J. Physiol. (1956) 133, 681–694

THE MECHANISM OF THE PERISTALTIC REFLEX IN THE ISOLATED GUINEA-PIG ILEUM

By H. W. KOSTERLITZ, VIVIEN W. PIRIE AND JUDITH A. ROBINSON

From the Department of Physiology, University of Aberdeen

(*Received* 11 *April* 1956)

In 1917 Trendelenburg demonstrated that a peristaltic reflex can be elicited in the isolated guinea-pig ileum by distension of the lumen. This reflex consists of two phases. In the first, or preparatory, phase the longitudinal muscle contracts without any appreciable amount of fluid leaving the lumen. In the second, or emptying, phase a contraction ring of the circular muscle travels in an aboral direction expelling the intestinal contents. The physiological basis of this reflex is still not fully understood; the experiments described in this paper were carried out in an attempt to analyse further the mechanism involved.

METHODS

Apparatus. The principle of the method used was to record simultaneously the tension developed in the isometrically contracting longitudinal muscle, the changes in intra-intestinal pressure and the amount of fluid leaving or entering the lumen. In some experiments the contraction of the longitudinal muscle was recorded isotonically. For the measurement of the intra-intestinal pressure an electric condenser manometer was used with a brass membrane of thickness 50–100 μ (Fig. 1). This was a modification of the manometer described by Griffith, Innes & Kosterlitz (1953). The main improvement, apart from increased mechanical stability, was the introduction of a variable air gap for the adjustment of sensitivity. The tension in the longitudinal muscle coat was measured with a condenser myograph of similar construction. The oral end of the ileum was tied and connected to a membrane 50 μ thick by means of a fine silver chain. For isotonic recording a lever of the type shown in Fig. 2 was used. It consisted essentially of an air condenser, the capacity of which was altered by the movements of the lever. The contractions were essentially isotonic as long as the lever did not move more than 25° from the horizontal.

The electrical circuit used for detecting the changes was in principle similar to that used for the heart rate counter (Griffith *et al.* 1953). Two important technical points arose in the course of the experiments. In view of the sensitivity of the apparatus to vibration it was necessary to use anti-vibration mountings; further, the screened box holding the condenser manometer had to be carefully lagged to minimize the effects of temperature changes, which caused drift of the zero point. The display unit consisted of a Cossor double-beam oscilloscope, each beam split again by a Carpenter high-speed relay switching at a frequency of 150–200 c/s. The relay, which was activated by the multivibrator circuit described by Attree (1950), was interposed between the analysing circuit and the amplifier of the oscilloscope.

The general experimental lay-out is shown in Fig. 3. The organ bath had a volume of 40 ml. The aboral end of the ileum was fixed to the vertical limb of a glass T-piece which passed through a rubber bung at the bottom of the organ bath *B*. All connexions between this T-piece and the membrane manometer M_2 or the resistance against which the gut worked were made of polythene tubing. The ileum emptied its contents through the resistance *E* into the air space *G*, the manometer M_2 and the capillary tube *E* being the only communication between the inside of the ileum and the rest of the apparatus. The standard resistance was a capillary glass tube of bore 1·75 mm and length 75 mm. The polythene connexions were of wide bore so that they contributed only little to the total resistance. When greater resistances were used, their relative values were

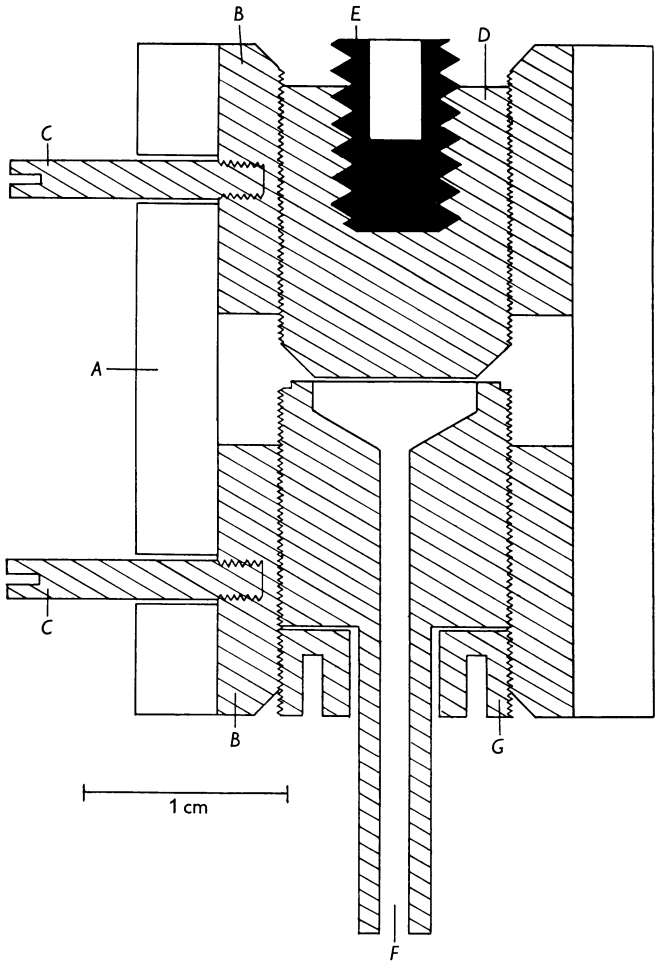

Fig. 1. Diagram of condenser manometer. *A*, Perspex cylinder; *B*, brass bushes, press-fitted; *C*, terminals; *D*, brass plug, fitted to the bush by a fine thread (80 turns/in.); *E*, socket screw firmly fixed in plug *D*; *F*, brass tube with soldered membrane, fitted to the bush in the same way as *D*; *G*, locking ring. In the myograph, the tube *F* is replaced by a wide cylinder and a fine silver chain is soldered to the centre of the membrane.

calculated from $R \propto l/r^2$, the standard resistance being given the value of unity. The air space could be varied; it was usually between 500 and 2000 ml.

To trigger off the peristaltic reflex the pressure was raised in the reservoir D to the desired value, usually between 1 and 3 cm H_2O. By opening tap T_4 for a second or so, the pressure was increased in the air space and therefore also in the lumen of the ileum. The increase in longitudinal tension during the preparatory phase of the peristaltic reflex was recorded by the myograph M_1, the rise in intra-intestinal pressure during the emptying phase by manometer M_2 and the rise in pressure

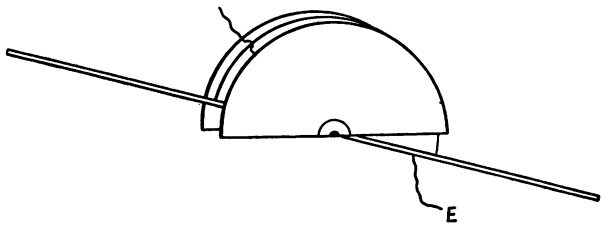

Fig. 2. Diagram of isotonic condenser lever. The centre plate holding the lever and the bearing are earthed (E).

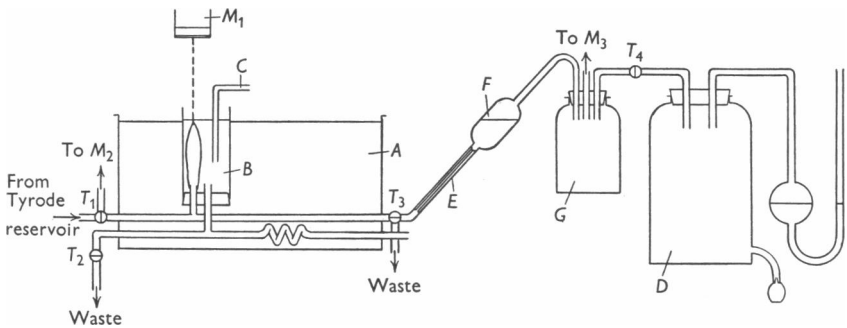

Fig. 3. Diagram of the organ bath and its connexions. A, thermostatically controlled water bath; B, organ bath with rubber bung; C, oxygen supply tube; D, pressure reservoir (5 l.) with pressure bulb and water manometer; E, capillary resistance; F, bulb of a 50 ml. pipette; G, air space; M_1, condenser myograph; M_2 and M_3, condenser manometers; T_{1-4}, glass cocks.

in the air space due to the ejection of fluid from the lumen of the ileum by manometer M_3. The volume of fluid ejected was calculated from the rise of pressure in the air space; e.g. the ejection of 1 ml. fluid caused a rise of 0·5 cm H_2O when the air space was 2000 ml. When such large air spaces were used the record of the changes in intra-intestinal pressure gave an approximate measure of the changes in mean velocity, since the pressure changes in the air space were small compared with those occurring on the intestinal side of the capillary resistance.

In a few experiments in which the effects of very small air spaces were studied, the gut emptied its contents into an air space without the intervention of a capillary resistance. In these experiments only one manometer (M_2) was used.

Isolated ileum. Adult guinea-pigs of both sexes were used. They were killed by decapitation and a piece of intestine 30 cm long was excised. The contents were gently washed out with Tyrode solution. About 10 cm of the ileum nearest to the ileo-caecal valve were discarded in view of the findings of Munro (1951) that the physiological reactions of this section were different from the rest of the ileum. A piece of the remaining ileum about 6–7 cm long was used and suspended at 35° C in oxygenated Tyrode solution with a $MgCl_2$ content of 0·01 g/l.

RESULTS

The time relations between the contractions of the longitudinal and circular muscle layers during the peristaltic reflex

Typical responses to subthreshold, submaximal and maximal increases in intra-intestinal pressure are shown in Fig. 4. To take up any slack, the preparation was slightly stretched until the tension in the longitudinal layer was 1 g. In the uppermost tracing (Fig. 4 A) the intra-intestinal pressure was raised to a value (1·3 cm H_2O) which did not trigger off the complete peristaltic reflex but led to a contraction of the longitudinal muscle layer. After a delay of about

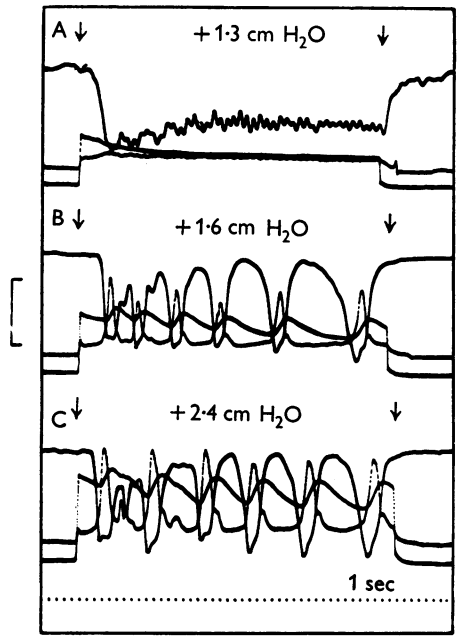

Fig. 4. Records of responses to subthreshold, submaximal and maximal pressure stimuli. In each record from above downwards: longitudinal tension, intra-intestinal pressure and pressure in air space of 1900 ml. Time marker: 1 sec. Increase in tension downward, increase in pressure upward. Initial longitudinal tension 1 g. Calibration: 3·3 g tension, 4·7 cm H_2O intra-intestinal pressure and 1·8 cm H_2O pressure in air space (=3·4 ml. volume change). Between arrows, intra-intestinal pressure raised in A by 1·3 cm H_2O, in B by 1·6 cm H_2O, and in C by 2·4 cm H_2O.

1·5 sec the tension in the longitudinal muscle increased rapidly from 1 to 5 g and then fell slowly to 3·7 g. It remained at this value for as long as the intra-intestinal pressure was kept raised, with oscillations of about 0·3–0·8 g at the rate of about 1/sec. The stimulus being subthreshold for a response by the circular muscle, there was no ejection of fluid. The intra-intestinal pressure

showed only small oscillations, more or less synchronous with the contractions of the longitudinal layer.

Raising the intra-intestinal pressure to a slightly higher value (1·6 cm H_2O) elicited the peristaltic reflex (Fig. 4B). After a delay of 2 sec the tension in the longitudinal muscle rose rapidly to 5·3 g. When the tension reached a value of 5 g, the emptying phase started, in which the circular muscle contracted causing a steep increase in the intra-intestinal pressure to about 4 cm H_2O in 0·75 to 1 sec. Then the intra-intestinal pressure fell as rapidly as it had risen, giving a spike-like trace. During such a cycle of rising and falling intra-intestinal pressures the contraction wave of the circular muscle proceeded in an aboral direction along the whole length of the preparation. When the ileum was completely empty the intra-intestinal pressure remained unchanged for about 0·5 sec at a level slightly higher than that found before the beginning of the emptying phase. This was due to the increase of pressure in the air space caused by the expulsion of fluid from the lumen of the ileum; with an air space of 2000 ml. it amounted to 0·5 cm H_2O when 1 ml. had been ejected. The spike-like appearance of the pressure curve indicated that the velocity at which fluid left the lumen increased steeply during the first part of the emptying phase and decreased as rapidly during the second part. This was corroborated by the sigmoid trace of the pressure changes in the air space.

The tension in the longitudinal layer started to fall very soon after the beginning of the emptying phase and was back at its original level of 1 g in the early stages of the filling phase. This phase, which lasted longer than the emptying phase, was initiated by a sudden relaxation of the circular muscle; the velocity at which the fluid returned to the lumen of the intestine diminished slowly until the distension of the ileum triggered off the next cycle of peristaltic activity. Usually half way through the filling phase, the tension in the longitudinal muscle layer started to increase while the circular muscle did not contract until filling was complete. In the second and later cycles the increase in longitudinal tension became more and more protracted although the final values were approximately the same in all cycles. At the same time, the amount of fluid entering during the filling phase and being ejected during the emptying phase increased gradually, e.g. from 0·7 to 0·95 ml. in the experiment shown in Fig. 4B.

When a greater pressure stimulus was used (2·4 cm H_2O), the events were not fundamentally different from those just described (Fig. 4C). However, as more fluid entered during the filling phase more was expelled (1·25–1·35 ml.) with each peristaltic cycle. Further, the intra-intestinal pressure reached a higher maximum (5–6 cm H_2O). The expulsion time was a little longer, 1·9–2·2 sec against 1·5–2·0 sec. Finally, the slowing of the rate of increase in longitudinal tension observed in later cycles was not so marked when the

stimulating pressure was 2·4 cm instead of 1·6 cm, and the intervals between the individual cycles were shorter.

Details of the pressure changes inside the intestine and in the air space were more readily seen when a faster moving paper was used (Fig. 5). In particular, the intra-intestinal pressure record of the emptying phase very often showed an inflexion in the ascending limb. There seemed to be no significant ejection of fluid from the lumen until this inflexion was reached.

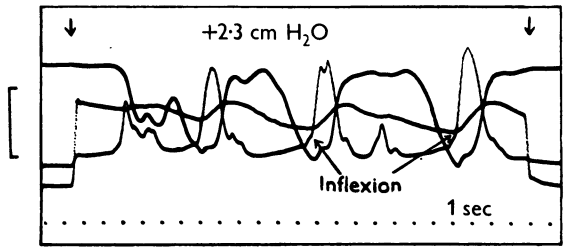

Fig. 5. Same preparation as in Fig. 4 but recorded with a faster moving paper. Records and calibration as in Fig. 4. Between arrows, ↓, intra-intestinal pressure raised by 2·3 cm H_2O.

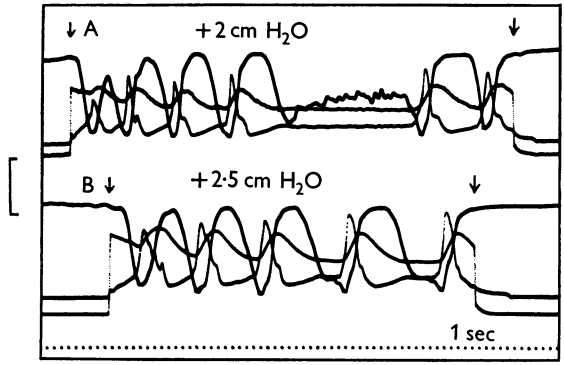

Fig. 6. Same preparation as in Fig. 4 but fatigued. Records as in Fig. 4. Initial longitudinal tension 1 g. Calibration: 3·5 g tension, 4·6 cm H_2O intra-intestinal pressure and 1·8 cm H_2O pressure in air space (=3·4 ml. volume change). Between arrows, intra-intestinal pressure raised in A by 2 cm H_2O and in B by 2·5 cm H_2O.

When the preparation had become fatigued, certain changes from the normal pattern were observed (Fig. 6). The individual cycles followed each other at longer intervals. For a given pressure, more fluid entered the lumen of the fatigued preparation and therefore more fluid was expelled, prolonging the expulsion time. The rate of rise in longitudinal tension was slowed. A change of great interest was the appearance of cycles in which the longitudinal tension rose more or less normally but remained increased for periods of up to 15 sec without any activity of the circular layer. When at the end of such a period

a peristaltic wave of the circular muscle was observed, this was always accompanied by a further rise in the longitudinal tension of about 1 g. The same phenomenon was also seen in fresh preparations when stimuli were applied which were just above threshold (Fig. 7). Although in normal reflex cycles no inflexion was seen in the record of the longitudinal tension, the observed phenomenon seems to suggest that the contraction of the longitudinal muscle consists of two phases, only the second of which is closely linked with the contraction of the circular muscle.

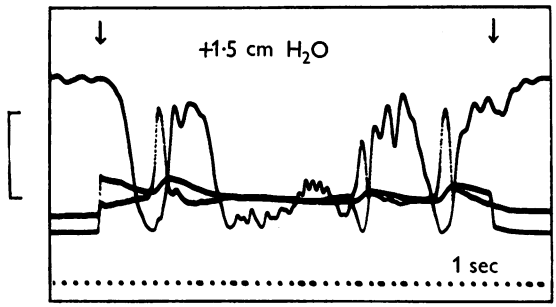

Fig. 7. Pressure stimulus near threshold. Records as in Fig. 4. Initial longitudinal tension 1 g. Calibration: 3·3 g tension, 4·8 cm H_2O intra-intestinal pressure and 2·5 cm H_2O pressure in air space (=4·8 ml. volume change). Between arrows, the intra-intestinal pressure was raised by 1·5 cm H_2O.

As far as the decrease in longitudinal tension during the emptying phase was concerned, there was never any significant delay whether the preparation was fresh or fatigued. When the circular muscle was fully contracted the relaxation of the longitudinal had always begun. However, sometimes the longitudinal tension had decreased only little (Fig. 4 B), or the relaxation was about half-way (Figs. 4 C, 6 A), or was almost complete (Figs. 5, 6 B), indicating that the two events were not interdependent.

Dissociation of the contractions of the longitudinal and circular muscle layers

The peculiar constancy of the time relationships between the contractions of the longitudinal and circular muscle layers raised the question whether the contraction of the longitudinal muscle triggered off the contraction of the circular muscle.

That the contraction of the circular layer but not that of the longitudinal layer is inhibited by ganglion-blocking agents was shown by Feldberg & Lin (1949) using tubocurarine and nicotine, and by Paton & Zaimis (1949) investigating the action of methonium compounds. By adding large doses of acetylcholine to the bath it was found possible to inhibit reversibly the contraction of the longitudinal muscle without affecting significantly the circular muscle (Fig. 8). During the period of inhibition, which was probably

due to a Cantoni & Eastman (1946) effect, the longitudinal muscle was quite insensitive not only to acetylcholine but also to histamine and 5-hydroxytryptamine. When the intra-intestinal pressure was raised in the presence of acetylcholine in concentrations of 5–10 mg/l., normal reflex contractions of the circular muscle took place while the contractions of the longitudinal muscle of the preparatory phase were almost completely suppressed (Fig. 8B). This insensitivity of the longitudinal muscle to intra-intestinal pressure, acetylcholine or histamine lasted a considerable time after washing out the large dose of acetylcholine (Fig. 8C). Normal responses were usually restored after an interval of about 1 hr (Fig. 8D).

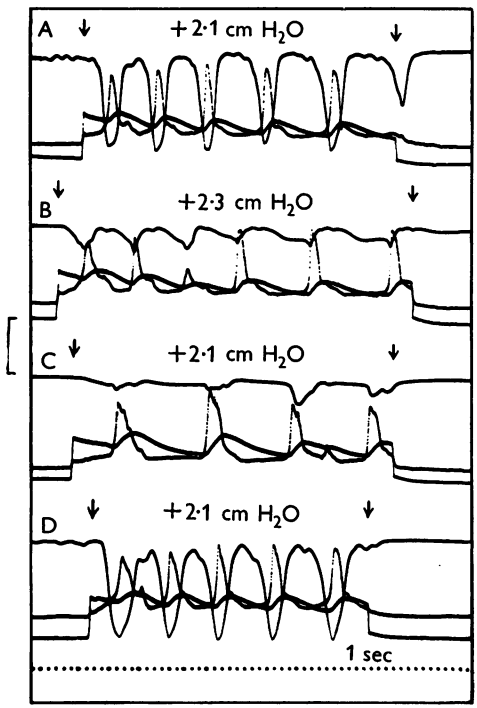

Fig. 8. The effect of large doses of acetylcholine on the peristaltic reflex. Records as in Fig. 4. Calibration: 3·3 g tension, 4·9 cm H_2O intra-intestinal pressure and 2·8 cm H_2O pressure in air space (=5·3 ml. volume change). Initial longitudinal tension 1 g. Between arrows, the intra-intestinal pressure was raised in A, C and D by 2·1 cm H_2O and in B by 2·3 cm H_2O. A, control response; between A and B two doses of 100 μg acetylcholine were added with an interval of 2·5 min, the second dose giving rise to a very small increase in tension; B was taken 5 min after the first dose of acetylcholine, the initial longitudinal tension being 1·5 instead of 1 g; after B the bath was washed twice and C was taken 12 min later, the longitudinal tension having returned to the initial value of 1 g; D was taken 33 min later, the bath fluid having been renewed 4 times.

Isometric and isotonic contraction of the longitudinal muscle

It was of interest to examine whether the actual shortening of the intestine contributed to the efficiency of the peristaltic reflex. The experiments with isotonic recording of the longitudinal muscle were performed either with a conventional isotonic lever or, when simultaneous records of the shortening and the changes in intra-intestinal pressure were required, with a lever attached to an air-spaced condenser. A load of 1 g was found most suitable; with 2 g performance was initially slightly superior but fatigue set in more readily, while a load of 0·5 g was insufficient, particularly when pressure stimuli near the threshold were used.

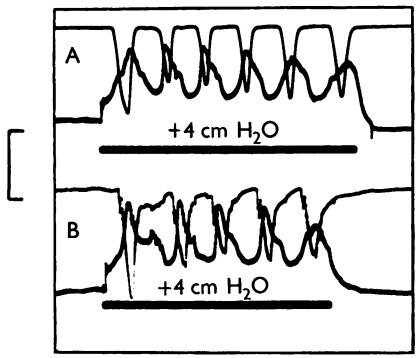

Fig. 9. Isometric and isotonic recording of the longitudinal muscle of the same preparation. Records from above downwards: tension or shortening of longitudinal muscle, intra-intestinal pressure and signal. Initial load or tension 1 g. Calibration: in A, 3·2 g tension and 5 cm H_2O intra-intestinal pressure; in B, 1·5 cm shortening and 4·4 cm H_2O intra-intestinal pressure. During signal, the intra-intestinal pressure was raised by 4 cm H_2O.

The tracings obtained from preparations contracting first isotonically and then isometrically showed no fundamental differences (Fig. 9). Over a wide range of varying conditions, the absence of shortening did not significantly reduce the pressure developed in the lumen nor the amount of fluid ejected (Fig. 10). Both types of preparation reacted in the same way to a reduction of the air space into which the contents were expelled: the rise in intra-intestinal pressure was increased to the same extent when the air space was decreased and in both instances the emptying became incomplete when the air space was smaller than 300–400 times the volume of fluid expelled. Sometimes the impression was gained that the ejection velocity was greater in isotonic than in isometric preparations, although this was by no means always the case.

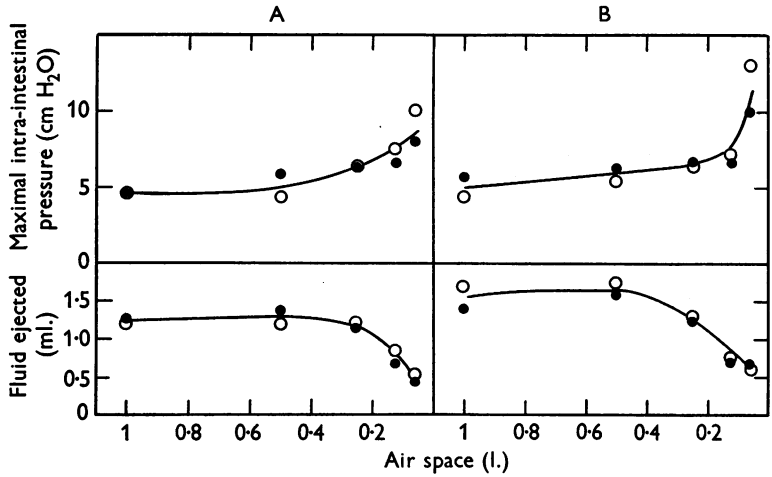

Fig. 10. Effect of isometric or isotonic recording on the maximal intra-intestinal pressure during the peristaltic reflex and on the volume of fluid ejected from the lumen. The same preparation was used for isotonic (●—●) and isometric (○—○) recording. Initial load or tension 1 g. The pressure stimulus was 2 cm H_2O in A and 3 cm H_2O in B.

The effect on the peristaltic reflex of reducing the air space into which fluid is expelled

The use of a restricted air space into which the intestinal contents were expelled led to a progressive increase in the pressure in the air space, rising to a maximum at the end of the emptying phase. This was of little importance when the air space was 500 to 2000 times as large as the volume of fluid ejected, the pressure in the air space varying then between 2 and 0·5 cm H_2O for a fluid volume of 1 ml. With such air spaces, the intra-intestinal pressure reached during the emptying phase was between 4·5 and 6 cm H_2O. When the air space was reduced to below about 300 times the volume of fluid ejected the pressure rose beyond these values but the intestine no longer emptied completely. Some of the fluid escaped through the contraction ring of the circular muscle towards the closed oral end of the ileum. Pressures as high as 20 cm H_2O were reached when the air space was about 30 times as large as the volume of fluid present in the lumen. With such small air spaces the maximum intra-intestinal pressure was reached later and maintained longer than with air spaces into which complete emptying was possible.

The effect of increasing the capillary resistance through which the fluid is expelled

When the resistance offered to the expulsion of the intra-intestinal contents was raised, not by reducing the air space but by increasing the capillary

resistance, and thus the circular muscle was forced to work from the start against a considerably raised resistance, then comparatively higher pressures were developed inside the intestine before failure and incomplete emptying set in (Fig. 11). With a resistance of 3 to 4 times the original value, the intra-intestinal pressure was 10 cm H_2O when the longitudinal muscle contracted

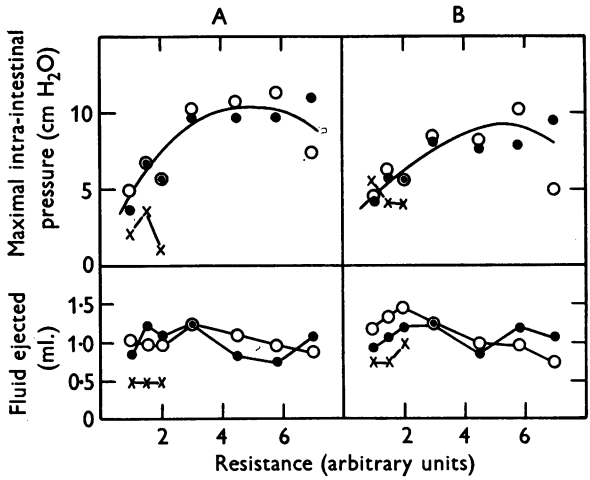

Fig. 11. The effect of increasing the initial resistance (capillary *E* in Fig. 3) on the maximal intra-intestinal pressure during the peristaltic reflex and on the volume of fluid ejected from the lumen. The same preparation was used for isotonic (A) and isometric (B) recording. Initial load or tension 1 g. The pressure stimulus was 1 cm (×), 2 cm (●) or 3 cm (○). The resistance of a tube of bore 1·75 mm and length 75 mm was taken to be one arbitrary unit.

isotonically and 9 cm H_2O when it contracted isometrically. There was no difference between the amounts of fluid expelled. Incomplete emptying was observed when the capillary resistance was greater than 4 times the original value. The duration of the emptying phase was prolonged; e.g. it was twice as long as normal when the value of the resistance was sevenfold.

DISCUSSION

When Trendelenburg (1917) first described the peristaltic reflex in the isolated guinea-pig ileum, he showed that a shortening of the longitudinal muscle layer was followed by a contraction of the circular muscle beginning at the oral end of the preparation. The difference in phase between the contractions of the two muscle layers was usually 90°; the circular layer started to contract when the contraction of the longitudinal muscle was about half completed and the contraction of the circular muscle was complete when the relaxation of the longitudinal had proceeded half-way.

It would appear from Trendelenburg's observations and from the findings presented in this paper that the contraction of the circular muscle follows that

of the longitudinal muscle in a more or less fixed pattern. The question arises whether the contraction of the circular muscle is triggered off by the contraction of the longitudinal coat. However, the fact that each of the two muscle layers can be selectively inhibited seems to rule out this possibility. The contraction of the circular coat is inhibited by ganglion-blocking agents; this strongly suggests that cholinoceptive synapses are present in the reflex arc activating the circular muscle. Evidence has recently accumulated that the contraction of the longitudinal muscle of the preparatory phase is also reflex in character, although the nature of the nervous elements involved is as yet unknown (Kosterlitz, Pirie & Robinson, 1955; Schaumann, 1955; Kosterlitz & Robinson, 1955, 1956). Why large doses of acetylcholine should inhibit the contractions of the longitudinal and not of the circular muscle is not understood.

A likely explanation of the pattern in which the emptying phase follows the preparatory phase may be found in the different degrees of distension necessary for eliciting the contractions of the two muscle coats. With a small filling pressure a contraction of the longitudinal muscle is obtained, while the circular muscle remains inactive. Further, in repetitive reflex activity, the longitudinal contraction always starts at an earlier stage of the filling phase than does the circular contraction. This lag between the two coats is increased when the stimulus is near the threshold for the circular muscle or when the preparation is fatigued. Since the lag is of the order of 1 sec or more, synaptic delay can play only a minor role.

The secondary rise in longitudinal tension, which accompanies the increase in intra-intestinal pressure at the beginning of the emptying phase, is seen particularly well in fatigued preparations or in fresh preparations with near-threshold stimuli. It never occurs in the presence of hexamethonium or when the pressure stimulus is too small to cause a contraction of the circular muscle. It would appear therefore that this secondary rise in longitudinal tension belongs to the emptying rather than to the preparatory phase and is evoked by a nervous mechanism involving cholinoceptive synapses.

The shape of the intra-intestinal pressure curve during the emptying phase is of some interest. This phase is initiated by a short-lasting small increase in pressure during which only little or no fluid is expelled. It coincides with the secondary increase in longitudinal tension already discussed. The spike-like rise or fall in pressure which follows the initial rise is an indication of the velocity with which fluid is ejected. The rise in velocity during the first part of the emptying phase may be due to an increasing rate of recruitment of circular fibres; there are, however, other possible explanations. Later, when the amount of fluid on which the circular fibres can exert pressure becomes less, the ejection velocity decreases again.

The contraction of the longitudinal muscle does not contribute materially to the efficiency of the ejection of fluid from the lumen, at least not in the

isolated ileum in which the distending pressure acts on the whole surface of the lumen. Allowing the longitudinal muscle to shorten makes no difference; even complete inhibition of its contraction has no significant effect. As the longitudinal muscle coat contracts with a smaller distending stimulus than the circular coat, its contraction may aid in the mixing of intestinal contents before peristaltic propulsion.

From the experiments in which the resistance to ejection of fluid was increased, either by decreasing the air space or by lengthening the capillary, it may be concluded that considerable obstacles can be overcome. An intra-intestinal pressure of about twice the value occurring during normal ejection can be produced by the circular muscle without failure when the resistance makes itself felt at an early stage of the contraction of the circular muscle. This situation would arise when the intestinal contents had to be forced through a region with increased tone of the circular muscle. On the other hand, if the contents have to be expelled into a restricted space, intra-intestinal pressures of up to four times the normal value may be observed, although the ejection soon becomes incomplete as some of the fluid passes in an oral direction through the incompetent ring of contracted circular muscle.

SUMMARY

1. An analysis was made of some of the mechanisms underlying the peristaltic reflex in the isolated guinea-pig ileum. Records were taken of the tension in the longitudinal muscle layer, the intra-intestinal pressure and the amount of fluid expelled.

2. With a subthreshold stimulus (0·5–1·5 cm H_2O intra-intestinal pressure) the only change was a rise in longitudinal tension. With submaximal or maximal stimuli (1·5–3 cm H_2O) the increase in longitudinal tension was followed by the emptying phase. While the contraction of the circular muscle travelled in an aboral direction, there was a spike-like rise and fall in intra-intestinal pressure, indicating that the ejection velocity increased at first and then decreased again. When volume of fluid ejected was plotted against time, a sigmoid curve was obtained.

3. In repetitive reflex activity the longitudinal tension started to increase early in the filling phase while the circular muscle only contracted when the distension of the lumen was maximal. The contractions of the two layers followed each other in an apparently fixed pattern. However, as the circular muscle could be selectively inhibited by ganglion-blocking agents and the longitudinal muscle by large doses of acetylcholine, the longitudinal contraction did not trigger off the circular contraction. The time lag between the contractions of the two layers was probably due to the fact that a greater distension of the lumen was required for the circular than for the longitudinal contraction.

4. The efficacy of the emptying phase was independent of an actual shortening of the longitudinal layer. It made little difference whether the contraction of the longitudinal layer was recorded isotonically, isometrically or was inhibited altogether.

5. When contracting against a large resistance the circular muscle was able to raise the intra-intestinal pressure to high values (up to 20 cm H_2O). However, emptying of the lumen became incomplete when the intra-intestinal pressure exceeded 6 to 10 cm H_2O.

Grateful acknowledgement is made of a grant by the Medical Research Council (to H. W. K.) which partly defrayed the expenses of this work. Valuable technical assistance was rendered by Mr W. J. Davidson and Mr J. McConnachie.

REFERENCES

ATTREE, V. H. (1950). An electronic stimulator for biological research. *J. sci. Instrum.* **27**, 43–47.

CANTONI, G. & EASTMAN, G. (1946). On the response of the intestine to smooth muscle stimulants. *J. Pharmacol.* **87**, 392–399.

FELDBERG, W. & LIN, R. C. Y. (1949). The action of local anaesthetics and D-tubocurarine on the isolated intestine of the rabbit and guinea-pig. *Brit. J. Pharmacol.* **4**, 33–44.

GRIFFITH, H. D., INNES, I. R. & KOSTERLITZ, H. W. (1953). The use of the condenser manometer for measuring the heart rate. *J. Physiol.* **121**, 29–30 *P.*

KOSTERLITZ, H. W., PIRIE, V. W. & ROBINSON, J. A. (1955). Contraction of the longitudinal muscle of the isolated guinea-pig ileum, caused by raising the pressure in the lumen. *J. Physiol.* **128**, 8–9 *P.*

KOSTERLITZ, H. W. & ROBINSON, J. A. (1955). Mechanism of the contraction of the longitudinal muscle of the isolated guinea-pig ileum, caused by raising the pressure in the lumen. *J. Physiol.* **128**, 18–19 *P.*

KOSTERLITZ, H. W. & ROBINSON, J. A. (1956). The effects of lowering the bath temperature on the responses of the isolated guinea-pig ileum. *J. Physiol.* **131**, 7–8 *P.*

MUNRO, A. F. (1951). The effect of adrenaline on the guinea-pig intestine. *J. Physiol.* **112**, 84–94.

PATON, W. D. M. & ZAIMIS, E. J. (1949). The pharmacological actions of polymethylene bistrimethylammonium salts. *Brit. J. Pharmacol.* **4**, 381–400.

SCHAUMANN, W. (1955). The paralysing action of morphine on the guinea-pig ileum. *Brit. J. Pharmacol.* **10**, 456–461.

TRENDELENBURG, P. (1917). Physiologische und pharmakologische Versuche über die Dünndarmperistaltik. *Arch. exp. Path. Pharmak.* **81**, 55–129.