STUDIES ON THE MECHANISM OF INTESTINAL INHIBITION BY CYCLOPROPANE ANESTHESIA *

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THE experiments performed by Miller (1), using dogs with intestinal fistulae, demonstrated that general anesthesia with some agents may result in severe intestinal inhibition while other agents have little or no inhibitory action on the intestine. Methods similar to that of Miller have been used to determine the effect of cyclopropane anesthesia on the intact intestine (2, 3). Burstein (2) concluded that cyclopropane causes an increase of both intestinal contractions and tone in III_1 and III_2 planes of anesthesia; and in the lower planes of III the contractions are inhibited but tone is maintained. Weisel, Youmans, and Cassels (3) reported that cyclopropane anesthesia causes a decrease in tonus and inhibits all types of movement in the intestine. Typically, the inhibition was found to be complete in the lower planes of stage III. The differences in results are understandable on the basis of differences in methods of recording intestinal motility. Burstein (2) recorded fluctuations in the volume of a balloon contained in the intestine which was working against pressure produced by a column of water in a burette (Jackson's method). Presumably, Burstein used a relatively low pressure. Weisel et al. (3) recorded the contractions of the intestine against a water-filled balloon and heavy tubing connected with a mercury manometer. This method is almost isometric, and no pressure is maintained in the intestine as a result of the recording device itself. Miller's method (1) differs from each of these in that it records changes in volume in the presence of constant pressure. It is customary to refer to an increased volume of the balloon and contents or a decreased pressure within the system or both as a decreased tonus; but these changes may be produced by a lengthened interval between rhythmic contractions in the absence of any decreased resistance to stretch, which is tonus in the true sense. Even though true tonus remains unchanged the higher the hydrostatic pressure in the balloon the greater will be the increase in volume as the interval between rhythmic contractions lengthens, because the balloon continues to fill until the onset of the next contraction. Moreover, the pressure in the balloon reflects changes in intra-abdominal pressure when the intestinal loop is in the form of a Thiry fistula. Both studies (2, 3) indicate that the rhythmic contractions of the intestine are inhibited in the lower planes of the

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third stage of cyclopropane anesthesia. It is this inhibitory action that is under consideration in the present study.

Since the rhythmic contractions in both the innervated and the extrinsically denervated intestine are inhibited during deep cyclopropane anesthesia the inhibition must be mainly on a humoral or chemical basis. However, it is difficult to demonstrate a direct inhibitory action of cyclopropane on the isolated rabbit intestine (4). These facts suggest that something other than cyclopropane itself is responsible for the direct inhibition of the intact intestine. This study was designed to determine if the inhibiting action of cyclopropane anesthesia on the intestine is dependent upon anoxemia or adrenalinemia.

METHODS

Eight dogs were used each of which had two Thiry fistulae of the jejunum. The motility of the intestinal segments was recorded by the balloon method identical to that used in the previous study (3). After determining the effect of cyclopropane anesthesia on the motility of the intestinal segments in dogs having all nervous pathways intact, the animals were subjected to various operations on the autonomic nervous system and adrenal glands. Following recovery from the operations the effect of cyclopropane anesthesia on the intestinal motility of the unpremedicated animal was determined. In all cases cyclopropane in oxygen was given by the closed CO_2 absorption method.

The operations performed were bilateral vagotomy, abdominal sympathectomy, and adrenal demedullation. The vagotomies were done by cutting the nerves along the esophagus just above the diaphragm. Adrenal demedullation was accomplished by burning out the adrenal medullae in two separate operations. Abdominal sympathectomy consisted of bilateral splanchnicotomy and removal of the lumbar sympathetic chains. Several or all of these operations were completed in some of the animals. The completeness of the sympathetic denervations was indicated by the elimination of the intestino-intestinal reflexes utilizing sympathetic nerves and by the absence of the pain response to severe intestinal distention.

RESULTS

The results with regard to the effect of cyclopropane anesthesia on intestinal motility in the dogs with all nervous pathways intact are in agreement with those previously reported (3). Inhibitory effects on the rhythmic contractions of the intestine were observed during the third stage of anesthesia in all of the dogs, and complete amotility associated with a decreased pressure in the balloon could be obtained in seven of the eight dogs by deep cyclopropane anesthesia.

Abdominal sympathectomy, by the method employed, results in destruction of the innervation of the adrenal medullae. It also results

in interruption of a large portion of the sympathin-producing pathways of the body. Five abdominal sympathectomized dogs showed fully as much intestinal inhibition under deep cyclopropane anesthesia as before the denervations; therefore, the inhibition of the intestine was not dependent upon reflex liberation of adrenalin. However, since a few drugs are capable of causing adrenalin liberation by direct action on the denervated adrenal medullae, the adrenals were demedullated in addition to the denervation in two of the dogs. These animals still showed complete inhibition of intestinal motility under deep cyclopropane anesthesia.

Bilateral vagotomy in four of the dogs did not reduce the inhibitory influence of cyclopropane on the intestine. One dog had all of the operations, and its intestine was still inhibited completely under deep cyclopropane anesthesia. This result is illustrated in figure 1.

Several of the dogs had one of the intestinal loops denervated in the mesentery in addition to the other operations. The loops having all extrinsic nerves cut were inhibited as much as either the sympa-
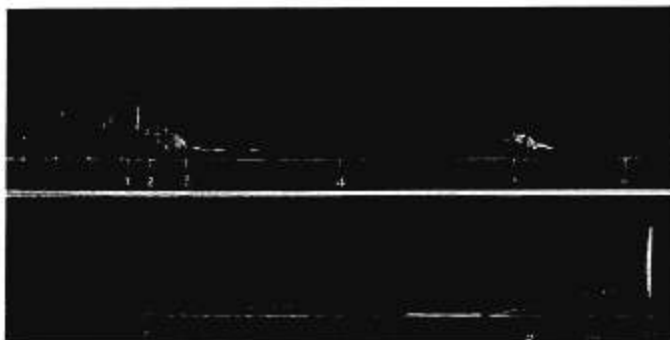

FIG. 1. *Intestinal inhibition by cyclopropane anesthesia in a vagotomized, abdominally sympathectomized dog having its adrenal glands demedullated.*

Balloon-mercury-manometer record from a jejunal Thiry fistula. The straight line indicates zero pressure. Time in minutes is marked by the upstrokes at the beginning of this line. The duration of the administration of cyclopropane was thirty-four minutes.

Protocol: Prior to 1 the dog was breathing oxygen. At 1 cyclopropane administration was begun. The rapid excursions between 2 and 3 are artefacts produced by excessive diaphragmatic activity. The animal was in the upper planes of stage III anesthesia between 3 and 4. After 4 the anesthesia was deepened preparatory to tracheal intubation, and at 5 the anesthesia lightened during the intubation. After 5 the animal was carried steadily down to respiratory arrest at 6. Between 6 and 7 the anesthesia was kept at stage IV and the dog was well ventilated artificially with the cyclopropane-oxygen mixture. After 7 the anesthesia was allowed to lighten up to III₃₋₄. Anesthesia was maintained at III₃₋₄ between 8 and 9, but the animal was kept well ventilated. At 9 cyclopropane administration was stopped and the bag was washed out with oxygen. The cough reflex returned at 10 so that the tracheal tube was coughed up and, characteristically, rhythmic intestinal contractions were rapidly returning. Vomiting occurred at 11.

thetically denervated or the parasympathetically denervated or the normally innervated loops.

Anoxemia, if severe enough, will produce intestinal inhibition, and it has been suggested that anoxia may be a factor in the inhibition of the intestine by anesthetics (5). There are several facts indicating that the intestinal inhibition seen under cyclopropane anesthesia is not dependent upon a low oxygen tension in alveolar air. In the first place, the anesthesia need not be carried to the point where there is a significant reduction in respiratory minute volume in order to produce intestinal inhibition. Secondly, the animals are breathing an oxygen-rich mixture and the mucous membranes remain red throughout the experiment. Finally, some of the animals were taken down gradually to respiratory arrest with complete intestinal inhibition resulting; they were then hyperventilated with the cyclopropane-oxygen mixture for several minutes, but the intestinal inhibition was still present. This procedure is illustrated in the figure.

The relative impotency of cyclopropane in producing inhibition of the rhythmic contractions of the isolated rabbit intestine (4) has been an obstacle to considering that the inhibition of the intact intestine observed under deep cyclopropane anesthesia is a result of direct action of the anesthetic agent. However, rhythmic contractions of the isolated intestine are diminished (4), and the failure to obtain greater inhibition may be the result of the low solubility of the gas in water.

SUMMARY

In the lower planes of the third stage and in the fourth stage of cyclopropane anesthesia there is marked inhibition or complete elimination of the rhythmic contractions of the dog intestine as recorded by balloon methods. Similar inhibitory effects of cyclopropane anesthesia on intestinal motility are observed in dogs having the adrenal glands denervated and demedullated. The inhibition is still present when the animal is hyperventilated with the cyclopropane-oxygen mixture required to produce deep anesthesia. Therefore, the inhibition of the extrinsically denervated intestine by cyclopropane anesthesia is not dependent upon the liberation of adrenalin from the adrenal medullae or upon a low oxygen tension in alveolar air.

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