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THE EFFECT OF DRUGS ON SPONTANEOUS MOTILITY AND ON RESPONSE TO STIMULATION OF THE EXTRINSIC NERVES OF THE GUT OF A TELEOSTEAN FISH

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Trout gut shows, in addition to changes in general muscle tone, longitudinal "pendular" rhythms, peristaltic waves, and longitudinal "colic" contractions. Both vagus and splanchnic nerves are motor and there is no evidence of antagonistic "sympathetic" and "parasympathetic" nervous control. A posterior autonomic nerve supplying the rectum stimulated or inhibited according to the duration and frequency of the electrical pulses applied. Acetylcholine increased the tone and amplitude of pendular movements in all regions of the gut, and produced strong contraction of the circular muscles. Both nicotine and hexamethonium antagonized the action of acetylcholine, suggesting that its principal site of action is the neurone. Adrenaline lowered the tone of the longitudinal muscle and abolished pendular activity in the intestine and rectum, but contracted the longitudinal and circular muscles of the stomach. Hexamethonium bromide abolished peristalsis but greatly increased the amplitude of pendular contractions.

The reaction of the trout intestine to both histamine and pilocarpine was slight, but nicotine, 5-hydroxytryptamine, eserine, and barium caused strong contractions. The actions of atropine and piperoxan (933F) are discussed. Evidence is presented which suggests that the postganglionic vagus nerve fibres supplying the trout stomach may be adrenergic, while both the splanchnic nerve fibres to the stomach and intestine, and the preganglionic vagal fibres to the stomach, may be cholinergic. It is also suggested that there is a continuous release of acetylcholine by cholinergic neurones in the gut wall.

Anatomical studies show that the vagus nerve of teleosts is limited to the stomach, whereas the splanchnic nerve innervates both the stomach and intestine (Young, 1931; Burnstock, 1958b). Both these nerves have a motor action on the gut (Müller and Liljestrand, 1918; Young, 1936; Barrington, 1942). Acetylcholine and adrenaline, however, were reported to have antagonistic actions throughout the alimentary tract (Backman, 1917; Dreyer, 1928; Frey, 1928; Bernheim, 1934; Young, 1936). This result indicated that there was no correlation between nervous and pharmacodynamic action in the teleostean gut, a situation which has not been found in other vertebrate classes (Nicol, 1952). The question has been re-examined in the present work, using the brown trout (*Salmo trutta*). It has been shown that while acetylcholine and adrenaline are antagonistic in the intestine and rectum, they are synergistic in the stomach.

The actions of some other drugs on the intestine of a tropical marine teleost, the yellow grunt (*Haemulon flavolineatum*), were described by Bernheim (1934). Atropine antagonized the action of acetylcholine. Nicotine and barium produced strong contraction, whereas histamine and eserine had little effect. Frey (1928) and Méhes and Wolsky (1932) discussed the action of several drugs on the gut of the tench (*Tinca vulgaris*). This fish, however, is atypical of its Class since the gut contains striated muscles throughout its entire length. Both smooth and striated muscles are supplied with motor fibres from the vagus nerve.

The objects of the present study were: first, to examine the nature of autonomic nervous control of the gut in a teleostean fish; second, to compare the actions of drugs on the gut of a teleost with their actions in other vertebrates.

The brown trout (*Salmo trutta*) was used because it belongs to a teleostean family that retains many primitive and generalized features; it has not adopted a specialized feeding habit, and it is easy to keep in captivity.

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Methods

Isolated preparations of the gut were suspended in nutrient salt solution, bubbled with 95% O_2 and 5% CO_2. Several salt solutions were tried including that recommended by Young (1932) for fresh water teleosts. A modified Krebs solution was finally chosen because it gave the strongest contractions for the longest period of time. The composition was: NaCl, 5.9; KCl, 0.25; $CaCl_2$, 0.28; $NaHCO_3$, 2.1; KH_2PO_4, 1.6; $MgSO_4$ $7H_2O$, 0.29; glucose 2.0, g./l.

Spontaneous pendular contractions of the longitudinal gut muscles were recorded from cylindrical segments of the stomach, intestine or rectum, suspended with open ends. Strips of longitudinal muscle were used in some experiments.

For recording circular muscle contractions, short cylinders of gut were suspended horizontally in the bath. One hook was attached to the middle of the preparation at right angles to its main axis and connected with the recording lever, while another hook held the opposite side to the bottom of the bath.

The vagus and splanchnic nerves were stimulated *in situ* electrically. In addition a nerve-muscle preparation of the stomach was used for stimulation of the vagus nerve *in vitro*.

The operculum and gills were removed from decerebrate fish to expose the vagus nerve. The pectoral girdle was dissected away. The visceral branch of the vagus was ligated near to its origin, and then dissected back to its point of entry into the oesophageal wall.

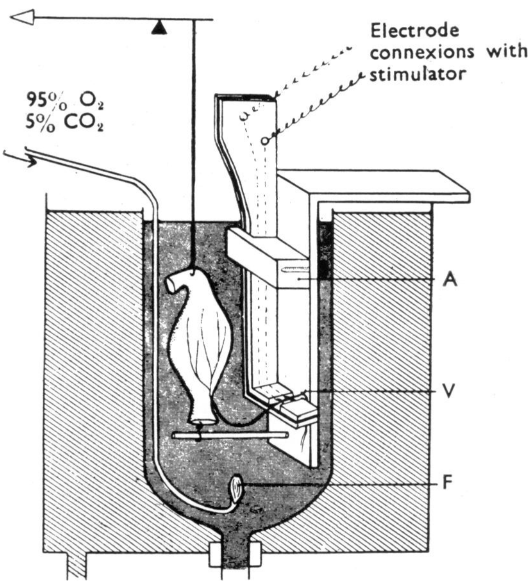

FIG. 1.—Diagram of the arrangement of the vagus-stomach preparation of the trout within the organ bath and the position of the stimulating electrodes. A, adjustable clamp; V, vagus nerve over electrodes; F, fluted glass distributor for 95% O_2 and 5% CO_2 gas mixture which is bubbled through the bath.

The stomach was severed behind the antrum and, on reflecting the ligated nerve forward, the anterior oesophagus was cut from the pharynx. The liver, swim bladder, and gonads were dissected away and the stomach with its attached nerve removed from the body cavity, after severing the other vagus nerve, the coeliacomesenteric artery and the splanchnic nerve. Connective tissue was carefully removed from the nerve trunk.

The oesophagus was tied to a perspex holder in a 100 ml. bath, while the antrum was connected to a light lever so that longitudinal contractions of the stomach were recorded. The vagus nerve was placed over bipolar platinum electrodes supported by a perspex shield. The final arrangement of the preparation in the bath is shown in Fig. 1. A rectangular pulse stimulator giving negative pulses was used to stimulate the nerve. Five second bursts of stimuli (usually of 0.3 msec. duration at 25/sec.) were applied at intervals of not less than ten minutes, so that fatigue was avoided.

The existence of a posterior autonomic nerve supplying the rectum of the trout has been demonstrated anatomically (Burnstock, 1958b). A nerve-muscle preparation was used for study of the action of this nerve on the rectum *in vitro*, using the same technique as for vagal stimulation of the stomach.

Results

Spontaneous Gut Motility

Three main types of spontaneous movement were seen in the trout gut in addition to changes in general muscle tonus.

Longitudinal Pendular Contractions.—Regular contractions of the longitudinal muscle occurred approximately once every 2 min. at normal environmental temperatures (8 to 14°) (Fig. 2).

These rhythms were more marked in the empty gut, being masked or modified to a large extent by peristaltic waves in those parts of the alimentary tract swollen with food. Figs. 2*a* and 2*b* show the range of amplitudes of contraction in different intestinal preparations under identical experimental

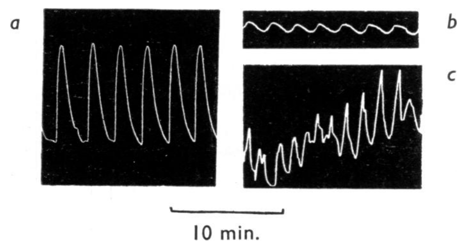

FIG. 2.—" Pendular " contractions recorded from the longitudinal muscle of the gut of the brown trout. Temperature 14°. (*a*) and (*b*), The extremes of amplitude of contractions encountered in the intestine and rectum under similar recording conditions. (*c*), Complex pendular activity often observed in the stomach.

conditions. In the stomach, pendular contractions were often more irregular (Fig. 2*c*). The rate of the pendular rhythm was very sensitive to temperature (Burnstock, 1958a) while the amplitude was affected by mechanical tension as well as temperature. No contractions corresponding to the longitudinal pendular movements were seen in the circular muscle.

Peristaltic Waves.—These occurred only when the gut was distended. The peristaltic wave moved slowly aborally (2 cm./min.) and was most prominently seen in the intestine and pyloric stomach, where it was always preceded by a powerful longitudinal contraction. Fig. 3*a* shows contraction of the longitudinal muscles superimposed over pendular activity during peristalsis. Fig. 3*b* shows contraction of the circular muscles of the stomach during peristalsis. In the cardiac stomach, antiperistalsis was commonly seen *in vivo* as well as *in vitro*.

Peristaltic waves originated in the cardia, the antrum, and in a region about one-third of the way down the intestine from the pylorus.

Longitudinal "Colic" Rhythm.—Strong, slow (1 beat/4 min.), longitudinal contractions were superimposed over the pendular activity. These contractions, like those of the circular muscle during the peristaltic wave, were triggered off by radial distension of the gut wall. They usually preceded the contractions of the circular muscles during a peristaltic wave, but this was not always so, particularly in the cardiac stomach. In the rectum, strong "colic" longitudinal contractions often occurred in the absence of circular muscle contractions (Fig. 3*c*).

No spontaneous rhythmical contractions were seen in the oesophagus. In trout with full stomachs, the circular oesophageal muscles were contracted, acting like a sphincter, preventing the regurgitation of food.

Effect of Drugs on Spontaneous Gut Motility

Acetylcholine and Adrenaline

Intestine and Rectum.—Acetylcholine (ACh) at concentrations between 10^{-4} and 10^{-8} g./ml. raised the general tone of the longitudinal muscle (Figs. 4*a* and 4*b*). The amplitude of pendular contractions was increased by concentrations of from 10^{-6} to 10^{-8} g./ml., the effect being more pronounced in preparations showing weak activity (Fig. 4*a*). Higher concentrations caused spasm during which pendular contractions were inhibited (Fig. 4*b*).

Adrenaline at concentrations between 10^{-8} and 10^{-5} g./ml. lowered the tone of the longitudinal muscle and completely inhibited pendular contractions (Fig. 4*c*).

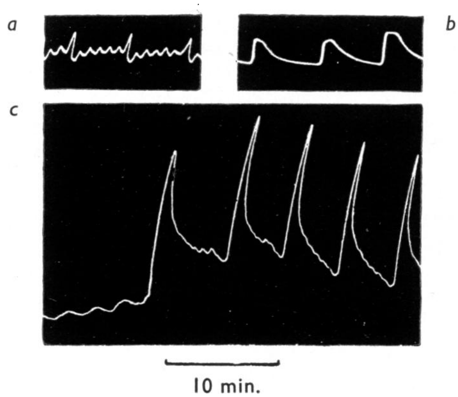

FIG. 3.—Peristalsis: 12°. (*a*), Record of the contractions of the longitudinal muscle of the intestine showing the strong peristaltic "colic" contractions superimposed over pendular activity. (*b*), The contractions of the circular muscles of the stomach during a peristaltic wave. (*c*), Longitudinal "colic" contractions, unaccompanied by peristaltic waves, as seen in the rectum. Temperature 16°

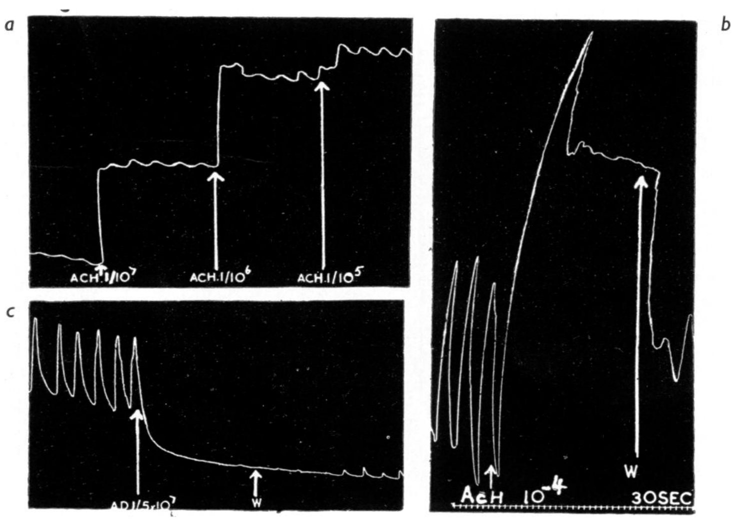

FIG. 4.—Action of acetylcholine (ACH) and adrenaline (AD) on the longitudinal contractions of the intestine. Temperature 14°. (*a*), The effect of increasing concentrations of acetylcholine on the tone and on the amplitude of pendular contractions. (*b*), The action of a high concentration (10^{-4} g./ml.) of acetylcholine. (*c*), The action of adrenaline (5×10^{-7} g./ml.). W = Wash.

Stomach.—As in the intestine, concentrations of ACh between 10^{-5} to 10^{-8} g./ml. raised the tone and increased the amplitude of the pendular contractions (Fig. 5*a*). ACh also caused strong contraction of the circular muscles, often inducing a series of regular contractions of decreasing amplitude to occur after the initial response (Fig. 5*b*). Unlike longitudinal muscle, the general tone of the circular muscle was never raised.

The reaction of the stomach to adrenaline, however, was different to that of the intestine. At concentrations of 10^{-6} to 10^{-8} g./ml., adrenaline caused a single strong contraction of the longitudinal and circular muscles, which was often followed by a depression of pendular activity (Fig. 5*b* and 5*c*). At the higher concentrations in particular, the amplitude of the pendular rhythm was decreased and there was sometimes a slight loss in general tone (Fig. 5*c*). Adrenaline applied to the stomach during an ACh-induced spasm did not cause relaxation—in contrast to the relaxation of an intestinal spasm.

On the stomach *in situ*, ACh caused longitudinal contraction and subsidiary after-contractions, whereas adrenaline produced one single contraction only. ACh and adrenaline had similar actions on the pyloric sphincter.

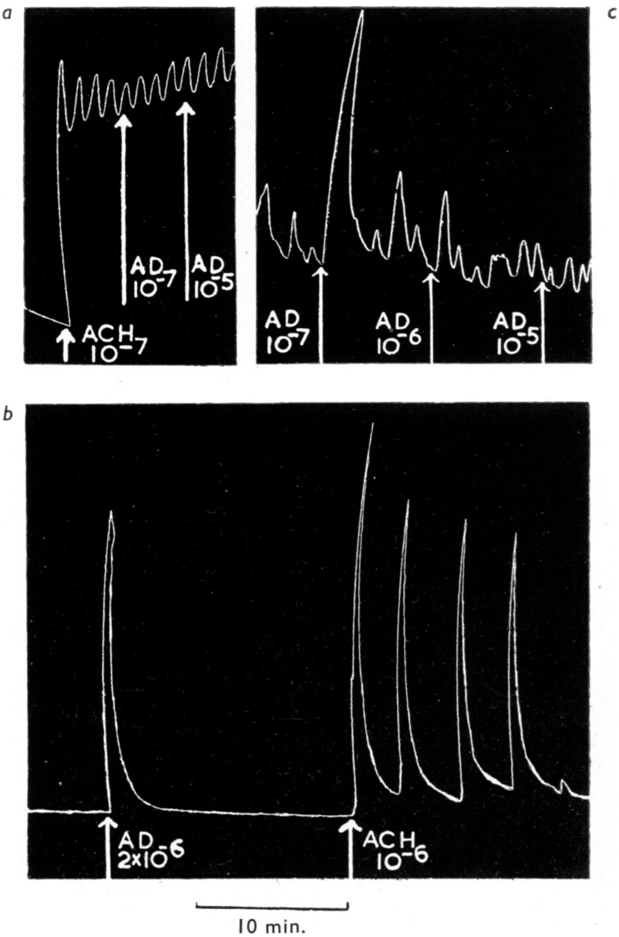

FIG. 5.—Action of acetylcholine (ACH) and adrenaline (AD) on the contractions of the circular and longitudinal muscles of the stomach. Temperature 14°. (*a*), The effect of acetylcholine (10^{-7} g./ml.) on the longitudinal muscle and the subsequent lack of response to adrenaline. (*b*), Stimulatory action of both adrenaline and acetylcholine on the circular muscles of the stomach. (*c*), The effect of adrenaline on the longitudinal muscle.

Hexamethonium

Hexamethonium bromide at concentrations of 5×10^{-4} g./ml. to 10^{-3} g./ml. stopped peristaltic activity. The action of hexamethonium on pendular contractions was very striking and was obtained consistently in over 20 experiments on the intestine and rectum, and in 10 on the stomach. At a critical concentration between 5×10^{-3} and 10^{-3} g./ml., the amplitude of the pendular contractions was greatly increased without alteration in rate (Fig. 6). This response was usually accompanied by an increase in tonus. Normal rhythm returned 15 min. after washing the

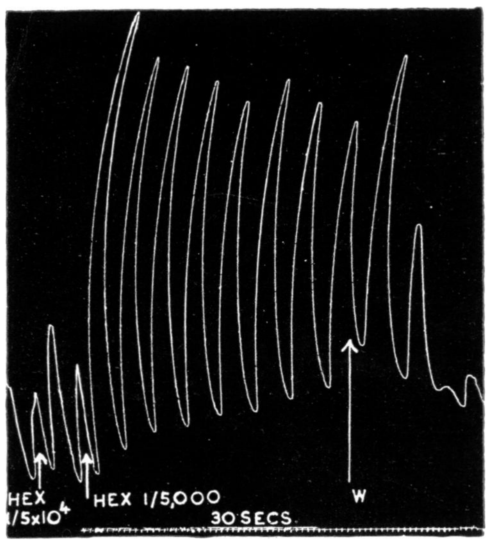

FIG. 6.—Action of hexamethonium bromide (HEX) on the longitudinal contractions of the intestine. Temperature 12°. W = Wash.

preparation. The reaction was usually more prominent in the intestine than in the stomach. The action of ACh was reduced after the application of hexamethonium.

Piperoxan (933*F*)

A concentration of 5×10^{-4} g./ml. increased the tone of the longitudinal muscle and decreased the amplitude of contractions both in the intestine and stomach (Fig. 7). Recovery from 933F took about 15 min. after washing the preparation with fresh Krebs solution.

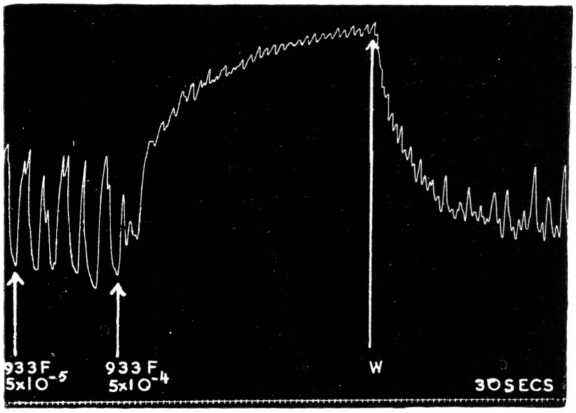

FIG. 7.—Action of piperoxane (933F) on the contractions of the longitudinal muscles of the intestine. Temperature 15°. W = Wash.

Atropine

The effects of atropine were variable. Atropine at concentrations as low as 10^{-8} g./ml. decreased the tone and abolished the pendular rhythm as well as peristalsis in the intestine and rectum of 12 out of 15 preparations (Fig. 8). In the other three preparations, atropine was ineffective alone but antagonized the action of acetylcholine. In the stomach, atropine had no effect on pendular activity in 8 out of 10 preparations, but always abolished peristalsis and antagonized the action of acetylcholine.

a b

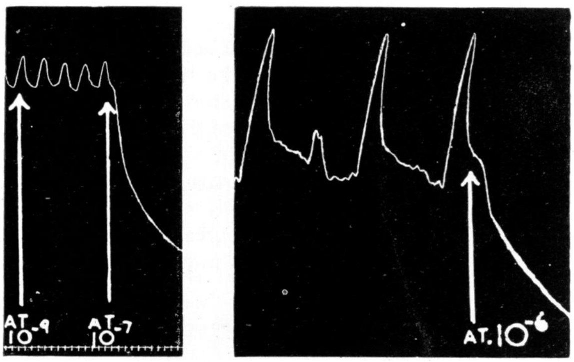

FIG. 8.—Action o f atropine (AT) on the longitudinal contractions of the intestine and rectum. Temperature 15°. Time, 30 sec. (*a*), Pendular contractions of the intestinal muscle abolished by atropine (10^{-7} g./ml.). (*b*), Colic contractions and pendular activity of the rectum abolished by atropine (10^{-6} g./ml.).

Nicotine

Nicotine in concentrations between 10^{-7} and 10^{-4} g./ml. produced a powerful longitudinal contraction of the intestine (Fig. 9). After low concentrations of nicotine (10^{-7} g./ml.) the preparation remained sensitive to low concentrations of ACh (10^{-7} g./ml.) (Fig. 9*a*). At high concentrations (10^{-4} g./ml.), however, the response to ACh was antagonized (Fig. 9*b*).

Nicotine had no effect in the presence of hexamethonium.

Eserine

In concentrations of above 10^{-5} g./ml., eserine increased the amplitude of pendular contractions (Fig. 10*a*). There was always a latent period of 2 to 3 min. before the response, in contrast to the almost immediate reaction to ACh. Application of eserine after hexamethonium, however, failed to produce a response (Fig. 10*b*). The eserine response was also abolished as soon as hexamethonium was added to the bath (Fig. 10*c*).

a b

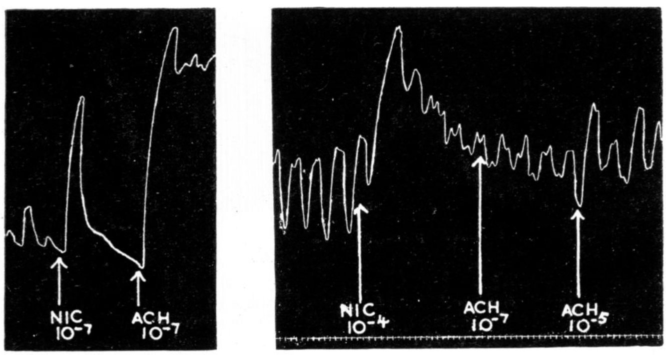

FIG. 9.—Action of nicotine (NIC) on the longitudinal contractions of the intestine. Temperature 14°. Time, 30 sec. (*a*), Effect of low concentrations of nicotine and the subsequent action of acetylcholine (ACH). (*b*), Effect of high concentration of nicotine and subsequent action of acetylcholine.

Barium Chloride

Barium chloride (10^{-3} g./ml.) caused great increase in tone and amplitude of pendular contractions in intestinal preparations. This reaction persisted, but to a slightly lesser degree, even in the presence of hexamethonium. Barium ions had little effect on stomach movements.

Histamine

Low concentrations of histamine were ineffective, but concentrations of 10^{-5} g./ml. produced a small increase in the amplitude of pendular contractions of the intestine as well as a rise in general tone. However, preparations normally at a high tonus failed to respond even to this concentration.

Pilocarpine

10^{-5} g./ml. caused a small increase in tone and amplitude of pendular contractions in the intestine, but the magnitude of the response was much less than that produced by ACh.

5-Hydroxytryptamine

Concentrations as low as 10^{-9} g./ml. caused a sustained increase in the tone of the longitudinal muscles of the stomach and intestine.

Response of the Gut to Stimulation of the Extrinsic Nerves

Fig. 11 shows the extrinsic nerves supplying the gut. The main vagus nerve trunks penetrate the wall of the oesophagus and run down the stomach, branching and anastomosing between the circular and longitudinal muscle coats. No vagal fibres extend beyond the stomach into the intestine. Stimulation of either of the vagus nerves produced contractions of the longitudinal muscles of the stomach, but had no action on the intestine or pyloric caeca. A fuller account of the form of the response and of the thresholds of stimulation has been reported elsewhere (Burnstock, 1958a).

The splanchnic nerve supplies both the stomach and intestine, branches penetrating the gut wall at intervals along its length. Stimulation of this nerve *in situ* produced contraction of both the intestine and stomach but to a lesser degree in the latter. In 5 out of 6 experiments atropine (10^{-6}) reduced this response but did not always abolish it. The existence of a posterior autonomic nerve supplying the rectum of the trout was demonstrated both anatomically and physiologically. It had a motor or inhibitory action according to the duration and frequency of the stimulating pulses applied (Fig. 12). Long duration pulses of high frequency caused inhibition of spontaneous motility, whereas pulses of short duration and low frequency stimulated the rectum.

Effect of Drugs on the Response of the Stomach to Stimulation of the Vagus Nerves

Adrenaline

It has already been mentioned that adrenaline in low concentrations caused a contraction

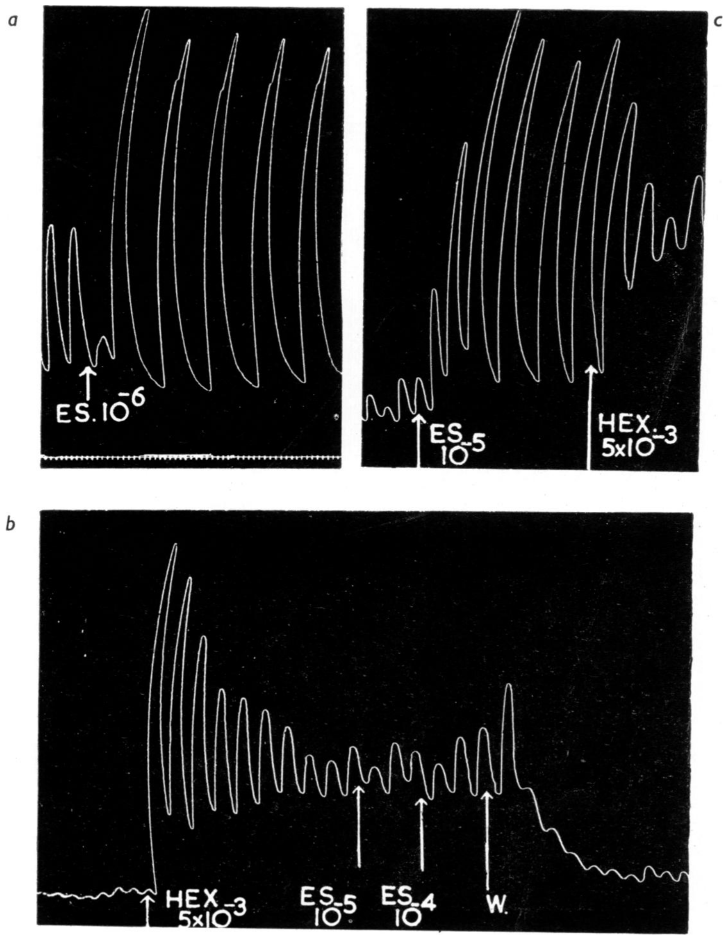

Fig. 10.—Action of eserine (ES) on the longitudinal contraction of the intestine. Temperature 14°. Time, 30 sec. W = Wash. (*a*), Effect of eserine (10^{-6} g./ml.). (*b*), Absence of the eserine action after the application of hexamethonium (HEX). (*c*), Inhibition of eserine response after the application of hexamethonium.

of the stomach. In preparations where the response to vagal stimulation was slight, treatment with adrenaline (10^{-7} g./ml.) invariably increased the amplitude of the response (Fig. 13*a*).

Nicotine

High concentrations of nicotine (10^{-4} g./ml.) always abolished the vagal response (Fig. 13*b*).

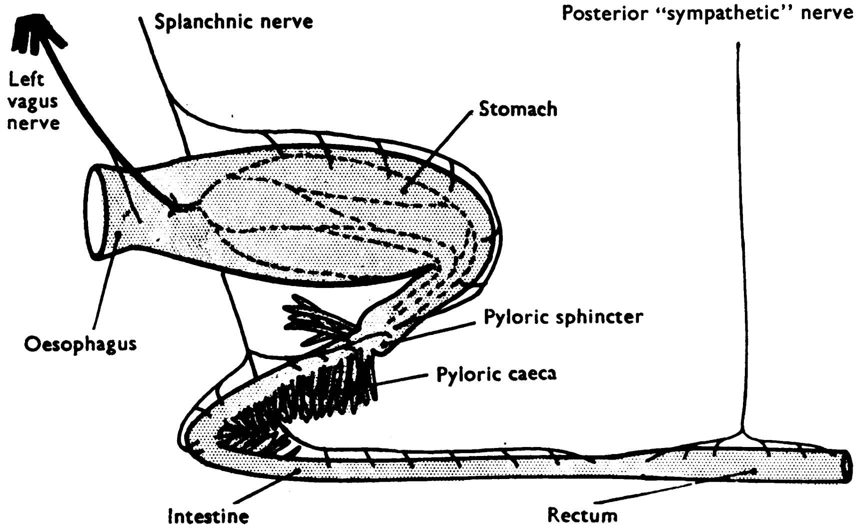

FIG. 11.—Diagram of the extrinsic innervation of the trout gut.

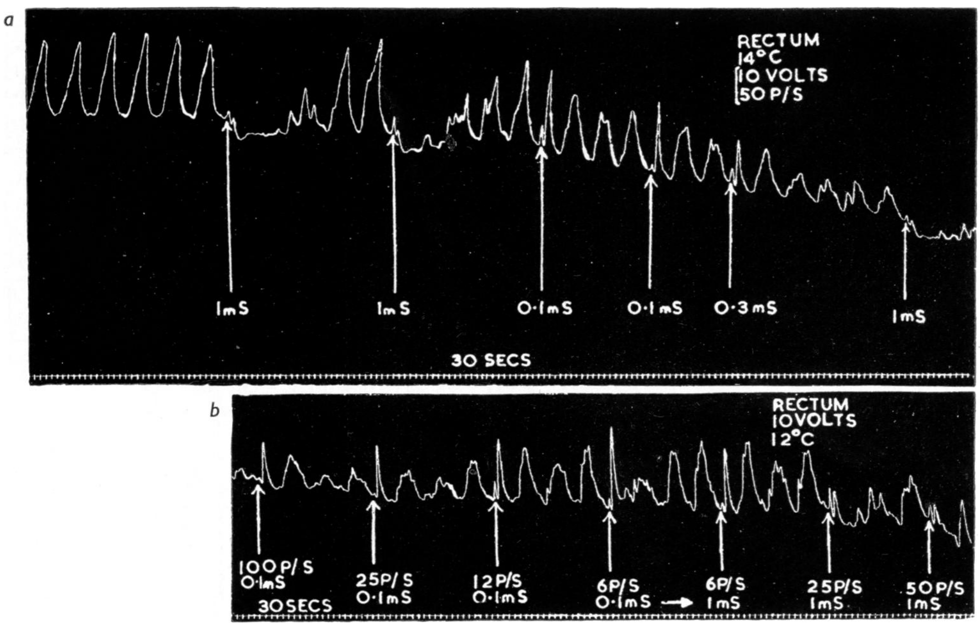

FIG. 12.—Stimulation of the posterior autonomic nerve supplying the rectum of the trout. (*a*), At a frequency of 50/sec. (P/S), pulses of long duration (1 msec.[mS]) inhibit spontaneous activity, while pulses of short duration (0.1 to 0.3 msec.) cause contraction. Temperature 14°. (*b*), Variation of the pulse frequency to show that high frequency pulses favour inhibition, while low frequency pulses cause contraction. Temperature 12°.

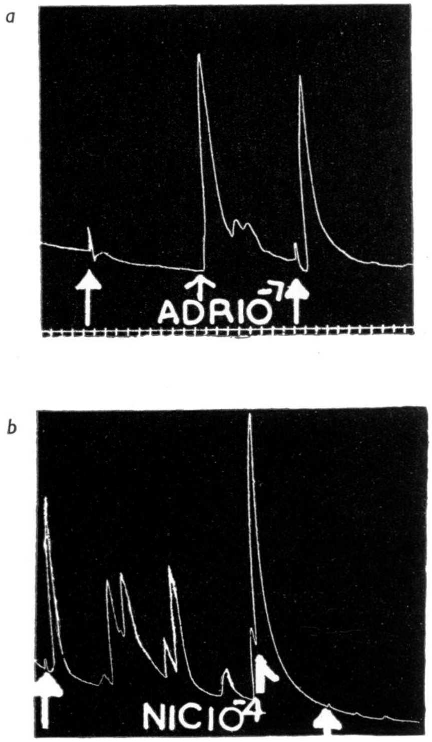

FIG. 13.—Effect of drugs on the response of the longitudinal muscles of the stomach to stimulation of the vagus nerves at arrows. Stimulus strength, 5 volts; frequency, 25 pulses/sec.; duration= 0.3 msec. Temperature 14°. Time, 30 sec. (*a*), Potentiation of the vagal response by treatment with adrenaline (ADR). (*b*), The vagal response abolished by treatment with nicotine (NIC).

Atropine

Atropine, even at high concentrations (10^{-5} g./ml.), had very little effect on the nature or magnitude of the vagal response, although the response to acetylcholine was abolished. In some experiments the amplitude of the vagal contraction was actually enhanced by atropine (Fig. 14*a*).

Hexamethonium

Concentrations of 5×10^{-3} g./ml. of hexamethonium bromide did not affect the response to vagal stimulation during the first 8 min. after its application. After this period, however, in 5 experiments out of 8, the response was abolished over the next 8 min., only to reappear in full strength after this period (Fig. 14*b*). In the other three experiments, the response was never completely lost after the application of hexamethonium.

Piperoxan (933*F*)

On the other hand, piperoxan, an adrenaline antagonist, when applied at concentrations of 10^{-5} g./ml., usually eliminated, and certainly reduced, the vagal response (Fig. 14*c*). Unfortunately 933F in concentrations above 10^{-5} g./ml. raised the general tone of the preparation to such a level that it cannot be certain whether failure of the vagal response was due to the drug or to the high tonus of the muscle.

DISCUSSION

Spontaneous Gut Motility

It has been shown that the spontaneous movements seen in the gut of the brown trout are similar to those in mammals—a regular "pendular" rhythm of the longitudinal muscle, peristaltic waves accompanied by powerful longitudinal "colic" contractions, and slow tonus changes. Unlike mammals, however, no myogenic rhythm occurs in the circular muscle coat, and no movements resembling "segmentation" (Cannon, 1902) have been identified in the trout gut. As the movements of isolated preparations resembled those seen *in vivo*, it seems that the extrinsic nerves only modify the intrinsic movements of the gut.

In mammals, pendular contractions occur 5 to 35 times/min., depending on the species (Garry, 1953); these are considerably higher rates than seen in the trout gut (1 every 2 min.). This difference, however, can probably be accounted for by the difference in normal environmental temperatures of the two Classes.

The pendular contractions found in the longitudinal and circular muscle coats of mammalian intestine are believed to be myogenic (Van Esveld, 1928; Feldberg and Lin, 1949; Evans and Schild, 1953; Ambache and Lessin, 1955). On the other hand, the peristaltic waves are considered to be neurogenic (Bozler, 1949; Evans and Schild, 1953; Kosterlitz, Pirie, and Robinson, 1956; Bülbring, Lin, and Schofield, 1958). Evidence is presented here that these conclusions also apply to the movements of the trout intestine. Peristaltic waves are abolished by nicotine and hexamethonium, while the "pendular" rhythm persists. Furthermore, on quickly raising the temperature of the gut, peristalsis disappears above 20° whereas the pendular rhythm persists up to 32° (Burnstock, 1958a). It has been suggested that the myenteric plexus is affected by temperature changes before the muscle cells (Ambache, 1946; Gillespie and Wishart, 1957; Innes, Kosterlitz, and Robinson, 1957; Burnstock, 1958a). It is probable, then, that the early elimination

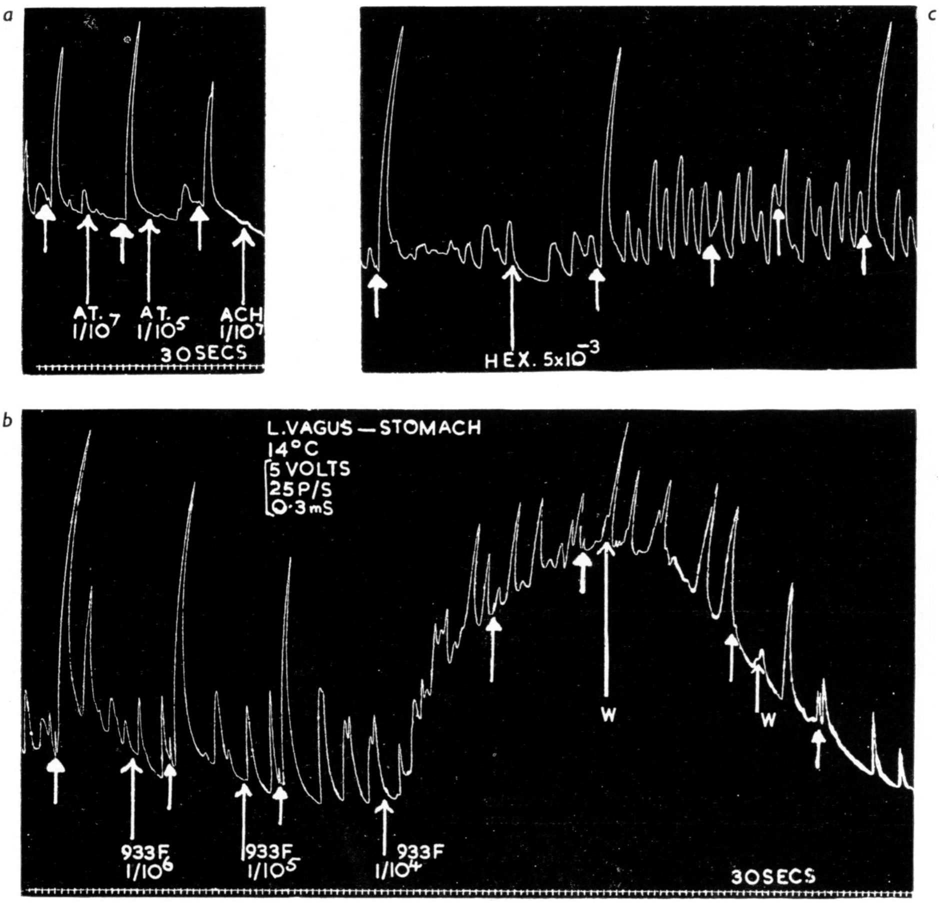

FIG. 14.—Effect of drugs (open arrows) on the response of the longitudinal muscles of the stomach to stimulation of the vagus nerves (closed arrows). Stimulus strength, 5 volts; frequency, 25 pulses/sec. (P/S); pulse duration, 0.3 msec. (mS). Temperature 14°. W=Wash. (*a*), Enhancing effect of atropine (AT) on the response of the stomach to stimulation of the vagus nerves. (*b*), Effect of treatment with hexamethonium (HEX) on the vagal response. (*c*), Effect of piperoxane (933F) on the vagal response.

of peristalsis by an increase of temperature results from inactivation of nervous structures.

Since in the trout intestine the action of ACh is always excitatory, and that of adrenaline always inhibitory, it seems likely that peristaltic contractions are mediated by cholinergic neurones. Both peristaltic waves and longitudinal colic contractions are elicited by radial distension of the gut wall. A similarly triggered myenteric reflex mechanism has been analysed in mammalian gut (Kosterlitz *et al.*, 1956).

The teleostean stomach movements appear to be less complicated than those described in the mammalian stomach by Alvarez and Zimmerman (1928). The antiperistaltic wave, so characteristic in the stomach of the trout, is probably a specialized feature of this fish, since it is not prominent in other teleosts (pike, char, perch). The absence of peristaltic waves and the prominence of powerful longitudinal muscle contractions in the rectum may also be a specialized characteristic of salmonoids.

There is no previous description of teleostean spontaneous gut motility available. From the few accounts of spontaneous gut movements described in other lower vertebrates, it seems clear that peristaltic waves occur in the stomach and intestine of both amphibians (Patterson, 1928, 1933) and elasmobranchs (Young, 1933; Nicholls, 1933, 1934; Babkin, 1946). In elasmobranchs, slow tonus changes and " small contractions with a fairly rapid rhythm " have been described (Alvarez, 1927). Presumably the latter movements can be equated with the " pendular " rhythm described in the trout gut as well as in mammals.

Eserine in concentrations of not less than 10^{-5} g./ml. markedly increases the amplitude of " pendular " contractions of the trout intestine. It is well established that eserine potentiates acetylcholine responses (Dale and Gaddum, 1930; Brown, 1937). If this is so in fish, the implication is that ACh is being continuously released in the trout's intestinal wall. The reaction of the gut to atropine supports this view. Such a mechanism has already been suggested for mammals, but, whereas Feldberg and Lin (1949, 1950) considered spontaneous release of ACh to be of non-nervous origin, both Ambache (1946) and Evans and Schild (1953) believed that postganglionic neurones in the myenteric plexus were involved. The fact that the response of the intestine to eserine is abolished by hexamethonium supports the latter view, as well as providing evidence for the nicotine-like action of ACh.

Piperoxan (933F) increases the tone of the longitudinal muscle and decreases the amplitude of pendular contractions, a response similar to the effect of high concentrations of ACh on gut movements. This implies that 933F removes an inhibitory action of adrenaline which may also be continuously released in the gut. Thus the amplitude of the myogenic pendular contractions may be controlled by a system of continuous antagonistic release of ACh and adrenaline in the gut wall. Whether the agents in such a system are of nervous or non-nervous origin remains to be seen. Burn (1950) put forward the view that adrenaline can be released locally in some organs. In mammals the existence of inhibitory adrenergic neurones in the wall of the gut has also been postulated (Ambache and Edwards, 1951).

Extrinsic Control of Gut Motility

The view that antagonistic " sympathetic " and " parasympathetic " nervous control of gut movements is absent in the lower vertebrates (Young, 1936) is supported by the present work. Both vagus and splanchnic nerves are motor to the trout gut. Moreover, the vagus nerve does not extend beyond the stomach, while the splanchnic nerve supplies the intestine as well as the stomach. It is not surprising, therefore, that the stomach and intestine often respond differently to drugs, and in particular to ACh and adrenaline, which are antagonistic in the intestine but synergistic in the stomach.

Previous workers found that ACh raised the tone and increased the amplitude of contractions in the stomach and intestine of teleosts (Backman, 1917; Dreyer, 1928; Frey, 1928; Bernheim, 1934; Young, 1936). This is also the response of the trout gut to ACh. The reaction of the trout gut to both nicotine and hexamethonium is similar to that reported in mammals (Cantoni and Eastman, 1946; Wien and Mason, 1951; Feldberg, 1951). High concentrations of nicotine or hexamethonium antagonize the response to ACh, suggesting that ACh has its principal action on the enteric neurones rather than on the neuromuscular junction or muscle fibres. Young (1936) presented evidence to support a view that the action of ACh on the bladder of the teleost *Uranoscopus* was also " nicotine-like."

Regarding the action of adrenaline there is some disagreement with previous work. Dreyer (1928), Bernheim (1934) and Young (1936) found that adrenaline caused marked loss in tone and inhibition of contractions in all regions of the gut of various marine teleosts. In the trout, this response is true for the intestine which is supplied solely by splanchnic nerves, but it is not the reaction produced in the stomach where there is vagal as well as splanchnic innervation. At low concentrations (10^{-7} to 10^{-8} g./ml.), adrenaline causes a single strong contraction of the longitudinal stomach muscles. At higher concentrations there is some decrease in the amplitude of pendular contractions, but usually only after producing a small initial contraction. These facts suggest that the postganglionic vagal motor fibres may be adrenergic, while the preganglionic fibres are cholinergic.

Some support for such a view is given by the effect of ACh and adrenaline antagonists on the vagal response. Atropine clearly does not abolish the vagal response, while piperoxan (933F), claimed to be an adrenaline antagonist in mammalian gut (Bovet and Bovet-Nitti, 1948), certainly reduces, though it does not always eliminate, electrically induced vagal contractions. In addition, pretreatment of the stomach with adrenaline usually increases the amplitude of the vagal response.

The inhibitory action of adrenaline on the intestine, together with the fact that both ACh and electrical stimulation of the splanchnic nerves produce motor responses throughout the gut, suggests that the splanchnic fibres are cholinergic. The fact that atropine reduces the effect of splanchnic stimulation supports this view.

As in teleostean fish, ACh increases the tone and contractions of the whole gut of both elasmobranch fish and amphibians (Epstein, 1931). Furthermore, both in the stomach of elasmobranchs (Dreyer, 1928; Lutz, 1931; Nicholls, 1934; Young, 1933; Babkin, Friedman, and MacKay-Sawyer, 1935) and of amphibians (Gruber, 1923; Friedman, 1935), adrenaline in low concentrations has been reported to have a stimulating action, while at high concentrations it causes inhibition of gut movements. Hence the stimulating action of low concentrations of adrenaline on the stomach of the trout is consistent with results obtained in other lower vertebrates. In addition, the results show that there is a closer correlation between nervous action and pharmacodynamic activity than was previously demonstrated in teleosts.

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