Esophageal Responses to Distension and Electrical Stimulation

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ABSTRACT The opossum esophagus contains only smooth muscle in the distal two-thirds; it can be used to study autonomic control of esophageal smooth muscle. Three different preparations of opossum esophagus were used: the esophagus in vivo, the isolated whole esophagus, and isolated strips of the three layers of esophageal smooth muscle. Responses were examined to localized distension and to electrical stimulation. Distension of the esophagus in vivo produced three separate responses: inflation of a distending balloon caused a brief contraction rostral to the point of distension, the *on response;* maintenance of distension produced shortening of the esophagus, sustained for the duration of the distension, the *duration response;* and deflation of the balloon caused a single brief caudal circumferential contraction, apparently propagated caudad, the *off response.* In the isolated whole esophagus distension produced the same three responses. Electrical stimulation in this preparation produced apparently identical responses. Electrical stimulation of isolated strips of the three muscle layers showed that the muscularis mucosae and the longitudinal layer of the muscularis propria always respond with a duration response only. The circular layer of the muscularis propria responds with on and off responses only. These observations suggest that both types of stimuli excite the same afferent nerve fibers in local reflex pathways. Peristalsis can be maintained by these reflexes in the smooth muscle part of the esophagus independent of central nervous connections.

INTRODUCTION

Striated muscle in the human esophagus is restricted to the proximal one-third (1); the distal two-thirds, containing smooth muscle, is often the major site of involvement in the esophageal motor disorders. Most current ideas about normal human esophageal function come from studies in vivo in man and in common laboratory animals (2) which are anatomically unlike man in the muscle composition of the esophagus. In dogs and most rodents the esophagus contains chiefly or only striated muscle; in cats, striated muscle makes up all but the distal one-fourth (3, 4). Experimental study of the autonomic regulation of movement in esophageal smooth muscle requires an animal whose esophagus more nearly resembles that of man. In the common opossum (*Didelphis virginiana*) the distal two-thirds of the esophagus is composed of smooth muscle. These experiments made use of various preparations of opossum esophagus. They were intended to show the responses of the intact and isolated distal esophagus to distension and electrical stimulation.

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METHODS

The opossum esophagus. Relevant anatomic details of the opossum esophagus have not been previously noted. We examined three fresh adult animals and two preserved specimens. Microscopic examinations were made on "Swiss-roll" preparations stained with hematoxylin-eosin and the Gomori one-step trichrome stain. We saw no significant variation among animals. The opossum esophagus is unusual in that after it traverses the diaphragm it passes downward to enter the stomach just above the pylorus. The intra-abdominal segment, 3–4 cm long in the adult, can be examined easily without disturbance of the nerve and blood supply. Inspection of the excised organ shows that orange-red striated muscle occupies the proximal 5–6 cm of the total length (15–18 cm), while pale pink smooth muscle makes up the remainder. Microscopic examination reveals a thick muscularis mucosae and a two-layered muscularis propria. The muscularis mucosae is smooth muscle throughout the esophagus with fibers oriented longitudinally. The thick inner layer of the muscularis propria contains transverse fibers which are smooth muscle in the distal two-thirds of the esophagus, and striated in the proximal one-third. The thin outer layer of longitudinal fibers also contains striated muscle only in the proximal one-third. At the striated muscle–smooth muscle junction in both layers both types of fibers intermingle over a distance of about 2 cm.

Studies of the esophagus in vivo. Seven adult animals, anesthetized with intraperitoneal sodium pentobarbital (50 mg/kg), received an intrathecal injection of 0.3 cc of 6% phenol between the first and second lumbar vertebrae. Each animal was tied to a warmed steel animal tray and the abdomen was opened. Two thin silver wire electrodes, sewn about 4 mm apart into the intra-abdominal segment of the esophagus, about 2 cm above the gastroesophageal junction, permitted bipolar recording of smooth muscle action potentials on a Beckman-Offner type R ink-writing recorder through an RC coupler (9806A).[1] Mineral-oil cotton pledgets were packed about the wires for electrical insulation. Two 10 × 4 mm water-filled thin-walled latex balloons (1 ml vol),[2] attached to water-filled PE 200 polyethylene tubing, detected intraluminal pressure changes in the esophagus. The tubes led to pressure transducers (Model 267A, Sanborn Co., Waltham, Mass.) whose outputs were recorded through linear voltage differential transformer (LVDT) couplers (9805) on the Beckman-Offner recorder. One balloon was inserted through an incision in the stomach into the distal esophagus to the level of the electrodes; it was kept in place by a ligature placed around the polyethylene tubing and sewn through the stomach wall. The other balloon was passed perorally. A third identical balloon, attached through a PE 200 polyethylene catheter to a syringe, was passed perorally for local distension of the esophagus. Preliminary experiments showed that a 5 ml inflation, producing a balloon diameter of about 2 cm, excited maximal responses. Marks on both peroral tubes permitted precise localization of stimulating and proximal recording balloons. The proximal recording balloon was kept about 1 cm above the stimulating balloon.

The isolated whole esophagus. We removed the entire esophagus, including a cuff of stomach, from 14 adult animals, given intraperitoneal sodium pentobarbital. The esophagus was divided transversely about 2 cm above the smooth muscle–striated muscle junction and the distal segment was mounted as shown in Fig. 1. The esophagus was fixed at the distal end; the proximal end was mounted on a glass spool sliding freely over a supporting tube. This spool was connected, through a pivoting lever, to a force-displacement transducer (model FT.03C[3]) to record longitudinal tension through a strain-gage coupler (9853) on the Beckman-Offner recorder. The bath, filled with Krebs solution (5), was bubbled with 95% O_2–5% CO_2 at 36.0°–38.0°C. The esophagus was marked in some experiments with small sutures sewn at 1 cm intervals along its length to facilitate observation of longitudinal contractions. Circular muscle contractions were recorded in some experiments by balloons inserted between the spokes of the fixed spool at the distal end of the esophagus. One recording balloon was fixed 1 cm above the gastroesophageal junction; the other was moved freely along the esophagus, being kept about 2 cm above the distending balloon, as in the studies of the intact esophagus. In other experiments we used two externally attached force-displacement transducers placed 1 cm and 4 cm above the gastroesophageal junction (Fig. 1). These recorded the force of contracting circular muscle by means of strain-gage couplers. Stimulation was achieved in some experiments by distension of a balloon, as described before, inserted from the distal end of the esophagus. In later experiments we used electrical stimulation with a Grass model S8 square-wave stimulator and a model SIU 4678 stimulus isolation unit. Stimuli were delivered through a pair of silver wires, mounted 3 mm apart in a handle, lightly applied to the external surface of the esophagus. We did not systematically explore the effects of varying stimulus characteristics, but arbitrarily used a monophasic square wave, duration 1 msec, frequency 20 cycles/sec. In brain, a pulse duration longer than 1 msec does not increase effectiveness but greatly increases the likelihood of tissue injury; frequencies of 20–30 cycles/sec are probably optimal for stimulation of peripheral autonomic nerves (6). We usually used 30 v, and train duration was varied freely.

Isolated muscle strips. 2 × 1 cm strips, cut from the distal esophagus, were each mounted in a 50 ml bath of warmed gassed Krebs solution and attached with a fine silver chain to a Grass force-displacement transducer. In strips cut transversely, with or without the mucosa intact, shortening represented contraction mainly of the circular muscle layer. In strips cut longitudinally with mucosa removed, shortening represented contraction mainly of the outer longitudinal layer. Longitudinal strips of mucosa were used to study responses of the muscularis mucosae separately. Two silver wires, mounted in a handle 3 mm apart, were applied to one end of each strip to deliver electrical stimuli from the Grass S8 stimulator; stimulus characteristics were the same as described for the isolated whole esophagus.

RESULTS

Distension responses of the esophagus in vivo. In preliminary experiments with balloon distension we observed that deep sedation depressed responses, probably because of respiratory depression and because body temperature falls greatly in the sedated opossum. The maintenance of body temperature by external warming and the use of low initial doses of sodium pentobarbital permitted good responses for periods up to 5 hr.

Responses depended upon the location of the stimulating balloon. Distension at the level of the larynx produced swallowing as shown by movements of the tongue, pharynx, and thyroid cartilage. Distension below this level caused esophageal responses not initiated by swallowing. In this analysis we ignored those responses initiated by swallowing. Distension of the esophagus produced three distinctly separate responses. The act of inflation of the balloon produced a single brief contraction rostral to the distending balloon and recorded as a pressure peak in the proximal recording balloon. If distension was maintained this was often repeated once or twice. We have called this the *on response*. The act of deflation of the stimulating balloon produced a single brief circumferential contraction of the abdominal esophagus, registered as a pressure peak in the balloon fastened in the abdominal esophagus. It was always accompanied by a burst of spikes in the bipolar electrical record from the electrodes implanted over the balloon. It appeared to be propagated from the level of the distension since there was always a delay between the act of balloon deflation and the response. The duration of the

[1] Offner Division, Beckman Instruments, Inc., Schiller Park, Ill.

[2] London Rubber Industries, Ltd., North Circular Road, Chingford, London E.4.

[3] Grass Instrument Co., Quincy, Mass.

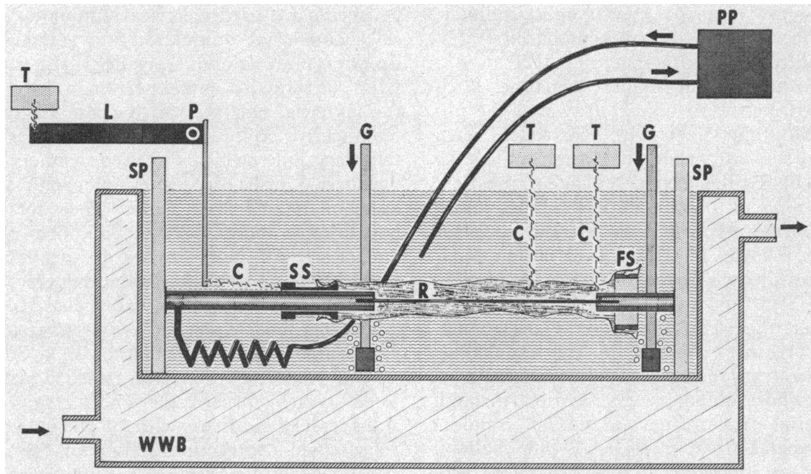

FIGURE 1 Apparatus for studying responses of the isolated whole esophagus. *SP*, stationary post; *T*, force-displacement transducer; *PP*, perfusion pump; *C*, fine silver chain; *FS*, fixed spool; *SS*, sliding spool; *R*, glass rod; *G*, gas: 95% O–5% CO_2; *L*, lever; *P*, pivot; *WWB*, warm water bath. The esophagus is tied at each end to a spool. The fixed spool (*FS*) at the distal end is fastened to a plexiglass tubing by means of radial spokes. The proximal spool (*SS*) slides freely over another plexiglass tubing and moves a lever (*L*) which acts on a force-displacement transducer (*T*). A thin glass rod (*R*) lies between the two plexiglass tubes to support the esophagus. Fine silver chains (*C*) support the esophagus with hooks and lead to transducers (*T*) placed 1 and 4 cm above the distal end. A perfusion pump (*PP*) circulates bath fluid through a polyvinyl tube to a warming coil leading to a lateral opening in the proximal plexiglass tube; the fluid perfuses the lumen and escapes between spokes supporting the distal fixed spool. Aeration stones at each end of the tank disperse the gas in the bath. A circulating constant-temperature water pump (not shown) circulates warm water through the jacket of the bath.

TABLE I
Responses to Distention

	Date	No. of stimuli	On response only	Duration response only	Off response only	On response and off response
Upper 1/3	1/20/68	16	11	0	1	0
	1/23/68	15	7	0	0	3
	1/30/68	42	13	0	2	20
	Totals	73(100)	31(42.5)	0(0)	3(4.1)	23(31.5)
Middle 1/3	1/20/68	33	2	0	5	21
	1/23/68	15	0	0	2	8
	1/30/68	67	0	0	37	28
	Totals	115(100)	2(1.7)	0(0)	44(38.3)	57(49.6)
Lower 1/3	1/20/68	11	0	0	0	2
	1/23/68	38	0	0	2	2
	1/30/68	52	0	0	13	1
		101(100)	0(0)	0(0)	15(14.8)	5(4.9)

* Figures in parentheses indicate responses as per cent of total stimuli. Duration responses were identified from records rather than by observation. Observation showed many duration responses not registered by the recording balloons. Each date represents one animal.

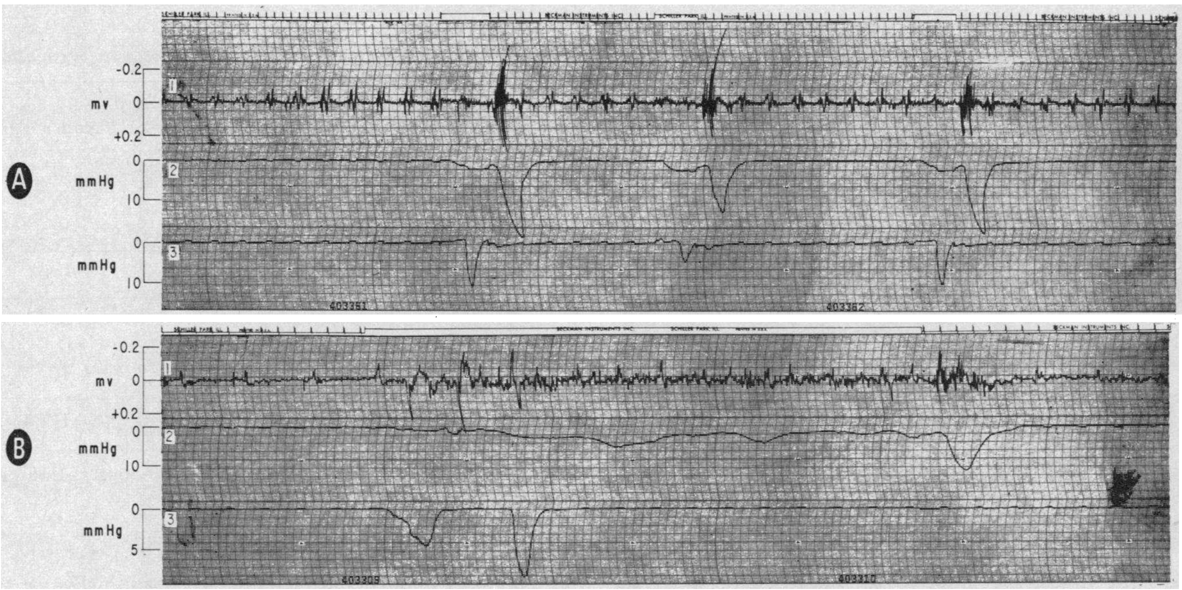

FIGURE 2 Distension responses of the esophagus *in situ*. Electrical records are calibrated in millivolts. Pressure tracings show millimeters of mercury above atmospheric. In A, channel *1* represents electrical activity recorded from two electrodes sewn into the abdominal esophagus; a regular signal represents respiratory artifacts, and bursts of spikes accompany contractions at that level. Channel *2* represents intraluminal pressures at that level and shows off responses. Small sustained rise of pressure before the monophasic off response reflect shortening of the esophagus as described in the text. Channel *3* represents intraluminal pressure about 1 cm above the distending balloon and shows on responses. The time scale (top) shows 1 sec marks and is interrupted for periods which represent the duration of balloon distension (5 ml) at about 5 cm above the gastroesophageal junction. In B the channels are the same as in A. Prolonged distension 7 cm above the gastroesophageal junction clearly separates on from off responses. The on response is repeated once. The duration response is evident in channel *2*.

*of the Esophagus In Vivo**

On response and duration response	Off response and duration response	All three responses	Total on response	Total duration response	Total off response	No responses
0	0	0	11	0	1	4
0	0	0	10	0	3	5
0	0	0	33	0	22	7
0(0)	0(0)	0(0)	54(74.0)	0(0)	26(35.6)	16(22.2)
0	4	1	24	5	31	0
0	1	4	12	5	15	0(0)
0	0	2	30	2	67	0
0(0)	5(4.3)	7(6.1)	66(57.4)	12(10.4)	113(98.3)	0(0)
0	3	5	7	8	10	1
0	4	30	32	34	38	0
0(0)	13	25	26	38	52	0
0(0)	20(19.8)	60(59.4)	65(64.4)	80(79.2)	100(99.0)	1(1.0)

TABLE II
Responses to Distention of

	Date	No. of stimuli	On response only	Duration response only	Off response only	On response and off response	On response and duration response
Middle 1/3	3/26/68	13	0	0	1	2	0
	3/27/68	31	0	0	0	0	0
	3/28/68	30	0	0	0	0	0
	Total	74(100)	0(0)	0(0)	1(1.3)	2(2.7)	0(0)
Lower 1/2	3/26/68	10	0	0	0	4	0
	3/27/68	33	0	0	0	0	0
	3/28/68	29	0	0	0	0	1
	Total	72(100)	0(0)	0(0)	0(0)	4(5.6)	1(1.4)

* Figures in parentheses indicate responses as per cent of total stimuli. Duration responses were identified by observation only. Each date represents one animal.
‡ These responses are tallied separately since they are atypical in location.

delay was directly related to the distance between the distending balloon and the gastroesophageal junction. This contraction was often repeated once or twice. We have called this the ***off response.*** If the distending balloon was maintained at inflation for a long period, the lower balloon registered a small constant or slowly rising pressure. This pressure was sustained as long as the stimulating balloon was held inflated and ended in an off response upon deflation. This constant pressure was accompanied by visible shortening of the intraabdominal segment, with rostral sliding of the esophagus into the diaphragmatic hiatus and some elevation of the stomach. This appeared to be a contraction mainly of the longitudinal muscle; we have called this the ***duration response.*** We could not tell from observation if this shortening represented contraction of the longitudinal muscle of

TABLE III
Responses to Electrical Stimulation

Date	Total stimuli	Terminal transducer only	Proximal transducer only	Distal transducer only	Terminal and proximal only	Terminal and distal only
					Stimulation 1–4 cm above	
2/19/68	46	1	0	0	5	0
2/21/68	25	0	0	0	11	0
2/26/68	25	1	0	0	1	6
2/27/68	20	4	0	0	9	1
2/28/68	18	0	0	0	1	2
2/29/68	13	0	0	0	0	2
Totals	147(100)	6(4.1)	0	0(0)	27(18.4)	11(7.5)
					Stimulation between proximal	
2/19/68	30	2	0	3	0	20
2/21/68	17	0	0	0	0	6
2/26/68	27	5	0	0	0	17
2/27/68	14	1	0	2	0(0)	6
2/28/68	14	1	0	3	0	9
2/29/68	15	4	0(0)	0	0	7
Totals	117(100)	13(11.1)	0(0)	8(6.8)	0(0)	65(55.6)

* Figures in parentheses indicate responses as per cent of total stimuli. Only duration and off responses are indicated except in the column at right where the rare on responses are tallied separately. Proximal strain-gage transducer at 4–5 cm and distal transducer at 1 cm above gastroesophageal junction record circular contractions; terminal transducer records longitudinal tension. Each date represents one animal.

*the Whole Esophagus In Vitro**

Off response and duration response	All three responses	Total on response	Total duration response	Total off response	No response	On response at distal balloon‡	Off response at proximal balloon‡
11	1	3	12	13	0	0	9
0	31	31	31	31	0	0	3
0	30	30	30	30	0	0	3
11(14.8)	62(83.7)	64(86.4)	73(98.5)	74(100)	0(0)	0(0)	15(20.2)
2	4	8	6	10	0	0	4
2	31	31	33	33	0	0	1
0	28	29	29	28	0	5	4
4(5.6)	63(87.6)	68(94.5)	68(94.5)	71(98.7)	0(0)	5(6.9)	9(12.5)

the abdominal esophagus or if it was passive shortening produced by local contraction of the longitudinal muscle in the thoracic esophagus. Fig. 2 shows representative records of these three responses to balloon distension.

These three responses occurred alone or in various combinations with the majority of stimuli in the distal two-thirds of the esophagus. The distending balloon was never passed into the intra-abdominal esophagus because of artifacts it produced in the recording devices at this level. We saw all these responses in preliminary experiments in four animals. Table I presents appropriate data from three subsequent experiments indicating the relative frequencies of the responses alone and in various combinations.

Distension responses in the isolated whole esophagus. The chief disadvantage of the preparation in vivo was

*of Whole Esophagus In Vitro**

Proximal and distal only	Terminal proximal and distal	Total terminal	Total proximal	Total distal	No response	On response at proximal transducer
proximal lateral transducer						
0	40	46	45	40	0	1
0	14	25	25	14	0	0
0	17	25	18	23	0	10
0	6	20	15	7	0	0
0	15	18	16	17	0	0
0	11	13	11	13	0	0
0(0)	103(70.0)	147(100)	130(88.4)	114(77.5)	0(0)	11(7.5)
and distal lateral transducers						
0	5	27	5	28	0	0
0	11	17	11	17	0	0
0	5	27	5	22	0	4
0	5	12	5	13		0
0	1	11	1	13	0	0
0	4	15	4	11	0	0
0(0)	31(26.5)	109(93.2)	31(26.5)	104(88.9)	0(0)	4(3.4)

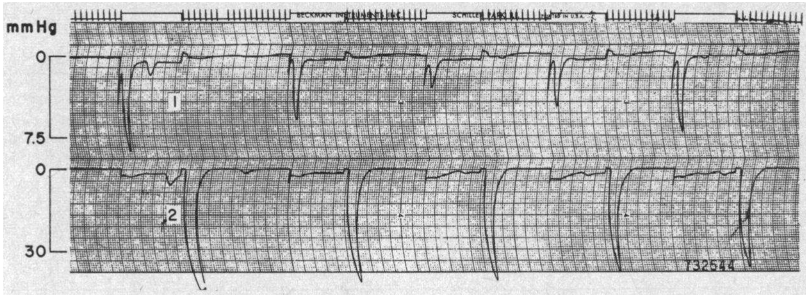

FIGURE 3. Distension responses of the isolated esophagus. The record shows a 5 ml distension 6.5 cm above the gastroesophageal junction, repeated five times. Channel *1* represents intraluminal balloon pressure, in millimeters of mercury above atmospheric pressure, 1 cm about the distension and shows the on response each time. Channel *2* represents intraluminal balloon pressure 5 cm below the point of distension (1 cm above the gastroesophageal junction) and records an off response with each stimulus. Both channels show small artifacts from abrupt inflation and deflation of the stimulating balloon.

our inability to observe directly the spatial correlation of responses. The isolated whole esophagus permitted direct observation. Good responses could be obtained for periods up to 5 hr. As described before, the preparation included only the distal two-thirds, the smooth-muscled part of the organ. In eight experiments using balloon distension we saw responses like those described in vivo, but more details were apparent. The on response occurred as a concentric contraction about 1 cm above the distending balloon. It was usually confined to this location, but it was very rarely seen to move caudad, below the balloon, appearing to have passed over the distending balloon. The duration response involved visible longitudinal contraction over the distending balloon. The length of esophagus involved in this contraction varied but the contracted segment appeared to extend about 1 cm rostral and 2–3 cm caudal to the midpoint of distension. It continued as long as the balloon was distended. The off response began as a localized concentric contraction at or just below the distending balloon and moved rapidly to the distal end of the esophagus. On some occasions it appeared to be nearly simultaneous at all levels below the point of distension. Fig. 3 shows a series of distensions in an isolated whole esophagus preparation. Figure 4 A shows two off responses to distention; the first is simultaneous at two point below the level of distention, the second is propagated. Fig. 4 A shows, in addition, the duration response to distension. Graphic records of the duration response were usually somewhat distorted by the artifact of balloon distension. The duration response could be seen easily, however, so duration responses were tallied by observation rather than from inspection of graphic records (Table II). Table II indicates the incidence of the three responses alone and in various combinations, in three experiments.

Electrical responses of the isolated whole esophagus. Since balloon distension involved a considerable length, about 2 cm, of the organ, we sought a means of more localized stimulation. Preliminary experiments were carried out with various kinds of electrical stimulation. At first we stimulated between a single silver wire applied to the surface and a thin silver rod extending throughout the lumen of the esophagus. Each transmural stimulation produced the same responses as bipolar stimulation; bipolar stimulation was used chiefly because it is technically simpler. Electrical stimulation produced the same kinds of responses as distension. Initiation of the stimulus produced contraction at or just above the point of stimulation, apparently identical with the on response to distension but occurring much less frequently than with distension. The longitudinal muscle about the point of stimulation remained contracted as long as the stimulus train was maintained, a response apparently identical to the duration response to distension. Termination of the stimulus train was followed by a localized concentric contraction beginning at or just below the point of stimulus and moving distally. This was apparently identical to the off response to distension. Since the responses to electrical stimulation appeared to be the same as the responses to distension, we retained the same terms for these responses.

We recorded these responses in six preparations using the apparatus shown in Fig. 1. One transducer (the terminal transducer) registered shortening of the esophagus; two others (the proximal and distal lateral transducers) registered circular contractions at 1 and 4 cm above the distal end of the organ. When stimuli were delivered above the points of attachment of the lateral transducers, a duration response almost always occurred. The off response was usually propagated distally to the end of the esophagus but sometimes went only part of the way. Rarely, it skipped the proximal transducer to show only at the distal transducer. On other occasions it appeared to be simultaneous at all points below the point of stimulation. When stimuli were delivered between the two lateral transducers, the on response, registered by the proximal lateral transducer, was weak and inconstant. An off response sometimes occurred at the levels of both transducers if the stimulus was delivered just below the proximal lateral transducer. Some of the variations in these responses are evident from Table III. Fig. 4 B, C, and D, and Fig. 5 illustrate the duration and off responses obtained in these experiments.

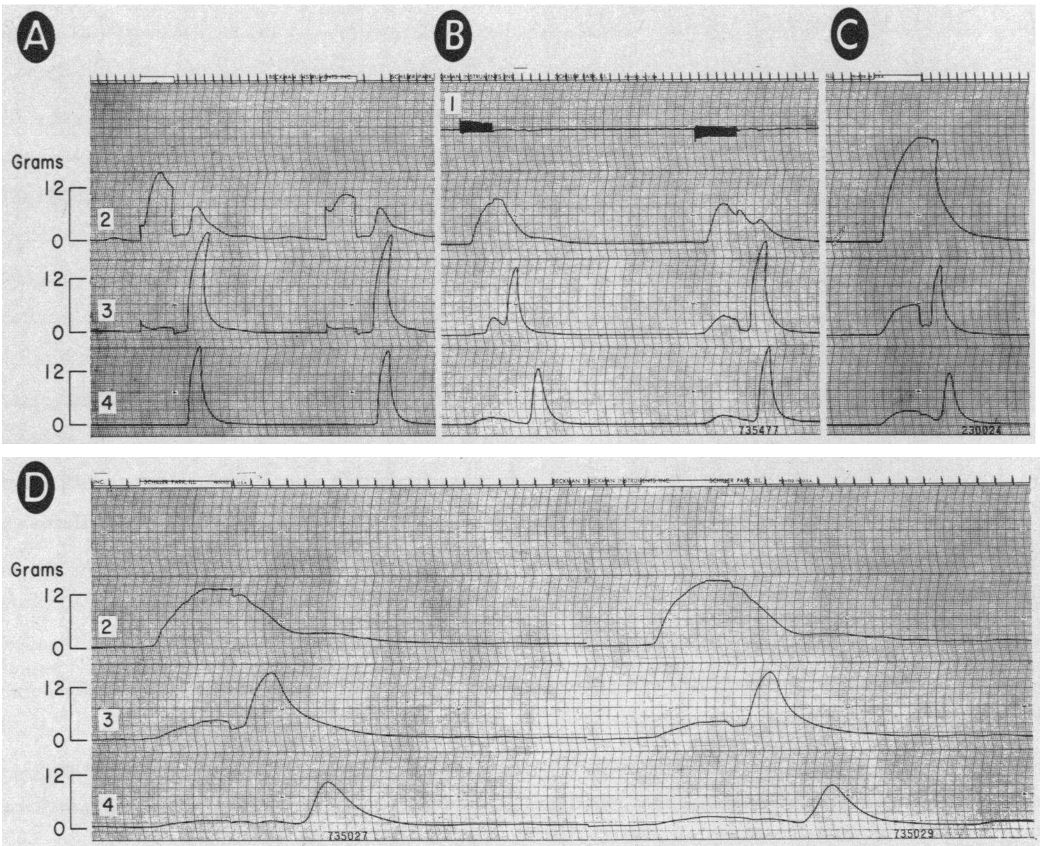

FIGURE 4 Responses of the isolated whole esophagus to distension and electrical stimulation. Scales show grams of tension recorded by force-displacement transducers. In A the esophagus was distended twice with a 5 ml inflation 7 cm above the gastroesophageal junction for the duration indicated on the 1-sec time scale at the top. Channel *2* shows shortening of the esophagus registered by the terminal transducer; channels *3* and *4* represent records from the two lateral transducers 4 cm and 1 cm, respectively, above the gastroesophageal junctions. Sharp deflections in channel *2* represent inflation and deflation of the balloon, but additional rises in tension indicating active shortening of the esophagus are recorded in both cases. The off response to deflation is simultaneous in the first case, peristaltic in the second. In B the esophagus was stimulated transmurally twice 7 cm above the gastroesophageal junction for the duration indicated by the dense spike burst in channel *1*. Channel *1* is a recording of the stimulus from electrodes immersed in one corner of the bath. Channel *2* represents shortening, recorded by the terminal transducer; the lateral transducer records are shown on channels *3* and *4* from 4 cm and 1 cm, respectively, above the gastroesophageal junction. The time scale, at top, shows seconds. In both cases the off response is peristaltic. To some degree, duration and off responses are recorded by both terminal and lateral transducers, but they are easily differentiated by their magnitude. In C and D the esophagus received bipolar stimulation 7 cm above the gastroesophageal junction. The three channels represent the outputs of the three transducers as described above. The interruptions of the time scale at top, showing seconds, represent the duration of the stimulus. The duration and off responses are clearly differentiated and the off response is peristaltic in all three cases.

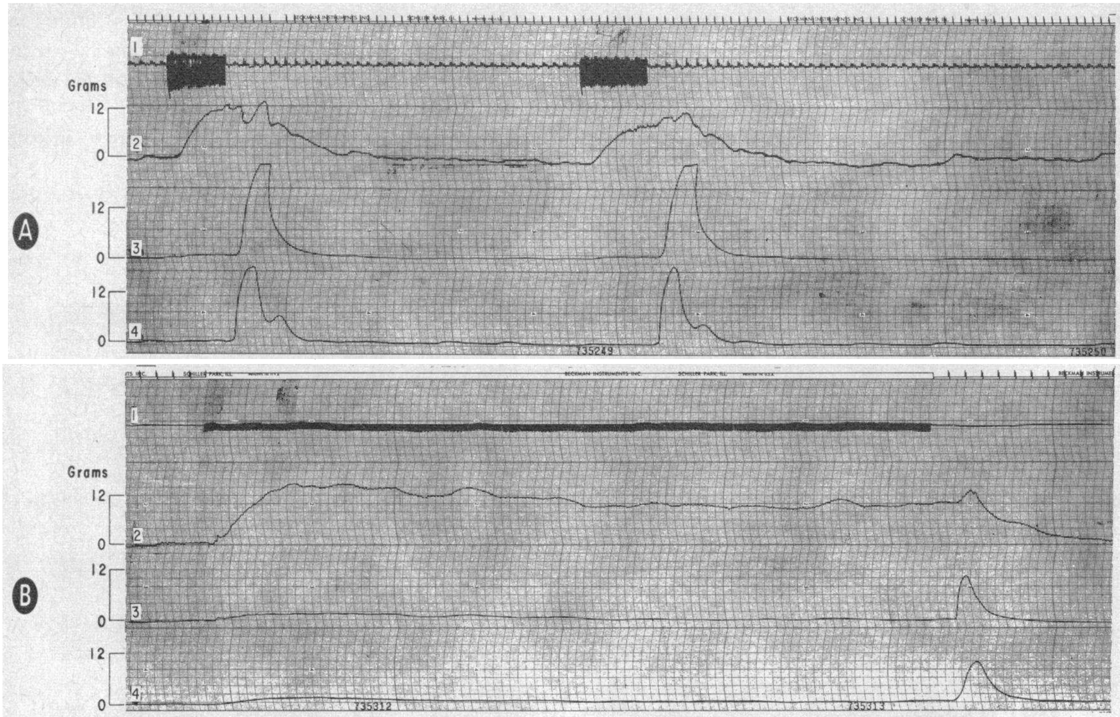

FIGURE 5 Responses to electrical stimulation in the isolated whole esophagus. In A, channel *1* shows the period of stimulation as a dense burst of spikes, recorded from two sensing electrodes immersed in the bath. Channel *2* represents changes in esophageal length as recorded by the terminal force-displacement transducer. Channel *3* represents the output of the proximal lateral force-displacement transducer 4 cm above the caudal end of the esophagus. Channel *4* shows the output of the distal lateral force-displacement transducer 1 cm above the caudal end of the esophagus. Transducer records represent force in grams. In this tracing both transducers show only the off response. In B, a similar record shows the responses to a prolonged stimulus. Stimulation used square waves, 1 msec, 20 cycles/sec, 28 v, delivered 2 cm above the caudal end of the esophagus. The time scale shows 1 sec marks.

Electrical responses of isolated muscle strips. Isolated strips also contracted in response to electrical stimulation. These experiments showed that the three responses could be attributed solely to one or another of the muscle layers. Only the duration response occurred in longitudinal strips of muscularis propria and muscularis mucosae. In transverse strips of the muscularis propria only the on and off responses occurred.

TABLE IV

Classification of Responses of the Three Muscle Layers Examined Separately

	Total No. of strips	No. of strips showing response: On response	Duration response	Off response
Longitudinal strips of *muscularis propria*	8	0	8	0
Transverse strips of *muscularis propria*	12	9	0	12
Longitudinal strips of *muscularis mucosae*	10	0	10	0

Representative tracings are shown in Fig. 6. Table IV indicates the incidence of the three responses in the three layers.

DISCUSSION

Esophageal distension in man excites responses which vary with the character of the stimulus. Transient small distension with a fixed balloon excites secondary peristalsis below the point of distension. The initiating event is usually deflation of the balloon (*7*, 8). Prolonged distension of greater magnitude excites other responses. A force oriented to drive a fixed balloon caudad develops immediately upon inflation, is sustained as long as the balloon is inflated, and may ocur in the absence of contraction in the esophagus above or below the balloon (9). Others (*7*, 8) have described contractions above the balloon after esophageal distension, as well as sustained contraction during inflation at the level of distension. Distension of the opossum esophagus in vivo produces the same general responses as those described in man. There appear to be no qualitative differences

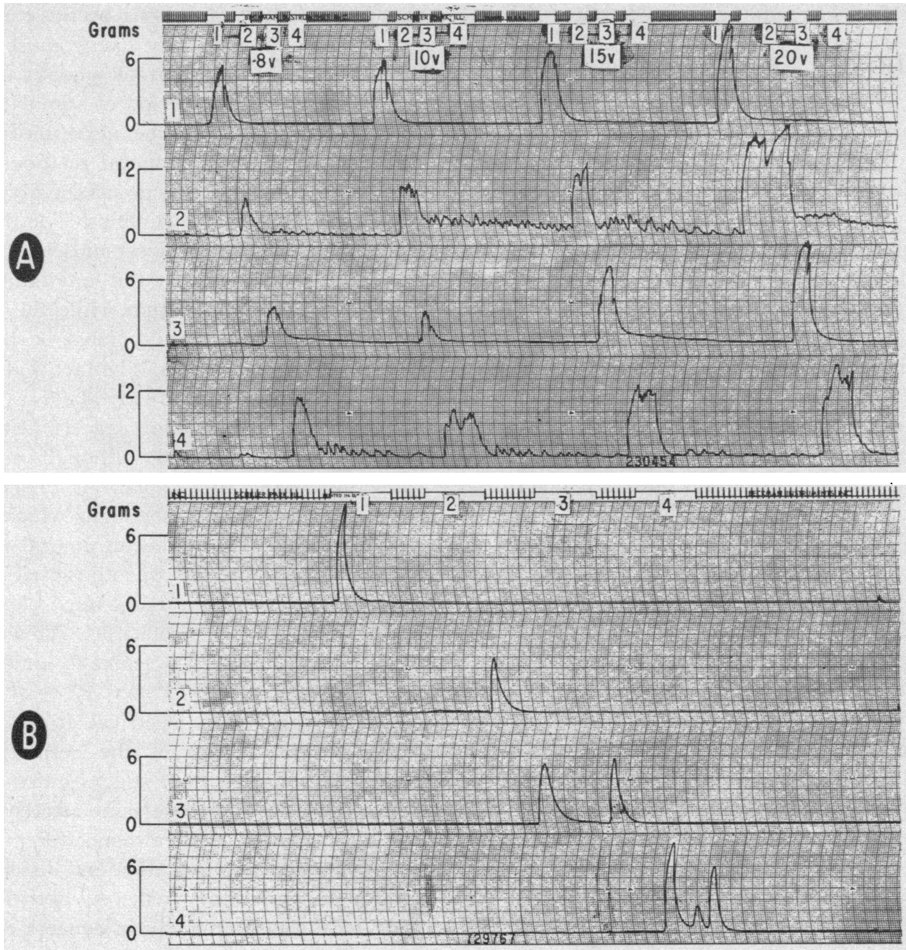

FIGURE 6 Electrical responses of various layers of esophageal muscle, recorded with force-displacement transducers, in grams. The scales are different for the different layers of muscle. In A, channels *1* and *3* represent contraction of longitudinal strips of *muscularis mucosae;* channels *2* and *4* represent longitudinal strips of the *muscularis propria.* The time scale shows stimuli delivered to the strips separately as indicated by the numbers. Stimuli were trains of square waves, 1 msec, 20 cycles/sec, with voltages as shown. All strips show only duration responses. In B all four channels represent contractions of transverse strips of *muscularis propria.* The time scale (top) shows seconds. Interruptions of the time scale indicate stimuli delivered separately to the four strips. Stimuli were trains of square waves, 1 msec, 20 cycles/sec, 35 v. Channel *1* shows an on response, channel *2* an off response, channel *3* both on and off responses, and channel *4* a repeated on response and an off response.

between the human and opossum esophagus in these responses.

Our observations permit a more precise definition of the responses to distension than have human studies. The on response is a transient, sometimes repeated, contraction of circular muscle rostral to the point of stretch, initiated by the act of deformation of the wall. It appears to be the same response as the proximal contractions caused by a distending balloon in the human esophagus. The duration response is a contraction occurring during stretch and confined to longitudinal muscle surrounding but mostly distal to the point of stretch. Since the longitudinal muscle contraction is mostly distal to the point of stimulation, this response tends to draw the point of stimulation caudad, though the actual movement depends upon the relative fixation of the two ends of the esophagus. The temporal characteristics of this response make it seem likely that this is a major component of the "esophageal propulsive force" described by Winship and Zboralske (9). The off response is a propagated peristaltic wave, initiated by balloon deflation or removal of the stretch, beginning below the point of stretch and moving to the end of the esophagus. This seems clearly to be secondary peristalsis as seen in man in similar circumstances (8).

These three responses probably depend upon reflexes initiated by different kinds of mechanoreceptors. There is little information about such receptors in the esophagus. Mei (10) described two kinds of mechanoreceptors in the cat esophagus; "on-off" receptors fire only during active inflation and deflation of an intraluminal balloon, while distension receptors fire continuously as long as the balloon remains inflated. His observations support the hypothesis that the duration response is distinct from the on and off responses.

Mei (10) detected these receptors by recording action potentials from the nodose ganglion during balloon distension of the cat esophagus. This observation suggests that the receptors activate reflex pathways through the central nervous system. Central pathways have also been implicated in peristalsis in the human esophagus, largely as a result of observations on the effects of unilateral and bilateral high vagal section on peristalsis in dogs. Primary peristalsis, resulting from the volitional act of swallowing, may be more dependent upon central control than secondary peristalsis (which results from local esophageal distension); Ingelfinger (2) cites evidence to indicate that the basic mechanisms of both kinds of peristalsis are quite similar. Our ability to induce secondary peristalsis in the isolated esophagus establishes that local reflexes are sufficient to maintain peristalsis, at least in the smooth-muscle segment, though central nervous connections could still have some supporting role.

The requirement of an intact central innervation for secondary peristalsis has been the subject of considerable controversy (2, 12). Siegel and Hendrix (12) concluded that central nervous connections are essential from studies in one dog after healing of a transection and reanastomosis of the proximal esophagus. In this animal transient balloon distention below the point of transection elicited relaxation of the upper sphincter and a transient contraction above the level of transection, just as it had preoperatively. The contraction may not have been peristaltic since it was recorded from only one point above the level of transection. It could represent persistence of local reflexes outside the esophagus in the nerves of the para-esophageal spaces of the mediastinum (11). Or, the dog may respond differently than the opossum and man because the canine esophagus is wholly striated muscle while in the latter species it is mainly smooth muscle.

The similarity of the responses of isolated esophagus to distension and electrical stimulation, is surprising. Electrical stimulation of various smooth muscle preparations may cause contractions by affecting local nervous structures or may directly excite muscle. Responses to direct electrical excitation of smooth muscle would be continuous during the period of stimulation. The on and off responses appear to be nerve-mediated because of their transience, their temporal relationship to the stimulus, and because they occur maximally a short distance away from the point of stimulus. The duration response could be a response to direct muscle stimulation. If so, it must be postulated that the longitudinal layer is susceptible to direct stimulation while the circular layer is not, since stimulus intensity must be the same in both layers in our preparations. The fact that the longitudinal contraction can be seen to extend several centimeters beyond the bipolar electrode suggests instead that the response is nerve-mediated, although muscle cell-to-cell conduction could also explain it. There are abundant nerve structures in the esophagus which could be stimulated. Ganglion cells of the intramural plexuses are distributed throughout the smooth-muscle segment. There are also elements of the esophageal plexus lying on the outer surface of the esophagus. This plexus contains nerve cell bodies which presumably innervate the esophagus (5, 11).

If the responses to electrical stimulation are nerve-mediated, the identity of the responses to electrical stimulation and distension suggests that electrical stimulation excites mainly those same afferents which are excited by distension, rather than efferents. It is probable that both electrical stimulation and distension excite both excitory and inhibitory reflexes. Both kinds of reflexes acting locally and remotely in concert could account for the consistent patterns of responses.

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