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Patterns of Dog Gastrointestinal Contractile Activity Monitored in Vivo with Extraluminal Force Transducers

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PREVIOUS WORK[13, 14] has established that the extraluminal force strain-gauge transducer is a reliable method for assessing contractile activity of gastrointestinal longitudinal and circular muscle separately and simultaneously in vivo. The transducer was modified so that compared to previous models an increased life expectancy and transducer sensitivity was obtained. The present study was concerned with obtaining and analyzing control patterns of dog gastrointestinal (stomach, duodenum, jejunum, ileum, and colon) contractility so as to develop baseline control values for future investigations. Patterns of contractile activity were obtained during the 2 physiological control states—digestive and interdigestive. In-vivo physiologic correlations of simultaneous contractility of various areas of the gastrointestinal tract are presented. Advantages of using the method to study drug action on the gastrointestinal tract are also presented.

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MATERIALS AND METHODS

The principle of the method is unchanged from that described by Jacoby *et al.*,[13] i.e., the measurement of strain in a small metal strip completely enclosed in Silastic and sutured to the wall of the gut. Increased sensitivity was obtained by using 2 miniature etched-foil gauges bonded to the metal strip. The transducer configuration (Fig. 1) was modified from that used previously to approximate better the transverse curvature of the gut and to record more accurately longitudinal axis contractile activity.

Fabrication

Two etched-foil strain gauges (No. EA-09-090DG-120) * were bonded 1 each to the convex and concave surfaces of a cleaned, heat-treated, 2.5% beryllium-copper shim stock with dimensions of 0.2 mm. in thickness, 4 mm. in width, and 6.5 mm. in length (Fig. 1). The bond was accomplished with a thin layer of Tatnall GA-5 epoxy cement using approximately a 1-psi clamping pressure and a 120° F. curing temperature for 1 hr. Lead wires (Teflon insulated, 36 gauge, 7 stranded, 3 conductor) were soldered to the soldering tabs of the 2 gauges using special strain-gauge solder and a fine-tip soldering iron. The transducer was waterproofed by applying several coats of a nitrile rubber

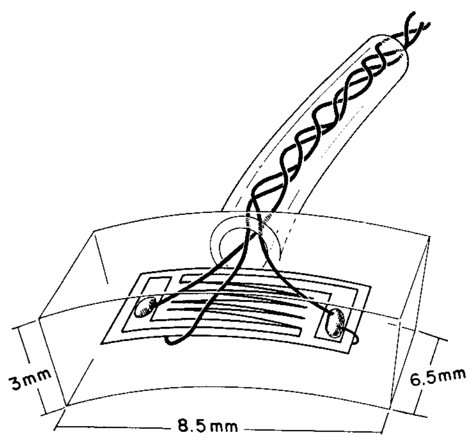

Fig. 1. Extraluminal contractile force transducer. Diagrammatic illustration of transducer and initial portion of lead wire in Silastic tubing. Second strain gauge (not shown) is bonded to concave side of beryllium-copper metal shim stock. Entire exterior surface of unit was medical grade Silastic heat-vulcanized silicone rubber.

solution (Gagekote No. 2).† The free ends of the wire were drawn through a 30-in. length of Silastic silicone rubber tubing, and enough extra wire (6–8 in.) was coiled in the tubing to allow for tubing stretch during periods of animal movement. The silicone rubber tubing was medical grade Silastic,‡ 0.062 in. I.D., 0.125 in. O.D. The metal strip assembly was placed in a mold

*Micro-Measurements, Inc., Romulus, Mich.

†William T. Bean, Inc., Detroit, Mich. Most of the materials in this section were obtained from this company.

‡Dow Corning Corporation, Midland, Mich.

and raw Silastic placed around the assembly. A thin sheet of Dacron mesh was also embedded in the raw Silastic to prevent tearing. Appropriate heat and pressure were applied to the mold to vulcanize the raw Silastic and seal the wire-containing tubing into a 1-piece transducer with the metal assembly.* Transducer working life now has been extended to more than 6 months.

The lead wires were soldered to a Cannon electrical connector and fixed in position with an acrylic-type plastic. A covering of room-temperature vulcanizing Silastic (Dow Corning RTV No. 382) was poured over the Silastic tubing ends and acrylic plastic to waterproof the connector and to fix the position of the Silastic tubing. Up to 8 transducers were placed on a single 25-prong Cannon connector.

Transducer Circuit

A balanced Wheatstone bridge circuit was used in the study. The transducer was connected to the strain-gauge coupler and chopper preamplifier of an ink-writing oscillograph (Dynograph Type R)† Five volts of DC activation voltage were employed.

Transducer Calibration

After completing the electrical circuit to the recorder, the transducer's tubing was fastened to a small supporting rod with tape (Fig. 2). Mersilene 3-0 suture

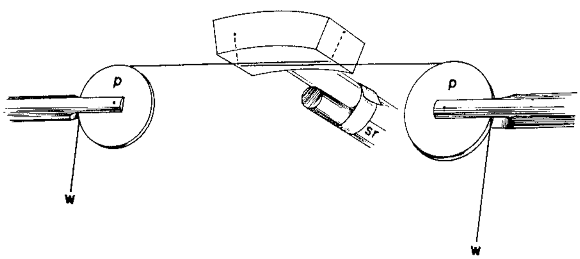

Fig. 2. Calibration procedure. Transducer was stabilized by taping tube to supporting rod (*sr*). A suture was placed at each end of transducer, led over opposite pulley (*p*), and weights (*w*) added simultaneously to each side to determine curve of transducer bending (contraction). Curve for relaxation was then obtained by passing each of 2 sutures over their respective adjacent pulley.

material (Ethicon R-552) was passed through each end of the transducer and led over a small pulley opposite that transducer end. Weights were hung on the free end of the Mersilene and pen deflections obtained. Mean calibration figures for 10 transducers are summarized on the upper line of the calibration chart in Fig. 3. Each transducer was linear in response for the range of con-

*This encapsulation, using medical grade Silastic 372 heat-vulcanized silicone rubber, was performed by the Medical Division, Dow Corning Corporation, Midland, Mich.

†Spinco Division, Beckman Instruments, Lincolnwood, Ill.

tractile forces found in dog gastrointestinal extrinsic musculature. Determination of the percentage bending and later correlation with observed maximum amplitudes show recordings to be principally isometric, i.e., less than 10% bending at maximum force development.

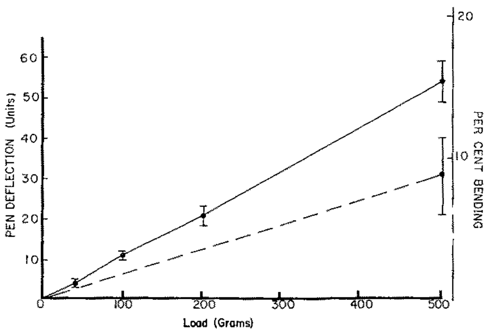

Fig. 3. Calibration curves for transducers. Upper calibration line (solid line) for pen deflection simulating contraction. Each point represents mean ± S.E. of different transducers (n = 10). Each transducer was linear. Abscissa represents sum of weights added, i.e., 200 gm. indicates 100 gm. added to each side of transducer (Fig. 2). Lower dashed line for percentage bending (see text).

Experimental Design

Following calibration, the transducers and tubing were cleaned with a warm-water solution of Ivory Flakes, rinsed thoroughly in warm water, and immersed for at least 12 hr. in benzalkonium chloride solution (1:750), then rinsed and immersed in sterile water (several changes) for 24 hr. to remove any benzalkonium chloride retained in the Silastic. Strain gauges and cements are now available for construction of transducers that can be autoclaved. Healthy mongrel dogs of either sex were anesthetized with 30 mg./kg. of sodium pentobarbital intravenously. Under sterile operating conditions, a 1-in. incision was made in the left flank, about 1 in. below the thirteenth rib. A similar incision was made at the cephalic border of the mid-scapula area. A 0.75-in. diameter stainless steel trocar was passed subcutaneously from the scapular to the flank skin incisions. The transducers were threaded through the trocar. The trocar was withdrawn from the flank incision leaving the tubing subcutaneous. A 6-in. midline incision was made, and the transducers and tubing were brought through the abdominal wall into the abdominal cavity at the point of the left-flank incision. The transducers were sutured to gut wall in the manner shown in Fig. 4. When circular muscle was to be monitored, the transducer was oriented in the transverse axis on the bowel with the 3-0 Mersilene sutures. When the longitudinal muscle was to be monitored, 3-0 Mersilene suture was placed in each corner of the transducer, which then was oriented in the longitudinal axis on the bowel and shallow, barely snug ties were used to fix the 4 corners of the transducer to the bowel. Midline closure was accomplished by peritoneal, subcutaneous, and subcuticular suture lines. The dog was fitted with a harness that had a protective metal housing. The plug end of the transducer assembly was bolted firmly to this metal housing. An animal sensor plug* has been successfully used to replace this harness arrangement.

A rubber mat was provided for the dog to lie on and once trained, the dog lay quietly on the mat for many hours. Colon studies were done in a small room equipped with a 1-way window simulating cage conditions (wood shavings on floor, water ad libitum, and companion dogs). Contractile activity was studied during the fasted (interdigestive) and the fed (digestive) states. Following at least a 20-hr. fast, recording sessions lasted 4 hr., usually 2 hr. before feeding and 2 hr. after feeding. In certain experiments, recording sessions persisted for 6–12 hr. after feeding. Effects of drug injection were recorded for 2–4 hr.

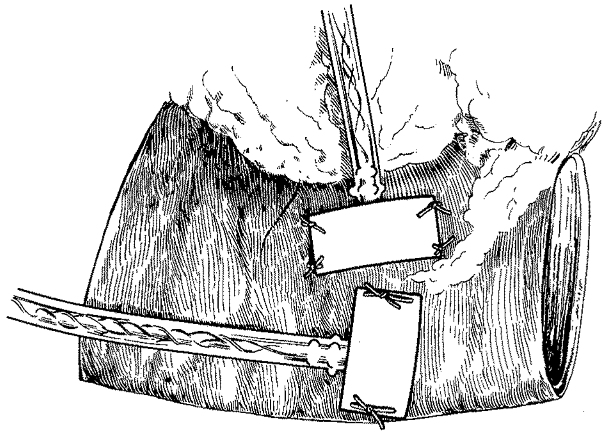

Fig. 4. T configuration of 2 transducers for measurement of longitudinal and circular muscle contractile activity of same level of bowel. Circular muscle transducer was sutured with 2 deep sutures, longitudinal muscle transducer with 4 shallow sutures.

Respiration can be monitored by a transducer sutured to the peritoneal side of the left hemidiaphragm at the time of bowel transducer implantation. In several animals a duodenal and/or gastric vitallium cannula† was inserted.

Small-intestine contractile activity always preceded the return of gastric contractile activity following surgical implantation of the transducers. Seven to ten days postoperation contractile activity was reproducible from day to day.

RESULTS

Control Contractile Activity Patterns of Small Intestine and Stomach

The 3 general patterns of gastrointestinal contractile activity, as recorded and described by Jacoby *et al.*[13] for the duodenum, namely, basal, burst, and intermediate, were observed in this study. Basal activity consisted of low-amplitude contractions (less than 10% of the segment maximum monitored

*Model No. 8500, Biometrics Inc., Plano, Tex.

†Austenal Co., New York, N. Y.

in a particular animal) with no prominent tonal changes (Fig. 5). Burst activity interrupting the basal pattern consisted of grouped high-amplitude contractions (25–100% of the segment maximum) that were usually superimposed on tone increases (Fig. 5). As noted by Jacoby[14] episodes of duodenal burst activity among dogs have a variable duration. Duration of episodes ranged from 30 sec. to 15 min. for all areas of the stomach and small intestine. The third contractile activity pattern, intermediate activity, consisted of varying-amplitude ungrouped contractions (10–100% of the segment maximum), often superimposed on low-amplitude tone changes. These patterns were recorded whether transducers were placed singly or in pairs forming a T (Fig. 4).

Small Intestine

The 3 patterns of contractile activity were recorded from the jejunum and ileum as well as the duodenum. Figure 6 illustrates ileal contractile activity monitored by 2 pairs of transducers 15 and 10 cm. from the ileocolic junction. Basal and burst patterns were recorded in the interdigestive state. The intermediate pattern of the digestive state was not recorded from the ileal transducers for some time after feeding. The onset of intermediate pattern activity in any segment of the small intestine beyond the duodenum likely paralleled the time when chyme reached the segment.

Stomach

The same 3 general patterns of contractile activities recorded from the small intestine were also recorded from areas of the stomach. Minor differences exist

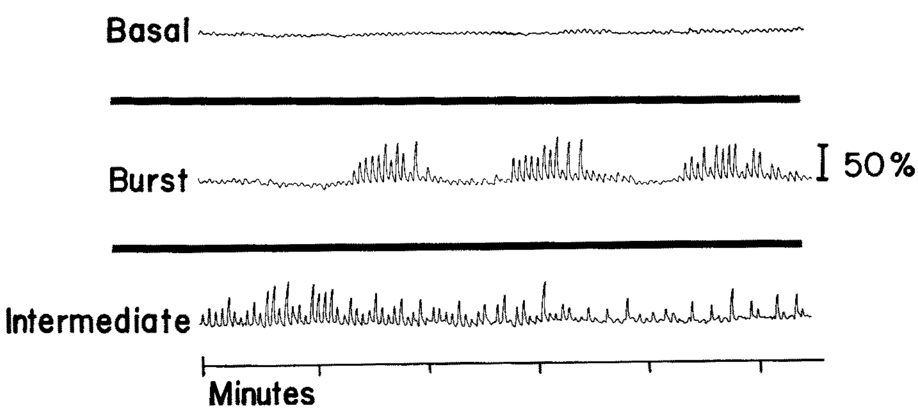

Fig. 5. Duodenal contractile activity patterns (transverse axis). Examples of 3 major patterns of contractile activity monitored from circular muscle of small intestine of dogs. Transducer position was 5 cm. distal to pylorus. Basal and burst patterns obtained from dog fasted 20 hr. Intermediate pattern obtained from same dog 10 min. after feeding canned dog food. Fifty per cent represents percentage of maximum contractile force recorded for recording life of animal.

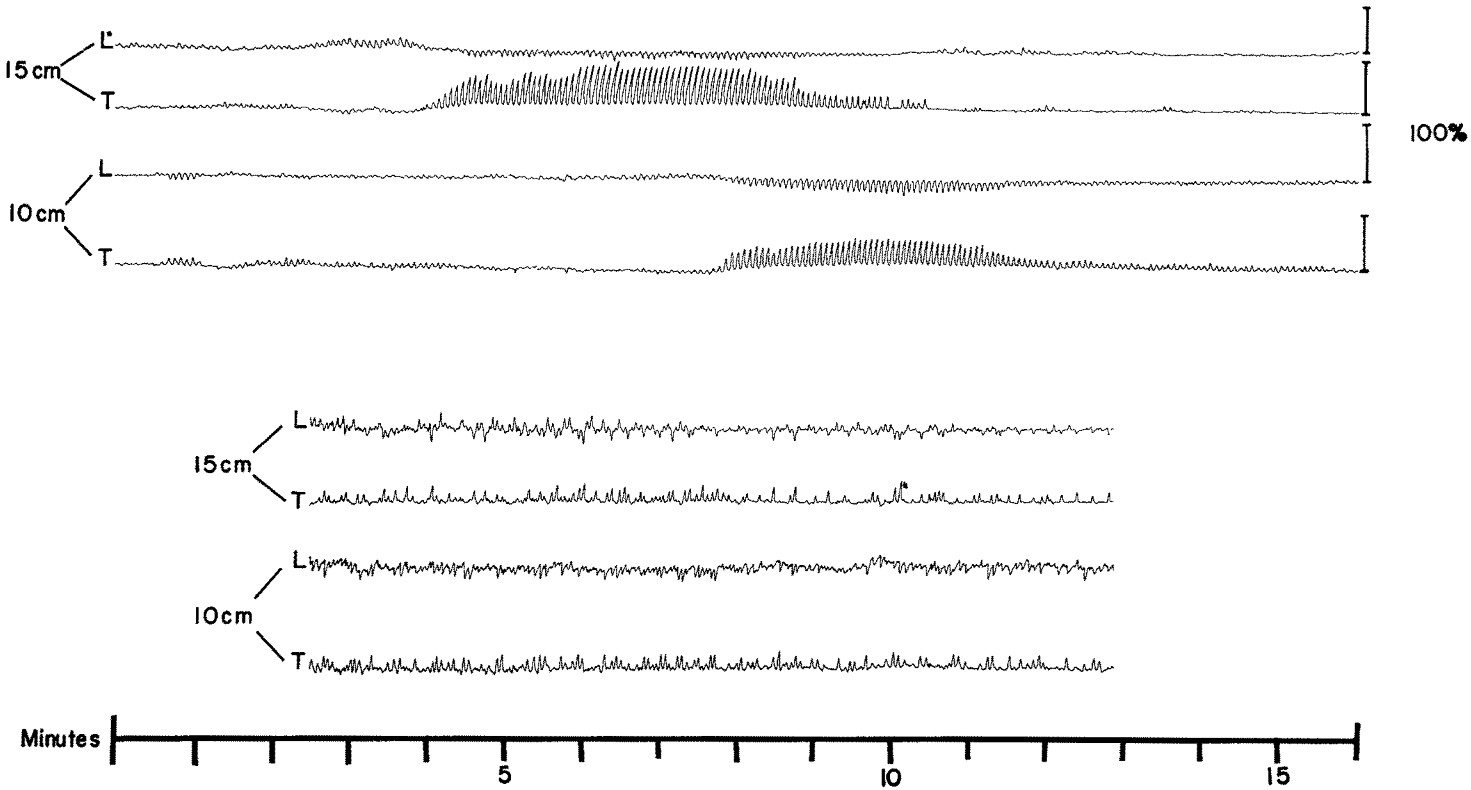

Fig. 6. Ileal contractile activity patterns. Examples of 3 major patterns of contractile activity obtained from circular and longitudinal muscle layers of small intestine of dogs. Two pairs of transducers on ileum (each pair in T configuration (Fig. 4)) 10 and 15 cm. proximal to ileocolic junction. Fasted state record (at top) monitored after 20-hr. food fast. Fed state record (at bottom) obtained from same animal, 4 hr. after meal of canned dog food. One hundred per cent represents maximum contractile force attained for each lead in recording life of animal. T indicates transverse axis; L, longitudinal axis.

in that (1) the number of grouped high-amplitude contractions in a single gastric burst was small compared to the small intestine; and (2) intermediate activity of the gastric body in both axes is characterized by steadily recurring contractions of rather constant amplitude (Fig. 7) compared to the ungrouped

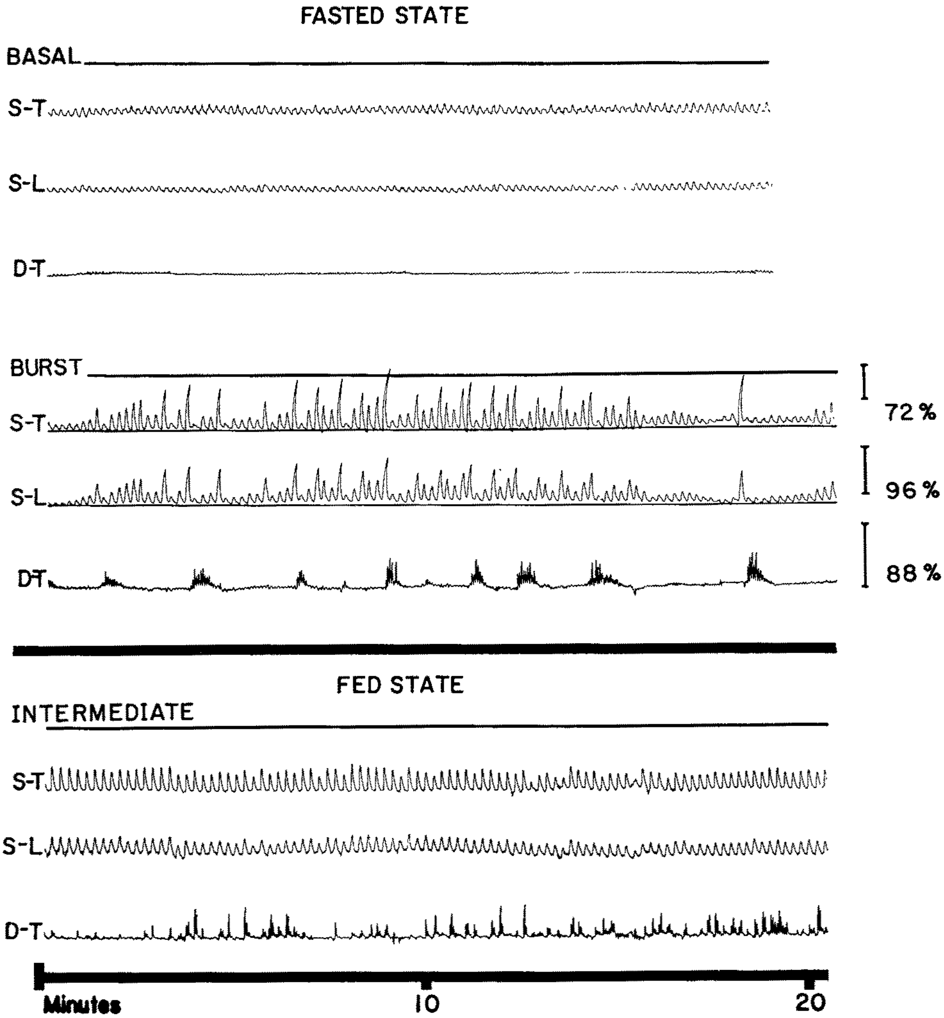

Fig. 7. Gastric contractile activity patterns. Examples of 3 major patterns of contractile activity obtained from circular (*S-T*) and longitudinal (*S-L*) muscle layers of dog gastric body. Simultaneous recording of duodenal circular (*D-T*) muscle layer (5 cm. distal to pylorus) from same dog included for comparison. Burst and basal patterns obtained after 20-hr. food fast. Intermediate pattern monitored in same dog 30 min. after feeding canned dog food. Calibration bars represent percentage maximum contractile force recorded for each lead for recording life of animal.

varying-amplitude contractions of the gastric antrum and small intestine (Fig. 13). To preserve simplicity, however, the same nomenclature was assigned to all patterns from the stomach and small intestine.

Burst Activity Pattern of Stomach and Small Intestine

During the interdigestive (fasted) state the predominant basal activity was interrupted by burst activity. Burst activity distribution varied among dogs but was reproducible in each dog from day to day. Total burst time per 2-hr. period, however, was essentially the same among dogs. For example, an animal that grouped burst activity in 1 continuous 20-min. episode with 100 min. between burst episodes showed this type pattern during the fasted state recording day after day. Another animal spaced 20 episodes of burst activity, each of about 1-min. duration, among basal periods lasting about 5 min. and did so every day.

It was observed that when gastric and duodenal burst activity was monitored along with the collection of secretions from a duodenal cannula, coordinated burst activity in both areas coincided with the expulsion of mucinous secretions from the duodenal cannula.

It is well known that an increase in gastric motility usually leads to an increase in duodenal motility. Recording with extraluminal contractile force transducers clearly shows that although gastric-burst contractile activity precedes duodenal-burst contractile activity, the strength and number of gastric contractions do not solely determine the degree of induced contractile activity in the duodenum (Fig. 8 and 12). The temporary reflex inhibition of existing duodenal contractile activity by gastric antral contractile activity is also seen in Fig. 8.

A typical intestinal burst is presented in Fig. 9 to show the correlation of contractile activities of muscle layers at the same level of bowel. The sequence of events occurring during the burst is: (1) initially contractile amplitude and tone begin to increase in longitudinal muscle. (2) The tone of circular muscle decreases without alteration of contractile amplitude. (3) Tone and contractile amplitude suddenly increase in circular muscle, while tone decreases in longitudinal muscle simultaneously. (4) As circular muscle tone and contractility gradually decrease, longitudinal muscle tone and contractility also gradually return to preburst condition (basal state).

Intermediate Activity Pattern of Stomach and Small Intestine

Intermediate activity was the predominant type of contractile activity during the digestive (fed) state. This pattern sometimes occurred in the interdigestive state for a brief period prior to a burst. On feeding a can of dog food (Pard),* at least 3 events occurred (Fig. 13): first, burst activity rapidly ceased

*Swift and Co., Chicago, Ill.

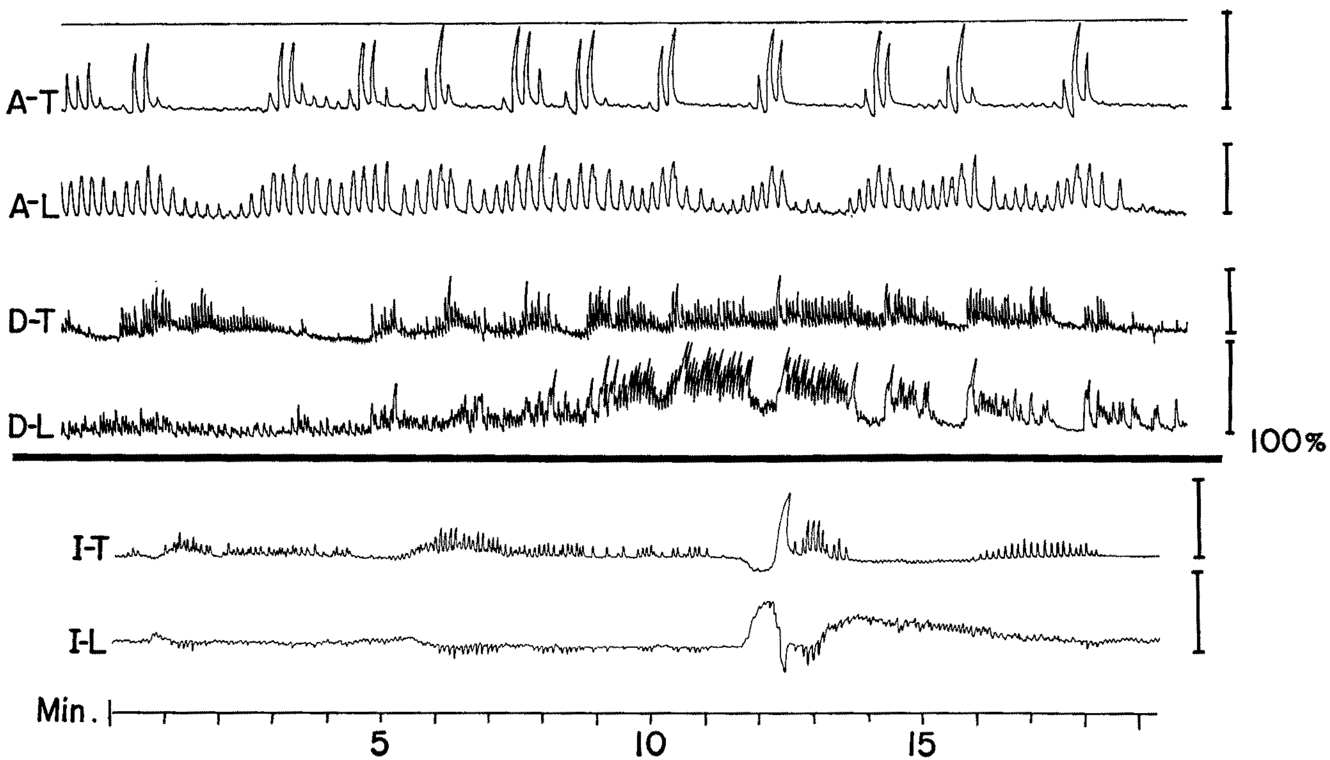

Fig. 8. Composite multiple-segment recording-burst pattern, for gastric antrum (*A*), duodenum (*D*), and ileum (*I*), in fasted state. Upper part of figure shows simultaneous recording of burst patterns from circular (*A-T*) and longitudinal (*A-L*) muscle layers of dog gastric antrum (3 cm. from pylorus) and duodenum (*D-T* and *D-L* respectively) 5 cm. from pylorus. Lower part of figure shows ileal burst patterns and a P wave at the 12–13-min. period obtained from same animal. All records from same dog fasted at least 16 hr., but upper and lower records obtained at different times. One hundred per cent represents maximum contractile force attained for each lead in recording life of animal.

in the stomach and duodenum; second, intermediate pattern activity began and persisted in the stomach and duodenum for 3–8 hr.; third, lower small-intestine contractile activity represented by terminal ileum in Fig. 6 remained similar to that recorded in the fasted state for some time, presumably until chyme entered it. Increased ileal contractile activity that occurred immediately after feeding, i.e., gastroileal reflex, persisted for only a few minutes before reverting to the fasted-state pattern.

A fourth type of contractile activity, the P wave, previously recorded by others[1, 10] occasionally interrupted burst activity in the ileum. The P wave was of maximum amplitude and was of long duration (Fig. 8). It was usually observed from 2 to 4 times during a continuous 12-hr. recording during the day. P waves most commonly occurred in the ileum following defecation.

There was no statistically significant difference among 3 areas of the tract used for this comparison (Table 1) regarding the amounts of time spent in the 3 contractile patterns during the fasted-state recordings. However, the differences between the amounts of time spent in the 3 patterns as measured pre- and postfeeding were all statistically significant in a paired comparison ($p < 0.01$).

Control Colonic Contractile Activity

Colonic contractile activity did not lend itself to being classified using the basal, burst, and intermediate nomenclature (Fig. 10). Tonal changes with and without rhythmic contractions of varying amplitude occurred. Periods of almost absolute quiet occurred in contrast to the basal activity of small intestine and stomach. The percentage of time the colon was observed to be

TABLE 1. TIME DISTRIBUTION OF CONTRACTILE ACTIVITY PATTERNS DURING FASTED AND FED CONTROL STATES

Site	No. dogs	Contractile pattern	*Fasted state** Minutes†	±SE	*Fed state‡* Minutes†	±SE
Stomach	8	Burst	12	±2.4	0	
		Basal	32	±4.4	7	±2.5
		Intermediate	16	±4.7	53	±2.5
Duodenum	8	Burst	11	±1.7	1	±0.4
		Basal	40	±2.5	9	±2.8
		Intermediate	9	±2.2	50	±2.7
Ileum	5	Burst	10	±1.6	7	±1.7
		Basal	39	±5.1	16	±5.0
		Intermediate	11	±3.6	37	±6.4

All dogs 14 days postoperative; all patterns of contractile activity in the fed state are statistically significantly different from the fasted state in each organ by paired comparison ($p < 0.01$).

*Fasted: 2-hr. recording after fast of 20–24 hr. Water ad libitum during fast.

†Minutes of pattern per hour.

‡Fed: 2-hr. recording immediately following Pard canned dog food (150–450 gm.).

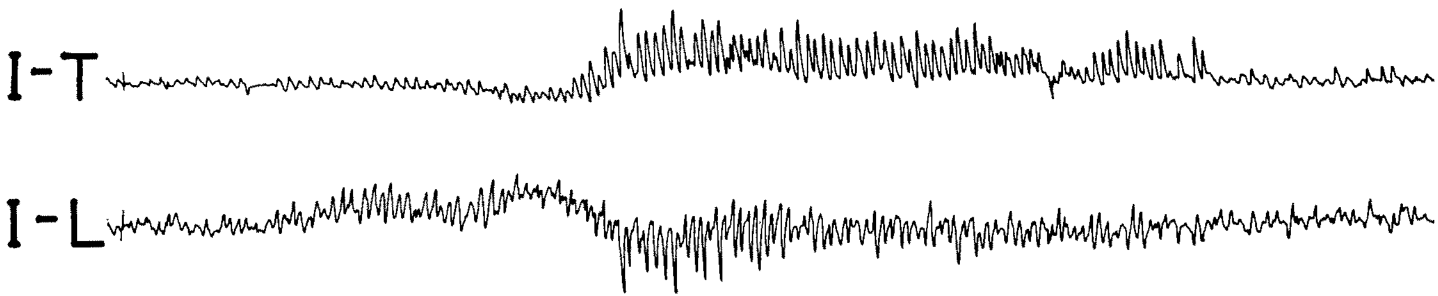

Fig. 9. Ileal burst pattern. One transducer (*I-T*) positioned to measure circular muscle activity; another (*I-L*) positioned to measure longitudinal muscle activity simultaneously and separately (T configuration) at same level of ileum.

inactive was similar to the percentage of time basal activity occurred in the remainder of the gastrointestinal tract. Feeding and defecation were both responsible for increased colonic contractility. The gastrocolic reflex was evident after feeding. In many cases this was often followed by defecation (Fig. 11). The P wave of the ileum was similar in duration and amplitude to those contractions of the descending colon noted during defecation. Following defecation, an increase in contractile activity occurred in all parts of the colon and persisted for several hours. Defecation without prior feeding was also followed by an increase in colonic contractile activity.

Drug Modification of Contractile Activity Patterns

Marked differences in contractile activity of several areas of the tract were obtained by using small doses of broadly classified GI smooth-muscle stimulant and depressant drugs. Prior to drug administration, the standard control patterns for the fasted (interdigestive) and fed (digestive) states were established over a period of at least 2 weeks. The control patterns for 1 such dog, used as an example here, are shown in Fig. 12 and 13. It is emphasized that identical drug-induced changes by each of the following drugs has been observed in at least 6 other dogs. As anticipated, paired rather than group comparison statistical analysis was best for the demonstration of subtle changes.

Histamine

The results of histamine administration to the animal whose control records are shown in Fig. 12 and 13 are shown in Fig. 14. The dose of histamine phosphate used (40 μg./kg. as the base, given subcutaneously) is the diagnostic dose for determining achlorhydria in man and the dose for maximally stimulating gastric acid secretion in the dog. Following a brief initial stimulation of the gastric body, note the conversion of the fasted (interdigestive) contractile activity to the "fed" (digestive) state pattern in all areas. In a dog with an implanted gastric cannula in place and given the same dose, 64 ml. of secretions was collected as opposed to a normal 5–16-ml. collection for a comparable period of time. Continuous collection of this histamine-induced secretion by aspiration ($<$ 10 mm. Hg) at another time in the same dog prevented the conversion to the fed (digestive) pattern.

5-Hydroxytryptophan

The marked initial increase in tone of the gastric body, but not gastric antrum, was seen not only with histamine but also with the administration of 5-hydroxytryptophan (Fig. 15). 5-Hydroxytryptophan (20 mg./kg.), unlike histamine, however, provoked strong continuous contractions of the antrum and duodenum for a period lasting 4 hr. A dose of 2 mg./kg., intravenously, increased contractile activity about 30 min.

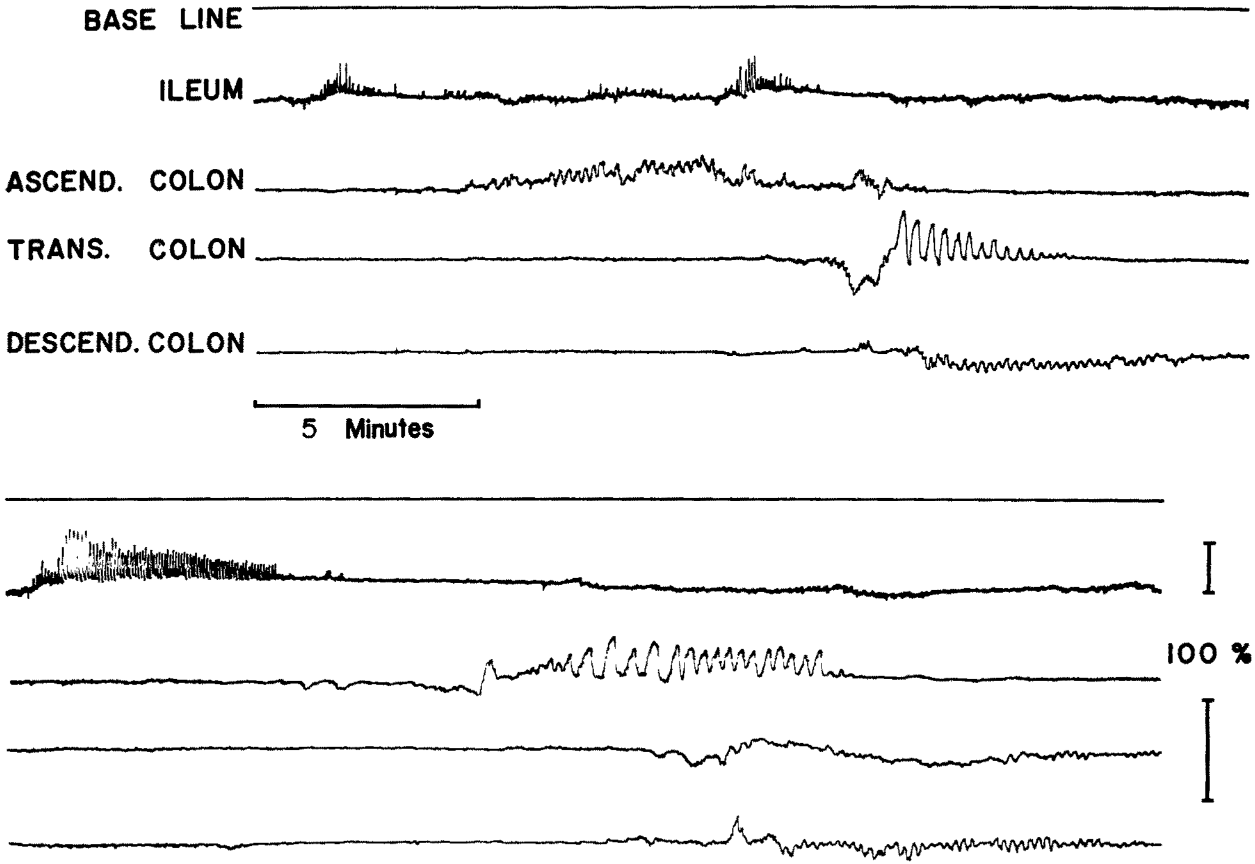

Fig. 10. Ileal and colonic circular muscle contractility, transverse axis. Animal fasted 24 hr. with water ad libitum during fast. Upper and lower records are continuous. One hundred per cent represents maximum contractile force recorded for each lead during recording life of animal.

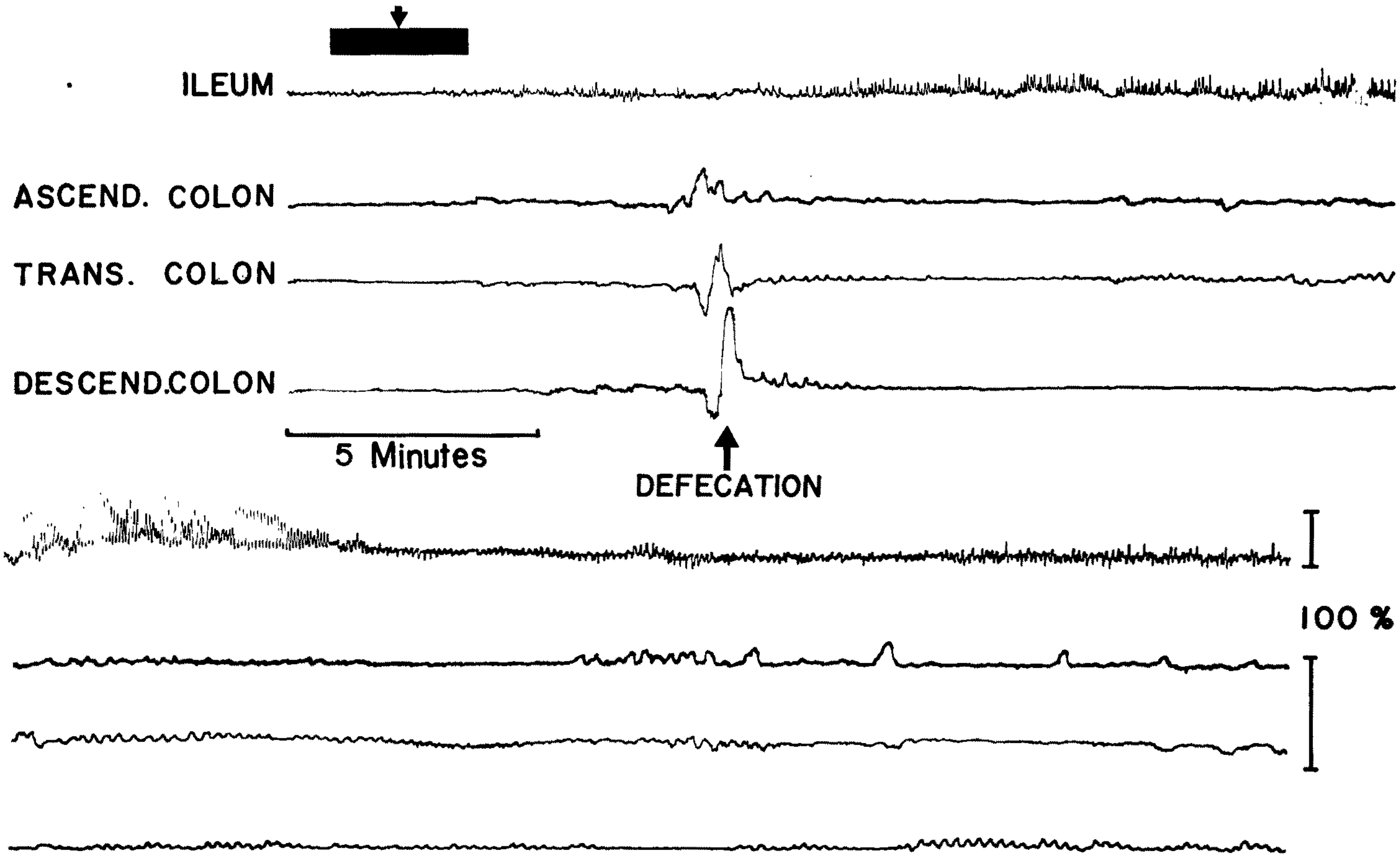

Fig. 11. Ileal and colonic circular muscle contractility. Animal had been fasted 24 hr. with water ad libitum during fast. Dog placed in 1-way observation pen on wood shavings. Animal ate 450 gm. of canned dog food in 2 min. (at arrow, top). Approximately 6 min. later, defecation occurred. Upper and lower records are continuous. Gradual and moderate increase in colonic contractility following defecation persisted for 3 hr. One hundred per cent represents maximum contractile force recorded for each lead during recording life of animal.

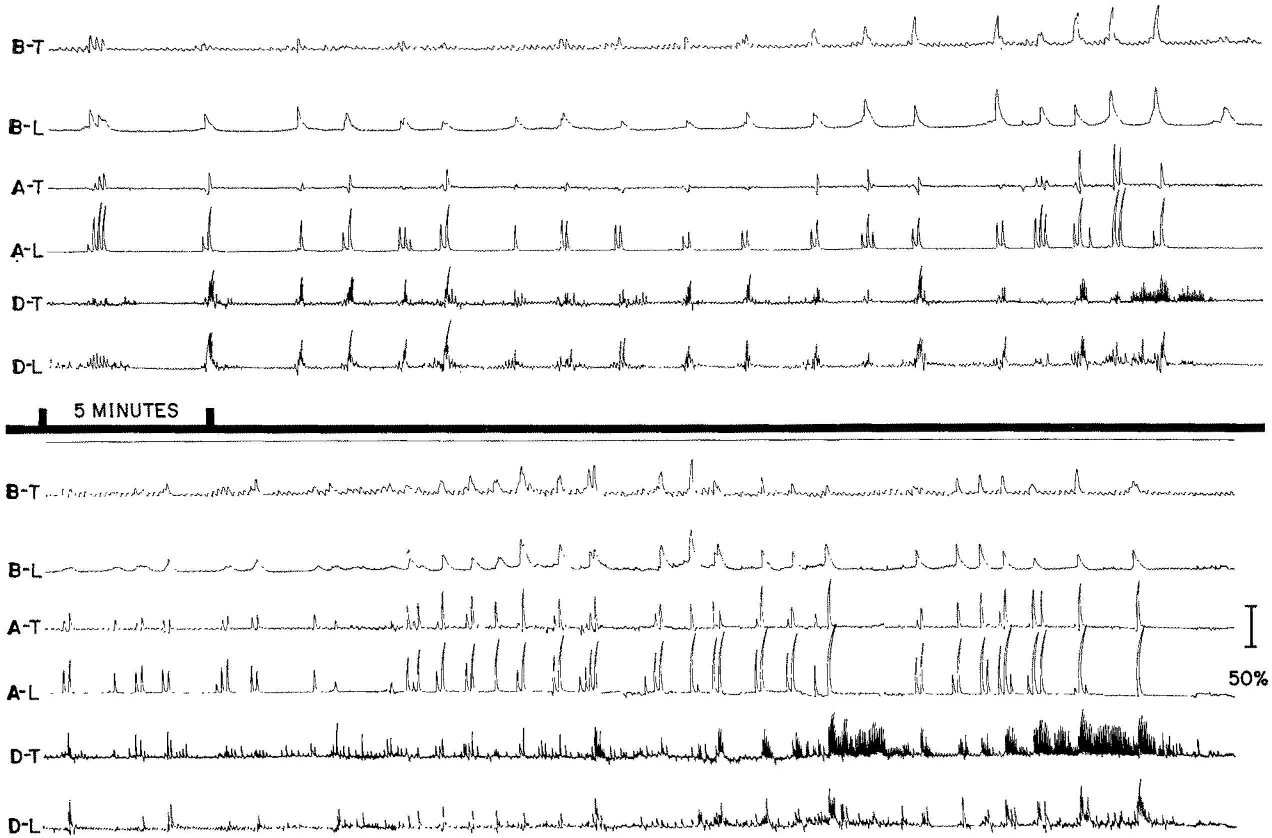

Fig. 12. Multiple-segment fasted-state contractile activity. Continuous and simultaneous recording of contractile activity of gastric body (*B-T* and *B-L*) with transducers located 15 cm. from pylorus, gastric antrum (*A-T* and *A-L*) with transducers located 3 cm. from pylorus, and duodenum (*D-T* and *D-L*) with transducers located 4 cm. from pylorus. All records taken 1 month postoperative. Fasted at least 18 hr., with water ad libitum during fast in all cases prior to recording. Fifty per cent refers to percentage of maximum contractile force recorded for all leads during recording life of animal.

Neostigmine

Neostigmine methylsulfate in a dose equivalent to that used in man for the treatment of adynamic ileus (15 μg./kg., as the salt, given subcutaneously) provoked the stimulation shown in Fig. 16 and 17. Longitudinal muscle layers were more sensitive to the drug than were circular muscle layers. Emesis appeared to be initiated after a profound tone change of the duodenum, just succeeding the point where licking (a presumed sign of nausea in the dog) was observed. Note that the gastric body was inactive during retching and emesis. A strong, maintained contraction of both muscle layers of the duodenum preceded strong gastric antral contractions prior to emesis.

Morphine

The effect of morphine sulfate (200 μg./kg., as the salt, given subcutaneously) on contractile activity during the interdigestive state is illustrated in Fig. 18. Note the continued stimulation of the duodenal circular muscle layer. On the other hand, note that duodenal longitudinal muscle was only briefly stimulated initially and then only during a time when the gastric antrum was stimulated. A prolonged depressant effect on contractility by morphine was observed for the next 4 hr. in all areas, including duodenal circular muscle.

Hexamethonium

Gastrointestinal circular and longitudinal muscle at the same level of the bowel were normally active at the same time. Morphine was not the only drug capable of interfering with the integrated activity. Figure 19 illustrates that hexamethonium bromide (100 μg./kg., intravenously) also led to burst activity in duodenal circular muscle but had no corresponding effect on duodenal longitudinal muscle. Note the profound depressant effect that followed in all leads. This drug, like atropine, was capable of abolishing basal activity in the small intestine.

DISCUSSION

Initially Jacoby,[14] using extraluminal contractile force transducers, determined the time distribution of the 3 major patterns of contractile activity in the fasted state for the dog duodenum. He noted that in 4 animals the burst, basal, and intermediate patterns per hour occupied an average of 9, 38, and 13 min. respectively. In the present study, with 8 dogs, we obtained 11, 40, and 9 min. respectively as the means for these same 3 patterns. During the fed state Jacoby found the same patterns in the duodenum occupied an average of 1, 15, and 44 min. per recorded hour, while in the present study, these mean values were 1, 9, and 50 min. This excellent agreement for both control states indicates that although there have been modifications of the geometry of the extraluminal transducer, the basic nature of the contractile patterns are unchanged.

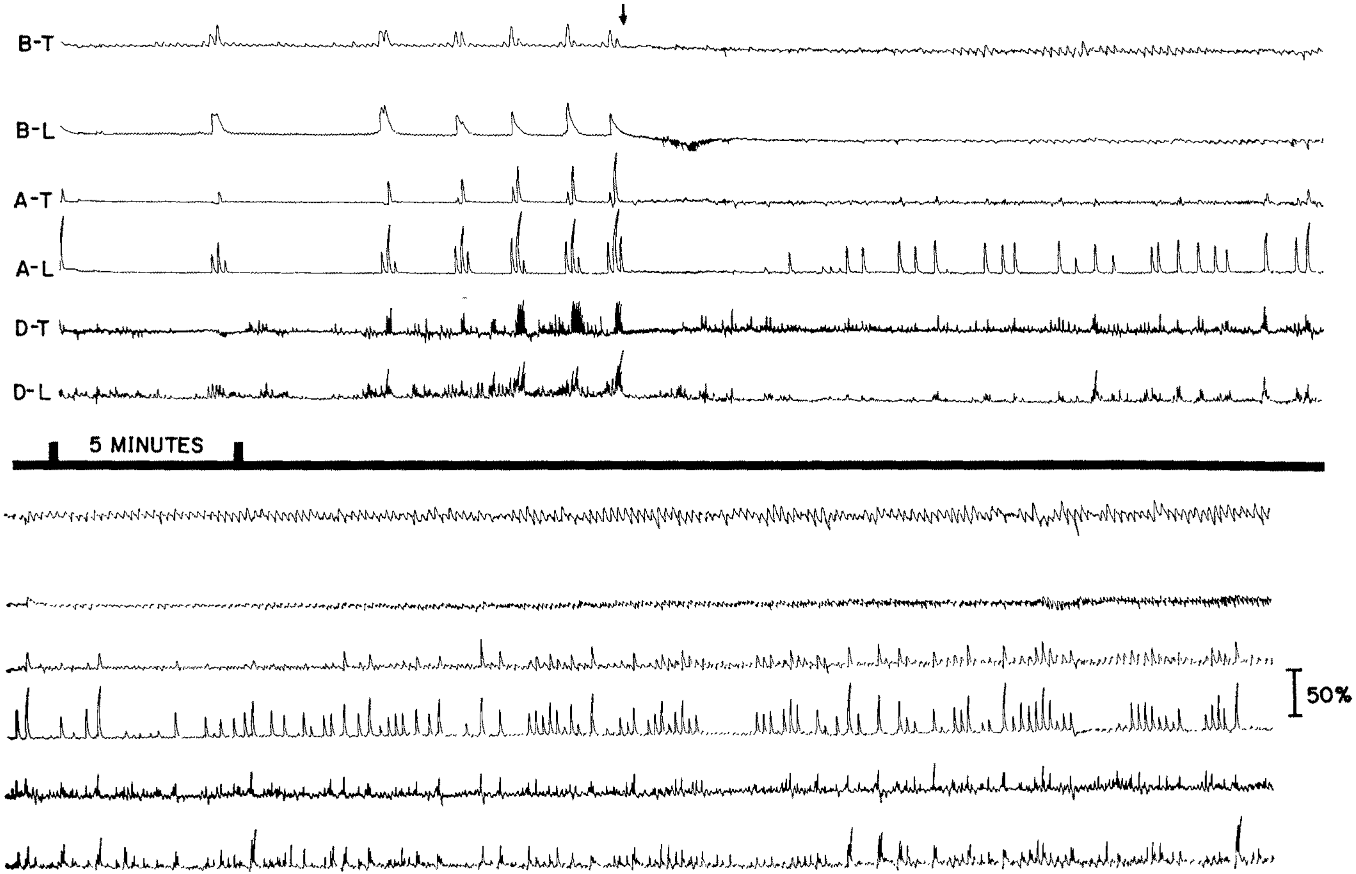

Fig. 13. Food-induced contractile activity. Recording from same animal as recorded for Fig. 12. Dog ate 200 gm. of canned dog food 2 min. after arrow. *B* indicates gastric body; *A*, antrum; *D*, duodenum; *T*, transverse axis; *L*, longitudinal axis.

Earlier investigators[1, 4, 7, 11] have studied small intestinal motility in unanesthetized dogs with exteriorized loops of intestine and have obtained results qualitatively similar to those obtained in this study, i.e., their fasted-state recordings consisted of quiesence interrupted by periods of increased motor activity at irregular intervals; feeding also increased motor activity. We note, however, that the patterns of this increased contractile activity in both fasted and fed states are different. Basal and burst patterns were characteristic of the fasted state while intermediate pattern was characteristic of the fed state.

The 3 major contractility patterns obtained by extraluminal force transducers were compared with intraluminal pressure patterns obtained by others. This is difficult, for not only has methodology changed in the latter area (large balloon, small balloon, open-tip) but also the nomenclature assigned to the results thereof is still in a state of flux.[8] In general, basal, intermediate, and burst contractility patterns correspond to Types I, II, and III pressure patterns.[6] The P wave in ileum and colon likely represents a Type IV pressure change. Friedman *et al.*[9] in a recent study have correlated cinefluoroscopic and intraluminal pressure changes. Despite the variations in amplitude and duration of contraction wave forms observed, they emphasize the presence of only 2 functions, mixing and propulsion. Thus, a more important correlation, i.e., function and contractile patterns, must wait until cinefluoroscopy can be used in the same animal simultaneously with extraluminal force transducers.

The basal pattern of activity predominated throughout the fasted-state recording of the stomach and small intestine. It is tempting to speculate that this pattern may be associated with the motility necessary to regulate blood flow to the resting gut or to aid in interdigestive secretory functions. However, it is also possible that this activity may have no function and may merely represent minimal contractile activity at a frequency characteristic of unitary smooth-muscle low-intensity pacemaker discharge in vivo.

Analysis of contractile activity patterns obtained in this study has reemphasized 1 principle, i.e., each animal can and should serve as his own control whenever possible. Each fasted animal had its own characteristic arrangement of burst pattern activity in an adequate (2–4-hr.) control period. The day-to-day consistency of this arrangement was striking. Boldireff[2] found that alkaline mucus was discharged from the dog stomach with periodic contractile activity. Our experiments with dogs with implanted cannulas revealed that gastric burst activity occurred just prior to, or coincided with, the expulsion of viscous fluids from the duodenal cannula. Those differences among animals with regard to burst pattern arrangement may then be related to individual differences in periodic interdigestive gastric secretory activity.

The fact that interdigestive secretions are viscous may account for the extent to which the gut contracts to accomplish this emptying. Hoelzel[12] made observations that correlate with this proposed function for burst activity. He found the volume of secretions of his own stomach to be very small at the end of a period of high-amplitude gastric contractions, but large at the end of a period

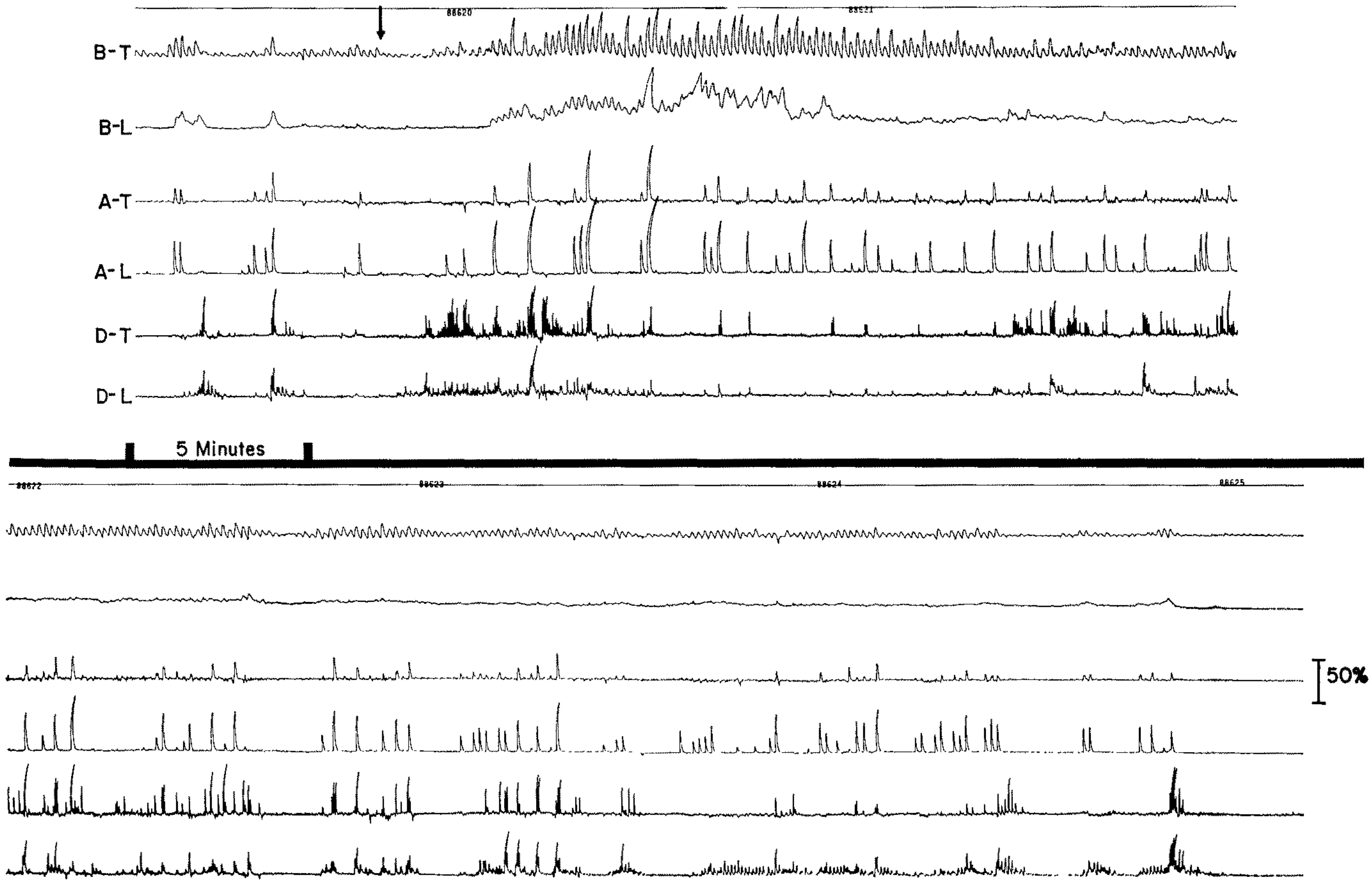

Fig. 14. Histamine-induced contractile activity; fasted state. Recording from same dog as in Fig. 12. Subcutaneous injection of histamine phosphate, 40 μg./kg., as base, given at arrow. *B, A, D, T,* and *L* as in Fig. 13.

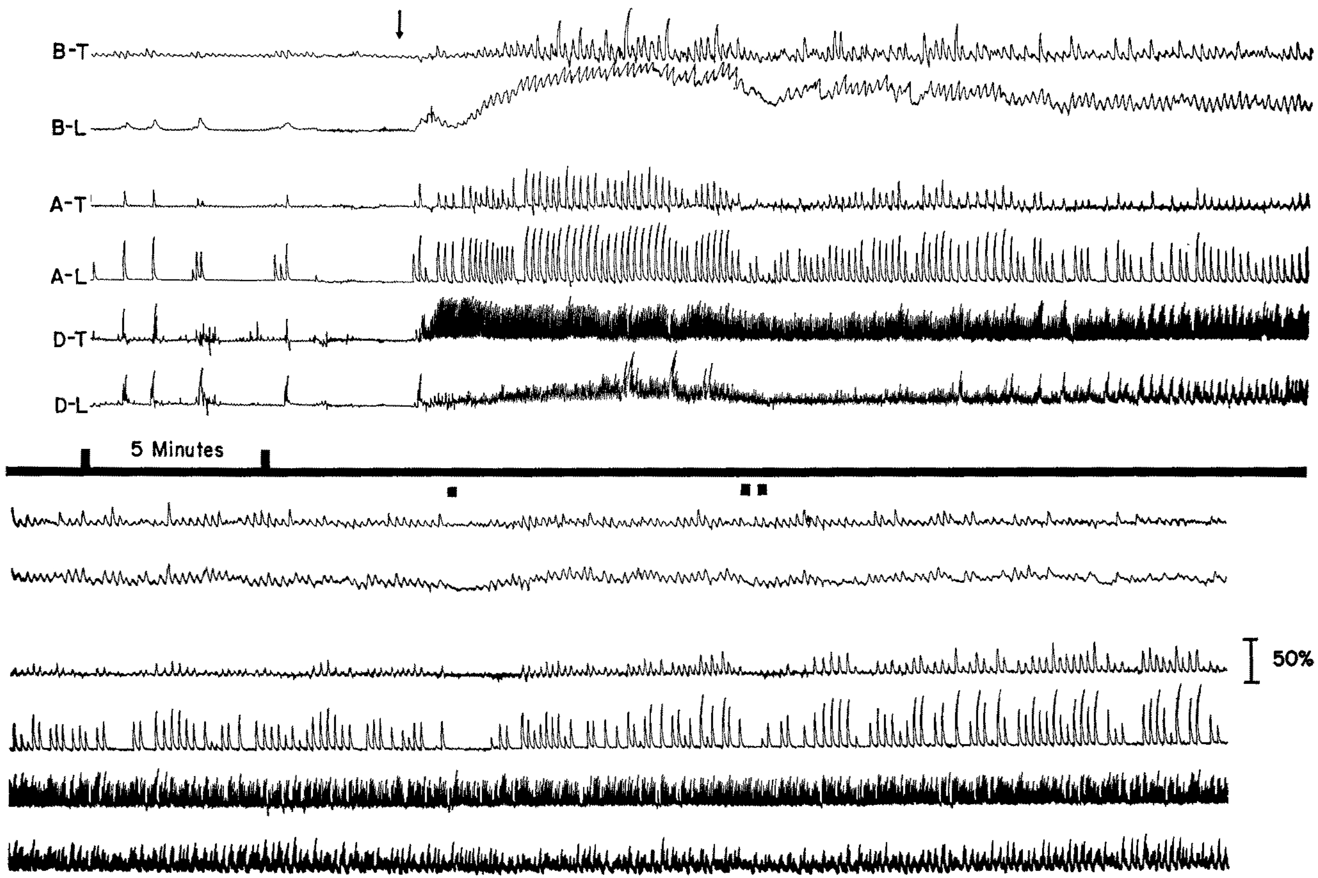

Fig. 15. 5-Hydroxytryptophan-induced contractile activity, fasted state. Recording from same dog as in Fig. 12. Intravenous injection of 20 mg./kg. 5-HTP given at arrow.

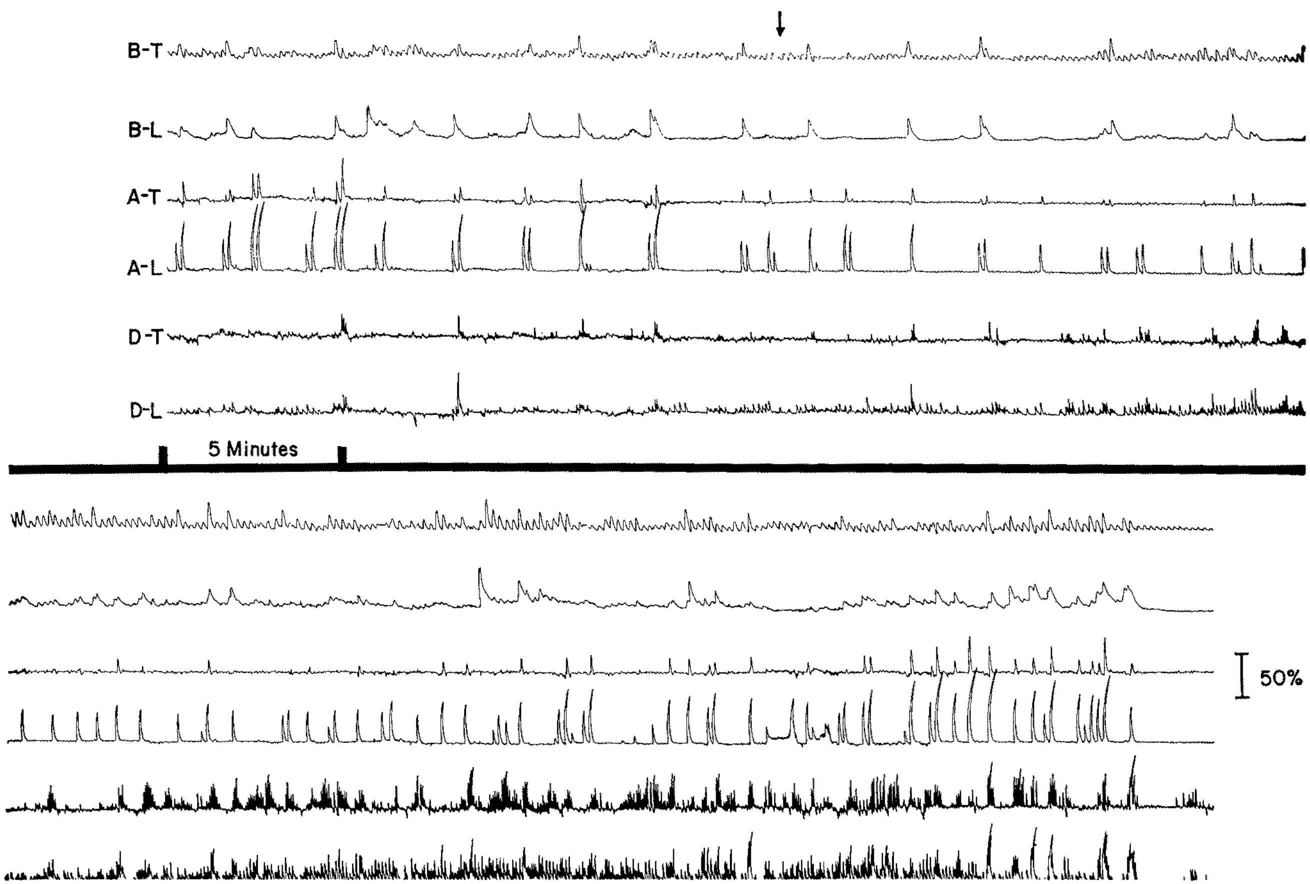

Fig. 16. Neostigmine-induced contractile activity, fasted state. Recording from same dog as in Fig. 12. Subcutaneous injection of neostigmine methylsulfate, 15 μg./kg., as base, given at arrow.

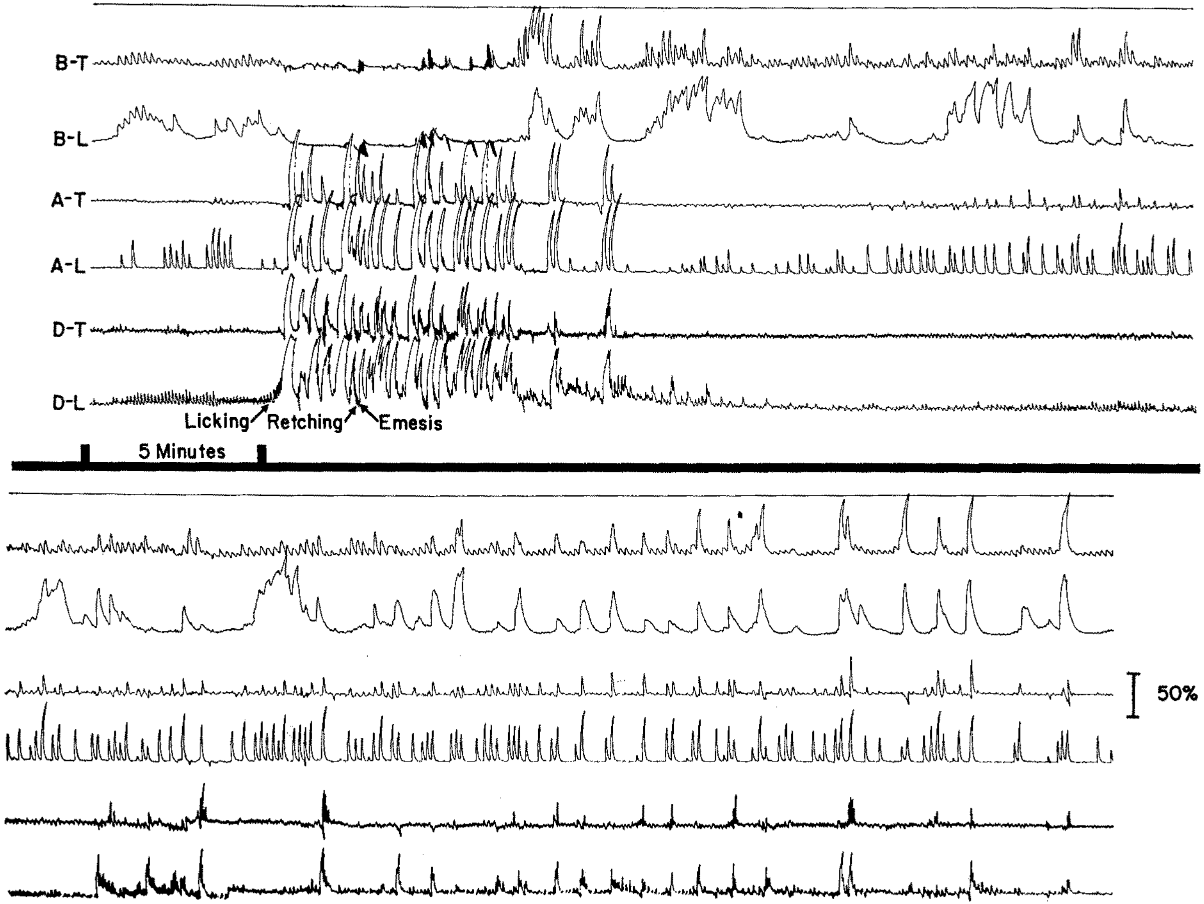

Fig. 17. Neostigmine-induced contractile activity, 120 min. after administration. Continuation of record shown in Fig. 16.

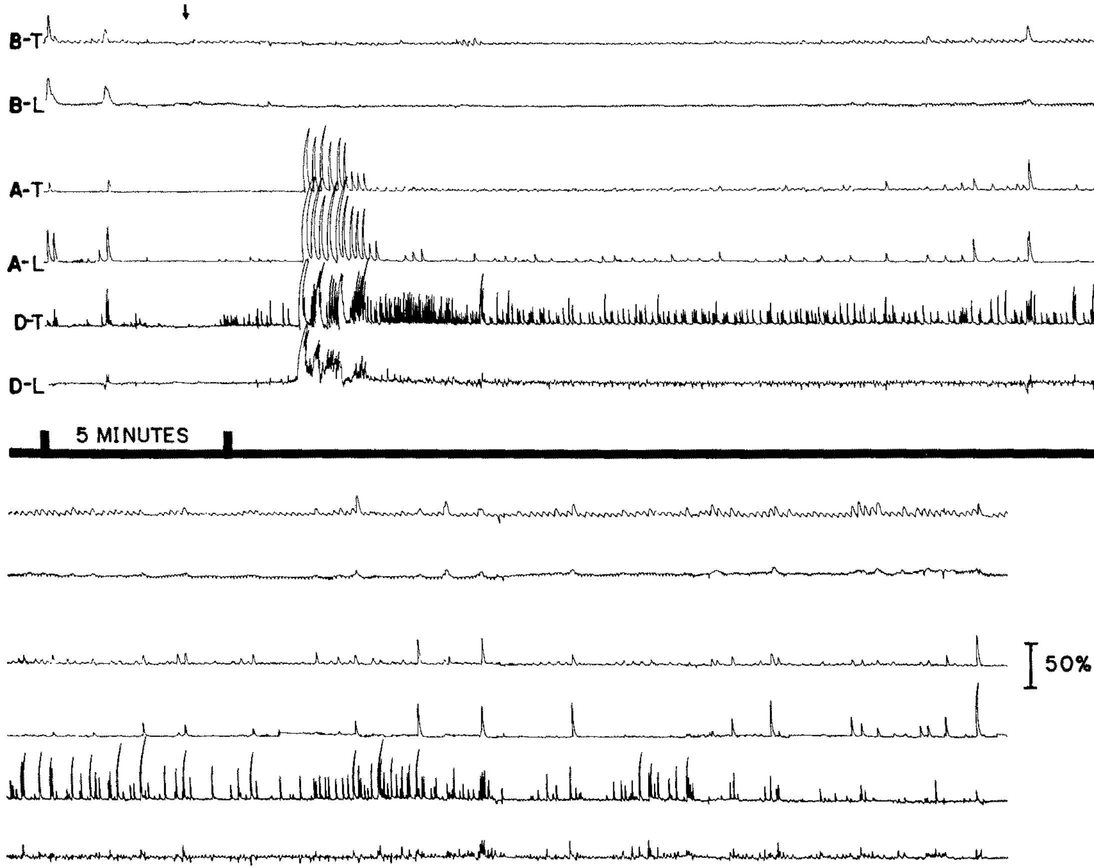

Fig. 18. Morphine-induced contractile activity, fasted state. Recording from same dog as in Fig. 12. Subcutaneous injection of morphine sulfate, 200 $\mu g./kg.$, as base, given at arrow.

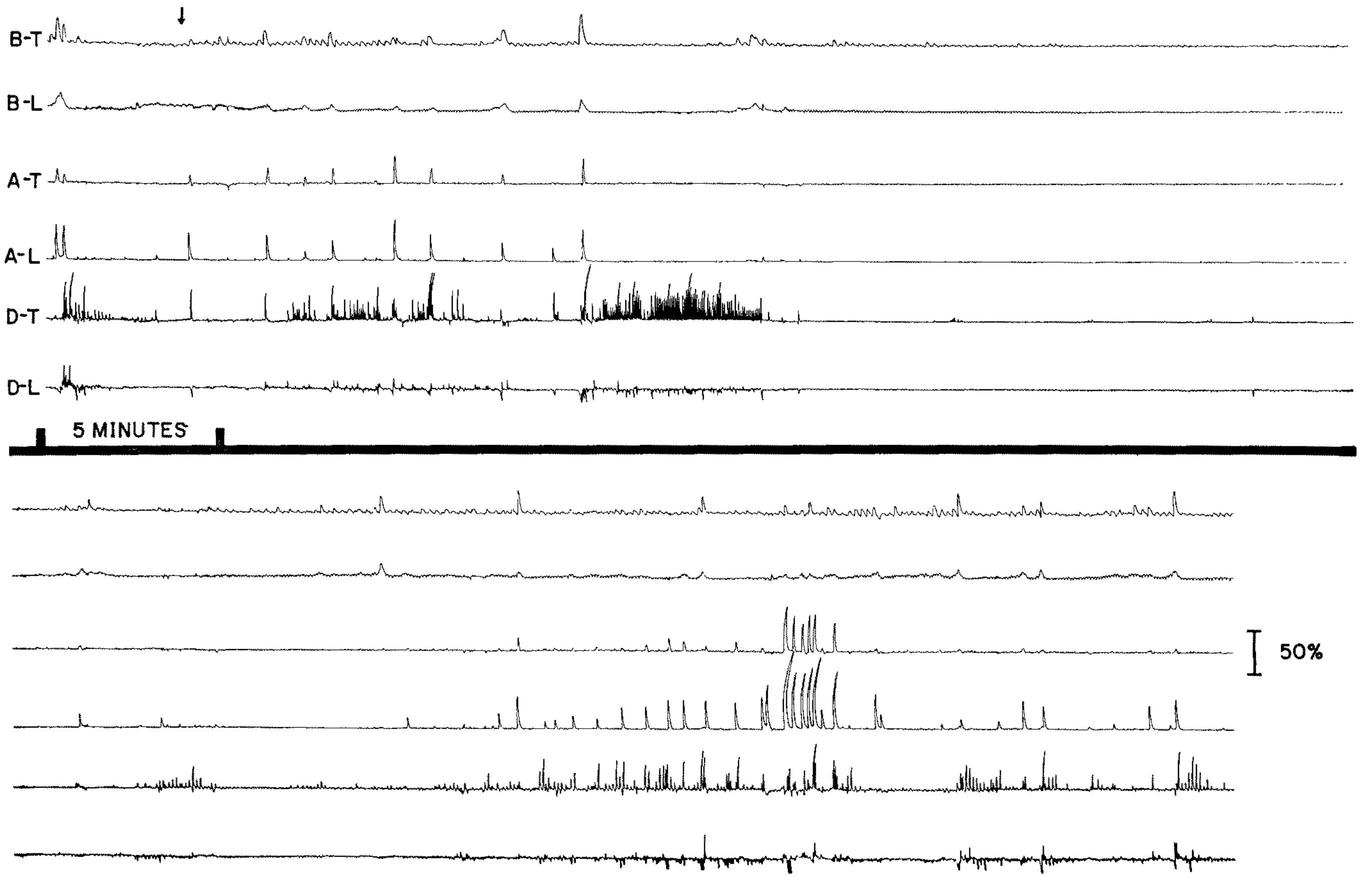

Fig. 19. Hexamethonium abolition of contractile activity, fasted state. Recording from same dog as in Fig. 12. Intravenous injection of hexamethonium bromide, 100 μg./kg., given at arrow.

of quiescence. Thus, the paradoxical finding of the strongest contractions occurring during the interdigestive state ("hunger contractions") compared to the digestive state may be explained if one assumes that they are needed to strip excess mucus from the walls of the stomach and intestine.

It is evident that the first contraction of a burst is often seen as a conducted sequential event passing from gastric body, to gastric antrum, and then to duodenum, e.g., Fig. 12. The same type of phenomenon is observed in the small intestine rather frequently if transducers are placed close to one another (1–5 cm.). Such conducted contractile activity may be observed over quite long distances, e.g., the colon during defecation (Fig. 11). These observations are noted to emphasize that this method may also lend itself to determine the effect of various conditions and drugs on the speed of conducted contractions in vivo. In addition, multiple and simultaneous recordings allow one to evaluate drug alterations of reflexes in vivo, e.g., gastroileal, gastrocolic, or reflex inhibition of existing duodenal contractile activity by gastric contractions.[15]

The in-vivo recording of a small-intestine burst (Fig. 9) and the sequence of events therein appears similar to the events recorded in vitro by Trendelberg[19] and later in situ by Raiford and Mulinos.[17] In their work as well as our own, the contractile activity of the longitudinal muscle layer preceded that in the circular muscle layer. It appears then that in-vivo intestinal-burst activity may also be the result of a myenteric reflex, perhaps elicited by accumulated interdigestive secretions. The normally occurring P waves of both muscle layers of the ileum probably represent a maximally elicited in-vivo myenteric reflex.

Intermediate contractile activity is dependent on the presence of luminal contents (Fig. 13). Immediately after feeding, the duodenal record did not reach a full intermediate pattern until the antral record showed considerable intermediate activity, which likely corresponded to the time of delivery of chyme to the duodenum. Recall also the 2–3-hr. delay after feeding before the ileum showed intermediate activity. Louckes *et al.*,[16] using the inductograph in unanesthetized dogs, recorded increased (from quiescence) pyloric sphincter and distal antral contractile activity immediately following feeding. Their recordings showed the rhythmic contractions continued for 60–90 min. We observed that such contractile activity in the antrum persisted for a somewhat longer period (3–6 hr.) following canned dog food (meat). An equal volume of water, 0.1 *N* HCl, or barium sulfate delivered through a gastric cannula produced the same effect but it seldom persisted for more than 20–30 min. Thus, distention alone appears to be sufficient stimulus to alter contractile activity. Duration of altered activity appears, however, to be related more to the character of the distending material.

It was not possible to classify colonic contractility in the same manner as stomach and small-intestine contractile activity. Chaudhary and Truelove, in a review of colonic motility,[5] also noted the inability of recent workers to use the Type I, II, III, and IV pressure-wave classification for the colon. Feeding is often followed in 5–15 min. by a gastrocolic reflex that sometimes results in defecation. Defecation is then followed by an increase in colon contractility resembling the fed (digestive) states in other areas. In the colon, this probably represents the beginning of refilling and again emphasizes that contractile activity of the colon, like any segment of the bowel, is related to local luminal contents as well as time before or after feeding.

The responses to small doses of 5 drugs are illustrated to show segment differences in sites of drug action. Exogenous histamine has a profound action on contractile activity and tone of the gastric body compared to the gastric antrum. An almost identical effect on gastric body tone is observed following administration of 5-hydroxytryptophan, but in addition, profound stimulation of gastric antral and duodenal contractile activity is also evident. Neostigmine has considerably more action on longitudinal than on circular muscle of the stomach and small intestine, an action anticipated in vivo in view of the higher sensitivity of the longitudinal intestinal smooth muscle to acetylcholine in vitro as shown by Bortoff.[3] Morphine's stimulant action is not present in gastric body but is present, although shortlasting, in gastric antrum. Morphine's stimulant action is profound in the small intestine, with circular muscle being stimulated to a much greater extent than longitudinal muscle. These discrete localizations of the site of drug action in vivo (either muscle layer and/or area of the GI tract) should allow for better selection of tissue for more meaningful physiologic and biochemical studies in vitro.

SUMMARY

The in-vivo extraluminal strain-gauge transducer, a method for the quantitative recording of contractile activity and tone of gastrointestinal muscle, has been modified to increase sensitivity and operational life. It was unnecessary to interrupt gut continuity, content flow, or nerve or blood supply. The transducers were implanted and recordings obtained from intact, unanesthetized, minimally restrained dogs for months. Respiration or normal body movements do not interfere with gut recording. Contractile activity of circular and longitudinal muscle layers was recorded separately and simultaneously. The method has been extended from studies on dog duodenum to record contractile activity patterns from gastric body, gastric antrum, jejunum, ileum, and colon.

Using these transducers, 3 major patterns of contractile activity were observed in the stomach and small intestine—basal, intermediate, and burst. Contractile activity of the large intestine did not lend itself to this kind of classification. These 3 patterns were probably similar to Type I, II, and III pressure waves respectively observed in small-balloon pressure technic records of unanesthetized humans. All patterns were present in the interdigestive state, when characteristically basal activity predominates (60%) and the remaining time was essentially divided equally between burst and intermediate

activities. It appeared that burst contractile activity represented principally a propulsive function—that of clearing viscous interdigestive secretions from an area. Characteristic findings of the digestive state were the virtual absence of the burst pattern and a much greater percentage of intermediate activity (80%) compared to basal activity (20%). It appeared that intermediate contractile activity represented principally a mixing function and a considerably inhibited propulsive function in order to aid digestion and absorption. A maximum contraction wave, a P wave, was occasionally recorded from both axes of the terminal ileum and colon. Such a contraction was likely a wall-movement counterpart of an intraluminal Type IV pressure wave as well as a maximally evoked myenteric reflex in vivo.

The above classification of contractile activity was appropriate not only for the stomach and small intestine, but also for both longitudinal and circular muscle in these areas. Longitudinal burst contractile activity characteristically preceded that of circular muscle at the same level of the bowel. Other than this latter exception, that contractile activity pattern observed in circular muscle under normal conditions was the same as that observed simultaneously in longitudinal muscle at the same level of the bowel.

There was considerable variation in the grouping of contractile patterns over an adequate control period (2–4 hr.) among dogs. However, the day-to-day constancy of this grouping of patterns for each individual animal was remarkable. There was also constancy among dogs concerning the time occupied by all patterns expressed as a percentage of contractile activity.

Examples of drug action on gastric body, gastric antrum, and duodenum were shown to stress that: (1) Drug doses equivalent to those used in man on a per kilogram basis and via the same route of administration produce significant changes in contractile activity using this method of recording. (2) Differential sensitivity to drugs was apparent not only for various areas of the gastrointestinal tract, but also for longitudinal and circular muscle at the same level of the bowel.

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