

## THE EFFECTS OF SOME HUMORAL AGENTS ON THE HORSE ILEUM

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(Received June 25, 1951)

In 1940 Tanaka and Ohkuho observed a marked contraction in isolated strips of horse ileum after the addition of adrenaline to the bath. This observation was confirmed and the effects of acetylcholine, histamine, and posterior pituitary extract studied in a similar manner (Alexander, 1949). It was found that acetylcholine and histamine caused a marked rise in tone and increased the magnitude of the rhythmic contractions, whereas the posterior pituitary extract was without effect. In other experiments with isolated blood-perfused ileum, similar responses were evoked with acetylcholine and histamine, whereas adrenaline inhibited motility and posterior pituitary extract caused a small contraction (Alexander, 1949). The experiments described here were designed to determine the response of the ileum in the living animal to adrenaline, carbamylcholine, histamine, and posterior pituitary extract.

### METHODS

Observations were made on three ponies with Biebl loops and one with a Thiry-Vella fistula. The surgical techniques involved in the preparation of Biebl and Thiry-Vella loops in the horse are described elsewhere (Alexander, 1951).

Recordings of movement in the Biebl loop were made with the double tambour system described by Douglas and Mann (1941) and from the Thiry-Vella loop by a balloon and water manometer.

Variations in the intestinal temperature were measured with two thermocouples and a galvanometer. The thermocouples were made from junctions of copper and eureka wire. The reference couple was placed in a vacuum flask containing water at about 37° C., along with a thermometer; the second couple was stitched through the exteriorized intestine so that the junction lay in or against the mucosa. A calibration curve for the galvanometer was constructed by plotting measured temperature differences between the two thermocouples against the galvanometer deflection produced. Thus it was possible, by reading simultaneously the galvanometer deflection and the temperature of the reference couple, to determine the temperature of the couple in the intestinal mucosa.

Aqueous solutions of adrenaline hydrochloride, carbamylcholine, histamine acid phosphate, and posterior pituitary extract were injected intravenously. The doses given were the least which consistently produced a measurable response; doubling this dose produced a similar but more lasting effect (Table I). It was considered unfair to subject the animals to undue distress by further increase of dosage. The effect of each drug was tested at least four times on each pony.

TABLE I  
The effects on intestinal movements and temperature of adrenaline, carbamylcholine, histamine, posterior pituitary extract, and isotonic saline

| Drug                        | Dose            | Effect                      |                 |                         |
|-----------------------------|-----------------|-----------------------------|-----------------|-------------------------|
|                             |                 | Motility                    | Tone            | Temperature             |
| Adrenaline .. ..            | 10 $\mu$ g./kg. | Inhibited                   | Slight increase | Decreased               |
| Carbamylcholine ..          | 20 $\mu$ g./kg. | Increased or made irregular | Marked increase | Unaffected or decreased |
| Histamine .. ..             | 20 $\mu$ g./kg. | Decreased                   | Marked increase | Decreased               |
| Posterior pituitary extract | 0.5 units/kg.   | Decreased                   | Unchanged       | Decreased               |
| Isotonic saline .. ..       | 5 ml.           | Unchanged                   | Unchanged       | Unchanged               |

## RESULTS

### *The contraction of the Biebl loop*

It was possible to distinguish two types of activity in this preparation, one characterized by regular rhythmic contractions, and the other by irregular strong slow contractions. The frequency of these rhythmic contractions was remarkably constant for an individual animal and varied very little from day to day. This is shown in Table II. The strong slow contractions were most frequently observed during the six hours following feeding. They became greatly reduced in magnitude and frequency after food was withheld for more than 24 hours. These different types of movement are shown in Fig. 1.

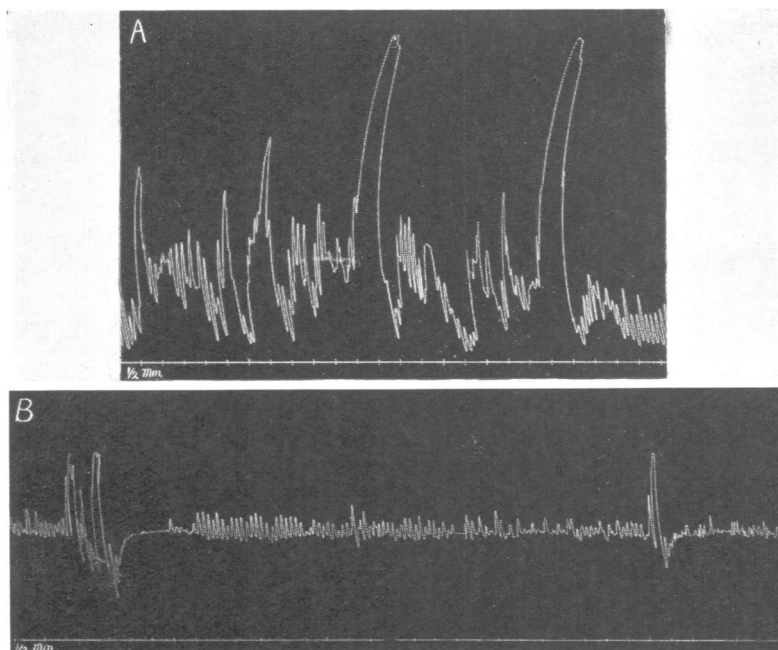


FIG. 1.—(A) Motility in a Biebl loop one hour after feeding; the large slow contractions predominate. (B) The same animal 24 hours after feeding; the large slow contractions occur infrequently.

TABLE II  
THE RHYTHMIC CONTRACTIONS OF THE HORSE ILEUM

|                        | Biebl loop            |                      |                      | Thiry-Vella loop    |
|------------------------|-----------------------|----------------------|----------------------|---------------------|
|                        | Pony I                | Pony II              | Pony III             |                     |
| Mean rate .. ..        | 10.23 $\pm$ 0.49/min. | 12.6 $\pm$ 0.95/min. | 10.5 $\pm$ 0.51/min. | 8.1 $\pm$ 0.69/min. |
| Range .. ..            | 9 to 11/min.          | 10 to 15/min.        | 10 to 11/min.        | 7 to 9/min.         |
| Period of observation  | 3 months              | 3 months             | 2 months             | 2 months            |
| Number of observations | 65                    | 102                  | 30                   | 32                  |

*The contractions of the Thiry-Vella loop*

The contractions shown by this preparation were similar to the rhythmic contractions of the Biebl loop. Their regularity is shown in Table II. Fasting for periods of 24 and 48 hours did not change the type or frequency of contraction. When isotonic solutions of sodium chloride and sodium bicarbonate, sodium dihydrogen phosphate and disodium phosphate were introduced into the oral opening they were forcibly ejected from the other opening, whereas the recording balloon was not propelled through the loop. Changes in tone were not conspicuous.

*The effect of drugs on ileal motility*

*Adrenaline.*—Adrenaline inhibited motility in both Biebl and Thiry-Vella loops (Fig. 2). This agreed with observations on the perfused ileum. The characteristic sweating produced by this drug on the horse was always observed.

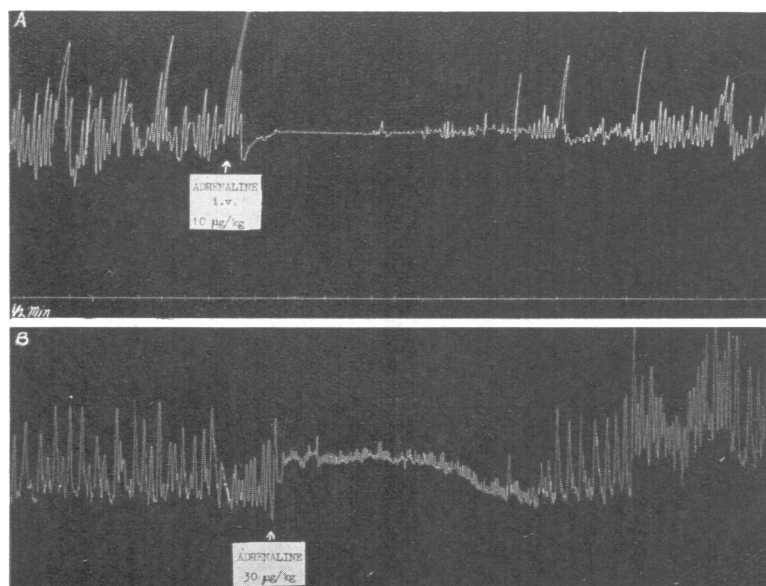


FIG. 2.—The effect of adrenaline on the movements of (A) a Biebl and (B) a Thiry-Vella loop.

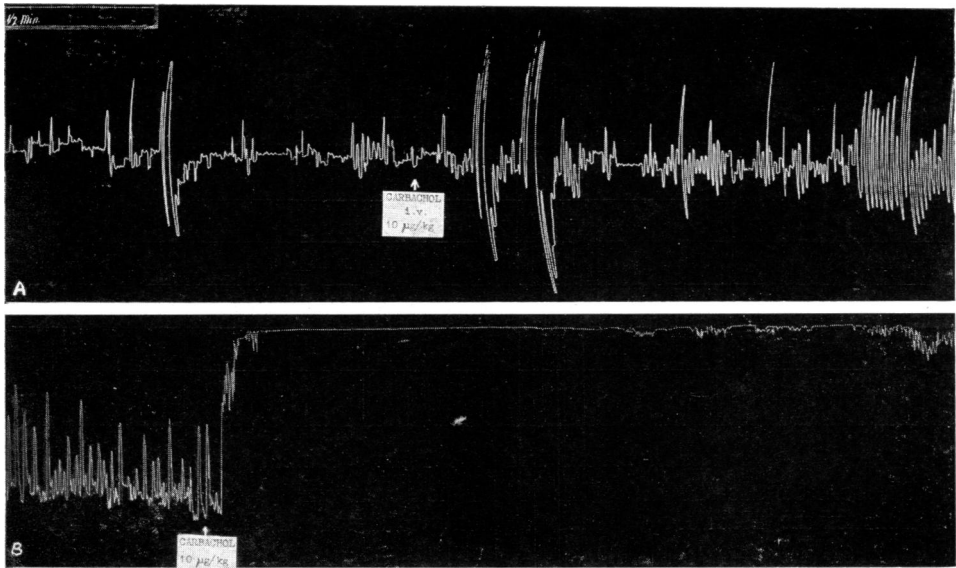


FIG. 3.—The effect of carbamylcholine on the motility of (A) a Biebl and (B) a Thiry-Vella loop.

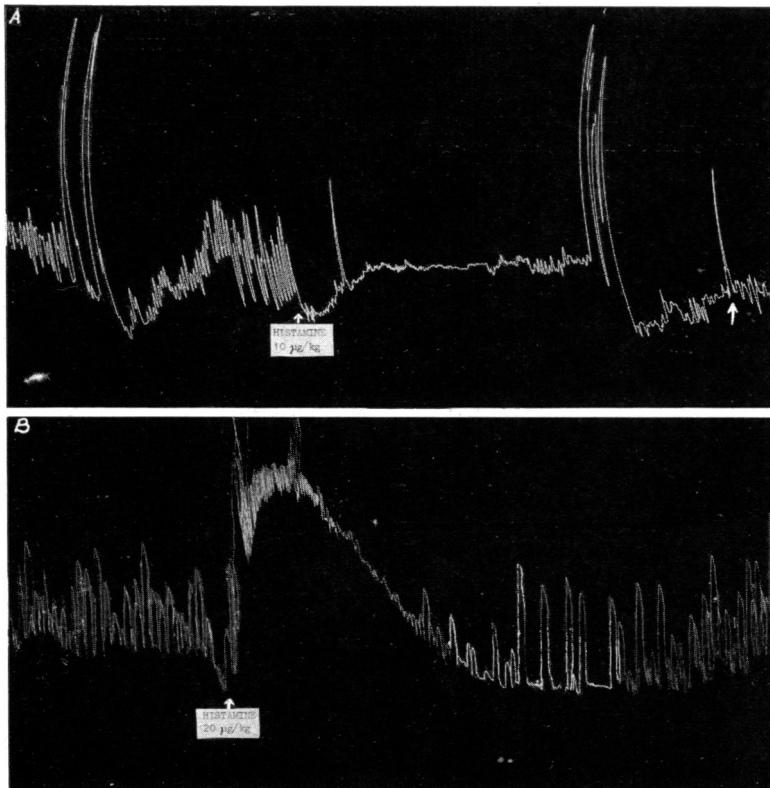


FIG. 4.—The effect of histamine on the motility of (A) a Biebl and (B) a Thiry-Vella loop.

*Carbamylcholine.*—In two ponies out of three with a Biebl loop carbamylcholine increased motility (Fig. 3). The third pony showed at different times increased and decreased motility. This different response can be explained by the recording technique, which did not distinguish between a long sustained contraction and inhibition. Such an explanation was supported by the experiments on the Thiry-Vella loop, which responded to carbamylcholine with a long sustained contraction. Hence the effect of this drug on the ileum of the living horse was similar to that on isolated preparations.

*Histamine.*—This drug appeared either to inhibit movements of the Biebl loop or to produce a long sustained contraction. However, as the Thiry-Vella loop

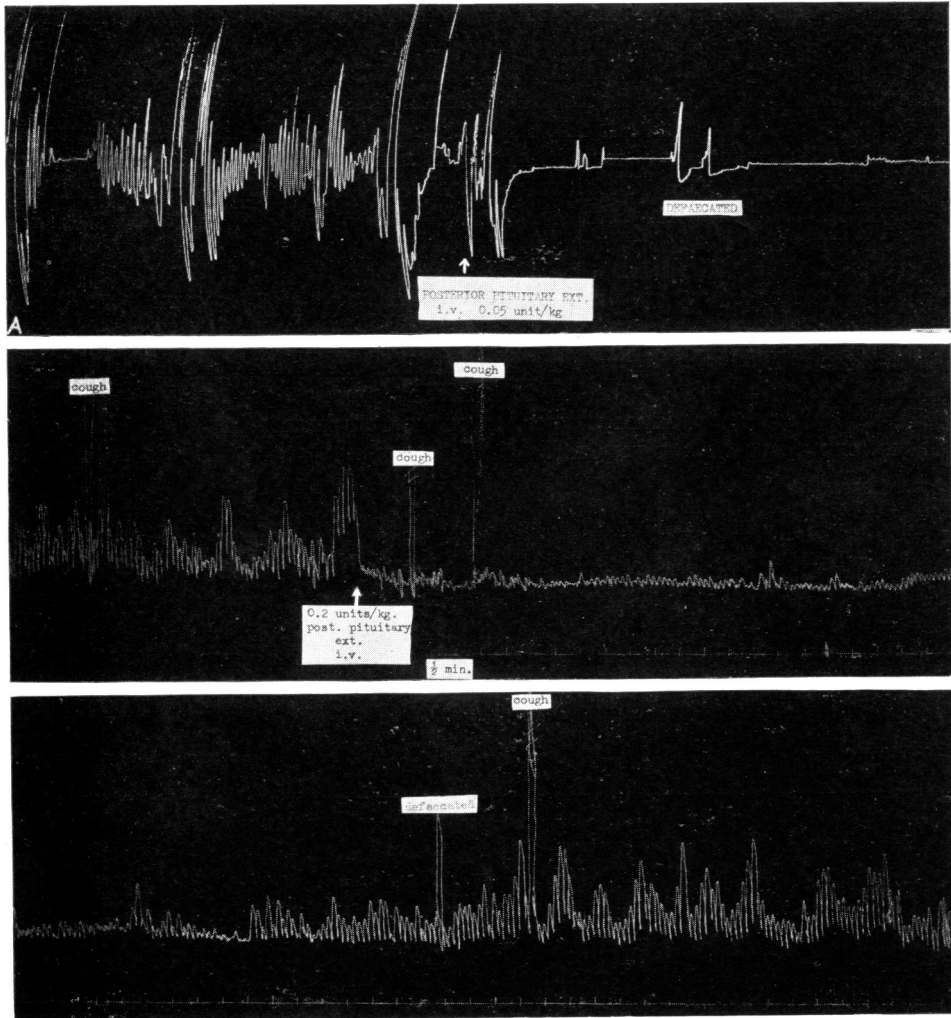


FIG. 5.—The effect of posterior pituitary extract on (top) a Biebl loop and (middle and bottom) a Thiry-Vella loop.

showed a marked rise in tone it is probable that the lack of movement shown by the Biebl loop (Fig. 4) was due to a sustained contraction. The response of the ileum of the intact animal, therefore, appeared similar to that of the isolated ileum (Alexander, 1949).

Immediately after the intravenous injection of histamine the animal showed a greatly increased respiratory rate, defaecation, and an increased secretion of tears and nasal mucus. The electrocardiograph showed an increased heart rate.

*Posterior pituitary extract.*—The injection of posterior pituitary extract was followed by inhibition in Biebl and Thiry-Vella loops (Fig. 5). This was unexpected in view of previous findings on the isolated strip and perfused ileum, when posterior pituitary extract had either no effect or caused a slight contraction (Alexander, 1949).

The recording balloon was not propelled through the Thiry-Vella loop by carbamylcholine, histamine, or posterior pituitary extract.

Various explanations of this disparity were considered. Earlier work (Alexander, 1949, 1950) had shown that the main factor influencing motility in the perfused ileum was the supply of oxygen. The possibility was therefore considered of the inhibitory effect of posterior pituitary extract being produced indirectly by the action of this drug on intestinal blood flow.

#### *The effect of drugs on the temperature of the ileum*

By observing the temperature of an exposed structure it is possible to infer whether the rate of blood flow has changed. This method, on account of its convenience, was used to study variations in blood flow through the Biebl and Thiry-Vella loop after the intravenous injection of the four humoral agents. The results of these experiments are shown in Fig. 6. It was clear that the inhibition of motility

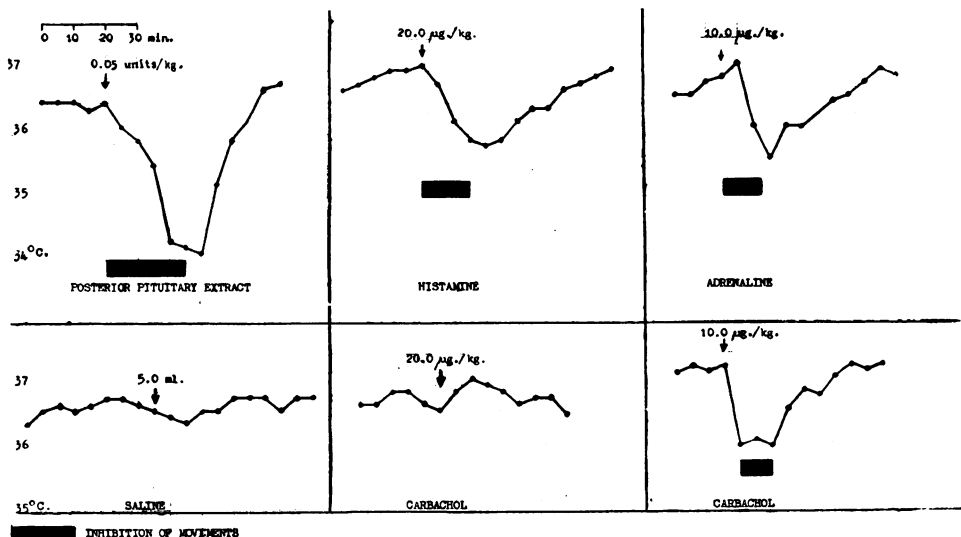


FIG. 6.—The effect of posterior pituitary extract, adrenaline, histamine, and carbamylcholine on the temperature of the intestine of the living horse.

after the intravenous injection of posterior pituitary extract was always accompanied by a profound fall in ileal temperature, and, in the Thiry-Vella loop, pallor followed by cyanosis of the exposed "cuff" of mucous membrane; simultaneously there was a marked slowing of the heart rate.

A fall in temperature always occurred after the injection of adrenaline, but the inhibition of motility preceded the fall by at least five minutes. This observation supported the agreement between the inhibitions produced by this drug *in vitro* and *in vivo*, thus showing adrenaline to have a direct effect on the ileum.

The irregularity of the response in the intestinal temperature after the intravenous injection of carbamylcholine was particularly interesting. The two ponies with Biebl loops which responded to carbamylcholine with increased motility did not show any fall in intestinal temperature. The third pony, which occasionally displayed an apparent inhibition of movement, showed, on these occasions, a fall in intestinal temperature.

In all instances where temperature of the mucosal "cuff" of the Thiry-Vella loop fell, the mucous membrane became cyanotic.

#### DISCUSSION

*Normal motility.*—The movements recorded from the Biebl loop in the horse were similar to those obtained from the Biebl loop in the dog (Castleton, 1934; Douglas and Mann, 1939). The records from the Thiry-Vella loop, however, showed only regular rhythmic contractions, but not the propulsive contractions exhibited by similar preparations in the dog (Krueger, Lampe, and Reid, 1936). Further, there seemed no tendency for the balloon to traverse the loop; this agreed with the observations on the isolated perfused ileum, where only about one loop in four showed rapid propulsion (Alexander, 1950). These findings suggest that the large slow contractions shown by the Biebl loop might be associated with the propulsion of digesta through the ileum.

*The effect of drugs.*—The effect of adrenaline on the ileum was essentially the same in the living animal as on isolated tissues (Alexander, 1949). The inhibitory effect of this drug preceded by at least five minutes any reduction of intestinal temperature, and showed that its effect was produced directly on the ileum.

Carbamylcholine usually increased the motility of Biebl loops, and the marked rise in tone produced by this substance would account for the apparent inhibition which was occasionally recorded. It was, however, of some note that on the occasions where an inhibitory effect was recorded there was an associated fall in intestinal temperature.

The effects of histamine on the preparations of horse ileum *in vivo* and *in vitro* were not difficult to reconcile. The apparent inhibition produced by this drug on the Biebl loop could be due to the associated increase in tone. However, this drug always caused a fall in intestinal temperature which accompanied the inhibitory effect recorded from the Biebl loop.

The most interesting observation was, however, the disparity between the inhibition produced by posterior pituitary extract on the ileum of the living horse and the lack of effect of this drug on the isolated ileum. Since the inhibition was shown by both preparations of the ileum in the living animal it could not be due to any artifact in the recording technique. Earlier work (Alexander, 1950) had shown that

the main factor influencing motility in the perfused ileum is the supply of oxygen. Moreover, it has long been known that posterior pituitary extract decreases the portal blood flow in cats (Clark, 1928). The intestinal temperature in both Biebl and Thiry-Vella loops showed a profound fall after the injection of this posterior pituitary extract, and, in the Thiry-Vella fistula, cyanosis of the mucous membrane. It seemed clear, therefore, that the intestinal blood flow had been greatly diminished, and this, in view of the earlier work (Alexander, 1950), would account for the decreased motility. The effect of posterior pituitary extracts on the alimentary tract has been reviewed recently by Stehle (1950), who states that, "In the intact animal the intense constriction of the splanchnic blood vessels caused by the pressor hormone makes one think of the possibility of an indirect action." The experiments on the horse support this idea.

The occasional inhibition which followed the injection of carbamylcholine was always associated with a fall in intestinal temperature, suggesting that even the well-marked intestinal stimulation usually produced by this drug could be masked by its action on the circulation. Further, with a well-recognized inhibitor of intestinal movement such as adrenaline, the ileal inhibition preceded the fall in temperature by at least five minutes, showing that the inhibition was direct and not secondary to a reduced blood flow.

The concurrence of reduced motility, a fall in intestinal temperature, and cyanosis of the ileal mucosa lends strong support to the evidence from the perfused ileum (Alexander, 1950) that, in the horse, ileal motility is greatly influenced by any interference with its supply of oxygen.

#### SUMMARY

1. Ileal motility has been studied in three ponies with Biebl loops and one with a Thiry-Vella loop.
2. The movements of the exteriorized ileum in the recently fed pony with a Biebl loop comprised a mixture of strong slow contractions and quicker rhythmic contractions. In the fasting animal the rhythmic contractions predominated. The Thiry-Vella fistula showed only rhythmic contractions.
3. Adrenaline inhibited, and carbamylcholine usually increased, ileal motility in the living animal.
4. Posterior pituitary extract diminished contractions in both Biebl and Thiry-Vella loops and caused a prolonged fall in ileal temperature.
5. A fall in ileal temperature was always associated with inhibition of motility.
6. It is suggested that intestinal motility in the horse is greatly influenced by drugs which affect intestinal blood flow.

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