In-Vivo Force, Frequency, and Velocity of Dog Gastrointestinal Contractile Activity

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THE EXTRALUMINAL FORCE transducer method allows continuous recording of gastrointestinal contractility patterns during digestive and interdigestive periods in the intact awake animal. An analysis and discussion of these patterns have been presented.[15] This method, coupled with high-speed recording, allows analysis of single contractions with respect to such parameters as wave shape, force, frequency, and velocity of contraction. A detailed analysis of these parameters is the basis of the present communication.

METHOD

The fabrication, calibration, and surgical implantation of the extraluminal strain-gauge force transducer has been described.[15] Most of the 33 mongrel dogs successfully implanted for that study were likewise used to obtain data for this study. Experimental design was similar except for the procurement of more records at fast-recording speeds, e.g. 250 mm./min. or 25 mm./sec.

Maximum contractile force or maximum amplitude was determined by measuring the greatest force developed for a single contraction after examining all control records obtained during the entire recording period of an animal. Such recording periods represented almost daily records obtained for at least 2 weeks and often for 8–12 weeks. Maximum contractile force was obtained as gm./sq. mm. by dividing the maximum contractile-force value by the concave surface area of the transducer. Frequency of contraction per minute was determined by 2 methods. First, frequency was determined by counting the actual number of consecutive contractions for a period of time (at least

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1 min.), provided all contractions measured for the period were within a designated range of amplitude. Second, frequency was determined by dividing this mean total-contraction time (sec.) into 60 sec. to give the possible number of contractions per minute. Velocity of contraction was expressed in the following manner: Peak time is the time required to reach a certain percent maximum amplitude beginning from the first visible evidence of the onset of the contraction. Peak time is reciprocally related to contraction velocity. We elected to use peak time as an index of contraction velocity.

RESULTS

Contractile Amplitude

Maximum contractile force was determined (gm./sq. mm.) and compared for both extrinsic smooth muscles of the stomach and of the small intestine. The results are shown in Fig. 1. Only those data are presented in which the transducer was shown to be in correct alignment at the time of autopsy. The "small intestine" data include those obtained for duodenum, jejunum, and ileum because no statistically significant differences are observed among the maximum forces developed in these 3 areas. For the same reason, the "stomach" data include those obtained from transducers on the antrum as well as the body of the stomach.

Gastric circular muscle develops a greater mean maximum force, 3.6 gm./sq. mm., than gastric longitudinal muscle, 2.0 gm./sq. mm. ($p < .05$), and the mean maximum force for both layers of the stomach was greater than for

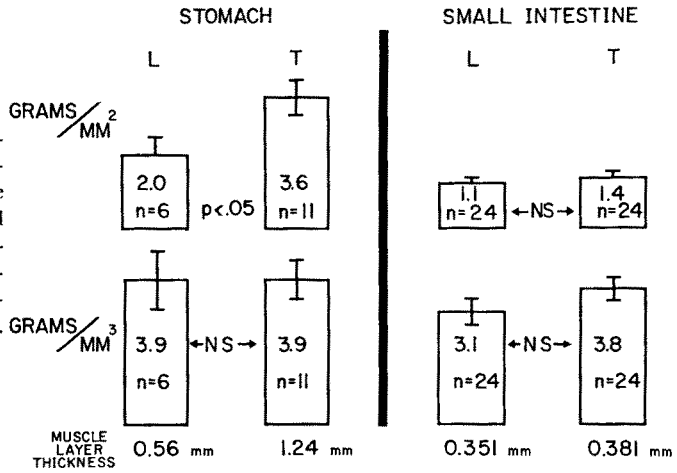

Fig. 1. Maximum contractile force of gastrointestinal muscle (see text). *L*, longitudinal muscle; *T*, circular muscle; *n*, number of transducers; *NS*, no statistically significant difference.

either muscle layer in the small intestine ($p < .05$). No statistically significant difference was found between the mean maximum forces developed by the extrinsic muscle layers of the small intestine. The muscle layer thickness data listed in Fig. 1, obtained from the work of Mall[11] and coupled with mean

maximum force data obtained in this study, allowed us to calculate the mean maximum forces developed on a gm./cu. mm. basis. The calculation and comparison of such contractile force per unit volume of smooth muscle yielded 2 findings: (1) There was no statistically significant difference between the maximum forces developed by equivolumes of longitudinal and circular smooth muscle either of the stomach or small intestine. (2) There was no statistically significant difference between the maximum forces developed by equivolumes of smooth muscle of the stomach and small intestine.

More marked baseline tone changes in small intestine longitudinal muscle were noted either spontaneously or in response to drugs.[15] Because of these observations, mean maximal contractile force was also determined for both extrinsic muscle layers of the small intestine on the basis of the number of gm.-force/sq. mm. from the lowest tone (maximal point of relaxation or minimum force) and the highest contraction level (maximal force) observed during the recording life of the animal. Maximum force values for longitudinal and circular muscle of small intestine in this instance were 1.50 and 1.58 gm./sq. mm., respectively, compared to 1.10 and 1.40 gm./sq. mm. when the point of maximum relaxation was not taken into account. Thus, longitudinal muscle of the small intestine did possess more baseline tone in vivo than circular muscle. Either method of calculating mean maximum contractile force however led to the same finding that longitudinal muscle had the same maximum force capability as circular muscle on a gm./sq. mm. or gm./cu. mm. basis in the small intestine.

Contractile Wave Shape

For purpose of analysis, various portions of a contraction wave were arbitrarily defined (Fig. 2). Peak time (PT) was the time required from onset to peak of the contraction. Mid-relaxation time (MRT) was the time required from contraction peak to relax to one-half the amplitude of contraction. Mid-relaxation time was occasionally used because small tone changes which occur at or near the end of relaxation made it difficult to determine the precise end of muscle relaxation. Interval time (IT) was the time from the end of relaxation (return to same level where onset of contraction measured) to the onset of the following contraction. Total time (TT) was the time from the onset of a contraction to the onset of the next consecutive contraction.

There is a difference in small-amplitude contractile-wave forms of longitudinal and circular muscle of the small intestine (Fig. 2). Listed are mean contraction-time values ($n = 20$) for small (left-hand column) and large (right-hand column) contractions of both circular and longitudinal muscle from the same area (duodenum) and same animal. The small contractions shown are approximately 10% of maximum amplitude for both muscles while the larger contractions are approximately 60% of maximum amplitude. The contraction examples shown are traced, actual contractions. Grossly,

small contractions of circular muscle are somewhat spike-shaped with an interval between contractions. Small longitudinal muscle contractions on the other hand are rather sinusoidal in shape. These findings were noted in the jejunum and ileum as well as the duodenum.

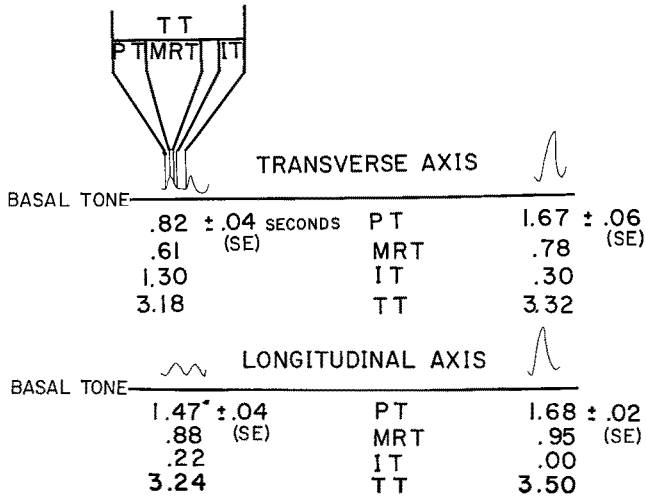

Fig. 2. Traced small and large contractile wave forms of circular and longitudinal muscle layers at same level of same dog duodenum. *PT*, peak time; *MRT*, mid-relaxation time; *IT*, interval time; *TT*, total time.

Small-amplitude contractile waves of both extrinsic muscle layers of the gastric body are sinusoidal in shape. Small amplitude contractile waves of both extrinsic muscle layers of the gastric antrum are spike-shaped. Thus, the small-amplitude wave form is regional but not muscle layer related in the stomach, whereas, the reverse situation occurred in the small intestine. This wave-shape difference between extrinsic muscle layers of the small intestine gradually disappeared as contractile amplitude increased to near-maximum as seen in Fig. 2.

Contractile Frequency

Following the time analysis of single contractile waves and the comparison of various amplitude contractions, it was obvious that the total time required for a small-amplitude contraction in either muscle layer (3.18 and 3.24 sec.) was less than for a large-amplitude contraction (3.32 and 3.50 sec., respectively). This frequency difference (possible number of contractions per unit time) was based on amplitude and was definitely present for all areas of the gastrointestinal tract (Table 1). The data for Table 1 was obtained by selecting at least 40 contractions (circular muscle layer) for each of the areas listed. Twenty of these contractions were approximately 10% and 20 were approximately 60% of maximum contractile amplitude. It is emphasized that only those contractions were accepted and analyzed in which there was: (1) a return to exactly the same tone level which was present prior to the contraction, and (2) a maintenance of that tone level prior to the onset of the

TABLE 1. FREQUENCY COMPARISON OF LARGE VERSUS SMALL CONTRACTIONS DETERMINED FROM INDIVIDUAL CONTRACTIONS

Area	*Large**	*Small†*	*P*
Gastric body	4.41 ± 0.13‡	5.21 ± 0.14	<.001
Gastric antrum	5.20 ± 0.13	5.49 ± 0.09	<.05
Duodenum	17.76 ± 0.40	18.87 ± 0.39	<.05
Jejunum	16.99 ± 0.40	18.08 ± 0.30	<.05
Ileum	14.12 ± 0.34	15.57 ± 0.46	<.02
Transverse colon	3.26 ± 0.14	5.03 ± 0.20	<.05
Descending colon	3.18 ± 0.11	4.33 ± 0.09	<.05

*Over-all mean of 59.4% of maximum amplitude.
†Over-all mean of 11.3% of maximum amplitude.
‡Mean ± S. E.

next contraction. In this manner, any possible alteration of frequency of contraction as a result of a change in baseline tone was eliminated and only contractile amplitude and frequency are compared.

Two possible ways of determining frequency of contraction per minute are: (1) determine the mean total contraction time for single contractions and divide this value into a minute (possible number of contractions per minute), and (2) count the number of consecutive contractions for 1 min. (actual number of contractions per minute). If frequency is to be compared with amplitude, then one can select and determine mean total contraction time for 2 levels of contractile amplitude as was done in Table 1. In the second method of determining frequency, however, if one wishes to correlate amplitude and frequency, it is necessary to select areas of recording where consecutive contractions of approximately equal amplitude are present and occurring for at least 1 min. This was done for small (approximately 10%) and large (approximately 60%) contractions. Figure 3 shows that when the sec-

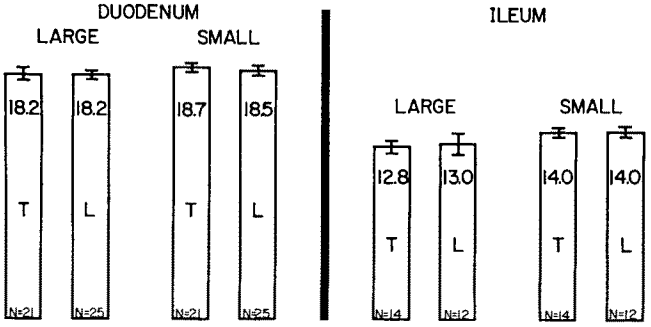

Fig. 3. Paired comparison of frequency (actual no./min.) of consecutive large versus consecutive small contractions in circular (*T*) and longitudinal (*L*) muscle layers of duodenum ($p < .01$) and ileum ($p < .001$).

ond method of determining frequency of contraction for small and large contractions was used, there was also a statistically significant faster frequency for smaller contractions. Further, this frequency difference for varying-sized contractions existed in both the longitudinal and circular muscle layers of

the small intestine. No significant difference existed in the frequency of contraction of the longitudinal and circular muscle at the same level of the intestine. The latter was true, of course, only if one compared contractions from each muscle layer which were of equal per cent maximum amplitude.

Contractile Velocity

Once able to determine the maximum contractile amplitude and express all other contractions as a per cent of that maximum, it was possible not only to explore contractile frequency–force but also contractile velocity–force relationships.

A straight-line relationship of peak times and amplitudes for both extrinsic muscle layers of the stomach and small intestine existed between 10 and 75% of maximum amplitude. Correlation coefficients and regression equations calculated from data in this amplitude range for longitudinal and circular muscle from several regions of the gastrointestinal tract are shown in Table 2. Graphs of such regression lines for the stomach are shown in Fig. 4 and for the small intestine, in Fig. 5. All correlation coefficients were statistically significant ($p < .05$). The data for the regression equations and correlation coefficients shown in Table 2 were obtained from 30 contractions of the muscle layer in question. Ten contractions each of low (10–30%), moderate (30–60%), and high (60–80%) maximum force were randomly selected. All data for muscle layers of the small intestine were taken from 1 animal. Another animal was used for all data for muscle layers of the stomach. Data obtained from other animals were similar to that shown. Paired-comparison contractile

TABLE 2. RELATION OF % AMPLITUDE AND TIME TO CONTRACTION PEAK OF CANINE GI TRACT

Area	*Axis*	*r**	*y*†
		STOMACH	
Gastric body	T‡	0.92	2.80 + 0.066x
	L§	0.77	3.40 + 0.030x
Gastric antrum	T	0.90	0.98 + 0.035x
	L	0.91	1.56 + 0.012x
		SMALL INTESTINE	
Duodenum	T	0.95	0.62 + 0.014x
	L	0.44	1.50 + 0.004x
Jejunum	T	0.90	0.91 + 0.012x
	L	0.66	1.05 + 0.003x
Ileum	T	0.85	0.99 + 0.022x
	L	0.78	1.02 + 0.012x

*r is the correlation coefficient.
†Regression equation: $y = a + bx$.
‡T is the transverse axis.
§L is the longitudinal axis.

velocity data yielded less variation than group-comparison data for the 2 muscle layers at the same level of the bowel.

At comparable force of contraction, contractile velocities for both muscles of the gastric body were considerably slower than both muscles of the gastric

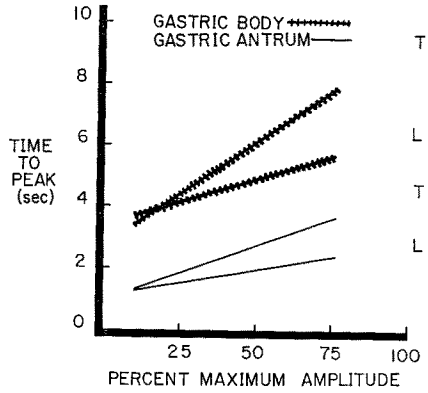

Fig. 4. Regression lines (transverse, *T*, and longitudinal, *L*, axis) of peak time versus % maximum amplitude in stomach.

antrum (Fig. 4). Contractile velocity for gastric-body longitudinal muscle was considerably faster than gastric-body circular muscle. The same relationship was observed in the gastric antrum. Circular muscle of the small intestine was also slower than longitudinal muscle except in the duodenum (Fig. 5). Too, there was a tendency for a slower velocity of circular-muscle contraction farther along the small intestine. Of the 10 regression lines shown, only duodenal longitudinal muscle appeared to be the exception to the rule. Its velocity was actually slower than duodenal circular muscle, a paradoxical relation which was observed in many animals. Initial data of this type were obtained by Jacoby[10] for the duodenum.

DISCUSSION

Farrar[5] has stressed the need for methodology capable of quantitatively evaluating contractile activity in vivo of the longitudinal and circular muscle layers of the gastrointestinal tract. Intraluminal-pressure devices frequently trigger mucosal reflexes and stimulate motility. Such devices may not actually record the occurrence of a segmental contraction, for a contraction in 1 segment, coupled with relaxation in an adjacent segment, may lead to no change in intraluminal pressure.[4, 16, 17] The extraluminal-gastrointestinal force transducer recorded in-vivo contractile activity directly, allowed quantification, was capable of measuring contractile activity in both extrinsic muscle layers separately and simultaneously, and did not possess the disadvantages of intraluminal-pressure devices. The extraluminal force transducer has recently been made more sensitive and durable and its value in simultaneous multiple segment recording has been presented.[15] Farrar[5] and Menguy[12] in recent

review articles on motor function of the alimentary tract have indicated the desirability of correlating the results of 2 or more technics used simultaneously. In this regard, an in-vivo correlation of electrical and contractile force activities of the 2 extrinsic muscle layers in dog duodenum was recently presented by Bass and Wiley.[3]

Initially, we expressed contractile force in terms of grams of force developed per transducer.[9] We noted that the control maximum contractile force was not increased by known stimulant drugs.[15] This emphasized that contractile amplitude, contractile activity per unit time, and/or persistence of strong contractions (spasm, tentanus, etc.), but not *maximum* contractile amplitude may be increased by stimulant drugs. The recorded maximum force depended on the size of the transducer, gut wall thickness, and region of the gastrointestinal tract that was monitored. We now express contractile force as a per cent of maximum amplitude. Using per cent maximum amplitude, it is possible to classify and compare control patterns of contractile activity among transducers in the same dog and among different dogs. Thus, meaningful comparisons of data obtained by this method used in different laboratories should be possible if the same general type and size of transducer is used and if contractile force is expressed as per cent maximum force.

The present study revealed that no difference in absolute maximal force development (gm./sq. mm.) was observed between the 2 extrinsic muscle layers of the small intestine. Using the muscle layer thickness data obtained by Mall[11] in the dog stomach and small intestine, we conclude that there is no statistically significant difference between the maximum forces developed in vivo by equivolumes (gm./cu. mm.) of smooth muscle of the gastric body, gastric antrum, duodenum, jejunum, and ileum. Earlier data presented by Jacoby,[10] concerning only the duodenum, allowed the same conclusion. No other comparable in-vivo data are available.

A recent analysis[1] of some mechanical aspects of intestinal smooth muscle in vitro may be appropriate to this discussion. Aberg and Axelsson[1] report that the mean maximum isometric force developed by 19 pieces of taenia coli muscle of the guinea pig was 1.82 ± 0.52 kg./sq. cm. where the area represents

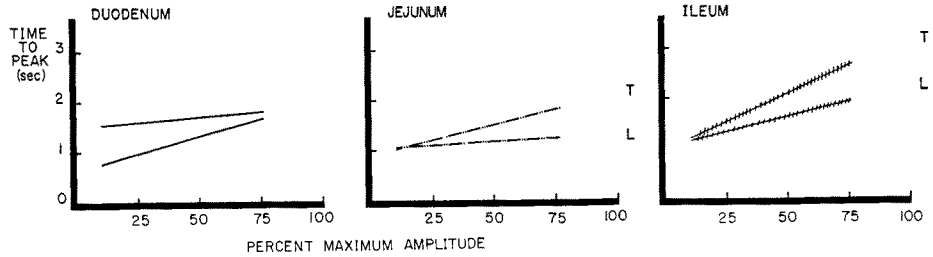

Fig. 5. Regression lines of peak time versus % maximum amplitude in small intestine. (*T*)—Transverse axis. (*L*)—longitudinal axis. Duodenum: upper line—(*L*), lower line (*T*). Corresponding lines for jejunum and ileum are reversed compared to duodenum.

the mean cross-sectional area of each muscle piece. The only examples of lengths of these pieces of muscle given by these authors, were 7.5 and 19.0 mm. If we assume a range of 5–20 mm. for the 19 muscles, then the calculated maximum force developed would range from 3.64 to 0.73 gm./cu. mm. The extraluminal-force transducer method was also essentially isometric, i.e., less than 10% bending at maximum force development.[15] Our in-vivo data for muscle layers were in (gm./cu. mm.) : stomach longitudinal, 3.9; stomach circular, 3.9; small-intestine longitudinal, 3.1; and small-intestine circular, 3.8. The mean maximum isometric forces determined in the 2 studies are comparable. Aberg and Axelsson used chemical stimulation, i.e., acetylcholine and carbachol, to effect maximum contraction. It was unnecessary for us to do this to determine maximum amplitude of contraction in the design of our experiments. Neostigmine elicited contractions which equalled but did not exceed the control maximum force.[15]

One of the major advantages of being able to quantify gastrointestinal muscle contractile force in vivo is to be able to correlate this data with other measurable physiologic properties of such muscle in vitro. A possible correlation between contractile force and contractile frequency was one of the first examined. Steggerda, in an editorial on the physiologic gradient of the intestine, summarized current thinking in this area.[18] He pointed out that not only is the frequency gradient of myogenic origin but it also was dependent upon the integrity and continuity of the enteric plexus. In our study, an in-vivo inverse correlation of contractile frequency and force was observed at all levels of the tract studied and in both extrinsic muscle layers of the bowel. Force of contraction may be an afferent stimulus operating through the enteric plexus which, in part, controls contractile frequency. This inverse correlation would predict that the aboral end of a gut segment might be contracting at a faster frequency than the oral end depending upon the degree of contractile force at each end. The prediction appears valid, for it was noted that the polarity of the well-known frequency gradient was occasionally reversed in vivo over short segments of bowel as a result of differences in contractile force. Such differences in contractile force result in local temporary reversals of the polarity of the frequency gradient which may slow propulsion of intraluminal contents and allow for more efficient digestion. Hasselbrack and Thomas,[7] following local cooling of the dog duodenum in vivo, note that a decrease in frequency was accompanied by a marked increase in amplitude. However, this finding was not discussed.

Any possible correlation between contractile force and contractile velocity was also examined in our studies. A correlation was expected in view of the differences noted in contractile wave shapes. Low-amplitude contractions of small-intestine longitudinal muscle and both extrinsic muscles of the gastric body are sinusoidal while small-intestine circular muscle and both extrinsic muscles of the gastric antrum were spike-shaped with a quiet interval period. Nelsen[13, 14] measured gastrointestinal muscular activity by multiple implanted

silicon strain gauges. Recordings from the body, antrum, and pylorus of the dog stomach were shown in Nelsen's papers. Axial position of the transducer was not always specified. The wave shapes of the contractions of the body and antrum are identical to those contractions we recorded from similar areas. The author does not acknowledge or comment on such differences in contractile wave shapes. Foltz *et al.*[6] illustrated records of ileal contractile wave shape obtained from strain gauges directly embedded in silicone rubber and sutured to the serosa of the monkey ileum. Again, axial position is not specified but a diagram in the text suggests that only circular muscle of the ileum was being recorded. Spike-shaped contractile waves with quiet interval periods are apparent in some of the records. As a result of the present analysis we conclude that such differences in wave shapes are, in part, due to differences in contraction velocity.

Aberg and Axelsson[1] note that great differences exist in contraction velocity between different types of smooth muscle in vitro. They also note that velocity of in-vitro contraction is limited by the rate of conduction of an action potential along the muscle, and higher velocities can be obtained on high-frequency electrical stimulation over the entire muscle length. Admittedly, the differences in velocities of contraction observed in our in-vivo study may be due to differences in nervous innervation of gastrointestinal musculature. However, this proposition can now be tested by nerve transection and drugs which interfere with nerve conduction.

We have shown that the contraction velocity of duodenal longitudinal muscle is slower at low contractile force levels than would have been expected from the remainder of the data obtained in the small intestine. It was also shown that duodenal longitudinal muscle contractile velocity was similar to antral longitudinal muscle at low contractile force levels. We note with interest that only longitudinal muscle traverses the pylorus,[8] and a partial relationship between antral and duodenal electrical activity has been observed.[2] Antral longitudinal muscle may regulate the velocity of contraction of duodenal longitudinal muscle. Any further discussion of the significance of the similarity in contraction velocities must await studies following transection and reanastomosis of the longitudinal muscle which traverses the pylorus.

SUMMARY

It has been possible in vivo to determine quantitatively the contractile force developed by the extrinsic smooth muscles of the gastrointestinal tract using, primarily, isometric extraluminal force transducers. Contractile amplitude can be expressed as gm./sq. mm. derived from calibration force values and the concave surface area of the transducer. The maximum contractile force of the thicker circular muscle layer of the dog stomach was greater than that recorded from the thinner longitudinal muscle layer. Both muscle layers of the stomach had a maximum contractile force greater than either muscle layer

of the small intestine. No difference was observed in the maximum contractile force developed between the circular and longitudinal layers of the small intestine. It is suggested that an equal volume of gastrointestinal smooth muscle in vivo, regardless of layer or location, has the same maximum contractile capacity, gm./cu. mm.

When contractile force was expressed as a per cent of maximum force developed, meaningful comparisons of control or drug-altered contractile activity in and among dogs were made possible regardless of the variation in the absolute level of force developed.

The well-known correlation of frequency of contraction and region of the gastrointestinal tract (frequency gradient) was observed. However, a heretofore undescribed in-vivo inverse correlation of frequency and force of contraction was observed in both longitudinal and circular muscle layers of the stomach and small intestine and circular muscle layer of the large intestine. It was noted that the polarity of the well-known frequency gradient was occasionally reversed in vivo over short segments of bowel as a result of differences in contractile force.

Because of the capability of discrete measurement of small-amplitude contractions coupled with high-speed recording, it was possible to study the wave shapes of circular and longitudinal muscle contractions of varying amplitude in vivo. An analysis of these wave shapes from various areas of the tract shows that as contractile amplitude is increased: (1) the velocities of contraction of both extrinsic muscles of the gastric body were slower than those of the extrinsic muscles of the gastric antrum; (2) contraction velocity of longitudinal muscle is faster than that of circular muscle in both gastric body and antrum; and (3) contraction velocity of longitudinal muscle in jejunum and ileum is more rapid than that of circular muscle. However, in the duodenum the contraction velocity of longitudinal muscle is slower than circular muscle.

This latter finding in the duodenum appears to be due to the fact that contraction velocity of duodenal longitudinal muscle is slower on an absolute basis than would have been expected from the remainder of the data on the small intestine. Instead, contraction velocity of duodenal longitudinal muscle is similar to gastric antral longitudinal muscle.

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