFECT OF ANEMIC ANOXIA

It is now in order to examine briefly the effect of anemic anoxia on the absorption of a few simple substances from the intestine. The study of anemic anoxia is now a timely one, because soldiers suffer from hemorrhage on the battlefield and then, too, many people nowadays are donating their blood for blood banks.

In our laboratory it was found (20) that if dogs are bled somewhat less than one-half of their calculated blood volume, which indeed constitutes a severe hemorrhage, the absorption of isotonic glucose solution from the small intestine is unaffected, but there is some decrease in the amount of water absorbed. The amount of absorption of physiologic saline solution, however, is significantly increased.

It may be said, then, that neither anoxic nor anemic anoxia has an important effect on intestinal absorption. It seems reasonably safe to assume that neither a fairly severe degree of anoxia nor a pronounced hemorrhage will interfere seriously with the absorption of food substances from the small intestine.

#### THE EFFECT OF SOME ANESTHETIC AGENTS ON GASTRIC MOTILITY

The effects of a number of anesthetic agents on the gastric emptying time (21) have been studied in our laboratory. These studies were carried out on dogs. The procedure was as follows: A standard test meal was used, which has been described elsewhere (22). Several determinations of the normal gastric emptying time were made fluoroscopically. The anesthetic agents studied were: chloroform, diethyl ether, nitrous oxide, ethylene, cyclopropane and divinyl ether. The animals were maintained under a light surgical anesthesia for fifteen minutes. Twenty minutes after the anesthetic was discontinued the animals were fed the standard test meal and the gastric emptying time was again determined. The experiments were repeated several times, but not on the same day.

Gastric emptying time was prolonged by chloroform about 60 per cent, by ether about 40 per cent, by nitrous oxide 15 per cent and by ethylene, cyclopropane and divinyl oxide about 7 per cent. The relative delays expressed as a ratio would be: chloroform, 9; ether, 6; nitrous oxide, 2; ethylene, cyclopropane and divinyl oxide, 1.

It is of interest that the two agents, namely, chloroform and diethyl ether, which produced a definite prolongation of gastric emptying, also markedly depressed the motility of the colon, as will be mentioned later.

Nitrous oxide, which produced a mild prolongation of gastric emptying, however, affected the motility of the colon about the same as did ethylene, cyclopropane and divinyl ether.

#### THE EFFECT OF SOME ANESTHETIC AGENTS ON THE MOTILITY OF THE COLON

During this past year my colleagues, Drs. Northup and Stickney, and I have made a comparative study of a number of general anesthetic agents on the motility of the intact colon of the dog. The agents studied were: sodium barbital, chloroform, diethyl ether, divinyl ether, ethyl bromide, ethyl chloride, nitrous oxide and cyclopropane.

Although these studies are still in progress and will be reported in a later paper, it might be in order to give a brief resume of our findings thus far. It should be stated that we were mainly interested in ascertaining whether any of these anesthetic agents produced similar effects to those of anoxia (6).

The experiments were performed on lightly barbitalized dogs. After the colon had been exposed, the movements of the longitudinal muscles were taken by means of an enterograph described by Lawson (23) and those of the circular muscles by means of a balloon.

The findings were briefly as follows: chloroform, diethyl ether and divinyl ether produced a decrease in muscle tone and practically abolished colonic contractions. Divinyl ether was not as effective in these respects as diethyl ether. Cyclopropane, ethyl bromide, ethyl chloride and nitrous oxide all produced a spasm of the longitudinal muscles as soon as they were administered. Since it is known that anoxia is often present when high concentrations of nitrous oxide are administered, it is of interest that this agent produced a spasm of the colonic musculature.

There has been considerable controversy in regard to the action of barbiturates on the gastrointestinal tract. We have studied the effects of various sized doses of sodium barbital on the movements of the colon. Although our studies are not completed, we observed that in most instances even large doses of sodium barbital did not appreciably influence colonic activity, nor was the intestinal tone changed. We are still studying this phase of the problem.

#### SUMMARY

Both anoxic and anemic anoxia are capable of causing a decrease in gastric and colonic motility. The motility of the small intestine, however, appears to be quite resistant to anoxia.

Anoxic and anemic anoxia also produce a decrease in gastric secretion; the latter type of anoxia causes the greater decrease. Both of these forms of anoxia have some influence on the absorption of certain substances from the small intestine. It seems safe to assume, however,

that the absorption of food substances in general is not materially affected by ranges of anoxia compatible with life.

Under carefully controlled conditions, the effects of several anesthetics on the gastric emptying time were studied. It was observed that chloroform prolonged gastric emptying 60 per cent, diethyl ether 40 per cent, nitrous oxide 15 per cent and ethylene, cyclopropane and divinyl ether about 7 per cent.

The effects were studied of seven general anesthetic agents on the motility of the longitudinal muscles of the colon of lightly barbitalized dogs. Chloroform, diethyl ether and divinyl ether had a pronounced depressing effect on the colonic musculature. On the other hand, cyclopropane, ethyl bromide, ethyl chloride and nitrous oxide all produced a spasm of the longitudinal muscles of the colon.

Sodium barbital given intravenously even in large doses seemed not to affect greatly colonic motility; further work, however, is needed on this point.

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For the information of anesthesiologists who are contemplating application for certification by the American Board of Anesthesiology, Inc., or who are training physicians for the specialty, the following questions have been employed for Part I (written) examinations in the past in *Physics and Chemistry*:

1. The atmosphere in an oxygen tent can be tested for its oxygen content and for its carbon dioxide content.
  - a. What are the chemical principles or reactions involved?
  - b. What is the technic of carrying out the tests with the use of a typical analyzing apparatus?
2. a. What are the atomic weights of carbon, hydrogen, nitrogen, oxygen?
  - b. What is the molecular weight of carbon dioxide, cyclopropane, ethylene, helium, nitrogen, nitrous oxide, oxygen?
  - c. Are these data used in calibrating flow meters on an anesthesia machine? Why?
  - d. Can you use a flow meter calibrated for carbon dioxide to measure the flow of nitrous oxide? Why?
3. a. What is the weight in kilograms of a woman who weighs 100 pounds? How is the conversion from pounds to kilograms made arithmetically?
  - b. If an endotracheal tube is 10 inches long, what is its length in centimeters?
  - c. If normal body temperature is 98.6 F., what is the reading in centigrade? How is the conversion from Fahrenheit to centigrade made arithmetically?
  - d. If the boiling point of a substance is 37 C., what is the reading in Fahrenheit? How is the conversion from centigrade to Fahrenheit made arithmetically?