PHARMACOLOGICAL EFFECTS ON THE MECHANICAL AND ELECTRICAL ACTIVITIES OF THE SURGICALLY ALTERED CANINE GASTRODUODENAL JUNCTION

BY

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PHARMACOLOGICAL EFFECTS ON THE MECHANICAL AND ELECTRICAL ACTIVITIES OF THE SURGICALLY ALTERED CANINE GASTRODUODENAL JUNCTION

Herbert Stowell Ormsbee, III

Under the supervision of Professor Paul Bass

This study was designed to characterize alterations in the pharmacological and physiological responses of the surgically altered canine antral-duodenal segment and to gain insight into the mechanisms of coordination between the antrum and duodenum. Antral and duodenal circular muscle contractile patterns were investigated following parietal cell vagotomy (PCV), truncal vagotomy (TV) and Heineke-Mikulicz pyloroplasty (P). Circular muscle contractile activity, electric activity and gastric emptying were also examined following pyloroplasty alone.

The PCV and P procedures were performed through a mid-line abdominal incision. In the PCV procedure, the anterior and posterior gastric nerves were sectioned from the incisura angularis to and around the gastroesophageal junction. Pyloroplasty was performed by suturing transversely a 5 cm longitudinal incision made through the gastroduodenal junction (GDJ). The TV procedure removed 1-2 cm segments of right and left vagus through a left thoracotomy. Contractile activity was monitored with chronically implanted extra-luminal force transducers. Chronically implanted platinum

wire sero-muscular electrodes were used to record electric activity. Following P, gastric emptying was evaluated with a 300 ml liquid test meal of trisodium citrate with 10 mN oleic acid suspended by 0.5% Tween 80 (citrate-fat). Contractile and electrical patterns were studied in the dogs during the interdigestive and digestive states, following citrate or citrate-fat test meals and after the administration of bethanechol (0.1 mg/Kg sc), insulin (0.5 U/Kg iv), pentagastrin (1 μg/min iv), metoclopramide (2 mg/Kg iv) and atropine (1 mg sc).

Following PCV, the basal, burst sequence was apparent and bethanechol stimulated the antrum and the duodenum. Insulin stimulated the antrum after a 20-30 minute delay. Following TV, the basal, burst sequence appeared but activity was reduced. Bethanechol stimulated the antrum and the duodenum. Insulin stimulated the duodenum immediately after administration, but did not stimulate the antrum. When P was added to either PCV or TV the results were not different from those for the vagotomies alone. Pyloroplasty alleviated gastric retention of solids following TV. All of the vagotomy and pyloroplasty procedures showed typical motor gradients for the liquid test meals.

Heineke-Mikulicz pyloroplasty enhanced the gastric emptying of the citrate-fat test meal. Following P, antralization of the duodenum was recorded with force transducers. A greater motility index was found for the terminal antrum than the orad antrum for the digestive state and after

pentagastrin. A steep antral-duodenal digestive motor gradient after metoclopramide was observed only in control dogs. Following P, recordings of antral electric activity demonstrated arrhythmias and tachygastria. Such abnormal electric activity could be corrected by feeding, pentagastrin, metoclopramide and bethanechol administration, but was present after atropine. The duodenal BER was recorded on the antrum and the antral BER could be recorded on the duodenum after P.

It was concluded: 1) that denervation of the body of the stomach does not affect responses of the antral-duodenal segment to bethanechol or insulin, or affect the emptying of liquids or solids, 2) denervation of the whole stomach demonstrates a peripheral action on duodenal smooth muscle for insulin, 3) TV causes retention of solids which is alleviated by a liquid diet or by P, 4) P alone appears to affect normal emptying of liquids, 5) following P, the duodenal inhibitory reflex in the burst period is impaired, 6) P may delay the emptying of solids by enhancing retropulsion, 7) delayed emptying due to pentagastrin may be due to increased retropulsion, 8) P appears to affect the ability of metoclopramide to produce a steep antral-duodenal motor gradient, 9) abnormal electric activity appears in the antrum after P, and 10) electric activity after P suggests that the GDJ prevents the spread of the BER in either direction across this "insulatory zone".

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Professor Paul Bass Date

INTRODUCTION

A. Anatomy and Physiology of the Gastroduodenal Junctional Segment

1. Anatomical considerations

The anatomy of the gastroduodenal area was described by anatomists in the 1920's and 1940's and has been recently reviewed by Edwards and Rowlands (1968). According to these authors the area is described in the human as follows:

a) Greater than 50% of the longitudinal smooth muscle fibers interdigitate with the circular fibers at the terminal portion of the antrum. This means that less than 50% of the longitudinal smooth muscle traverses from antrum to duodenum.

b) There is a distinct separation of the circular smooth muscle of the stomach from the circular smooth muscle of the duodenum.

c) The type of mucosal cell changes between the antrum and the duodenum. (This appears to be the reason for the distinct difference in skin-to-mucosa potential difference measured in these two regions by Andersson and Grossman (1965).)

d) The mucosal lining of the antrum is much more loosely attached to its submucosa than that of the duodenal mucosa.

e) The antrum and duodenum each possess a different characteristic basic electric rhythm (BER).

These characteristics apply to the gastroduodenal junction (GDJ) of the dog and the cat as well (Bass et al., 1961b; Bortoff, 1965). In addition to these factors, it has been shown that Auerbach's plexus, the myenteric plexus, crosses the GDJ completely intact (Alvarez, 1948). Alvarez also demonstrated that the gastric lymphatics are totally separate from the lymphatics of the small bowel. From these facts it appears obvious that the GDJ is a transition zone between two organs and it is strictly hypomuscular in nature.

The nature of the anatomy of this segment has caused considerable confusion concerning the properties of the GDJ. At the terminal antrum the circular muscle becomes enlarged as it terminates and interdigitates with the longitudinal smooth muscle. This enlargement occurs in a ringlike fashion at this location and consequently has been referred to as the "pyloric sphincter". Such nomenclature has influenced many investigators in their analyses of the function of the GDJ and its role in the emptying of the stomach. The search for the characteristics of the "pyloric sphincter" has endured many years of research and today the debate continues. Both in vitro and in vivo methods have been used to investigate the properties of such a sphincter. D. D. Bass and his co-workers have shown that the reciprocal response of the human and canine gastrointestinal sphincters to pharmacologic stimulation in vitro cannot be shown at the GDJ as it can at the gastroesophageal or ileocecal junctions (Bass et al., 1970). More recently, electrical field stimulation

of 2 mm wide transverse muscle strips from the GDJ area of opossums, cats, some dogs, and one human specimen has demonstrated relaxation of the strip from the terminal antrum (Anuras *et al.*, 1974). The authors propose a distinct innervation for the segment where relaxation occurred and suggest that this may indicate a sphincteric function. The significance of such a narrow muscle strip is unknown.

In vivo work in the dog and man using water-filled or air-filled open-tipped tubes or balloons has demonstrated both an area of elevated pressure at the GDJ (Brink *et al.*, 1965) or none at all (Edwards and Rowlands, 1968). Fisher and Cohen (1973) used a refined manometric technique to show an area of elevated pressure which they claim is the pyloric sphincter in man. In contrast, the most recent study by Mehta and associates (1974) in man using a circumferentially-sensitive miniature transducer assembly failed to detect any evidence for a pyloric sphincter. Clearly, there is not general agreement concerning the question of a sphincter. Anatomically, however, there does not appear to be any independent sphincteric segment between the stomach and duodenum. A reasonable hypothesis stated by Alvarez over twenty-five years ago which is still valid today is as follows:

> . . . the pyloric ring behaves simply as the distal end of the thickened band of muscle which surrounds the pars pylorica, and that when waves reach this terminal segment it contracts exactly as did the segments orad to it. (Alvarez, 1948, p. 382)

Thus, even though a physiological sphincter may be present,

three anatomical areas exist in this region. These are the antrum, the GDJ (the hypomuscular segment) and the duodenum, which begins with the segment known as the duodenal cap.

2. Coordination between the antrum and duodenum

Since the time Beaumont (1833) observed the motions of Alexis St. Martin's stomach, investigators have been interested in gastric motility, stomach emptying, and what the correlation was with the motor action of the duodenum. W. B. Cannon, a major figure in gastrointestinal motility, reviewed the literature of the late 1800's on stomach emptying and devised experiments to test the mechanism of the "pylorus". From this work he theorized that acid controlled the pylorus which means that free acid in the area of the "sphincter" opened it and acid in the duodenum acted to close it. This is the classical "keeper-of-the-gate" hypothesis (Cannon, 1911). Objections were raised to Cannon's hypothesis since it did not seem to apply to fats or to liquids. In 1934 Cesare Gianturco, working with W. C. Alvarez, implanted lead shot under the serosa of the antrum, GDJ, and duodenum of cats and studied the passage of various barium meals roentgenocinematographically. In addition to concluding that the "pylorus" responds mechanically similarly to the rest of the antrum, he stated that food leaves the stomach when the antrum and duodenum are relaxed at the same time and that when only the terminal part of the

antrum is relaxed, food does not pass into the duodenum (Gianturco, 1934). Gianturco showed that the chemical as well as the physical nature of the food were important factors in regulating emptying, not the amount of free acid secreted.

Three years later Crider and Thomas (1937) reported the results of experiments in dogs fitted with gastric and duodenal fistulas and a cannula between these placed so as to hold the GDJ open and yet allow liquids to pass through. They concluded that the "pylorus" was ". . . not an essential part of the mechanism that regulates the emptying of certain liquids," (Crider and Thomas, 1937, p. 299). In addition, they suggested that the GDJ prevents duodenal reflux into the stomach.

Quigley and Loucke (1962) advanced the concept of the "gastric pump"; that is, waves of contraction over the body of the stomach proceed to the antrum where stronger contractions produce a gradient of pressure between the antrum and duodenum. This allows chyme to empty from the stomach. This mechanism which propels chyme into the duodenum when the duodenum is relaxed has been more fully described by Carlson, Code, and Nelson (1966). Using unanesthetized dogs with duodenal and gastric cannulas or with exteriorized antral-duodenal zones, they observed the passage of a barium meal cineradiographically. The work showed that a terminal antral contraction (TAC) resulted also in retropulsion of antral contents back into the body of the stomach and was

followed by duodenal contractions. These authors proposed that a message crossed the GDJ resulting in the 1-3 bandlike duodenal contractions when retropulsion occurred in the antrum. The concept was established that the antrum, GDJ, and duodenum act as a unit in a coordinated contractile sequence.

When food enters the stomach inhibitory stimuli in the chyme act on the duodenum to regulate the amount of chyme subsequently passed to the duodenum. These inhibitory substances can diminish the action of the gastric portion of the contractile sequence thereby reducing the amount of material which is emptied. In addition to releasing hormones which may affect gastric emptying the food can slow emptying by interacting with duodenal receptors responsive to salts of fatty acids, osmotic pressure, and acids. The use of liquid test meals in the study of stomach emptying and the influences of the inhibitory substances have been discussed in an excellent review (Hunt and Knox, 1968).

The mechanisms underlying the duodenal inhibition of antral motility have not been fully elucidated. One important study of this topic has been reported by Weisbrodt et al. (1969). This work has shown that the difference in emptying times for 300 ml liquid test meals of 200 mOsM glucose, trisodium citrate or 10 mN oleic acid suspended in trisodium citrate can be correlated with circular muscle contractile activity of the antrum and duodenum. The liquid test meal with the slowest rate of emptying, the meal with the

oleic acid, produced significantly fewer contractions in the antrum and significantly more contractions in the duodenum than the meal with the fastest emptying rate, the citrate meal. It appears that gastric emptying is regulated in part by the ratio of contractile activity in the antrum and duodenum, and that the substances emptied into the duodenum can affect the relative amounts of contractile activity in each organ. This study does not explain how the motor activity was coordinated. Three possibilities appear to exist as possible mechanisms for the coordinated contractile sequence between the antrum and duodenum. These have been discussed by Edwards and Rowlands (1968) and can be summarized as follows. First, the coordination could be the result of electrical continuity between the two organs. This electric continuity could be through Auerbach's plexus, which is known to be prominent in the GDJ as it passes from stomach to small bowel. Also, a small percentage of the longitudinal muscle crosses the GDJ, so an electric-myogenic link may exist. Second, the possibility exists of a hormonal or neural pathway involving extrinsic nerves. The third possible mechanism, which would appear to be supported by Weisbrodt's data, results from the mechanical, osmotic, or chemical stimulus of chyme as it is emptied into the duodenal cap. None of these has been proved to be the sole integrating mechanism, which may even be a composite of effects from all three possible mechanisms.

B. Techniques for Chronically Recording Mechanical and Electrical Activity of the Gastrointestinal Tract

Due to the number of drawbacks to the intraluminal monitoring of gastrointestinal motility (e.g., inhibition of flow, elicitation of abnormal reflexes), an extraluminal recording technique has been developed (Jacoby et al., 1963; Reinke et al., 1967; Anderson et al., 1968). This technique uses strain gage force transducers bonded back to back or onto either side of a small copper-beryllium strip. Wires are soldered to each unit so that two arms of a Wheatstone bridge are within the gage. Epoxy is applied to the solder joints to waterproof them and the gage is encapsulated in silicone rubber. As many as eight gages may be connected to one Cannon electric plug making a set ready for sterilization and chronic implantation in the dog, cat, or monkey. Each gage may be sewn wherever desired on the serosal surface of the stomach, small bowel, or colon. The Cannon connector, encapsulated in epoxy, is brought through the skin through a circular incision below the left scapula lateral to the spine and the wires are led through a trocar subcutaneously to the mammary ridge. They enter the abdomen through a stab wound. An advantage of the force transducers is that the strain gages may be oriented in the longitudinal or transverse axis so that either longitudinal or circular muscle contractions (or both) may be recorded from a single site (Reinke et al., 1967; Anderson et al., 1968). The strain gage technique does not require any special surgical alteration of the

gastrointestinal tract, but the effects on motility of various surgical procedures may be monitored with these gages (e.g., Ludwick et al., 1969). In addition, it should be apparent that many fixed sites of the gastrointestinal tract may be monitored simultaneously under numerous conditions (e.g., before and after food or drugs). Repeated tests may be performed in unanesthetized animals for long periods of time with strain gage force transducers. The importance of the use of unanesthetized animals to study the physiology and pharmacology of the gastrointestinal tract has been discussed (Bass and Weisbrodt, 1971).

It has been known for some time that depolarizations of groups of smooth muscle fibers of the gastrointestinal tract cause a recordable change in electrical potential difference when measured by surface electrodes. Such potential differences were measured in the 1920's by Alvarez and his coworkers and referred to as "electroenterograms" (Alvarez, 1948). Bass, Code and Lambert (1961a and 1961b) studied the electric activity of exteriorized Biebl loops of duodenum and of exteriorized antral-GDJ-proximal duodenal segments in unanesthetized dogs. Using needle electrodes, they were able to demonstrate two types of electric phenomena in the canine antrum and duodenum. The first was an "omnipresent", cyclically recurring pattern which they referred to as the basic electric rhythm (BER). The frequency of the BER in the antrum was 4.4/min. In the duodenal cap, the BER frequency was much more variable than in the distal duodenum,

where it was 17.6/min. The second pattern consists of bursts of spike potentials (fast changes in potential difference) superimposed on a particular portion of the BER cycle. When a pressure detecting catheter was placed in the lumen of the Biebl loop, increases in intraluminal pressure were correlated with the spike potentials. The conclusion drawn from this result was that spike potentials are indications of contractions in the bowel. This finding established the recording of gastrointestinal electric activity as a major technique in the study of gut motility. Spike potentials are also correlated with antral contractions (Carlson et al., 1966).

In 1963, McCoy and Bass reported the method of construction and described the utility of newly developed platinum surface electrodes for chronic implantation. This technique allowed the recording of surface potentials in an unanesthetized, essentially unaltered preparation. Recordings could be made over a long period of time and simultaneously at numerous sites. Data from this study confirmed the previous finding (Bass et al., 1961b) of attenuated electrical activity at the GDJ.

C. Alterations in the Pattern of the Basic Electric Rhythm (BER)

It is generally believed that under normal conditions the intact small bowel of many species generates an undaunted BER. Conditions are known which can influence the electrical

frequency of the small bowel. These include ligation (Bass and Wiley, 1965b), transection and reanastomosis (Bunker et al., 1967; Bass and Wiley, 1965a), and various drugs (Bass, 1968). The main effect noted in most of these cases is an alteration in the frequency but not the rhythm of the BER.

In the stomach, the BER originates from a pacemaking region in the orad portion of the corpus near the greater curvature (Weber and Kohatsu, 1970). From there it propagates over the corpus and antrum on its way to the GDJ. As the BER proceeds, the velocity of propagation increases with the greatest velocity in the terminal antrum (Kelly et al., 1969). Kelly and his associates noted that the frequency of the BER was usually the same in the body and antrum but the period of the gastric BER was occasionally irregular. Also, the voltage amplitude of the antral BER is greater than the voltage amplitude of the BER from the body. Thus, it appeared that some electrical characteristics of the smooth muscle of the antrum differed from those of the body of the stomach.

Using anesthetized dogs and close intraarterial injections of various drugs, Daniel has described some additional properties of the smooth muscle electrical activity of the stomach (Daniel and Irwin, 1971). When acetylcholine (0.01-0.1 μg) was injected, premature pacesetter potentials (PP, synonym for BER) were induced depending upon the time elapsed from the previous BER. This particular experiment demonstrated that there was both orad and aborad propagation of

the premature potentials, that a refractory period occurred after each BER and that the premature potential could alter the timing and spread of the normal BER. In addition to demonstrating that small doses of catecholamines inhibit spike potentials (the electrical correlates of contraction), Daniel showed that higher doses (e.g., 10 μg epinephrine) can eliminate the BER for a short time and allow orad propagation of the next BER to occur. In another series of experiments (Daniel, 1965), similar large doses of catecholamines caused arrhythmias which were defined as "rapid repetition of initial potentials without second potentials or contractions". Daniel further states that arrhythmias may be caused by atropine, morphine or large inhibitory doses of histamine, and has referred to this phenomenon under the general classification of the sympathetic dominance pattern (SDP). Phenoxybenzamine could antagonize the effects of norepinephrine and pronethalol could not. From these experiments it is apparent that alterations in the BER called arrhythmias may be pharmacologically induced in the anesthetized dog preparation. An earlier study (McCoy and Bass, 1963) had shown that antral arrhythmias could be produced by an infusion of epinephrine (16 μg/Kg min iv) in the unanesthetized dog.

Abnormalities of the antral basic electric rhythm have also been discovered following at least two surgical procedures. Both Kelly and Code (1969) and Nelson et al. (1967) recorded arrhythmias from their antral electrodes following

truncal vagotomy. The arrhythmias were present only during the early post-operative period in most dogs. It was suggested by Nelson and his co-workers that vagotomy removed a controlling influence on the normal pacemaker allowing the development of ectopic antral pacemakers. Further evidence for this suggestion has been presented by Wilbur and Kelly (1973) who observed antral arrhythmias in fasting dogs for a 1-2 month period after parietal cell vagotomy. In a study of the propagation of the canine gastric BER, Bedi and associates performed a 1 cm longitudinal myomectomy 5 cm from the GDJ in five dogs (Bedi et al., 1972). They recorded electric activity above and below the site of insult and found that the BER of one dog increased below the site to a frequency of 11 to 13 cycles per minute, more than a doubling of the normal BER frequency. This effect lasted at least two weeks, and if it can be assumed that the longitudinal layers did not grow back together during this time, the enhanced frequency must be due to the formation of an ectopic antral pacemaker.

Two recently published studies have further characterized the physiology of the gastric smooth muscle and are aids to understanding abnormal antral BER. The first study determined strength versus duration curves for the BER generated by chronically implanted bipolar stimulating electrodes in the dog (Kelly, 1974). In this study Kelly showed that the antrum had a smaller rheobase (i.e., the minimal strength of stimulus which will elicit a BER wave) and a

shorter chronaxie (i.e., the time necessary to reach threshold after giving a stimulus with twice the strength of rheobase). Kelly also demonstrated a shorter refractory period for the antrum. He concluded that the antrum was more excitable than the body of the stomach and possessed characteristics which might allow an antral pacemaker to appear. The second study (Sarna and Daniel, 1974) confirmed that the antrum had a shorter absolute refractory period than the corpus. In addition, Sarna and Daniel showed that atropine could reduce the threshold for the production of premature potentials and the duration of the absolute refractory period. Physostigmine, on the other hand, increased the threshold for the production of premature potentials and under certain circumstances increased the duration of the absolute refractory period. A reduced threshold and absolute refractory period in the antrum following truncal vagotomy may have resulted in the arrhythmias observed by Kelly and Code (1969) and Nelson et al. (1967).

In view of the studies on the excitability and refractoriness properties of the antrum, it is not surprising that abnormal electrical activity has been recorded in the unanesthetized normal dog implanted with chronic recording electrodes. Kelly and La Force (1972) noted periods of rapidly repeating antral potentials in one fasting intact dog which were returned to the normal BER by stimulating the stomach through a chronically implanted bipolar electrode. Even though the antrum and body can be uncoupled, the dominant

pacemaker is the corporal one.

In a very recent publication Code has described the extent and characteristics of abnormal electrical activity of the antrum observed over the course of two years work in the intact unanesthetized dog (Code and Marlett, 1974). In two dogs abnormal rhythms occurred spontaneously in the interdigestive state. In one of these dogs and a third dog abnormal electrical activity was observed following celiac and superior mesenteric ganglionectomy. Code observed two main types of abnormalities which he named arrhythmia and tachygastria. Arrhythmias were defined as

> "bursts of coupled, tripled, quadrupled, or irregularly grouped abnormally fast pacesetter potentials (which) were often followed by a compensatory pause - an interval in which one or more expected pacesetter potentials failed to occur."

This definition agrees well with that used previously by Daniel (1965). The second abnormality, tachygastria, was essentially a long arrhythmia. In Code's experiments tachygastria was recorded as long as 32 minutes, with frequencies ranging from 10.5 to 12.5 cycles per minute. Tachygastria and arrhythmia are antral phenomena apparently unrelated to the duodenal BER and assumed to be due to the presence of an ectopic pacemaker. They can be propagated in either direction from their site of origin, but only the compensatory pause (not the arrhythmia) reaches the corpus. This observation led Code to propose an orad feedback system which can influence the pacemaker. Lastly, these abnormalities were

only observed during the basal period of the interdigestive state and could be returned to the normal BER following ingestion of water or milk.

At least two reports are available of clinically observed antral arrhythmias. Sarna et al. (1974) recorded gastric BER from 9 patients following laparotomy for various reasons. Records were made throughout the first 5 post-operative days before the sero-muscular electrodes were removed. The BER demonstrated arrhythmias or tachygastria in all patients soon after closure of the abdomen lasting a mean of 14.6 hours (range 7-25 hr.). Spike potentials were not present during these irregular periods and the abnormal BER was propagated in either direction. These workers suggest that motility disorders such as impaired gastric emptying in the early post-operative state may be related to antral arrhythmia or tachygastria. This suggestion received support from a report by Barbara et al. (1974) on the gastric motility and emptying of patients with chronic atrophic gastritis. The BER in these patients was recorded with an intraluminal suction electrode. Antral arrhythmias were observed in three of seven patients with low or normal serum gastrin levels. Contractile activity did not occur while arrhythmias were present. All three of these patients had delayed gastric emptying and dilated, bag-like stomachs were observed radiologically. It appears that abnormal electrical activity observed in the dog stomach may have applications to clinical situations.

D. Vagotomy and Pyloroplasty

Truncal vagotomy with a pyloroplasty or an antrectomy is a current surgical treatment for duodenal ulcer. Dragstedt originally treated patients with truncal vagotomy alone (Dragstedt and Owens, 1943), but problems with gastric stasis necessitated the addition of pyloroplasty to the procedure (Dragstedt et al., 1949). It was traditionally felt that pyloroplasty alleviated the gastric retention and allowed the stomach to "drain" much more easily. Hence, pyloroplasty and other operations designed to achieve the same result have been called "drainage procedures". This terminology has been questioned by Kelly (1971) who noted that coordinated motor activity at the GDJ and not gravity is chiefly responsible for gastric emptying. Other sequelae such as diarrhea, dumping, bilious vomiting, and fullness after meals have led to the development of alternative vagotomy procedures to reduce the high acid secretion of duodenal ulcer patients without contributing to the side effects.

One alternative surgical approach was first tested in dogs by Griffith and Harkins (1957). This approach denervated the parietal cell mass of the stomach leaving the antrum innervated and the hepatic and celiac branches of the vagus untouched. This procedure-variously known as parietal cell vagotomy, proximal gastric vagotomy, and highly selective vagotomy (among at least four other names)-was begun in patients in England and Denmark in 1969 (Johnston and Wilkinson, 1970; Amdrup and Jensen, 1970). A number of

subsequent reports have indicated that as long as the antrum is innervated and bleeding or stenosis is absent, relatively normal gastric emptying should take place, and a pyloroplasty need not accompany the vagotomy (Johnston et al., 1971; Imperati et al., 1972; Grassi et al., 1973). Further clinical work has shown that upon early assessment of results parietal cell vagotomy has a lower incidence of diarrhea (Johnston et al., 1972) and dumping (Humphrey et al., 1972) associated with it than with truncal vagotomy or total selective vagotomy of the stomach. Clark and Alexander-Williams (1973) have shown that parietal cell vagotomy enhances initial emptying but that the overall emptying pattern appears to remain normal. These workers also suggest that dumping may be associated with pyloroplasty.

Cannon and Blake (1905) were probably the first investigators to study the effects on feline stomach emptying of Heineke-Mikulicz and Finney pyloroplasties. They concluded that these procedures did not destroy the normal emptying mechanism. In more recent studies in both man and dog (Hayden and Read, 1968; Lulu et al., 1971) no obvious differences in the effects of the two types of pyloroplasties were noted, but normal gastric emptying appeared to be impaired (at least when these procedures were combined with truncal vagotomy). Ludwick and co-workers (1969), using extraluminal force transducers in unanesthetized dogs, showed that Finney pyloroplasty alone or with truncal vagotomy disrupts the normally coordinated antral-duodenal

contractile activity. This appears to happen by making the GDJ segment one large compartment. These authors followed up this study with an investigation of the stomach emptying of liquid test meals following Finney pyloroplasty and vagotomy (Ludwick et al., 1970). These two studies taken together support the concept that pyloroplasty alters antral-duodenal coordination, and impairs stomach emptying.

When a Heineke-Mikulicz pyloroplasty is performed, the region of the caudad duodenal cap is approximated to the anterior aspect of the mid-antrum. This obviously disrupts the normal anatomical arrangement of the hypomuscular segment and surrounding terminal antrum and duodenal cap. In addition, this procedure brings into juxtaposition the smooth muscle of the antrum and duodenum without any connective tissue separation. This would allow the BER of both organs to be more closely positioned in respect to each other, and may alter the electrical and mechanical character of the area. In fact, Douglas and Duthie (1972), reporting on a series of patients who underwent Heineke-Mikulicz pyloroplasty following negative duodenal ulcer exploration, noted an incidence of post-operative symptoms (including dumping) similar to that following truncal vagotomy and pyloroplasty. The only electrical study following Heineke-Mikulicz pyloroplasty was performed on the acute, anesthetized dog using bipolar electrodes (Shiratori et al., 1965). Their results, which showed a prolongation of the interval between antral BERs, need confirmation.

An in depth analysis of the effects of various vagotomy and pyloroplasty procedures has been carried out in three laboratories on the dog. Wilbur and Kelly (1973) have reported their results on gastric emptying, intraluminal pressure, and electrical activity following parietal cell vagotomy, complete gastric vagotomy and after truncal vagotomy. They found enhanced emptying of liquid saline and glucose test meals following parietal cell vagotomy and complete gastric vagotomy, but only the glucose meal was enhanced after truncal vagotomy. When the emptying of radiopaque spheres was observed, parietal cell vagotomy did not change the rate of emptying, but both complete gastric and truncal vagotomy demonstrated delayed emptying of the spheres. Hallenbeck and Gleysteen (1974) have reported no change in emptying of saline and glucose test meals after parietal cell vagotomy when measurements were made at longer intervals than those of Wilbur and Kelly. In two studies from Dr. Paul Bass's laboratory on the stomach emptying of trisodium citrate and citrate with oleic acid test meals it was found that 1) truncal vagotomy with or without pyloroplasty has no significant effect on the emptying time of these liquid meals; 2) parietal cell vagotomy with or without pyloroplasty has no significant effect on the emptying time of these meals, and 3) truncal vagotomy caused retention of solid dietary meals (Springfield et al., in press; Weddle et al., 1974). Normal emptying of solids but not liquids is affected by altering the innervation of the GDJ segment.

When Wilbur and Kelly measured intraluminal pressures following the various vagotomy procedures they found that the pressure increased more with distention after all three vagotomies than before surgery. The vagus nerve has an important part in the stomach's ability to distend without great increases in intraluminal pressure.

The effects of truncal and parietal cell vagotomy on antral-duodenal contractility have also recently been investigated (Walker et al., 1974). The finding contained in this report is that both procedures are disruptive to the normal antral-duodenal contractile relationship. Parietal cell vagotomy only slightly altered the contractile pattern without significantly affecting the frequency or force of contractions in the interdigestive or postprandial state. Truncal vagotomy significantly reduced antral contractility in the interdigestive state and inhibited antral contractions in two of three dogs following food. The normal pattern of duodenal contractions was absent as well. It is important to note that Walker and associates had difficulty maintaining the health of animals following truncal vagotomy.

STATEMENT OF PROBLEM

The objectives of this study are fourfold.

1) The first objective is to examine the antral-duodenal circular muscle contractile patterns following parietal cell vagotomy (PCV), parietal cell vagotomy with pyloroplasty (PCV + P), truncal vagotomy (TV) and truncal vagotomy with pyloroplasty (TV + P). It is intended to analyze all four procedures so as to have a complete characterization, and to do so in healthy unanesthetized dogs.
2) The second objective of this study is to evaluate the effects of Heineke-Mikulicz pyloroplasty alone on the gastric emptying of a liquid test meal.
3) Thirdly, the effects of Heineke-Mikulicz pyloroplasty on the circular muscle contractile activity of the antral-duodenal segment will be evaluated.
4) The final objective is to investigate the patterns of electrical activity of the antral-duodenal segment following Heineke-Mikulicz pyloroplasty.

It is hoped that fulfilling these objectives will characterize the alterations in the physiological and pharmacological responses of the antral-duodenal segment caused by these surgical procedures. It is further hoped that this study will lead to a clearer understanding of the mechanisms involved in the motor coordination of the antrum and

duodenum in stomach emptying.

METHODS

A. Vagotomy and Pyloroplasty Procedures

1. Experimental design

Nine healthy mixed breed dogs (9.5-14.5 Kg) were used in this study. An outline of the surgical conditions and the experimental challenges investigated is shown in Table 1. The dogs were randomly divided into four groups corresponding to the surgical procedures, parietal cell vagotomy (PCV), PCV with pyloroplasty (P), truncal vagotomy (TV), and TV with P. Two dogs underwent both PCV and pyloroplasty procedures. Similarly, two dogs were tested after both truncal vagotomy and TV + P procedures. An additional dog was studied in three of the four groups, after either PCV, PCV + P or TV + P. Two additional dogs were studied following the truncal vagotomy procedure alone.

The dogs were housed in a constant temperature environment on alternating 12 hour light-dark cycles. The reason all dogs receiving PCV or TV were not continued into the PCV + P or the TV + P studies respectively (see Table 1) was due to morbidity of the dogs, or to transducer failure. In the early part of the study dogs with TV maintained on solid laboratory chow had a tendency to become morbid. For example, following truncal vagotomy, a healthy state was difficult to maintain due to food retention, vomiting, and electrolyte loss. Consequently, all dogs were maintained on a nutritionally balanced liquid diet, Carnation Slender®,

TABLE 1

Surgical conditions and experimental challenges used in the study of vagotomy and pyloroplasty procedures.

SURGICAL CONDITIONS

PARIETAL CELL VAGOTOMY	TRUNCAL VAGOTOMY
'TAFFY'	'SHEPHERD'
'FRANCIS'	'BLACKIE'
'WEAZEL'	'CLORIS'
	'BLONDIE'

PARIETAL CELL VAGOTOMY AND PYLOROPLASTY	TRUNCAL VAGOTOMY AND PYLOROPLASTY
'TAFFY'	'SHEPHERD'
'FRANCIS'	'LADY'
'BROWNIE'	'CLORIS'

EXPERIMENTAL CHALLENGES

CITRATE TEST MEAL

CITRATE-FAT TEST MEAL

BETHANECHOL

BETHANECHOL, CITRATE-FAT TEST MEAL

INSULIN

INSULIN, CITRATE-FAT TEST MEAL

throughout the remainder of the study. For these reasons we collected less data from animals with truncal vagotomy.

2. Surgical methods

All surgical procedures were performed under pentobarbital anesthesia (35 mg/Kg iv). Parietal cell vagotomy was performed after a midline abdominal incision as previously described (Weddle et al., 1974). After visualizing the vagus along the lesser curvature of the stomach, the branches of the anterior and posterior gastric nerves were ligated and sectioned from the incisura angularis to the gastroesophageal junction. The vagal branches to the liver and celiac axis are preserved during this procedure and the antrum is left innervated. The serosa just below the gastroesophageal junction was circumferentially "skeletonized" of all small vagal branches.

Truncal vagotomy was performed through a left thoracotomy. The dogs were artificially respired with 95% O_2-5% CO_2. The distal third of the esophagus was examined and the right and left vagal trunks were identified. These were ligated and approximately 1-2 cm segments of the trunks were removed along with a third communicating branch.

In this study, Heineke-Mikulicz pyloroplasties were performed following a midline incision and location of the gastroduodenal junction. A six cm longitudinal incision was made equidistant on the anterior surface of the antrum and duodenum. The mucosa and muscle layers were closed transversely with one layer of suture. A second transverse

suture layer was used to approximate the serosa. An adequate lumen was obtained in each case as shown by inspection at surgery and confirmed at the time of autopsy.

Circular muscle contractile activity was monitored with extraluminal strain gage force transducers as previously described. Briefly, each force transducer consists of two foil strain gages with the dimensions 8 mm X 5 mm (Micro-Measurements, Romulus, Michigan). The strain gages are bonded back to back and wires are soldered to each unit so that two arms of a Wheatstone bridge are within the transducer. The transducers are then waterproofed with epoxy, encapsulated in silicone rubber, and heat sterilized for implantation. Each unit consisted of five transducers connected to a Cannon plug. The transducers and lead wires were led through a circular skin incision, below the left scapula lateral to the spine, subcutaneously to the lower left quadrant. They entered the abdomen through a stab wound and each transducer was sewn on to the serosal surface of the organ to be studied. In this study, the transducers were oriented in the transverse axis to record circular muscle contractions. The body transducer was 10-15 cm, while the two antral and two duodenal transducers were 4-5 and 2-3 cm orad and aborad to the gastroduodenal junction.

At least ten days prior to any of the surgical procedures described above, six of the nine dogs had been implanted with a Teflon cannula in the cervical esophagus for administration of liquid test meals.

3. Test meals and drug challenges

Studies were begun following a 10 to 14 day recovery period after each surgical procedure. The antral-duodenal contractile activity was monitored in every dog following an 18 hour fast. Test meals or drugs were administered in an interdigestive basal period following an interdigestive burst. These terms have been described previously (Carlson et al., 1970). Briefly, the interdigestive state is recorded in dogs following an 18 hour fast and has been characterized by periods of alternate low level (basal) and high level (burst) activity on both the antrum and duodenum. The basal period lasts approximately 90 minutes. The burst period lasts approximately 15 minutes.

The liquid test meals consisted of either 300 ml of trisodium citrate (19.6 g/l) or 300 ml of trisodium citrate with 10 mN oleic acid suspended by 0.5% Tween 80. These were called the citrate and citrate-fat test meals respectively. Each had an osmolarity of 200 milliosmoles/liter which was determined by freezing point depression. The test meals were administered through a stomach tube placed through the esophageal cannula or passed orally into the stomach.

The effects of bethanechol chloride (0.1 mg/Kg sc) and insulin (0.5 units/Kg iv) alone and on the motility pattern of the citrate-fat test meal were examined. Bethanechol acts peripherally on smooth muscle muscarinic receptors while insulin stimulates the vagus nerve centrally by

induced hypoglycemia.

4. Data Analysis

Circular muscle contractile activity was recorded from the transducers on an 8-channel Beckman® Type R411 Dynograph® recorder. Records were evaluated for one hour following an interdigestive burst ("control" activity), either test meal, or drug administration. This time period was used for the analysis in this study since the $T_{1/2}$ for the normal stomach emptying of the citrate-fat test meal determined previously (Weddle et al., 1974) was approximately one hour (54.6 ± 9.1 min.). The citrate test meal data were also analyzed for 15 minutes since this is approximately the $T_{1/2}$ for the stomach emptying of citrate (13.2 ± 2.1 min.). Since the hypoglycemic effect of insulin on contractility is delayed, evaluations of experiments using insulin were begun 30 minutes after its administration. In each dog one specific antral and one specific duodenal transducer were picked for analysis of all records within one surgical condition. Contractions were analyzed by placing a transparent template over the record and manually counting the number of contractions within various calibrated force ranges for the hour test. Prior to implantation each transducer had been calibrated by recording the deflection in mm after hanging various weights on the transducer. The calibration was linear over the range of recorded values. A motility index was calculated for each area of the bowel under study by

multiplying the number of contractions falling within the various force ranges by a factor which weighted the force ranges and finding the sum. The force ranges used were 10-20 grams, 20-40 grams, 40-80 grams, and 80+ grams. The motility index (MI) may be represented by the formula:

$$MI = (N_1 \times 1) + (N_2 \times 2) + (N_3 \times 4) + (N_4 \times 8)$$

where N equals the number of contractions within a particular force range. This index is a number which represents the frequency and force of contraction for each experimental situation. In addition to the MI, the per cent activity was calculated for all of the experimental challenges. This number was found by dividing the observed frequency of contractions for 60 minutes by the number of contractions which theoretically could be produced under maximum cholinergic stimulation with bethanechol. By sampling peak bethanechol stimulation for 2 minutes the maximum possible number of contractions for an hour was extrapolated for each dog. Experimental challenges were replicated twice for each dog wherever possible and all data for each surgical condition were pooled. Both MI and % activity data were subjected to an analysis of variance of the four surgical procedures for each challenge and each organ. Whenever the F test was significant, the data were analyzed by a least significant difference procedure.

B. Heineke-Mikulicz Pyloroplasty - Gastric Emptying

1. Experimental design

Seven healthy mixed breed dogs (9.5-15.0 Kg) were used in this study. All animals were conditioned to the laboratory environment and to the passage of gastric tubes (20 Fr) through a bite block before beginning studies of gastric emptying. The index of gastric emptying in these experiments was the volume of a 300 ml citrate-fat liquid test meal remaining in the stomach after 45 minutes. This time period was chosen since it is approximately the $T_{1/2}$ for the citrate-fat test meal as previously determined in normal dogs (54.6 $\pm$ 9.1, Weddle *et al.*, 1974). At least three experiments were performed in each dog before and after a Heineke-Mikulicz pyloroplasty.

2. Surgical methods

Heineke-Mikulicz pyloroplasties were performed using pentobarbital anesthesia (35 mg/Kg iv) and sterile surgical technique. The gastroduodenal junction was located through a midline incision and a 5 cm longitudinal incision was made on the anterior surface of the antrum and duodenum. The incision extended 3 cm on the antrum and 2 cm on the duodenum. The mucosa and muscle layers were closed transversely with one layer of suture. A second transverse suture layer was used to approximate the serosa. An adequate lumen was obtained in each case and was confirmed at autopsy. A 10 to 14 day recovery period was allowed before repeating the

gastric emptying experiments.

3. Emptying procedure

The citrate-fat liquid test meal consisted of 300 ml of trisodium citrate (19.6 g/l) with 10 mN oleic acid suspended by 0.5% polysorbate (Tween) 80. The test meal also contained 40 mg/l phenolsulfonphthalein as a nonabsorbable marker to determine gastric volumes by a colorimetric method. The osmolarity of this test meal was 225 mOsM/l as measured by freezing point depression.

Following at least an 18 hour fast, the dog was placed in a stand in the laboratory and a tube was passed into the stomach through a bite block. One to two 50 ml rinses of distilled water were administered and aspirated through the tube to remove any residual food particles and secretions. The room-temperature citrate-fat test meal was then instilled and the tube was withdrawn. After 45 minutes the tube was reinserted, the stomach aspirated, and one 50 ml rinse administered and aspirated.

The optical density of phenolsulfonphthalein was measured in the original test meal, in the meal aspirated, and in the final rinse solution. This was performed by measuring the per cent transmittance at 560 nm (λmax) of solutions of 1 ml test solution and 7 ml of pH 9.2 boric acid-sodium hydroxide buffer (3.09 g/l H_3BO_4, 1.04 g/l NaOH, and 3.73 g/l KCl) and converting to optical density by standard conversion tables. The volume of test meal remaining

in the stomach was calculated from the following formula:

$$V(\text{remaining}) = Va \times \frac{Pa}{Po} + Vr \times \frac{Pr}{Pa}$$

where Va = volume of gastric aspirate, Vr = volume of rinse solution aspirate, Pa = optical density of phenolsulfonphthalein in gastric aspirate, Po = optical density of phenolsulfonphthalein in original test meal, and Pr = optical density of phenolsulfonphthalein in rinse solution aspirate. Since the optical densities are determined by the relative concentration of marker present, their ratios are proportional to the ratios of the actual concentrations of phenolsulfonphthalein.

4. Data analysis

In this study each animal served as its own control. The mean volume remaining in the stomach with its standard error was determined for at least three experiments before and three experiments after Heineke-Mikulicz pyloroplasty. These two means were then compared in each animal using the Student t-test. Also the grand means for all control experiments and all experiments following pyloroplasty were compared in this way.

C. Heineke-Mikulicz Pyloroplasty - Motor Activity

1. Experimental design

Eight healthy mixed breed dogs (9.5-16.5 Kg) were used in this study. The dogs were divided into four in a control group and four in a group which received Heineke-Mikulicz pyloroplasty. The motor activity of the gastroduodenal junctional area was monitored in all dogs under various challenges. Between experiments the dogs were maintained on solid laboratory chow and water ad libitum in a constant temperature environment with a 12-hour light-dark cycle.

2. Surgical methods

All surgical procedures were performed using sterile surgical technique and pentobarbital anesthesia (35 mg/Kg iv). Heineke-Mikulicz pyloroplasties were performed exactly as described in part B.2. of these methods. A 5 cm incision was closed transversely with 2 layers of sutures.

Each control dog and each dog in the pyloroplasty group was implanted with a unit of extraluminal strain gage force transducers. The construction and method of implantation of these transducers is described in part A.2. of these methods. Each unit consisted of five transducers connected to a Cannon plug located subcutaneously near the left scapula. In this study the transducers were sewn to the serosal surface in the transverse axis of the stomach and duodenum to record circular muscle activity. In the control group the body transducer was located 10-12 cm from the gastroduodenal

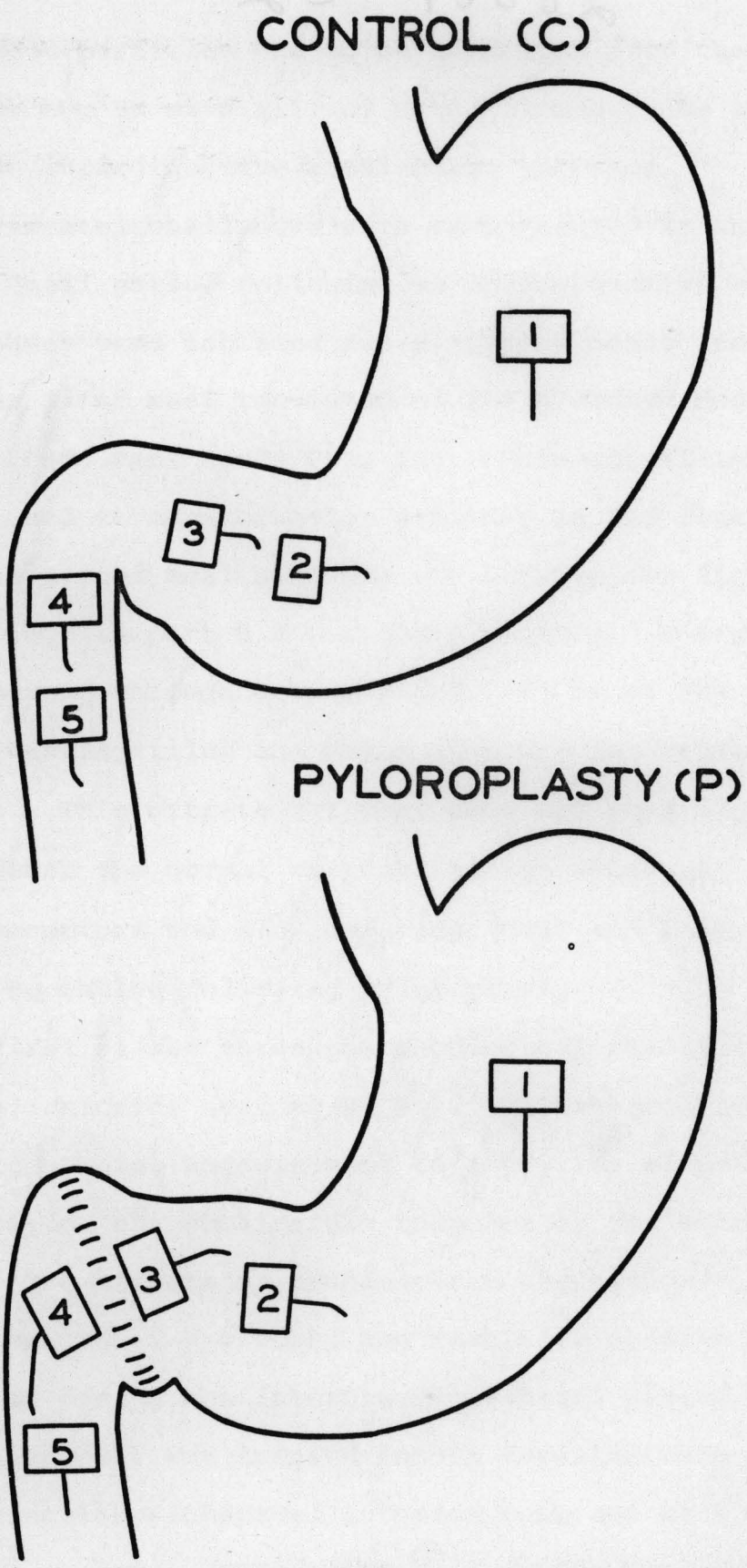
junction, two antral transducers were located 3 cm and 6 cm from the gastroduodenal junction, and the duodenal transducers were located 2-3 cm and 6 cm aborally from the junction. The transducers in the pyloroplasty group were implanted at the same distances from the gastroduodenal junction as those in the control group and then the pyloroplasty was performed. In this way essentially the same segments of muscle were recorded in all dogs even though in the pyloroplasty group the transducers closest to the gastroduodenal junction on the antrum and duodenum were next to the suture line of the pyloroplasty. The placements of the transducers are shown in Figure 1. Following surgery the animals were allowed to recover for 10 to 14 days before experiments were begun.

3. Test meals and drug challenges

A variety of physiological and pharmacological challenges were performed in each dog to study the motor characteristics of the gastroduodenal junctional area and to compare the results from the control dogs with those from the pyloroplasty group.

Circular muscle contractile activity was monitored in every dog following at least an 18 hour fast. Control interdigestive activity was collected in each animal for both the basal and burst periods of the interdigestive state. These periods are described in part A.3. of these methods. In some animals, particularly animals with pyloroplasties,

Figure 1. Illustrations of the positions of the extraluminal force transducers for the control (C) group of dogs (top) and for the pyloroplasty (P) group of dogs (bottom). Position 1 was on the body of the stomach, positions 2 and 3 were on the antrum, and positions 4 and 5 were on the duodenum. See text for exact distances from the GDJ.


CONTROL (C)
1
3
2
4
5
PYLOROPLASTY (P)
1
3
2
4
5

residual food particles had to be aspirated from the stomach with one or two 50 ml distilled water rinses to be able to observe the interdigestive basal-burst sequence.

Experimental challenges were administered in an interdigestive basal period following an interdigestive burst. The challenges used included two different meals and three drugs. The first meal consisted of 200 g canned dog food (Vets Dog Food, Peck Foods Co., Inc., Chicago, Illinois) which was used to monitor motor activity in the digestive state. The second meal used was the citrate-fat liquid test meal described in part B.3. of these methods. A stomach tube was passed through a bite block, 300 ml of the liquid test meal was instilled and motor activity was recorded for 45 minutes. This citrate-fat test meal was used to investigate whether the normal response to fat which can affect duodenal receptors and slow emptying (Hunt and Knox, 1968) was still operative following pyloroplasty.

The first of the three pharmacological challenges was bethanechol chloride (0.1 mg/Kg sc). Bethanechol is a cholinergic agonist and was used to study the effect of pyloroplasty on the cholinergic response of the antrum and duodenum. The effects of pentagastrin (Peptavlon®, Ayerst Laboratories, Inc., New York, New York, 1.0 µg/min) were also studied during the interdigestive basal period. Pentagastrin (20 µg/ml) was infused into a forelimb vein using a Harvard Apparatus Withdrawal/Infusion Pump set at 0.051 ml/min for a 10 cc syringe. A Butterfly® infusion set with a 19 g

or 21 g needle was attached to the syringe. Of interest was whether the surgery could alter the normal response to pentagastrin. Finally, the effects of metoclopramide HCl (Robins Research Laboratories, Richmond, Virginia) on the circular muscle contractile activity of the antrum and duodenum were investigated in the interdigestive basal period and during the digestive state. In both cases the dose given was 2 mg/Kg iv and in the latter case metoclopramide was administered 30 min after the animal was fed 200 g of canned dog food. Metoclopramide is a drug which has been claimed to enhance stomach emptying, but its mechanism of action is not yet proved. Data from two replicates of all of the above challenges was collected wherever possible for each dog.

4. Data analysis

The circular muscle contractile activity from the five positions in each dog was recorded on an 8-channel Beckman® Type R411 Dynograph® recorder. Records were evaluated manually for each challenge in every dog. The time of analysis differed from challenge to challenge, but was the same length in each dog for each individual challenge. The interdigestive burst period was analyzed for 10 minutes of peak activity and the basal period was analyzed for one hour. Activity from the digestive state was analyzed for one hour and the citrate-fat test meal was analyzed for the time period used in the gastric emptying study, 45 minutes. Contractile activity following

bethanechol and pentagastrin administration was analyzed for periods up to 30 minutes, and that due to metoclopramide was analyzed for one hour in either the digestive or interdigestive states. Data collected from all transducers except on the body of the stomach was subjected to quantitative analysis. A motility index was calculated for transducers numbered two through five by multiplying the number of contractions within four set force ranges by a factor which gave more weight to the larger amplitude contractions and then finding the sum. The force ranges used were 5-10 grams, 10-20 grams, 20-40 grams, and 40-80 grams. The lower range was selected as that which would include the smallest amplitude contractions which could be discriminated from baseline artifact or respirations. The motility index (MI) for these experiments is represented by the same formula used in the vagotomy and pyloroplasty experiments,

$$MI = (N_1 \times 1) + (N_2 \times 2) + (N_3 \times 4) + (N_4 \times 8)$$

where N equals the number of contractions within the particular force range. Since this index is a number which represents the frequency and force of contraction for a given experimental situation two other parameters were calculated to give a more complete picture of the results. These parameters were the frequency of contraction for a given challenge and a parameter called the mean motility index (MMI) found by dividing the motility index by the number of contractions for the time period analyzed. The

MMI is therefore a term which is an expression for the force of contraction for a given time period. For any experimental challenge, data from the control dogs and pyloroplasty dogs for the antrum were subjected to an analysis of variance using a completely random design with unequal replication due to failure of some transducers. A similar analysis of variance was used for all of the data from the duodenum. In some instances data collected from two positions on one organ in either the control or the pyloroplasty conditions was analyzed by a paired t-test (Steel and Torrie, 1960). The number of total degrees of freedom (df) used in any analysis was determined by testing the difference between the variance about the mean determined for all experiments in all dogs and the variances about the means for individual dogs. This was done with the conventional F-test. If F was significant (meaning the variance about the grand mean was greater than the variances about individual means) then total df = N - 1 where N was the number of dogs. If F was not significant then total df = N - 1 where N was the number of experiments (which was usually two experiments per dog). Whenever total df was calculated by the former method, the F value determined in the analysis of variance was considered to be a conservative estimate of real F. Whether the F values from the analyses of variance were significant or not, the difference between means was tested using a Bayesian Multiple Comparison Test with a "K" ratio of 100:1 which corresponds to the conventional 0.05 level of

significance (Waller and Duncan, 1970).

5. Validity of the motility index

The motility index (MI) has been used to analyze records of circular muscle contractile activity of the antrum and duodenum throughout the experiments described above in these methods. It has been assumed whenever the MI was used that it was a number which represented the number and force of contractions for the time period analyzed. Thus, the MI was assumed to represent the overall motor activity for a given time period. It is the purpose of this section to describe evidence which lends support to that assumption.

The formula for the motility index is,

$$MI = (N_1 \times 1) + (N_2 \times 2) + (N_3 \times 4) + (N_4 \times 8).$$

The motor activity is divided into four force ranges and the number of contractions within each (N) is counted. This formula can be interpreted by using a hypothetical period of analysis.

In this hypothetical interval four contractions occur, one in each of the four force ranges. Then, according to the formula, the contribution each contraction has to the overall motor activity would be proportional to the weighting factors 1, 2, 4, and 8. The contraction in the highest force range has the largest contribution to the overall activity and the other three contractions contribute

one-half, one-fourth, and one-eighth as much respectively as the largest contraction. If it can be assumed that as the force of contraction increases the base and height of the contraction also increase, then contractions in the higher force ranges should have greater areas than those in the lower force ranges and obviously contribute more to the overall area. If the further assumption is made that the total area of contractions in a given time period is related to the total motor activity and if total motor activity is represented by the MI, then the areas of contractions within the four force ranges of the motility index should on average be related by the numbers used as weighting factors in the motility index. More importantly, the total area of contractions should be related to the motility index. It was decided to assume that an appropriate measure of total activity would be the total area of contractions within a given time period. Determinations of this area were made by assuming a contraction to be an isosceles triangle. The areas of each contraction were determined by multiplying the height of the contraction in mm by the base at one-half the height in mm. From the chart speed and the calibration of the transducers the area of each contraction was reported in the units, gram·minutes. This analysis of total area was performed on at least two transducers in three dogs for either a 5 min segment of peak activity during an interdigestive burst period or a 5 min segment of pre-burst activity. These were compared with the motility index for the same

segment. The total area was plotted against the motility index for the stomach and the duodenum, and the correlation coefficient was calculated and tested for significance with a t-test. The data are shown in Figures 2 and 3. Ten points are plotted for the stomach (Figure 2). Two points for the body and four points for the antrum were from dog one, two points from dog two and two from dog three. For the duodenum (Figure 3), two points were from dog one and two were from dog two. As shown on the figures the correlation coefficient (r) for the stomach was 0.96 ($P < 0.001$) and for the duodenum $r = 0.93$ ($0.1 > P > 0.05$).

These data lend strong support to the hypothesis that the motility index is a valid criterion for the analysis of total motor activity, especially in the stomach. The total area of contraction was highly significantly correlated with the MI for the stomach. Although the correlation coefficient for the duodenum was large only four numbers contributed to its determination and it did not reach the 0.05 level of significance. Since the number of points determined for the duodenum was small, the lack of significance on the duodenum does not seriously limit its use on the duodenum or in any way affect the validity of using the MI for analyzing data from the antrum or body of the stomach. It is therefore concluded that motility index is a valid representation of total motor activity provided that individual organs of the gastrointestinal tract are analyzed separately. It was felt that the strong tendency toward significance of the

Figure 2. Correlation of the total area of contraction with the motility index for a 5 minute burst period on the stomach. Total area of contraction was determined by assuming gastric contractions were isosceles triangles, computing their areas, and finding the sum for 5 minutes. This was plotted as the ordinate against motility index (described within the text) on the abscissa to show the correlation.

Figure 2

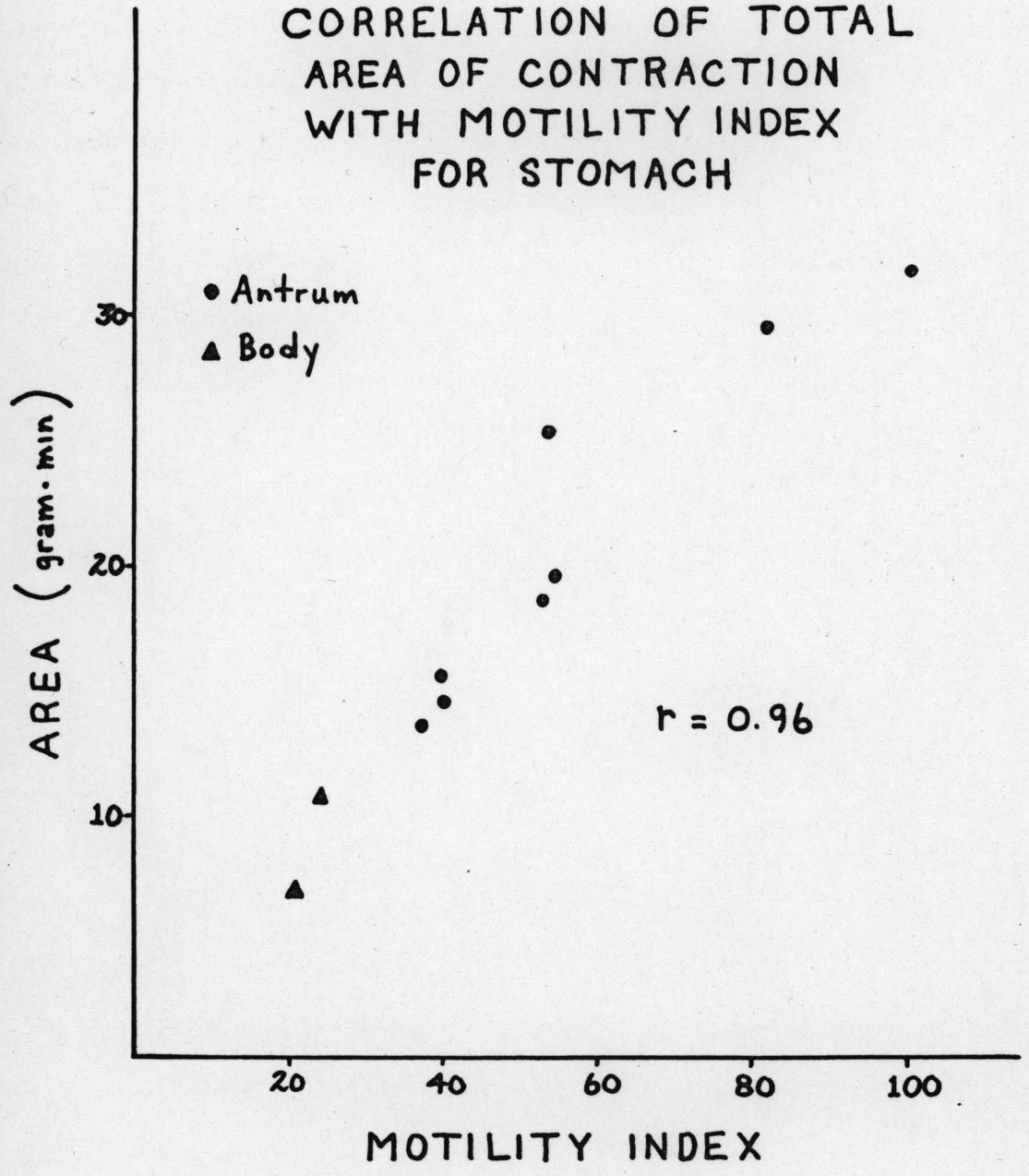
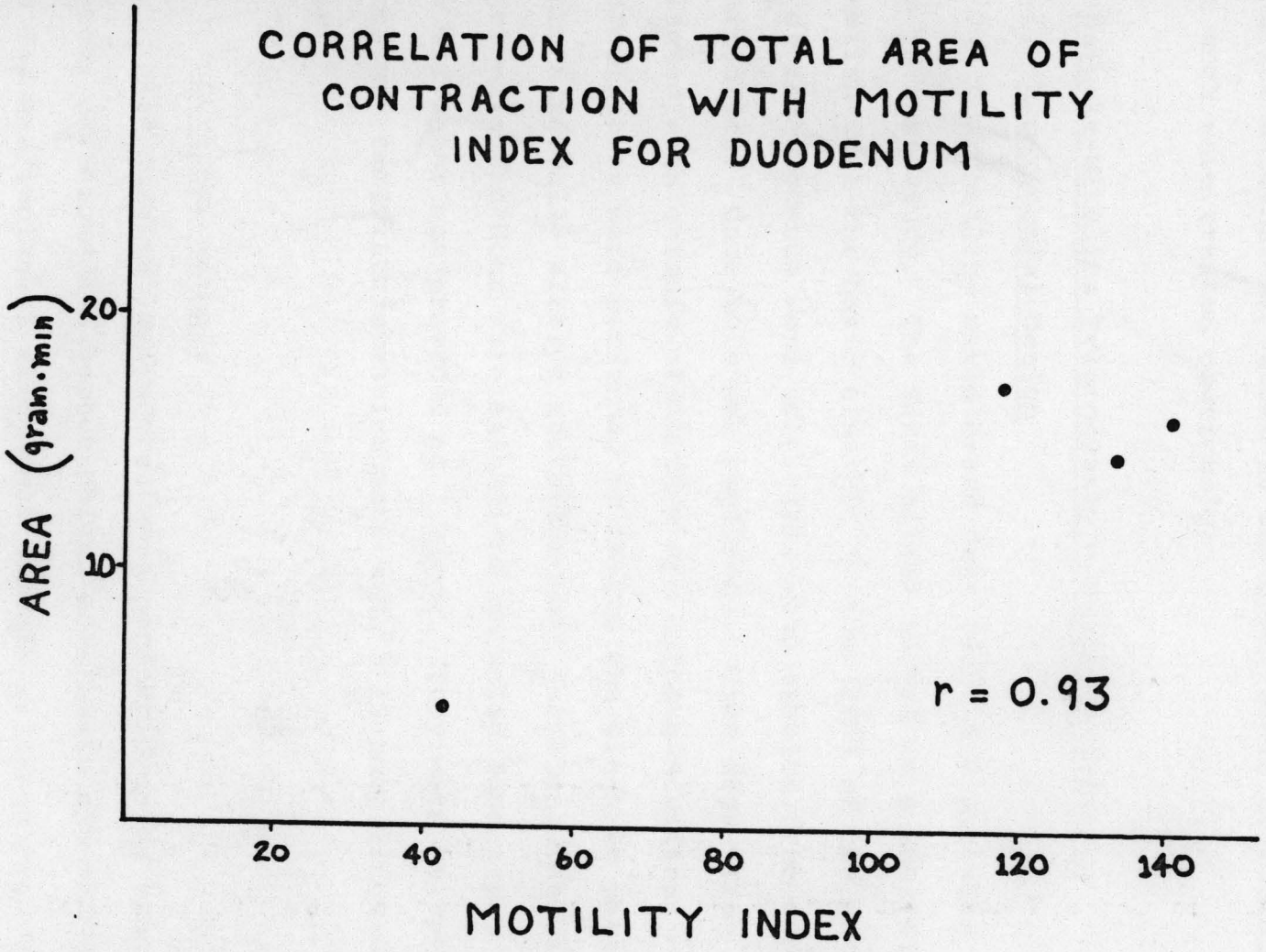

CORRELATION OF TOTAL AREA OF CONTRACTION WITH MOTILITY INDEX FOR STOMACH
• Antrum
▲ Body
AREA (gram·min)
30
20
10
r = 0.96
20
40
60
80
100
MOTILITY INDEX

Figure 3. Correlation of the total area of contraction with the motility index for a 5 minute burst period on the duodenum. Total area of contraction is described within the text and in Figure 2. Total area was plotted on the ordinate against motility index (described within the text) on the abscissa to show the correlation.

Figure 3


CORRELATION OF TOTAL AREA OF CONTRACTION WITH MOTILITY INDEX FOR DUODENUM
AREA (gram.min)
20
10
r = 0.93
20
40
60
80
100
120
140
MOTILITY INDEX

relationship of area and MI on the duodenum justified its use for the analysis of data from that organ. Any differences found for duodenal MI values in the experiments presented in this work were treated cautiously.

D. Heineke-Mikulicz Pyloroplasty - Electric Activity

1. Experimental design

Four healthy mixed breed dogs (9.5-15.0 Kg) were used in this study. The first animal served as a control to establish that the basic electric rhythm (BER) of the antrum and of the duodenum were consistent with results from other laboratories. Once this was confirmed, three dogs were implanted with chronic electrodes and Heineke-Mikulicz pyloroplasties were performed to define the electric patterns of the surgically altered gastroduodenal junction. Between experiments the dogs were maintained on solid laboratory chow and water was provided ad libitum. They were housed in a constant temperature environment with a 12-hour light-dark cycle.

2. Surgical methods

All surgical procedures were performed using sterile surgical technique and pentobarbital anesthesia (35 mg/Kg iv). Each dog was implanted with eight chronic platinum recording electrodes and a reference electrode all of which were connected by Teflon coated lead wires to a 15-pin Cannon connector plug. The plug was embedded in epoxy and covered

with silicone rubber. Recording electrodes were constructed by soldering a 5 mm length of 0.6 mm (approximately 0.3 inch) diameter platinum wire at right angles to a Teflon coated lead wire (16 inches long). A cast for the electrodes was made of beeswax which had been melted and then allowed to harden in a small tin weighing dish. The wax was removed from the dish and placed upside down under an infra-red heating lamp until it became soft. At this time a model electrode was pressed into the wax to form impressions for the new electrodes. A platinum wire connected to its lead wire was pressed into the center of each impression and epoxy (Dore' E-712, a 2-component epoxy, John L. Dore' Co., Houston, Texas) was poured into the impression and allowed to cure overnight. The electrodes were next removed from the mold by heating the wax; the wax was cleaned from the electrode and the epoxy was shaped to desired size. To facilitate suturing, two holes (1 mm (0.04 inch) diameter) were drilled through the epoxy such that the holes were on either side of the wire tip which protruded 2 mm from the center of the electrode. The overall dimensions of these electrodes were 8 mm X 4 mm X 3 mm. The reference electrode was a coil (approximately 4.5 mm overall diameter) of the platinum wire soldered to a 12 inch Teflon coated lead wire with the solder joint covered with epoxy. Each unit of eight recording electrodes and one reference electrode was tunneled subcutaneously, from a position lateral to the spine and caudal to the left scapula where the Cannon plug

was located, to the left mammary ridge. The recording electrodes were brought into the abdomen through a stab wound and the reference electrode was sewn to the facia overlying the rectus muscle near the entrance of the recording electrodes into the abdomen.

In the control dog four electrodes were sutured to the anterior surface of the antrum and four were sutured to the antimesenteric surface of the duodenum. Two antral and two duodenal electrodes were placed just next to, but not on, the gastroduodenal junction with the electrodes on the same organ approximately 1.5 cm apart. The remaining two antral and two duodenal electrodes were 3 cm and 6 cm respectively in either direction from the gastroduodenal junction. In the three dogs which received pyloroplasty five electrodes were placed on the antrum and three were sutured to the duodenum. First, two electrodes were sutured approximately 1 cm and 2-3 cm from the gastroduodenal junction on the posterior surface of the antrum. The Heineke-Mikulicz pyloroplasty was performed as described in part B.2. of these methods. A 5 cm incision was closed transversely with 2 layers of sutures. Finally, the remaining six electrodes were implanted. Two antral and two duodenal electrodes were sewn to the surface of the gastroduodenal junction just next to and on either side of the suture line of the pyloroplasty. The electrodes on the same organ were approximately 1.5 cm apart. One other antral electrode was sutured 3 cm from the suture line of the pyloroplasty and one other duodenal

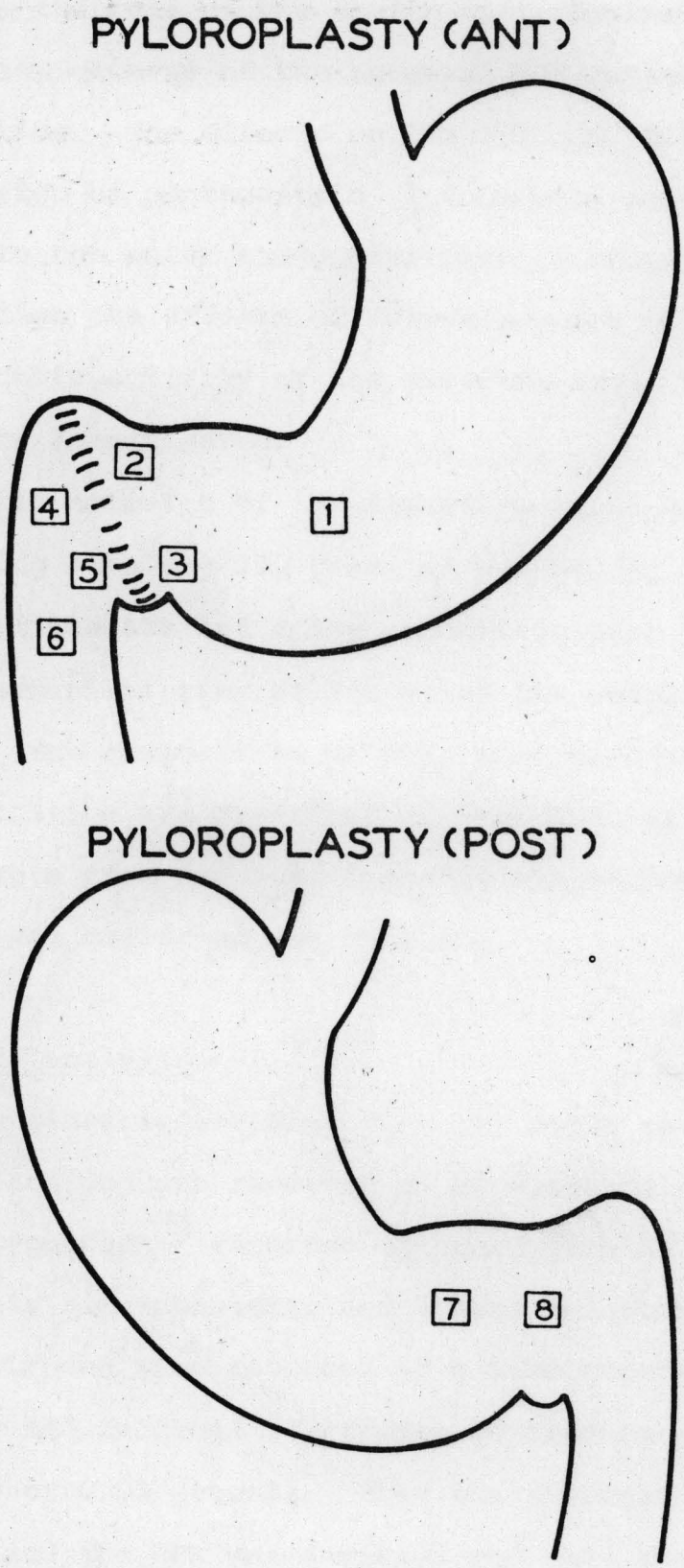
electrode was also sutured 3 cm from the suture line. The positions of the electrodes for dogs with pyloroplasty are shown in Figure 4. Following surgery the animals were allowed to recover for 10 to 14 days before experiments were begun.

3. Test meals and drug challenges

The electrical characteristics of the gastroduodenal junctional area following pyloroplasty were tested in a similar manner to the motor characteristics (described in part C.3. of these methods). Experiments were performed following at least an 18 hour fast. Routinely, the dog's stomach was rinsed with one or two 50 ml distilled water washes to remove any residual food particles. In addition, the animals were trained to lie quietly in stands to reduce noise artifact in the electrical records before any experimental challenges were given.

Electric activity from the antrum and duodenum of all dogs was recorded in the interdigestive and digestive states. In the interdigestive state both the basal and burst periods were recorded to establish the frequency of the BER in the antrum and duodenum and the incidence of spike potentials during these periods. Drugs and meals used in this study were always administered in a basal period following a burst. Cholinergic receptor stimulation and blockade were studied with bethanechol chloride (0.1 mg/Kg sc) and atropine sulfate (1 mg sc), respectively. These drugs were used to

Figure 4. Illustrations of the positions of the chronic recording electrodes on the anterior (ANT) and posterior (POST) gastric surfaces from a dog with a Heineke-Mikulicz pyloroplasty. Positions 1-3 are on the anterior antrum. Positions 7 and 8 are on the posterior antrum. Positions 4-6 are on the duodenum.


PYLOROPLASTY (ANT)
2
4
1
5
3
6
PYLOROPLASTY (POST)
7
8

investigate the role of the cholinergic nervous system in the electric patterns of the surgically altered gastroduodenal junction. The effects on the BER and spike potentials of an infusion of pentagastrin (1.0 μg/min) were studied similarly to the motor study described in part C.3. of these methods. Also the effects of metoclopramide HCl (2 mg/Kg iv) on the electric activity of the gastroduodenal junctional segment were investigated.

Electric activity of the digestive state was recorded after feeding each dog 200 grams of canned dog food. The responses of the BER and spike potentials were also recorded following administration of 300 ml of the citrate-fat liquid test meal. The composition of this test meal and the method of administration are described in part B.3. of these methods. Data from two replicates of all of the above challenges was collected for each dog.

4. Data analysis

The electric activity from the eight recording electrodes in each dog was recorded on an 8-channel Beckman® Type R411 Dynograph® recorder equipped with A-C couplers with variable time constants and a lead selector panel. Antral electrodes were recorded at a time constant of 0.3 seconds and duodenal electrodes at time constants of 3.0 seconds or 0.03 seconds. When the shortest time constant was used the BER was dampened and only the spike potentials were observed. The chart speed was generally set at

1 mm per second except during periods following an experimental challenge when it was changed to 5 mm per second to facilitate analysis.

Records from the antrum and duodenum were analyzed in 5 minute segments for one lead on either side of the pyloroplasty suture line for one of the dogs and in comparable positions in the preliminary control dog. Thus, a 5 minute analysis was obtained for the basal and the burst periods of the interdigestive state, and alternating 5 minute periods of analysis were obtained for other challenges. For each 5 minute segment the period of the BER was measured for a given electrode by measuring the time from the peak negative deflection of one antral wave to the next or the peak positive deflection of one duodenal wave to the next.

To facilitate the analysis of the variability of the gastric BER periodicity, the following method was used. The period of each cycle during the 5 minutes analyzed was measured and placed in an appropriate grouping. The groupings for the antrum were 2 seconds long ranging from 1 second to 31 seconds. The groupings for the duodenum were 0.5 second long ranging from 2.0 seconds to 5.0 seconds. The number of periods measured within each grouping was totaled for the 5 minute time periods to obtain a measure of the variability or stability of the BER. When the total number of periods counted was divided by the time (5 minutes) the frequency of the BER was found for that analysis. In addition, the number of spike potentials on the duodenum was

also measured during these 5 minute intervals. Since the total number of waves was known, the per cent spiking or per cent activity was calculated. The variability in the wave-form which could be correlated with contractions on the antrum prevented a similar analysis of per cent activity for that organ.

RESULTS

A. Vagotomy and Pyloroplasty Procedures

1. Interdigestive state

The basal and burst periods on the antrum and duodenum were present following each of the four surgical conditions (parietal cell vagotomy, parietal cell vagotomy with pyloroplasty, truncal vagotomy, and truncal vagotomy with pyloroplasty). The terminal portion of an interdigestive burst period recorded from a dog with PCV is shown at the top of Figure 5. Segments of duodenal inhibition characteristic of this period in the normal dog are apparent. Figure 5 also contains examples of the motor patterns recorded following administration of the liquid test meals and drugs in the PCV condition. Figures 6 and 7 show examples of the typical motor patterns for all of the experimental challenges given in the TV condition. Figure 6 (top) demonstrates that the interdigestive basal-burst sequence is present following truncal vagotomy. Although the burst period appears to have diminished activity compared to that in the PCV condition, segments of duodenal inhibition are apparent.

The contractility of the body of the stomach was not quantified. Qualitatively, this organ relaxed when either of the two test meals was administered. This relaxation occurred in the presence of all four surgical conditions and equalled approximately a 15 g decrease in baseline force (Figure 6). The body was observed to respond to the

Figure 5. Examples of circular muscle contractile activity from the canine antrum and duodenum following parietal cell vagotomy (PCV). Patterns from the inter-digestive state, following administration of citrate and citrate-fat test meals, insulin and bethanechol (alone or in the presence of the citrate-fat test meal) are shown. Vertical bars represent the calibration of the force transducers. The calibration is the same for all patterns shown. Time is given by the horizontal bars.

Figure 5

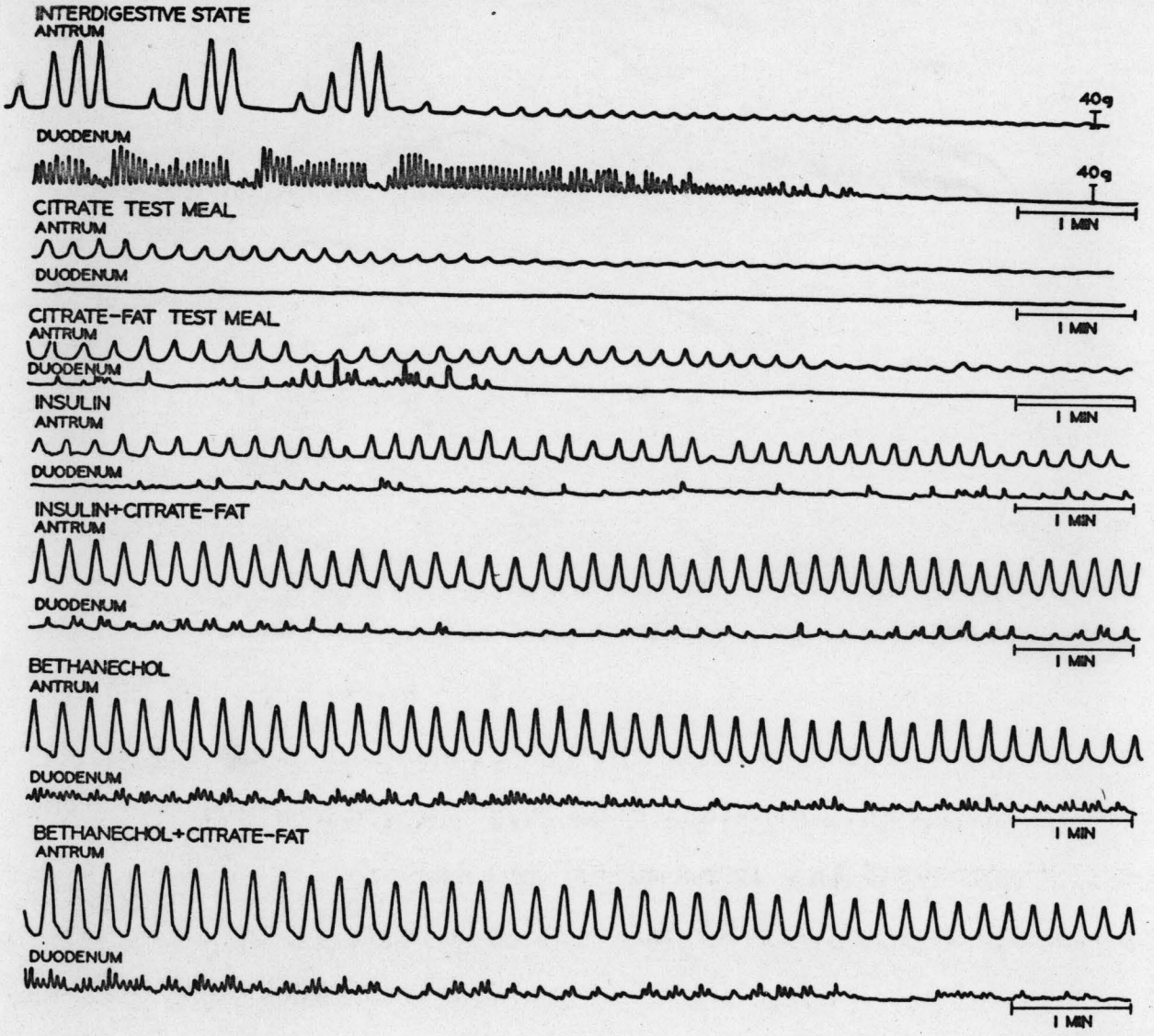

INTERDIGESTIVE STATE
ANTRUM
40g
DUODENUM
40g
1 MIN
CITRATE TEST MEAL
ANTRUM
DUODENUM
1 MIN
CITRATE-FAT TEST MEAL
ANTRUM
DUODENUM
1 MIN
INSULIN
ANTRUM
DUODENUM
1 MIN
INSULIN+CITRATE-FAT
ANTRUM
DUODENUM
1 MIN
BETHANECHOL
ANTRUM
DUODENUM
1 MIN
BETHANECHOL+CITRATE-FAT
ANTRUM
DUODENUM
1 MIN

Figure 6. Examples of circular muscle contractile activity from the canine gastric body and antrum and the duodenum following truncal vagotomy (TV). Patterns from the interdigestive state and following administration of citrate and citrate-fat test meals are shown. Vertical bars represent the calibration of the force transducers. Time is shown by the horizontal bar.

Figure 6

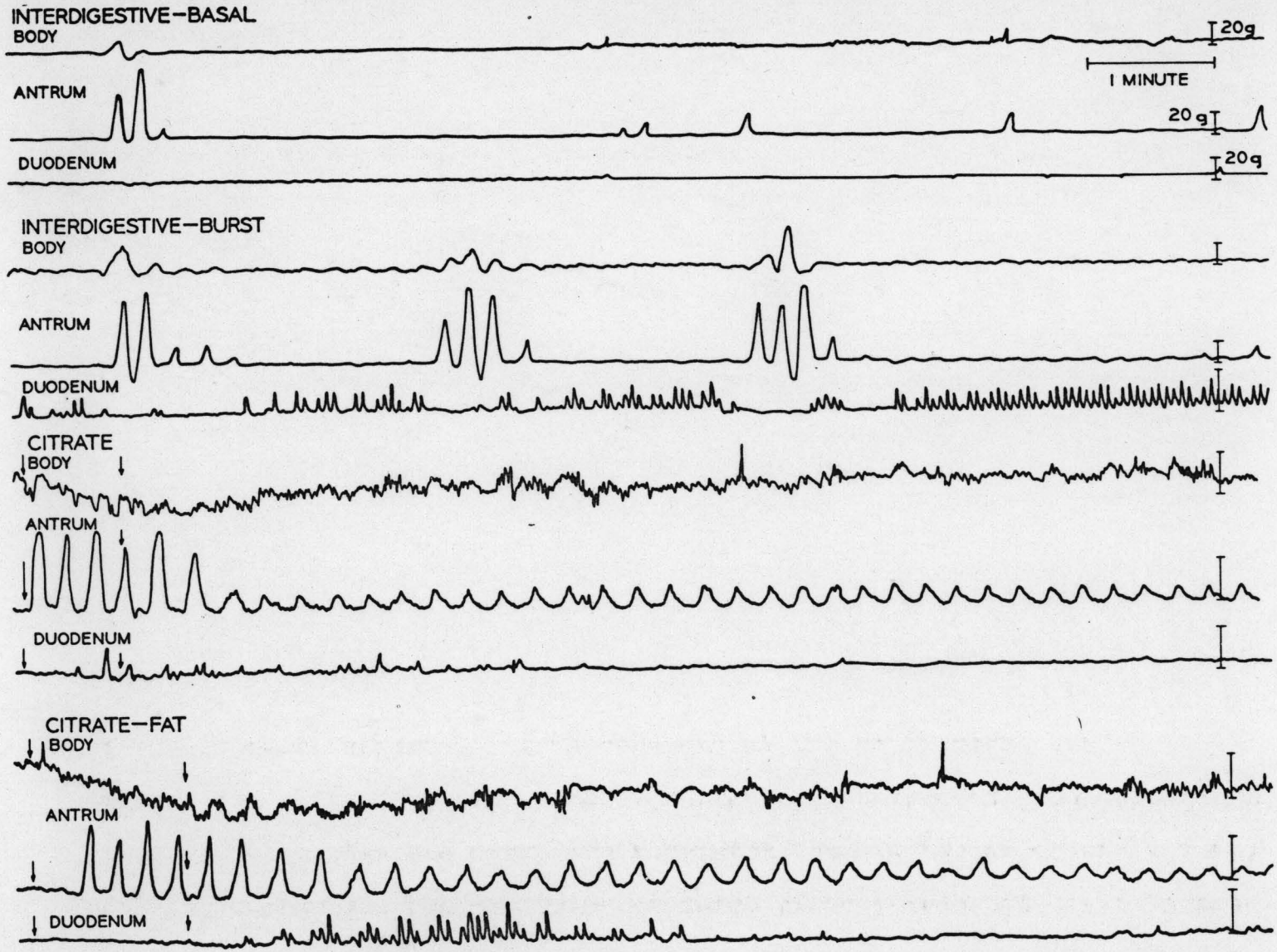
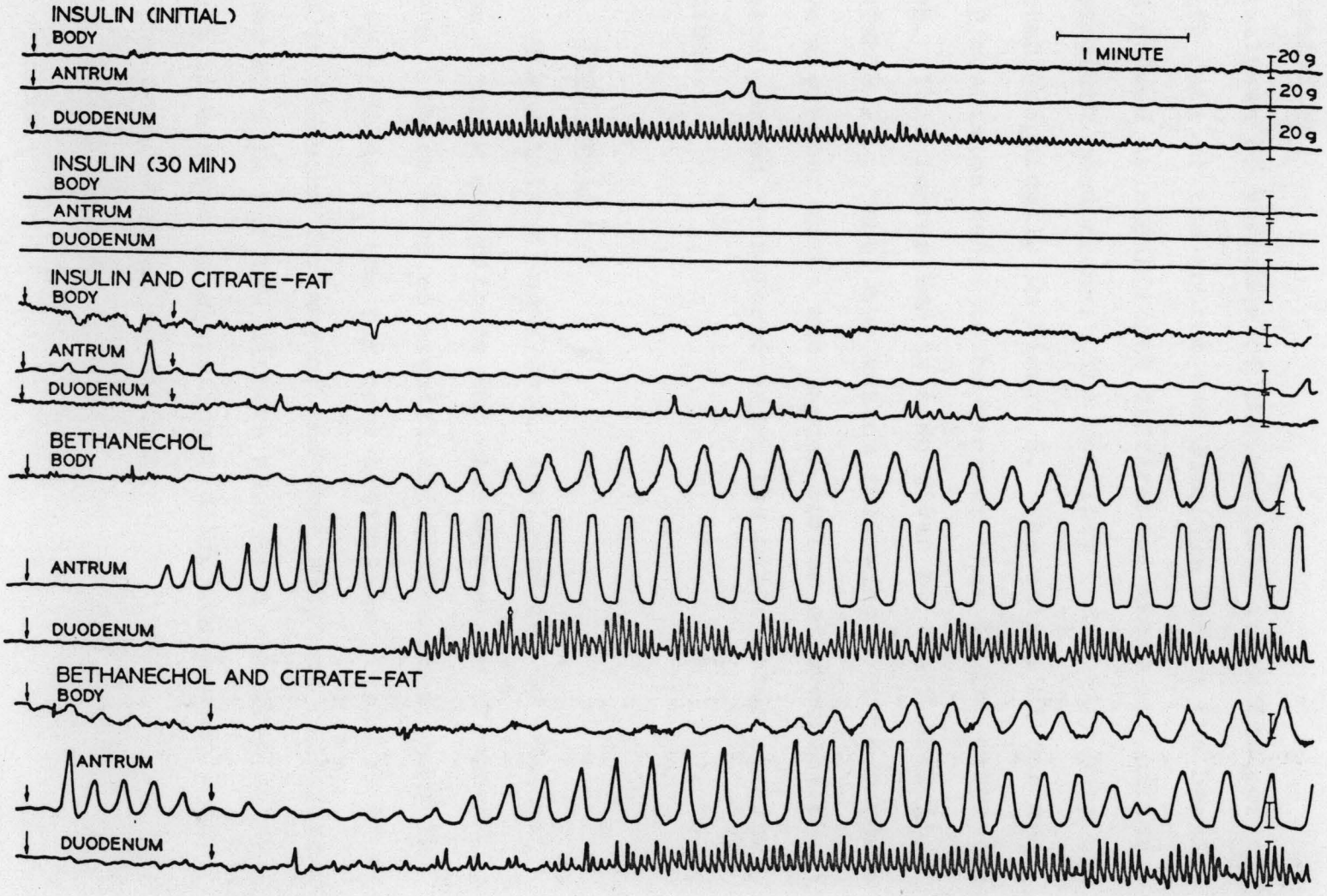

INTERDIGESTIVE–BASAL
BODY
20g
1 MINUTE
ANTRUM
20g
DUODENUM
20g
INTERDIGESTIVE–BURST
BODY
ANTRUM
DUODENUM
CITRATE
BODY
ANTRUM
DUODENUM
CITRATE–FAT
BODY
ANTRUM
DUODENUM

Figure 7. Examples of circular muscle contractile activity from the canine gastric body and antrum and the duodenum following truncal vagotomy (TV). Patterns following administration of insulin and bethanechol alone or in the presence of the citrate-fat test meal are shown. Vertical bars represent the calibration of the force transducers. Time is shown by the horizontal bar.

Figure 7


INSULIN (INITIAL)
BODY
1 MINUTE
20 g
ANTRUM
20 g
DUODENUM
20 g
INSULIN (30 MIN)
BODY
ANTRUM
DUODENUM
INSULIN AND CITRATE-FAT
BODY
ANTRUM
DUODENUM
BETHANECHOL
BODY
ANTRUM
DUODENUM
BETHANECHOL AND CITRATE-FAT
BODY
ANTRUM
DUODENUM

bethanechol challenge, but showed no response to insulin administration.

Analyses of variance of the motility index and per cent activity data of the antrum and duodenum during the basal period showed no significant differences among any of the four surgical conditions. The motility index (MI) data are presented graphically in Figure 8. The antral MI for the PCV + P condition tends to be greater than in the other conditions. This impression is also given by the % activity data (Table 2). Thus, the antrum following a PCV + P tends to have a greater force and larger number of contractions in the basal period than found under the other three surgical conditions.

2. Test meals

The motility index data, analyzed for 60 minutes, for the citrate and citrate-fat challenges are presented in Figure 9. There were no significant differences among the motility indices or the per cent activities (Table 2) of the antrum or duodenum for any of the four surgical conditions. When the MI data for the citrate meal were analyzed again for only 15 minutes no significant differences were found among the four surgical conditions.

3. Drugs

In animals with PCV with or without pyloroplasty insulin stimulated high antral and relatively low duodenal

Figure 8. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the interdigestive basal period. Comparisons were made among the four surgical conditions, PCV, PCV + P, TV, TV + P (see text for definitions) for each organ. Numbers on the abscissa represent the pooled numbers of experiments for each surgical procedure.

Figure 8

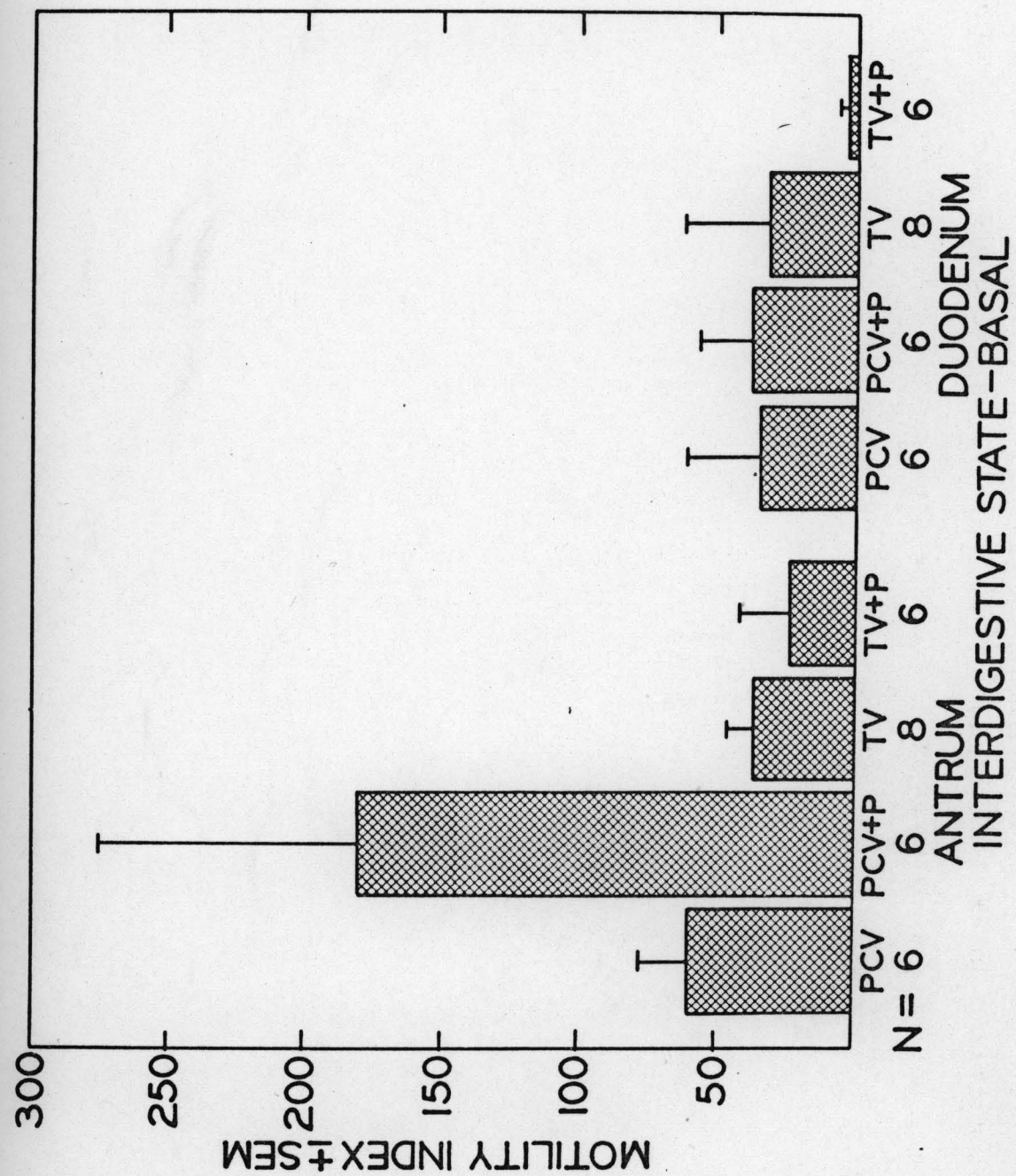

MOTILITY INDEX ± SEM
300
250
200
150
100
50
N = 6
PCV
PCV+P
TV
TV+P
6
6
8
6
ANTRUM
PCV
PCV+P
TV
TV+P
6
6
8
6
DUODENUM
INTERDIGESTIVE STATE-BASAL

Figure 9. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the citrate and citrate-fat test meals. The surgical conditions compared and the numbers shown on the abscissa are described in Figure 8.

Figure 9

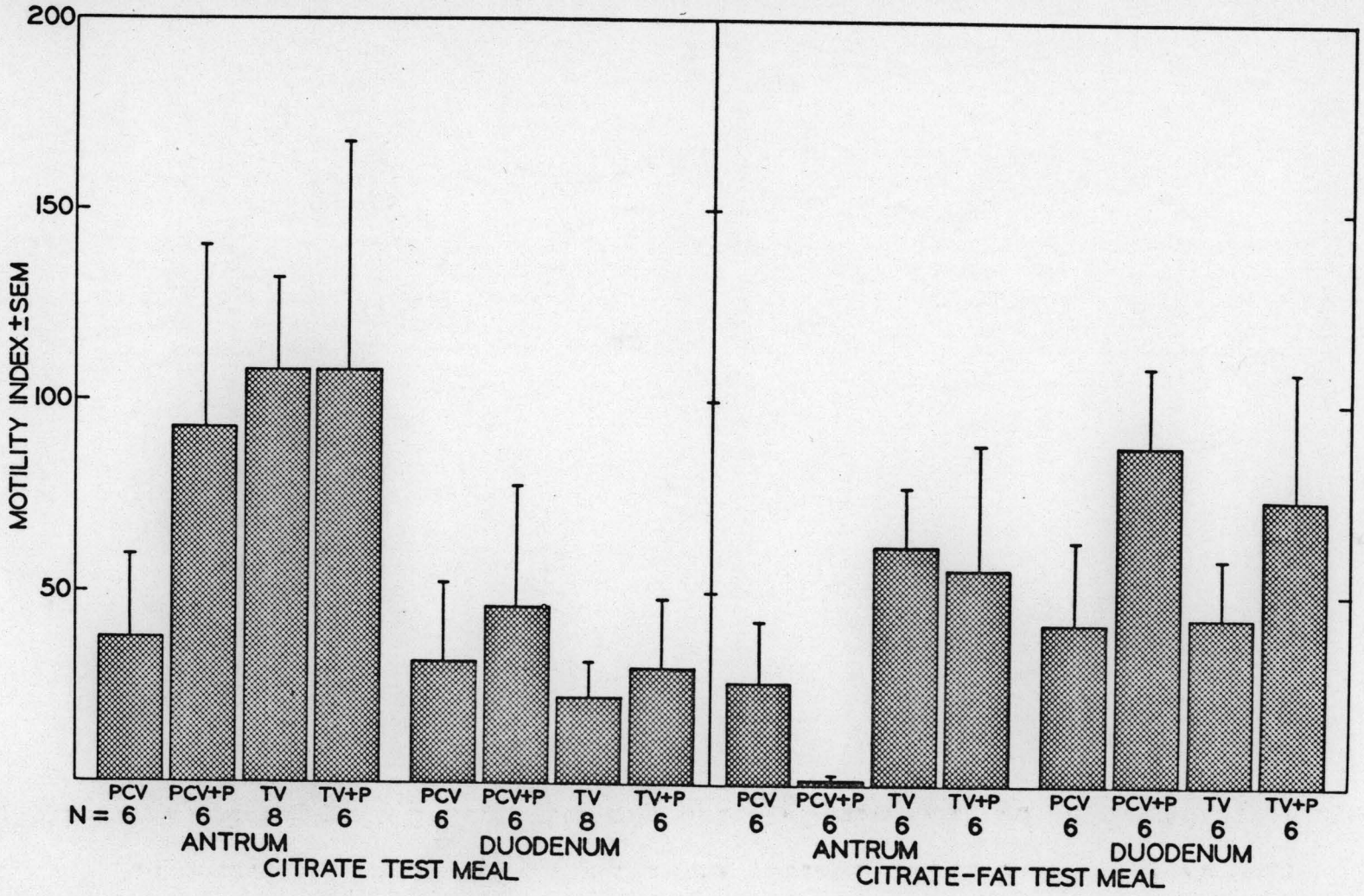

200
150
100
50
MOTILITY INDEX ±SEM
PCV
PCV+P
TV
TV+P
N = 6
6
8
6
ANTRUM
DUODENUM
CITRATE TEST MEAL
CITRATE-FAT TEST MEAL

TABLE 2

Per cent of maximum contractile activity[a] for the antrum and duodenum of dogs used in the study of vagotomy and pyloroplasty procedures.

SURG. COND.[c]	CHALLENGE	% ACTIVITY ANTRUM	% ACTIVITY DUODENUM	RATIO[b]
PCV	Basal Period	12.0 ± 5.8	2.0 ± 1.4	6.00
PCV + P	Basal Period	25.0 ± 13.1	2.8 ± 1.6	8.93
TV	Basal Period	7.2 ± 2.3	1.4 ± 1.3	5.14
TV + P	Basal Period	7.1 ± 4.9	0.2 ± 0.2	35.50
PCV	Citrate	6.8 ± 3.5	2.8 ± 1.8	2.43
PCV + P	Citrate	15.7 ± 6.5	3.9 ± 2.7	4.03
TV	Citrate	31.0 ± 6.2	2.3 ± 0.8	13.48
TV + P	Citrate	28.7 ± 15.3	2.2 ± 1.3	13.05
PCV	Citrate Fat	5.5 ± 2.5	2.5 ± 1.0	2.20
PCV + P	Citrate Fat	0.1 ± 0.1	6.0 ± 1.6	0.02
TV	Citrate Fat	18.4 ± 4.6	3.9 ± 1.3	4.72
TV + P	Citrate Fat	19.0 ± 11.9	6.3 ± 2.8	3.02
PCV	Insulin	46.0 ± 21.4	5.1 ± 1.8	9.02
PCV + P	Insulin	73.0 ± 14.5	9.7 ± 5.1	7.53
TV	Insulin	0.2 ± 0.2	0.5 ± 0.3	0.40
TV + P	Insulin	6.7 ± 3.1	0.5 ± 0.3	13.40
PCV	Insul. & Citrate Fat	56.5 ± 16.0	10.3 ± 3.4	5.49
PCV + P	Insul. & Citrate Fat	71.6 ± 21.6	12.0 ± 5.0	5.97
TV	Insul. & Citrate Fat	11.6 ± 7.3	1.4 ± 0.8	8.29
TV + P	Insul. & Citrate Fat	11.3 ± 5.9	9.7 ± 4.5	1.16

PCV	Bethanechol	62.7 ± 5.2	18.7 ± 2.7	3.35
PCV + P	Bethanechol	66.0 ± 9.2	25.2 ± 4.7	2.62
TV	Bethanechol	67.0 ± 7.2	11.2 ± 3.4	5.98
TV + P	Bethanechol	46.3 ± 6.7	20.3 ± 4.7	2.28
PCV	Beth. & Citrate Fat	43.9 ± 5.2	16.6 ± 1.7	2.64
PCV + P	Beth. & Citrate Fat	37.0 ± 5.4	22.2 ± 6.9	1.67
TV	Beth. & Citrate Fat	74.0 ± 9.9	12.8 ± 2.2	5.78
TV + P	Beth. & Citrate Fat	49.7 ± 3.0	15.3 ± 2.9	3.25

a. Per cent of maximum contractile activity was calculated by dividing the observed frequency of contractions for 60 minutes by the maximum possible number of contractions for that time period. The denominator was determined individually for each dog under maximal bethanechol stimulation, and the data were pooled for each surgical condition. The mean denominators for the antrum and duodenum were 260 and 1075 contractions per hour respectively. These values correspond to 4.33 and 17.9 contractions per minute.

b. Per cent activity ratios were determined by dividing the antral value by the corresponding duodenal value.

c. Abbreviations used: PCV = parietal cell vagotomy; PCV + P = parietal cell vagotomy with pyloroplasty; TV = truncal vagotomy; TV + P = truncal vagotomy with pyloroplasty.

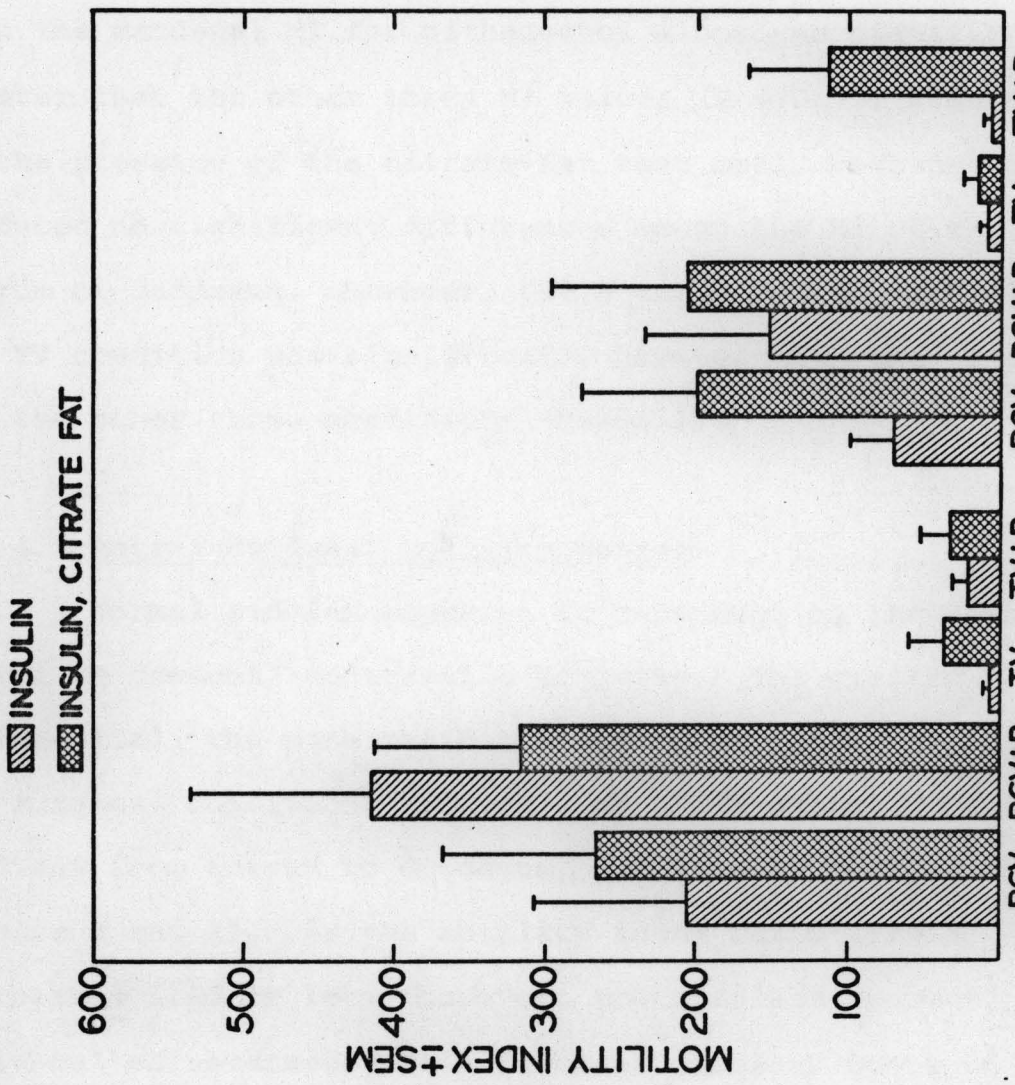
contractile activity (Figure 10). This degree of stimulation can be compared with the interdigestive basal state (cf. Figure 10 and Figure 8; antral-206 vs 52, duodenal-71 vs 34). The animals with truncal vagotomy with or without a pyloroplasty essentially had no response to the insulin (Figure 10). This differential response to insulin on the antrum was significant. The least significant difference procedure demonstrated that both TV and TV + P conditions differed significantly from the PCV + P condition ($P < 0.01$) but not from the PCV condition alone. The analysis of the % activity data parallels the motility index data.

In contrast to the antrum, the duodenal MI and % activity values following an insulin challenge were not significantly different. There was a tendency for smaller values under TV and TV + P conditions (Table 2, Figure 10). Insulin was capable of stimulating duodenal contractile activity in animals with truncal vagotomy (Figure 7).

When the citrate-fat test meal was administered 30 minutes after insulin, the response to insulin was essentially unaltered on the antrum and duodenum. As expected, in animals with PCV or PCV + P increased contractile activity was found on the antrum and duodenum (cf. Figure 10 and Figure 8). Animals with TV or TV + P demonstrated a normal response to the citrate-fat test meal which was not altered by the insulin. A significant difference existed for antral MI values and the % activity between the two types of vagotomy procedures ($P < 0.05$). No significant

Figure 10. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the insulin and insulin, citrate-fat challenges. The surgical conditions compared and the numbers shown on the abscissa are described in Figure 8.

Figure 10


INSULIN
INSULIN, CITRATE FAT
MOTILITY INDEX ±SEM
600
500
400
300
200
100
N=6 6 6 6 5 4 6 6 6 6 6 6 6 6 6 5 4 6 6
PCV PCV+P TV TV+P PCV PCV+P TV TV+P
ANTRUM
DUODENUM

differences were found for the duodenal MI values or % activities.

Bethanechol administered to animals in the basal period or in the presence of the citrate-fat test meal stimulated both the antrum and duodenum under all surgical conditions. The analysis of variance revealed that in the PCV + P condition the duodenal MI for bethanechol alone was significantly greater than the other three MI values ($P < 0.05$, Figure 11). In the presence of the citrate-fat test meal, bethanechol produced no significant differences among the MI of the antrum or duodenum. However, the % activity value (74%) for the TV condition was significantly greater than the values for the other three conditions (Table 2).

4. Antral-duodenal motility ratios

Normal stomach emptying is dependent on the ratio of antral to duodenal contractile activity. The greater the differential, the more rapid the emptying. Under each of the surgical conditions studied, the differential (i.e., the gradient from antrum to duodenum) was usually maintained (Tables 2 and 3). As the motility index ratio (Table 3) approaches 1.00 or less, however, the gradient becomes equivocal or reversed. This reversed gradient occurred in only six of the twenty eight tests. Four of these six "reversals" were found in animals with pyloroplasties. Similarly, % activity ratios less than 1.00 indicate a reversed contractility gradient (e.g., the PCV + P condition

Figure 11. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the bethanechol and bethanechol, citrate-fat challenges. The surgical conditions compared and the numbers shown on the abscissa are described in Figure 8.

Figure 11

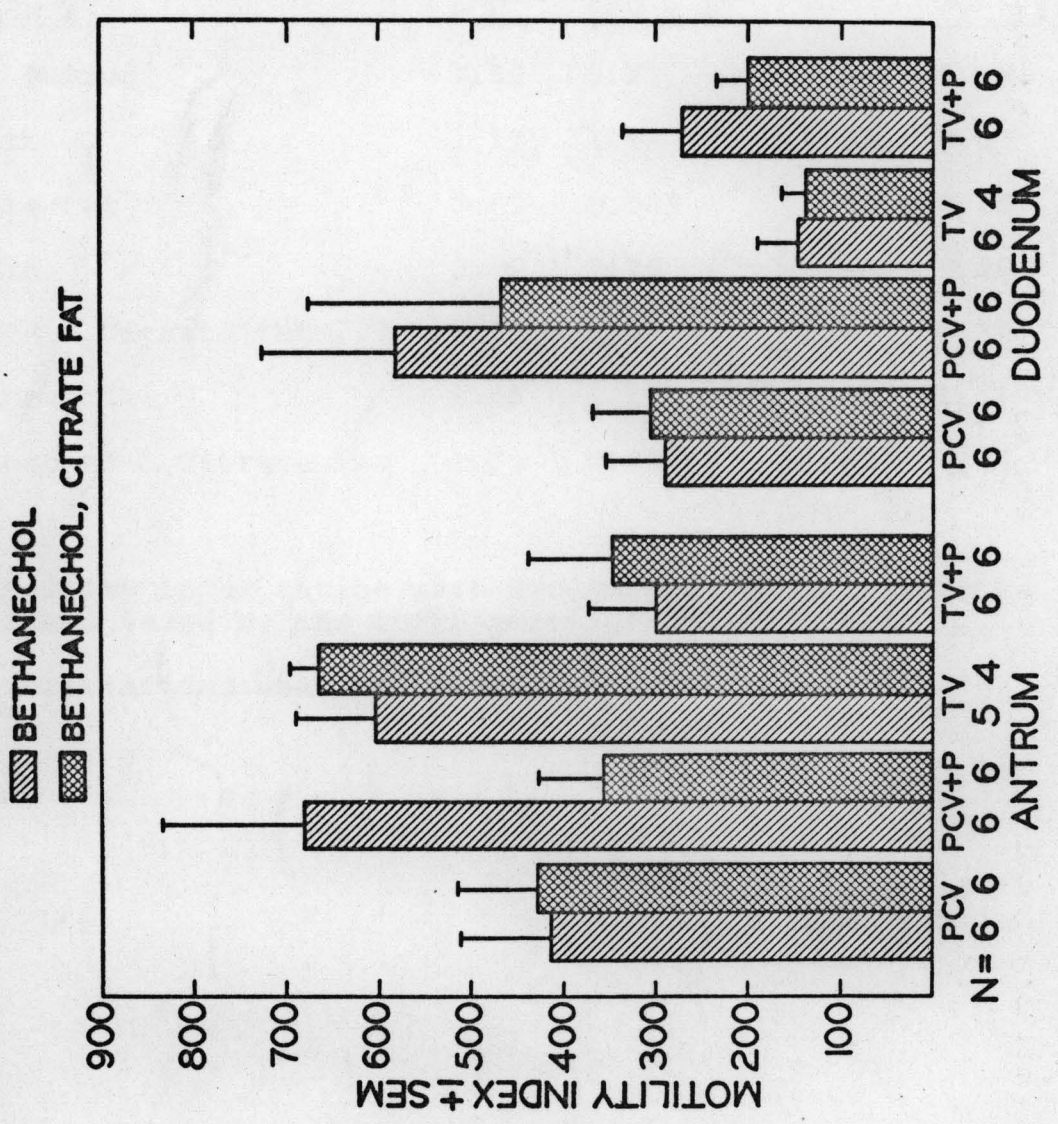

BETHANECHOL
BETHANECHOL, CITRATE FAT
MOTILITY INDEX ± SEM
900
800
700
600
500
400
300
200
100
N= 6 6 6 6 5 4 6 6 6 6 6 6 6 6 6 4 6 6
PCV PCV+P TV TV+P PCV PCV+P TV TV+P
ANTRUM
DUODENUM

TABLE 3

Motility index ratios[a] for the antral-duodenal relationship of dogs used in the study of vagotomy and pyloroplasty procedures.

	SURGICAL CONDITIONS			
CHALLENGES	PCV[b]	PCV + P[b]	TV[b]	TV + P[b]
Basal Period	1.52	3.21	1.14	8.59
Citrate	1.17	1.98	4.92	3.63
Citrate Fat	0.62	0.002	1.44	0.74
Insulin	2.90	2.78	0.16	3.28
Insulin & Citrate Fat	1.32	1.53	2.50	0.30
Bethanechol	1.45	1.17	4.26	1.11
Bethanechol & Citrate Fat	1.39	0.76	4.87	1.75

a. Motility index ratios were determined by dividing the antral value by the corresponding duodenal value.

b. Abbreviations used are described in text and Table 2.

challenged by the citrate-fat test meal (Table 3)). In general, high ratios were obtained when the surgical conditions were challenged by substances which enhance gastric emptying (i.e., the citrate test meal or insulin). In contrast, lower ratios were associated with the citrate-fat test meal challenge.

B. Heineke-Mikulicz Pyloroplasty - Gastric Emptying

The results for each of the seven dogs and the pooled results are presented in Table 4. Three of the seven dogs had significantly less test meal remaining in their stomachs after 45 minutes following Heineke-Mikulicz pyloroplasty. In all dogs the means were smaller (indicating more emptying) after surgery. When the values from all animals were pooled before and after surgery the difference between these grand means was highly significant. Pyloroplasty enhanced the emptying of the citrate-fat test meal.

C. Heineke-Mikulicz Pyloroplasty - Motor Activity

1. Interdigestive state

The basal and burst periods on the antrum and duodenum were present following pyloroplasty. On some days the dogs with pyloroplasty had their stomachs rinsed to remove food particles still remaining after an 18 hour fast. This maneuver always brought about the normal interdigestive basal-burst sequence. Figure 12 shows representative records of peak burst period activity from a normal dog (top)

TABLE 4

Gastric emptying of citrate-fat test meal before and after Heineke-Mikulicz pyloroplasty.

DOG	$\bar{V}_R \pm$ SEM[a] PRE-PYLOROPLASTY	$\bar{V}_R \pm$ SEM[b] POST-PYLOROPLASTY	P (SIGNIFICANCE LEVEL)
1	189.3 ± 11.5	124.8 ± 6.5	$P < 0.01$
2	206.6 ± 9.3	197.2 ± 3.0	$P > 0.05$
3	164.9 ± 1.2	151.1 ± 10.2	$P > 0.05$
4	205.9 ± 4.8	193.6 ± 3.5	$P > 0.05$
5	159.6 ± 4.0	133.8 ± 5.0	$P < 0.02$
6	194.1 ± 9.9	177.5 ± 1.2	$P > 0.05$
7	189.1 ± 5.5	141.9 ± 13.2	$P < 0.05$
Grand mean[c]	187.1 ± 7.0	160.0 ± 11.1	$P < 0.02$

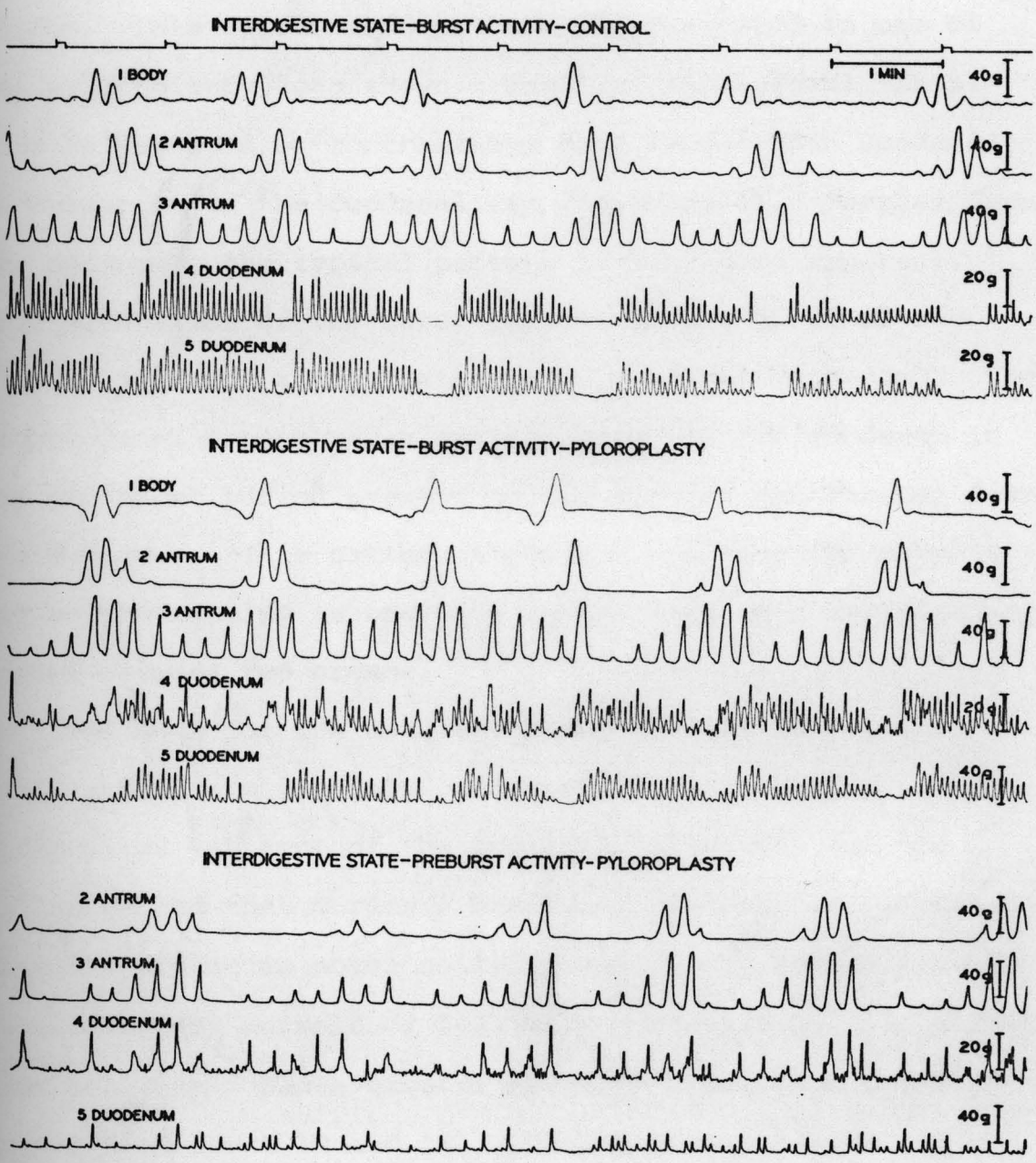
a. The mean amount remaining in the stomach after 45 minutes ($\bar{V}_R \pm$ SEM) before any surgery. At least three experiments contributed to each value.

b. Same as in a. following Heineke-Mikulicz pyloroplasty.

c. A paired t-test was performed using the means from three replicates from each dog. N = 7, df = 6.

Figure 12. Examples of circular muscle contractile activity from the canine gastric body and antrum and the duodenum. The upper panel shows the pattern from a normal dog during a burst period in the interdigestive state. The middle panel shows the pattern from a dog following Heineke-Mikulicz pyloroplasty during a burst period in the interdigestive state. The lower panel shows the pattern from the same dog as in the middle panel during the pre-burst period in the interdigestive state. Antralization of the duodenum is apparent on position 4. The numbers on the left of each panel refer to the positions of the force transducers shown in Figure 1. Vertical bars on the right of each panel represent the calibration of the force transducers. Time is given by the horizontal bar at the top.

Figure 12

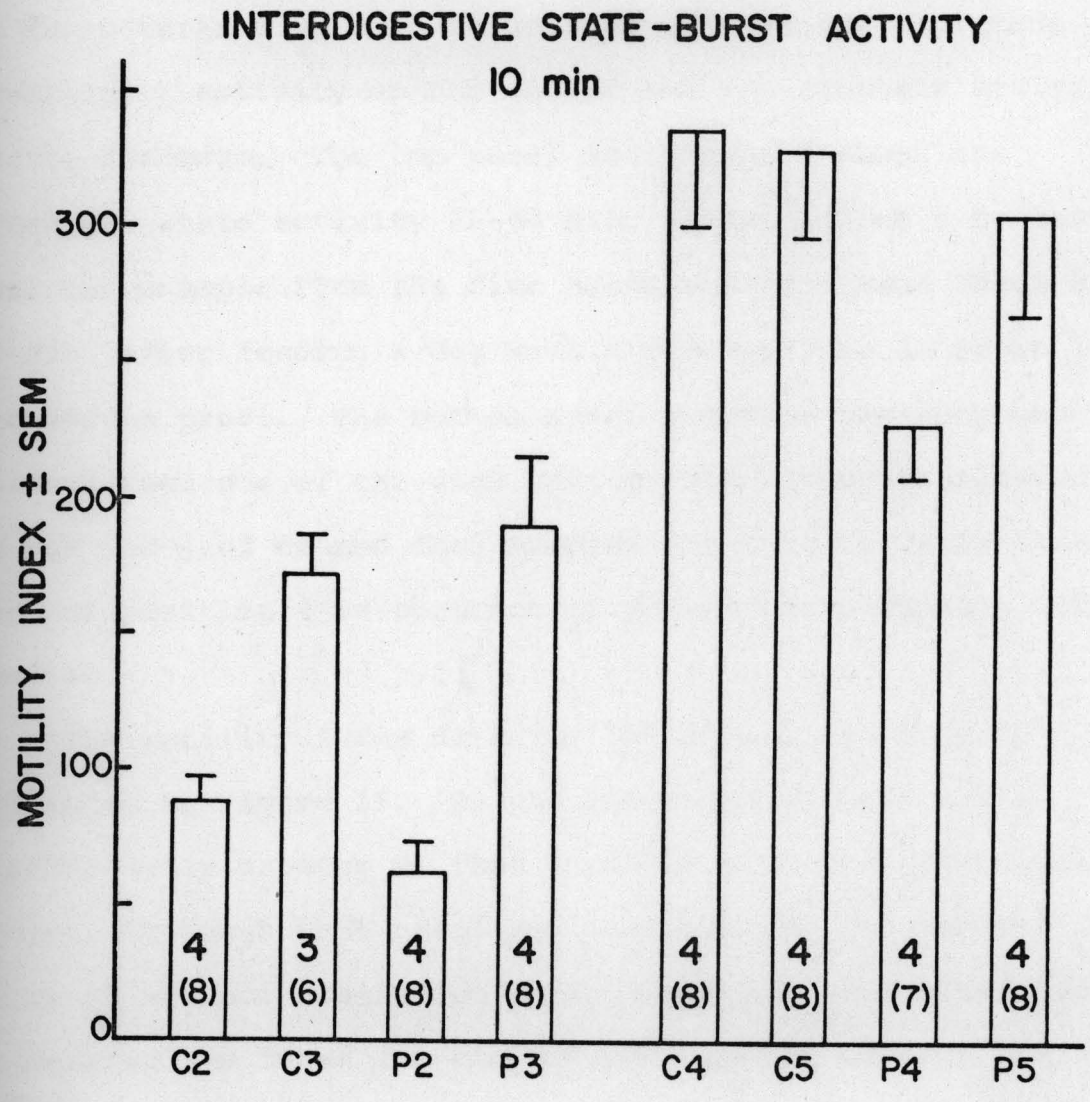

INTERDIGESTIVE STATE-BURST ACTIVITY-CONTROL
1 BODY
1 MIN
40g
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
20g
INTERDIGESTIVE STATE-BURST ACTIVITY-PYLOROPLASTY
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
40g
INTERDIGESTIVE STATE-PREBURST ACTIVITY-PYLOROPLASTY
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
40g

and a dog following pyloroplasty (middle). The control record demonstrates segments of duodenal inhibition coordinated with the greatest amplitude contractions on the antrum. This coordinated pattern was disrupted in one of the pyloroplasty dogs shown. The typical duodenal inhibition is replaced by contractions more antral than duodenal in character on the duodenal cap (position 4). Further down the duodenum, the typical pattern is much more apparent. This alteration of the motor pattern on the duodenal cap will be referred to as "antralization of the duodenum". The bottom panel demonstrates antralization of the duodenum in the pre-burst period present on the cap but not further down the duodenum. This pattern indicates that the GDJ segment may be contracting as one unit rather than in a coordinating effort between two organs.

The data for the motility index calculated for the burst period are presented graphically in Figure 13. The analysis of variance of the motility index data for the antrum showed that during a burst period there is a significant difference in motor activity within the antrum itself in the control animals or following pyloroplasty. In either case position 3 had a greater motility index than position 2 (refer to Figures 12 and 13). During the same time period no differences were found for either position monitored on the duodenum in the control or pyloroplasty animals.

Figure 13. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the interdigestive burst period. The four columns on the left represent the antral activity from control (C) and pyloroplasty (P) dogs. The four columns on the right represent the duodenal activity from the C and P groups of dogs. The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The bold numbers within the columns refer to the numbers of dogs from which data was obtained for that particular position. The numbers within parentheses in the columns refer to the total number of experiments contributing to the mean activity for that position.

Figure 13


INTERDIGESTIVE STATE-BURST ACTIVITY
10 min
MOTILITY INDEX ± SEM
0
100
200
300
4 (8)
3 (6)
4 (8)
4 (8)
4 (8)
4 (8)
4 (7)
4 (8)
C2
C3
P2
P3
C4
C5
P4
P5

2. Digestive state

Digestive state activity monitored after feeding the dogs 200 g of canned food was similar in control and pyloroplasty animals. As seen in Figure 14 this type of activity is characterized by a continuous pattern of low amplitude contractile activity on the antrum and intermittent activity on the duodenum. The top panel in Figure 14 shows the digestive state activity 35-40 min. after feeding a control dog. An example from the five recording positions taken 35-40 min. after feeding a dog with a pyloroplasty is shown in the middle panel. The bottom panel presents the response to feeding when one of the dogs with pyloroplasty was allowed to eat 200 g of canned food between the arrows. Antralization of position 4 is apparent in the interval shortly after feeding.

The motility index data for the digestive state is presented in Figure 15. On the antrum position 3 had a significantly greater MI than position 2 in the pyloroplasty group. Although this trend was apparent for the control dogs, it was not statistically significant. One significant difference was found for the duodenal values between position 5 in the control dogs and the same position in the pyloroplasty group. The MI was greater in position 5 following pyloroplasty.

Further analysis was performed to attempt to pinpoint the reasons for the differences in MI which were found. The number of contractions occurring for an hour after feeding

Figure 14. Examples of circular muscle contractile activity from the canine gastric body and antrum and the duodenum. The upper panel shows the pattern from a normal dog 35-40 minutes following ingestion of 200 g canned food. The middle panel shows the pattern from a dog following Heineke-Mikulicz pyloroplasty 35-40 minutes after ingestion of 200 g canned food. The lower panel shows the pattern during (between arrows) and immediately after feeding 200 g canned food to the same animal as in the middle panel. Antralization of the duodenum is apparent on position 4. The numbers on the left of each panel refer to the positions of the force transducers shown in Figure 1. Vertical bars on the right of each panel represent the calibration of the force transducers. Time is given by the horizontal bar at the top.

Figure 14

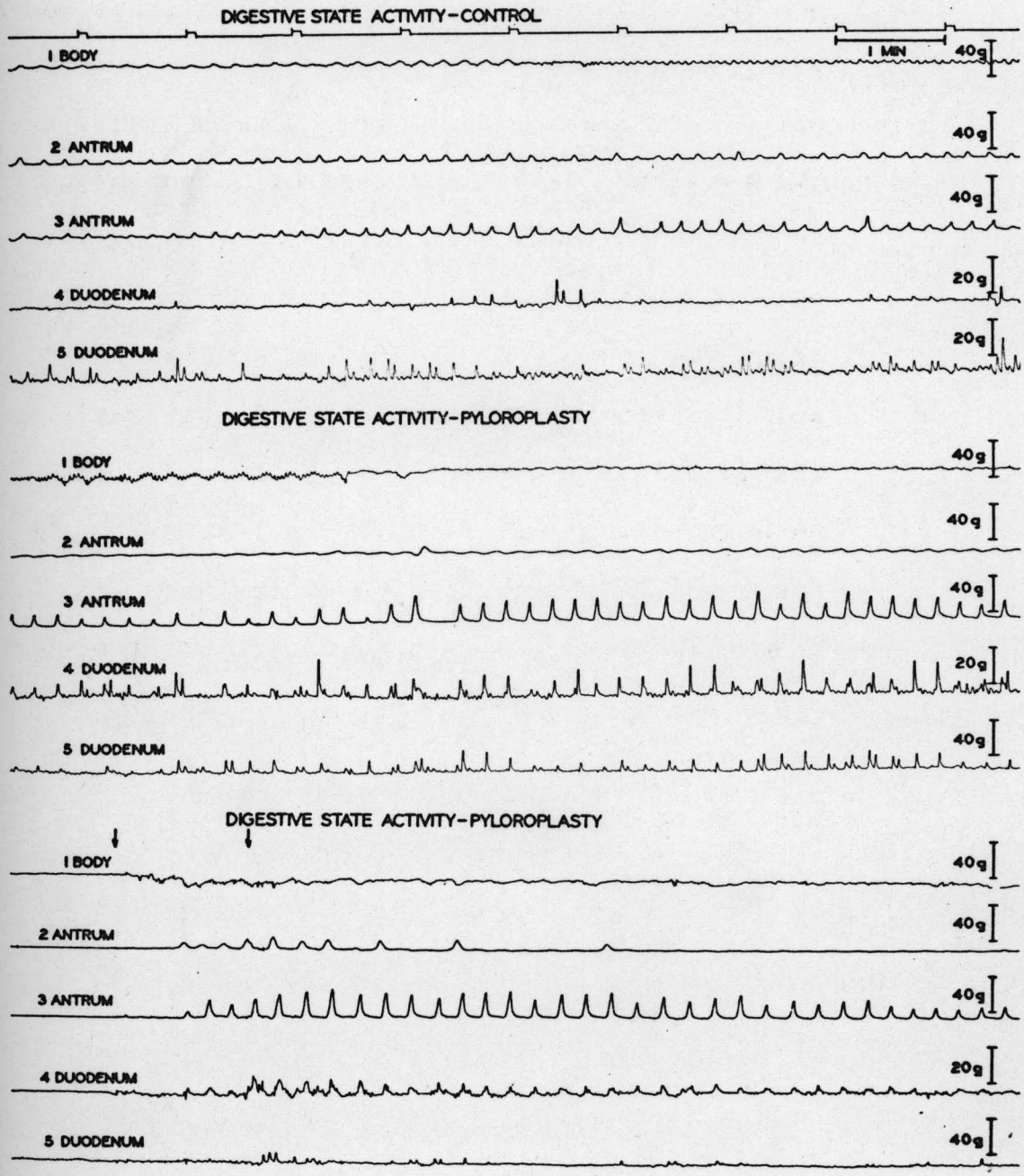
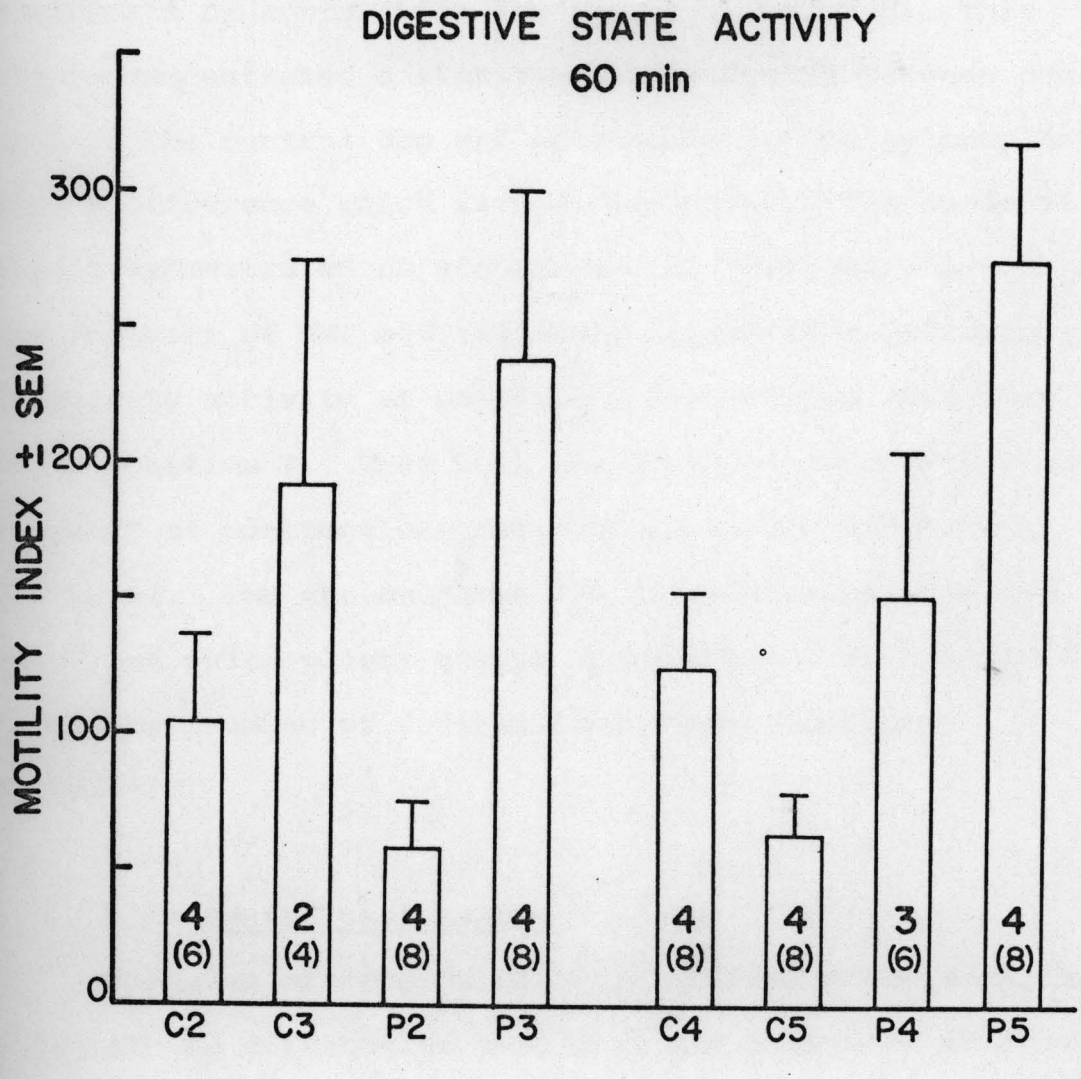

DIGESTIVE STATE ACTIVITY-CONTROL
1 MIN
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
20g
DIGESTIVE STATE ACTIVITY-PYLOROPLASTY
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
40g
DIGESTIVE STATE ACTIVITY-PYLOROPLASTY
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
40g

Figure 15. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the digestive state. The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The numbers within the columns are described in Figure 13.

Figure 15


DIGESTIVE STATE ACTIVITY
60 min
MOTILITY INDEX ± SEM
300
200
100
0
4 (6)
2 (4)
4 (8)
4 (8)
4 (8)
4 (8)
3 (6)
4 (8)
C2
C3
P2
P3
C4
C5
P4
P5

are shown graphically in Figure 16. This analysis showed no significant differences on the antrum. A significantly larger number of contractions occurred in position 5 following pyloroplasty. Figure 17 presents the data for the analysis of mean motility index (MMI), a term which indicates the strength of contraction for the hour analyzed. This analysis demonstrated a significant difference between position 2 in the control dog and position 3 in the pyloroplasty group, a difference which is not meaningful. The duodenal analysis demonstrated no significant differences. A look at these analyses of MMI and frequency showed that following pyloroplasty activity at position 2 tends to be less than that at position 3. Thus both the force of contraction and the number of contractions contributed to the difference found in MI. For the duodenum the difference between the control and pyloroplasty groups at position 5 is clearly due to a greater number of contractions there following pyloroplasty.

3. Citrate-fat test meal

Examples of records obtained following the administration of the citrate-fat test meal are presented in Figure 18. The citrate-fat test meal stimulated duodenal circular muscle contractility in control dogs and those with pyloroplasty. There appeared to be no stimulation of the antrum with this test meal in control dogs and some stimulation at position 3 in the pyloroplasty group of dogs. When these

Figure 16. Analysis of the circular muscle contractile activity of the antrum and duodenum for the digestive state. Frequency (FREQ) is plotted on the ordinate $\pm$ SEM. This is simply the number of contractions which occurred during the 60 minute period of analysis. The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The numbers within the columns are described in Figure 13.

Figure 16

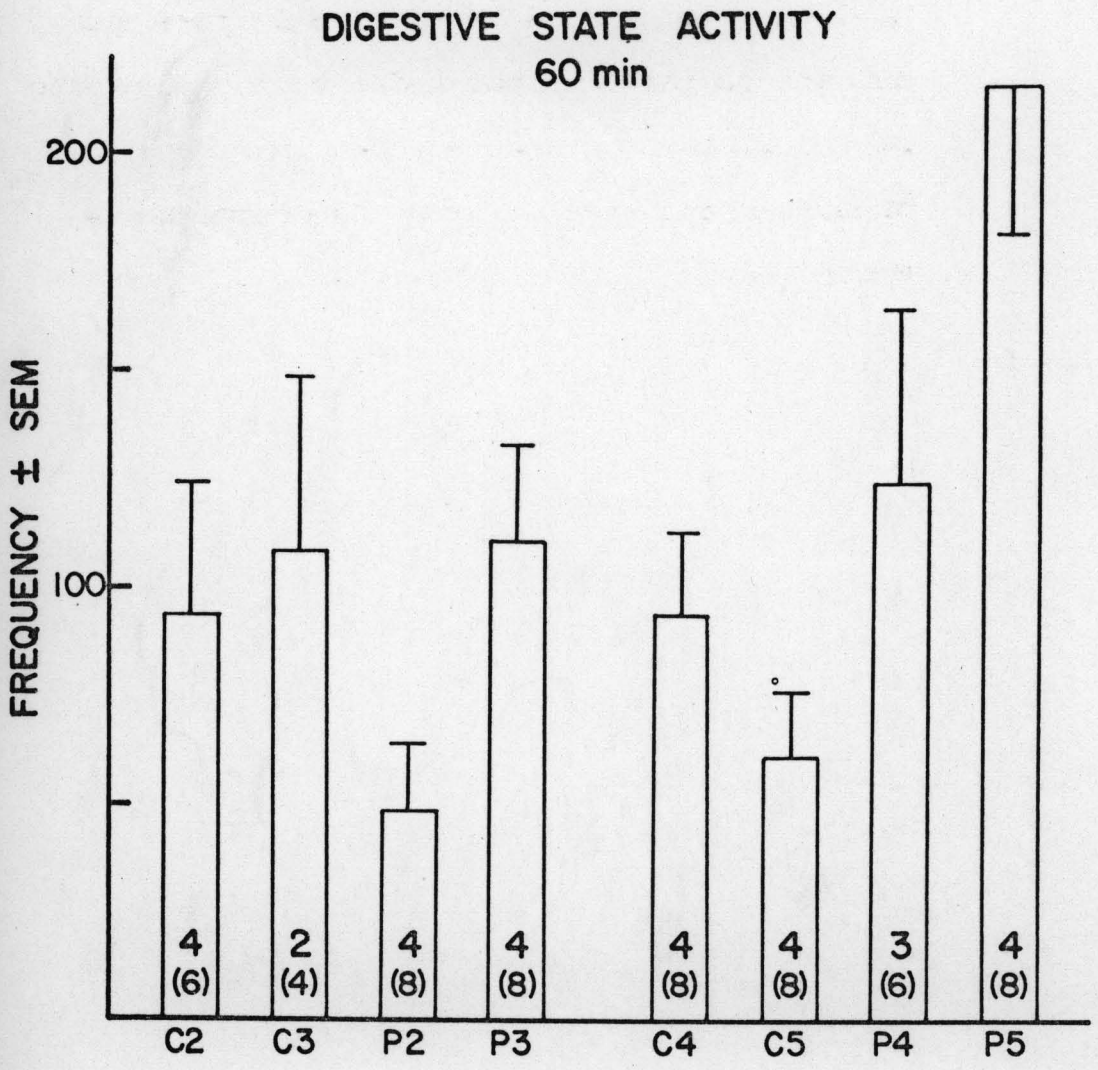

DIGESTIVE STATE ACTIVITY
60 min
FREQUENCY ± SEM
200
100
4
(6)
2
(4)
4
(8)
4
(8)
4
(8)
4
(8)
3
(6)
4
(8)
C2
C3
P2
P3
C4
C5
P4
P5

Figure 17. Analysis of the circular muscle contractile activity of the antrum and duodenum for the digestive state. Mean motility index (MMI) is plotted on the ordinate $\pm$ SEM. MMI was found by dividing the MI for the 60 minute analysis by the number of contractions occurring during that period (FREQ). The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The numbers within the columns are described in Figure 13.

Figure 17

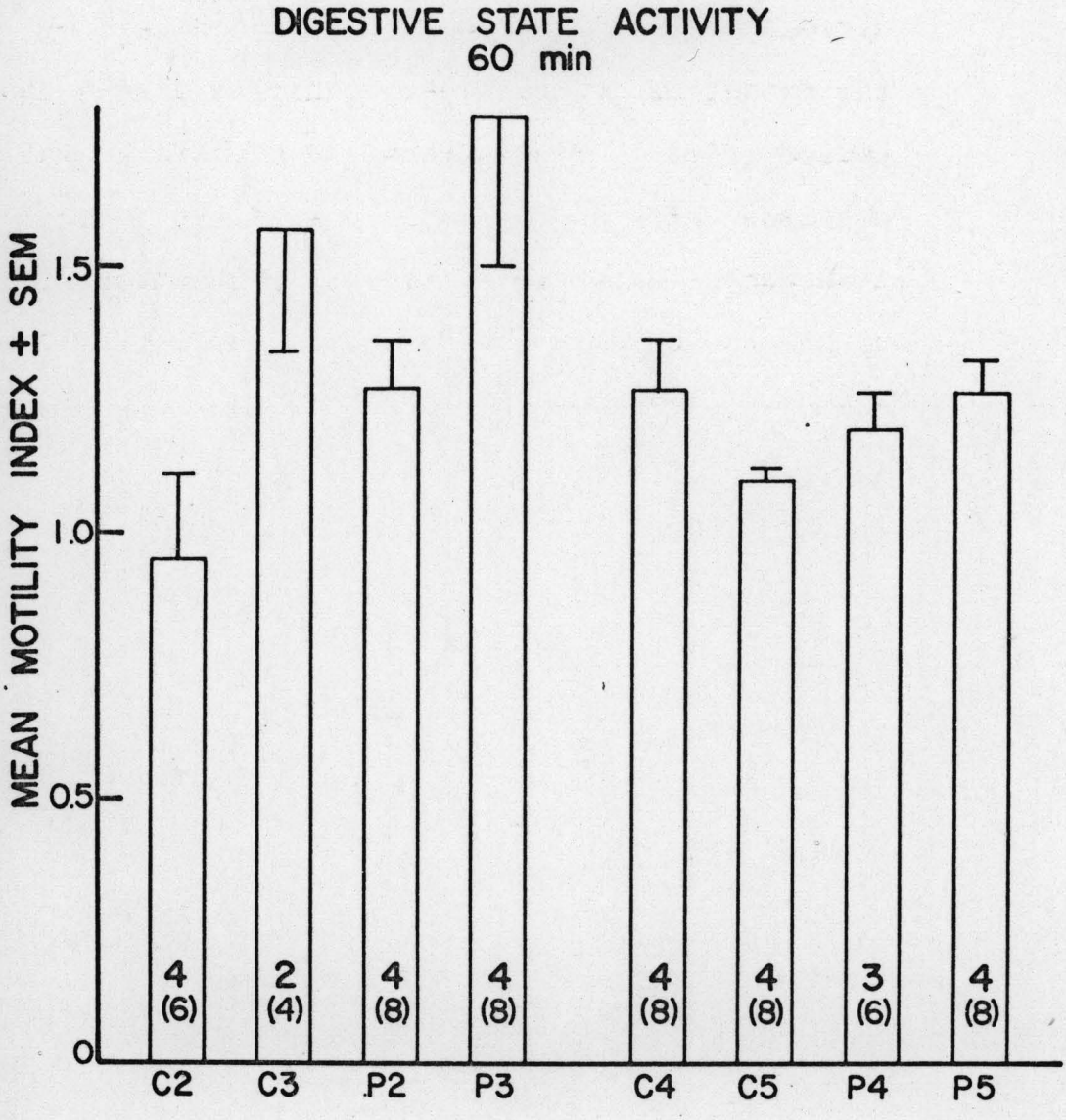
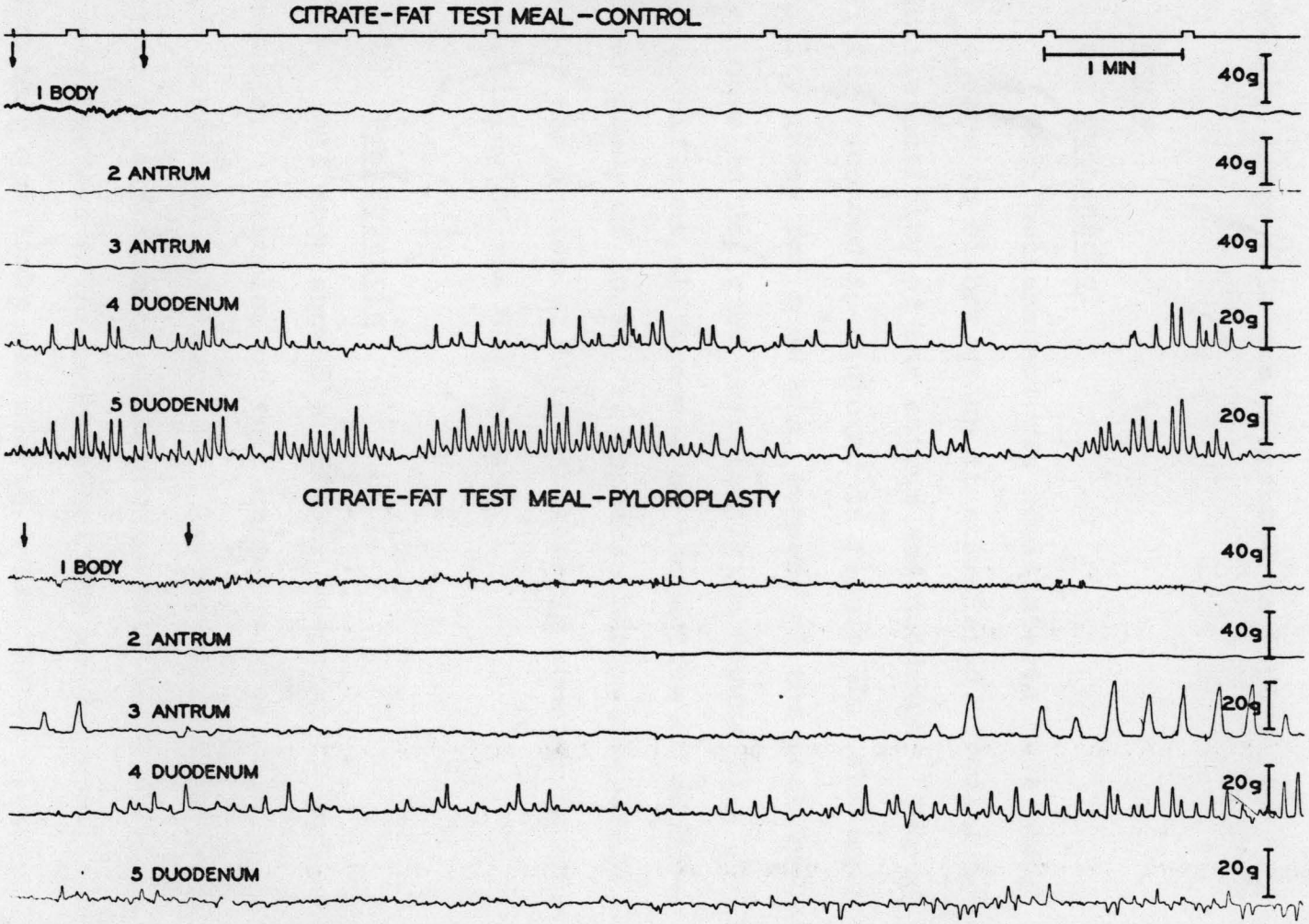

DIGESTIVE STATE ACTIVITY
60 min
MEAN MOTILITY INDEX ± SEM
1.5
1.0
0.5
0
4 (6)
2 (4)
4 (8)
4 (8)
4 (8)
4 (8)
3 (6)
4 (8)
C2
C3
P2
P3
C4
C5
P4
P5

Figure 18. Examples of circular muscle contractile activity from the canine gastric body and antrum and the duodenum for the citrate-fat test meal. The upper panel shows the pattern from a normal dog. The lower panel shows the pattern from a dog following Heineke-Mikulicz pyloroplasty. In each case 300 ml of citrate-fat was instilled into the stomach between the arrows. The numbers on the left of each panel refer to the positions of the force transducers shown in Figure 1. Vertical bars on the right of each panel represent the calibration of the force transducers. Time is given by the horizontal bar at the top.

Figure 18


CITRATE-FAT TEST MEAL-CONTROL
1 MIN
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
20g
CITRATE-FAT TEST MEAL-PYLOROPLASTY
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
20g
4 DUODENUM
20g
5 DUODENUM
20g

records were subjected to analysis of variance, no significant differences were found for the antrum or the duodenum. The motility index data are presented in Figure 19.

4. Drugs

a) Bethanechol

When bethanechol was administered in a basal period to dogs in either group it stimulated circular muscle contractile activity of the antrum and duodenum. The type of activity recorded is pictured in Figure 20. The analysis of motility index for a 30 min. segment of the peak bethanechol response is depicted graphically in Figure 21. There were no significant differences on the antrum or duodenum for either group of dogs. It appears that pyloroplasty did not affect the action of this cholinergic agonist on circular muscle activity of the GDJ segment.

b) Pentagastrin

All dogs showed a similar response to pentagastrin infusion. Examples of this response from each group of dogs are presented in Figure 22. Pentagastrin stimulated the antrum to a frequency of approximately six contractions per minute whereas after bethanechol the antrum contracted approximately 4.5 times per minute. The faster rate of contraction on the antrum was accompanied by very few contractions on the duodenum. In the bottom panel of Figure 22 some antralization occurs in position 4. This pattern was

Figure 19. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) $\pm$ SEM for the citrate-fat test meal. The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The numbers within the columns are described in Figure 13.

Figure 19

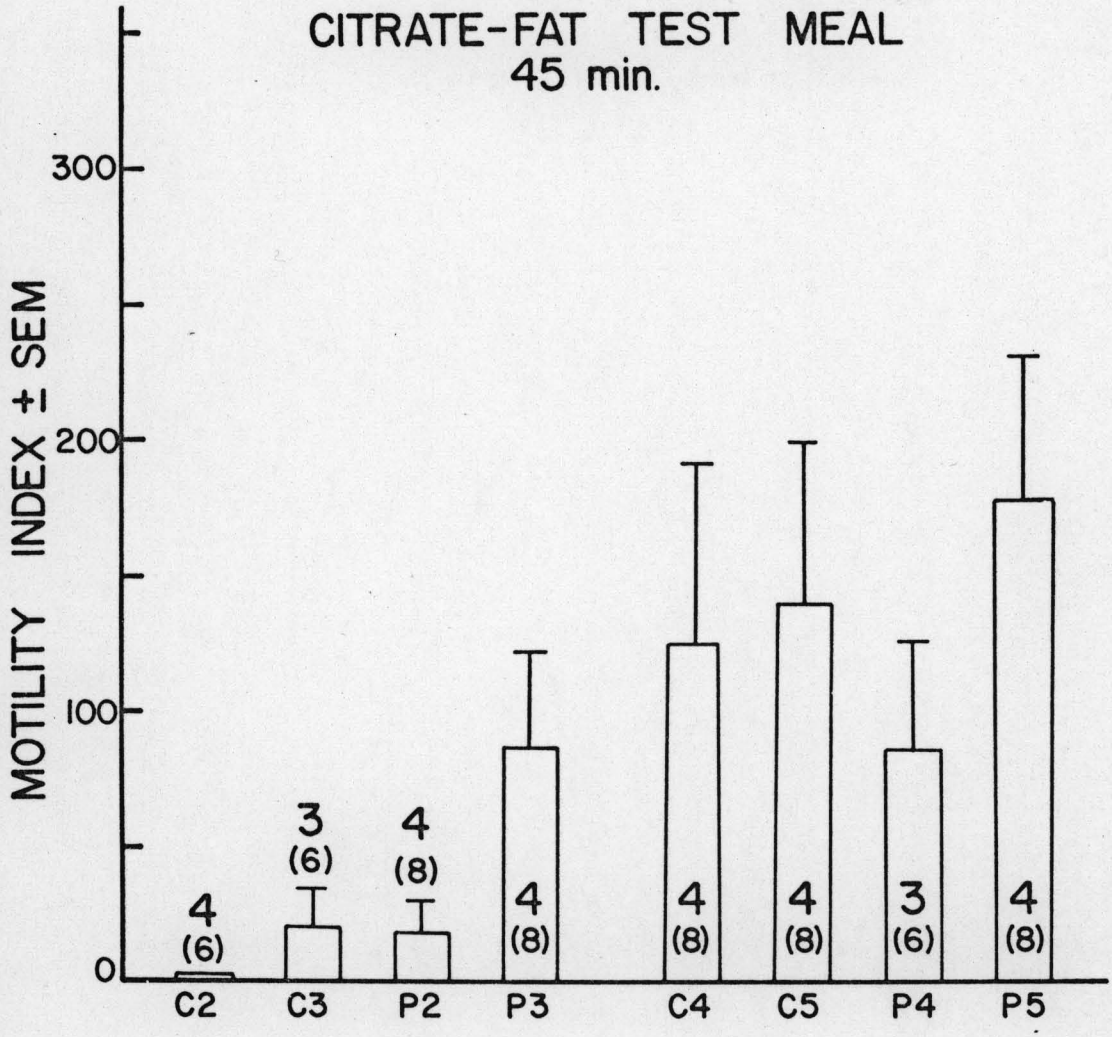

CITRATE-FAT TEST MEAL
45 min.
MOTILITY INDEX ± SEM
300
200
100
0
4
(6)
3
(6)
4
(8)
4
(8)
4
(8)
4
(8)
3
(6)
4
(8)
C2
C3
P2
P3
C4
C5
P4
P5

Figure 20. Examples of circular muscle contractile activity from the canine antrum and duodenum following administration of bethanechol (0.1 mg/Kg sc). The upper panel shows the pattern from a normal dog. The lower panel shows the pattern from a dog following Heineke-Mikulicz pyloroplasty. The numbers on the left of each panel refer to the positions of the force transducers shown in Figure 1. Vertical bars on the right of each panel represent the calibration of the force transducers. Time is given by the horizontal bar at the top.

Figure 20

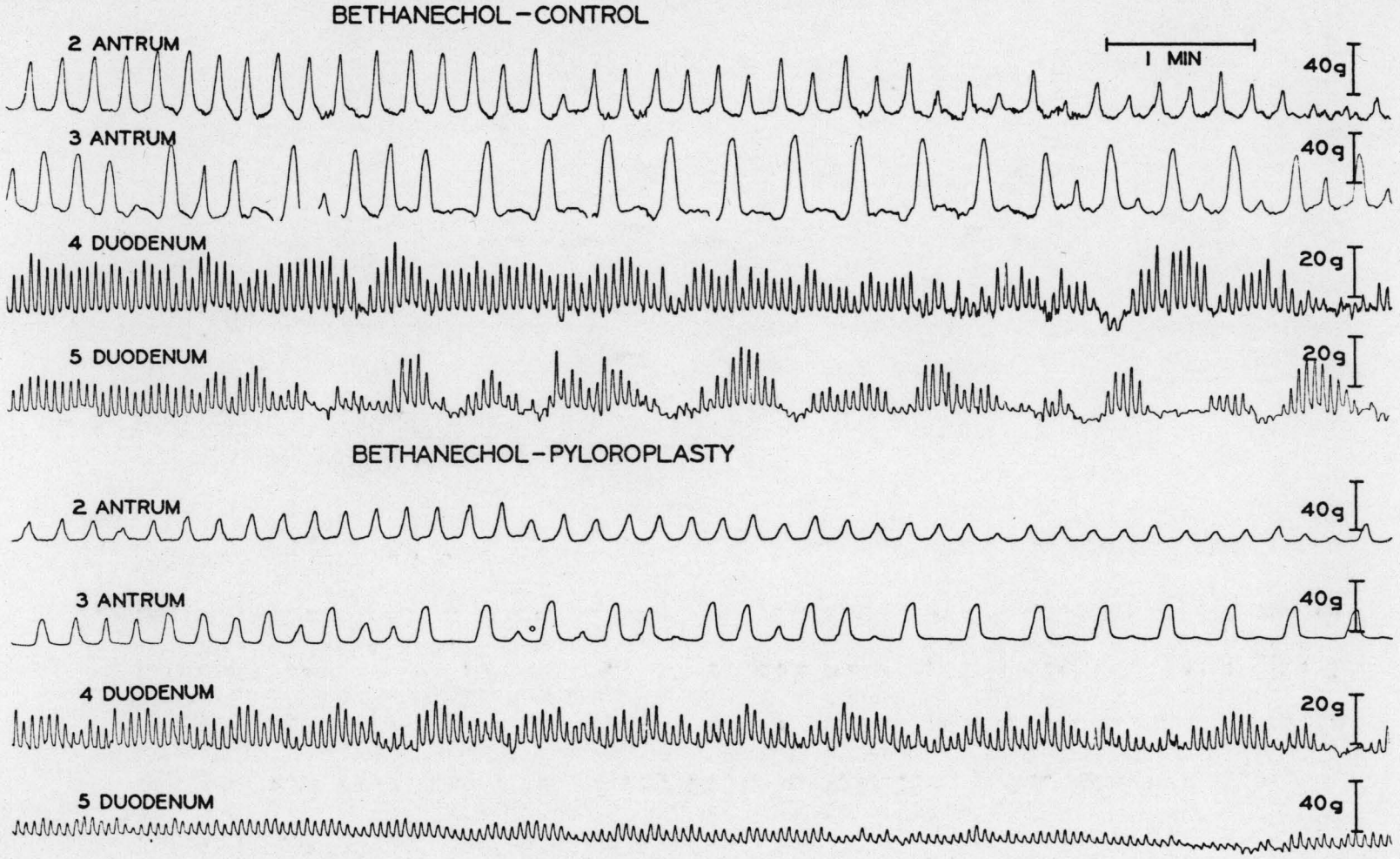

BETHANECHOL – CONTROL
2 ANTRUM
1 MIN
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
20g
BETHANECHOL – PYLOROPLASTY
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
40g

Figure 21. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the bethanechol response. The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The numbers within the columns are described in Figure 13.

Figure 21

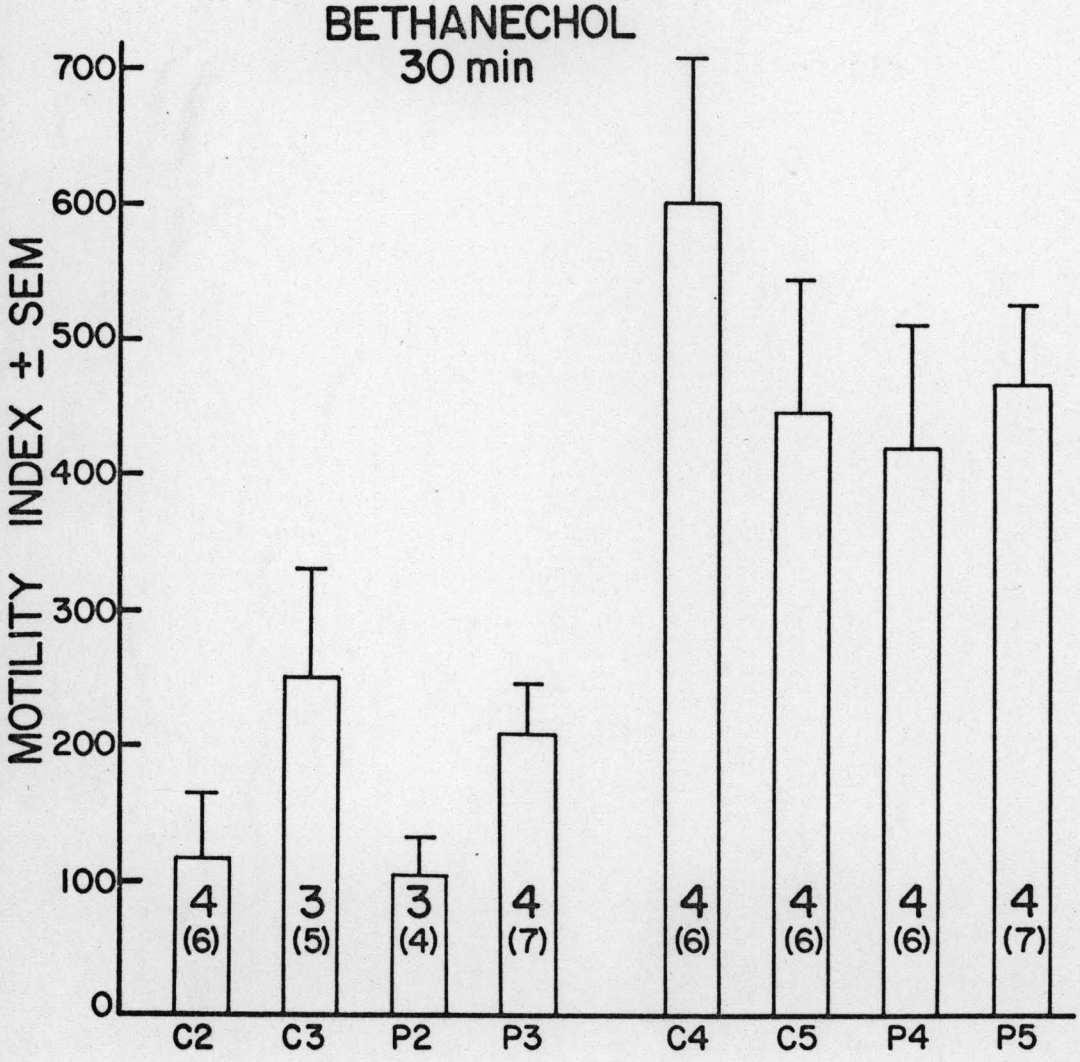
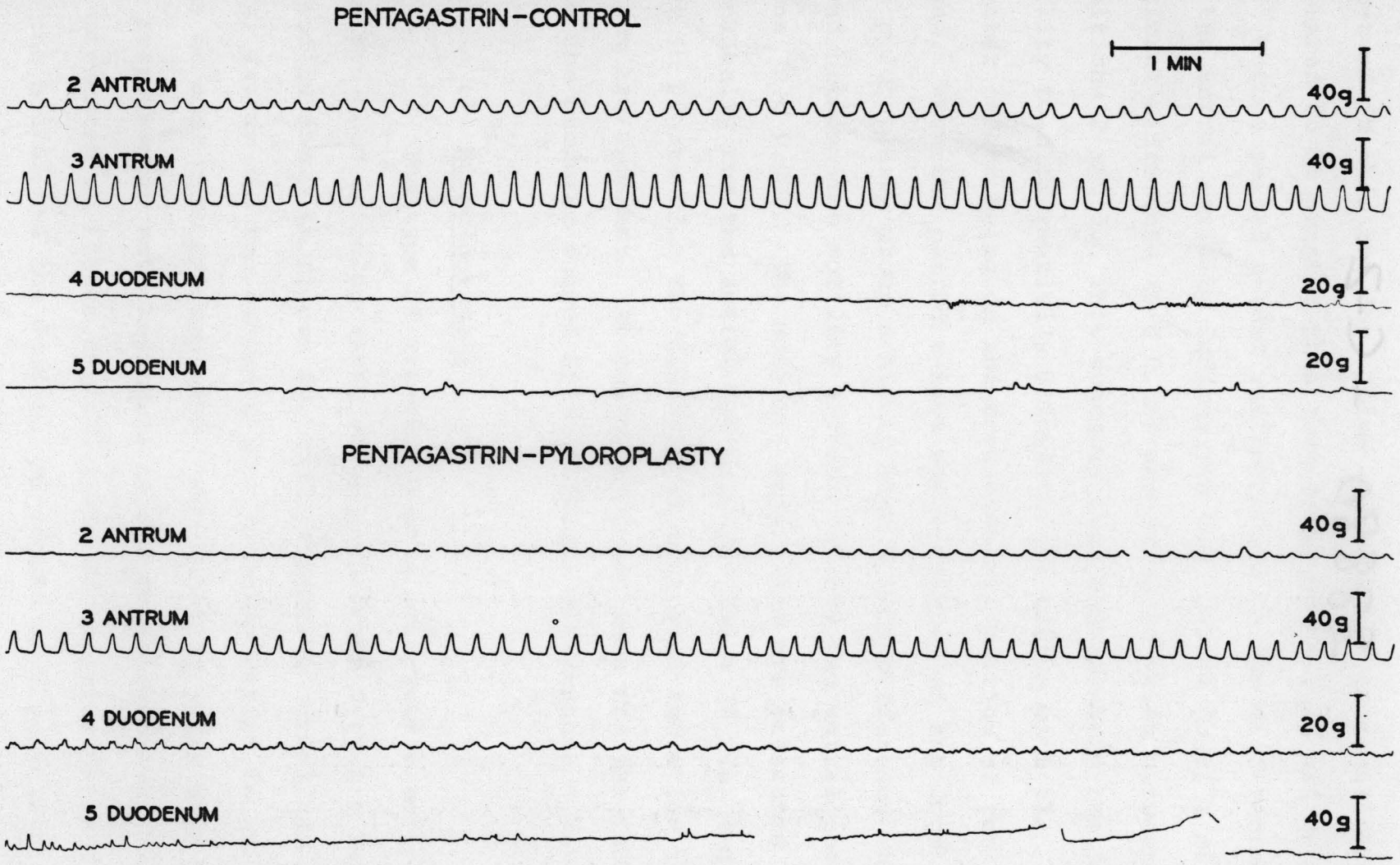

BETHANECHOL
30 min
MOTILITY INDEX ± SEM
700
600
500
400
300
200
100
0
4
(6)
3
(5)
3
(4)
4
(7)
4
(6)
4
(6)
4
(6)
4
(7)
C2
C3
P2
P3
C4
C5
P4
P5

Figure 22. Examples of circular muscle contractile activity from the canine antrum and duodenum during an infusion of pentagastrin (1.0 μg/min iv). The upper panel shows the pattern from a normal dog. The lower panel shows the pattern from a dog following Heineke-Mikulicz pyloroplasty. The numbers on the left of each panel refer to the positions of the force transducers shown in Figure 1. Vertical bars on the right of each panel represent the calibration of the force transducers. Time is given by the horizontal bar at the top.

Figure 22


PENTAGASTRIN – CONTROL
1 MIN
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
20g
PENTAGASTRIN – PYLOROPLASTY
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
40g

observed in this one dog. Also the activity at position 3 appeared to be greater than that at position 2 in all dogs.

When a paired t-test was performed on the differences in the antral motility indices for the control dogs, a significant difference ($P < 0.05$) was found to exist between positions 2 and 3. This suggests that pentagastrin has the ability to differentially stimulate the antrum with the greater effect being on the most terminal portion of that organ. When the paired t-test was performed on the dogs in the pyloroplasty group a highly significant difference was found between the motility indices for the two antral positions ($P < 0.01$). The motility index data are presented graphically for the antrum and duodenum for a 20 min. segment in Figure 23. The differences mentioned above for the antrum are apparent. An analysis of variance for the data from the duodenum showed no significant differences.

c) Metoclopramide

The type of circular muscle contractile activity observed when metoclopramide was administered during a basal period is shown in Figure 24. Metoclopramide stimulated the body, antrum and the duodenum to a variable extent in normal dogs or dogs with pyloroplasty. The motility index data for the responses to metoclopramide in the interdigestive state are presented in Figure 26. Analyses of variance performed for the antral and the duodenal MI showed no significant differences within either organ or between the control and

Figure 23. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the pentagastrin response. The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The numbers within or above the columns are described in Figure 13.

Figure 23

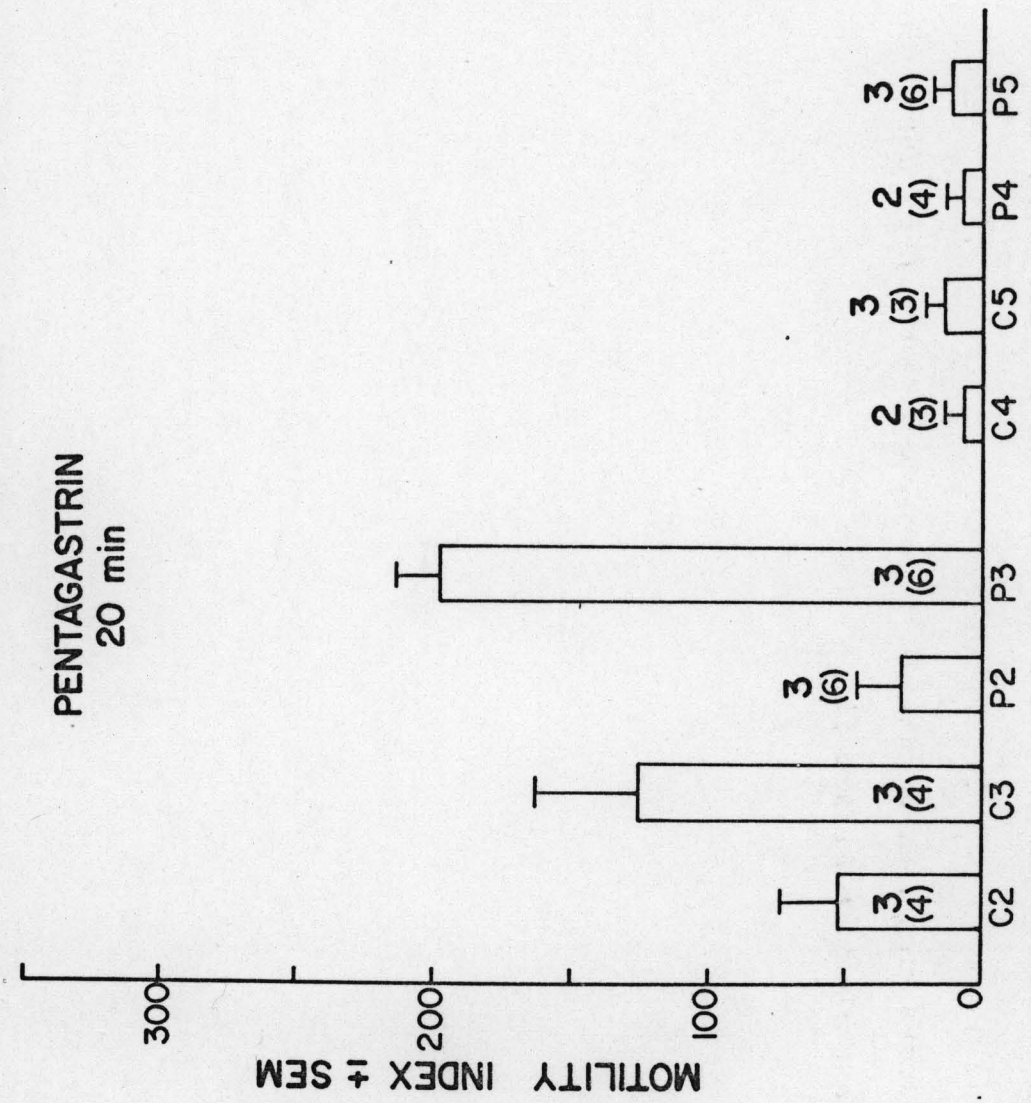
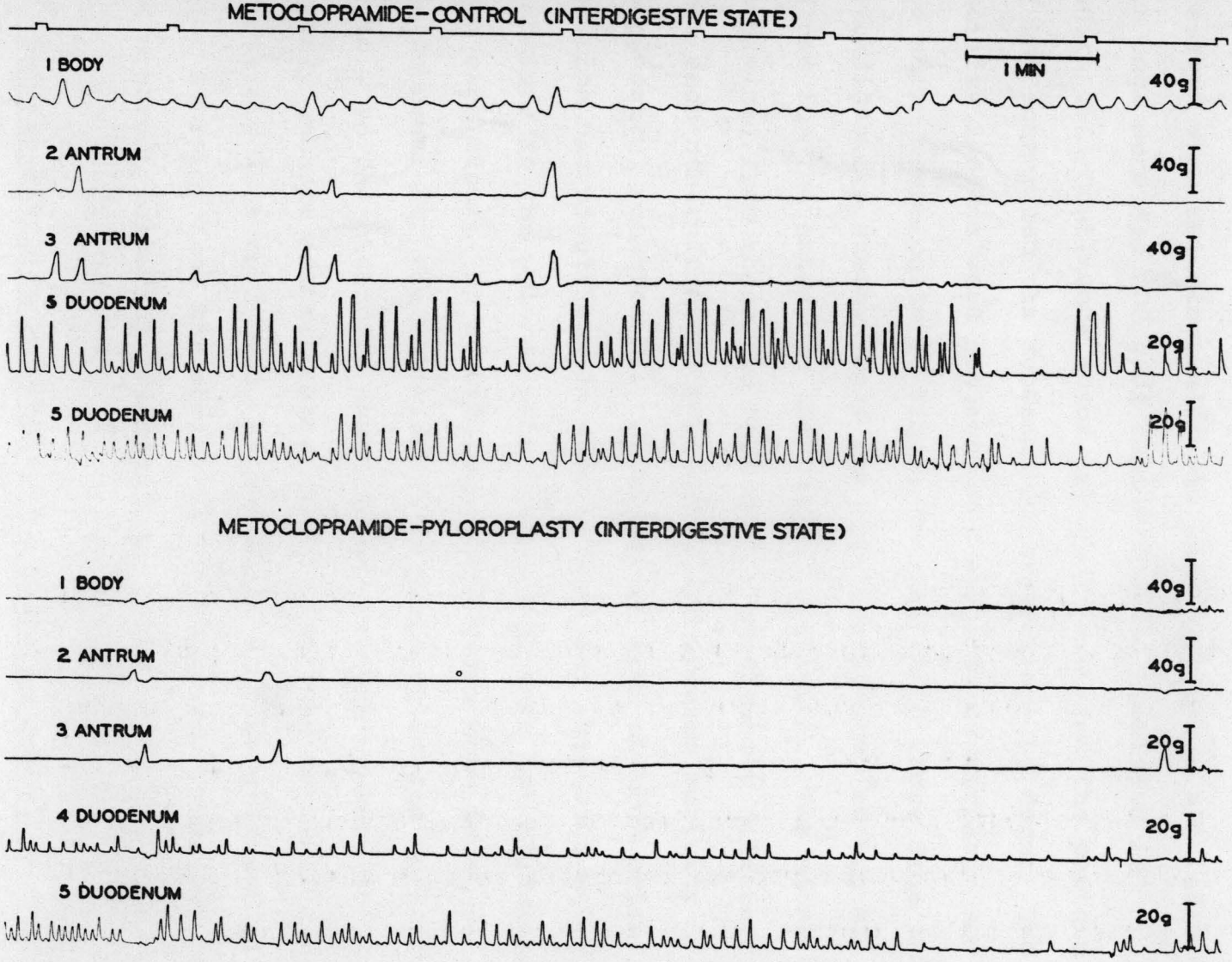

PENTAGASTRIN
20 min
MOTILITY INDEX ± SEM
300
200
100
0
3 (4)
3 (4)
3 (6)
3 (6)
2 (3)
3 (3)
2 (4)
3 (6)
C2
C3
P2
P3
C4
C5
P4
P5

Figure 24. Examples of circular muscle contractile activity from the canine gastric body and antrum and the duodenum following administration of metoclopramide (2 mg/Kg iv) during a basal period of the interdigestive state. The upper panel shows the pattern from a normal dog. The lower panel shows the pattern from a dog following Heineke-Mikulicz pyloroplasty. The numbers on the left of each panel refer to the positions of the force transducers shown in Figure 1. Vertical bars on the right of each panel represent the calibration of the force transducers. Time is given by the horizontal bar at the top.

Figure 24


METOCLOPRAMIDE-CONTROL (INTERDIGESTIVE STATE)
1 BODY
1 MIN
40g
2 ANTRUM
40g
3 ANTRUM
40g
5 DUODENUM
20g
5 DUODENUM
20g
METOCLOPRAMIDE-PYLOROPLASTY (INTERDIGESTIVE STATE)
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
20g
4 DUODENUM
20g
5 DUODENUM
20g

pyloroplasty group of dogs.

The type of circular muscle contractile activity observed when metoclopramide was administered 30 min. after the dogs were fed 200 g of canned food is displayed in Figure 25. Continuous motor activity dominated the pattern of the antrum and the duodenum in both groups of dogs. The motility indices were subjected to analyses of variance and are shown graphically in Figure 26 along with those from the interdigestive state. Only two dogs contributed to the MI values for the antrum in the control condition. The means determined from these two dogs were significantly different from each other (control position 3 had greater activity than control position 2). In addition, each control antral position had significantly greater activity than both antral positions in the pyloroplasty group which were not different from each other. No significant differences were found on the duodenum for the metoclopramide response in the digestive state. In the digestive state metoclopramide appears to greatly enhance antral contractility more than duodenal contractility in normal dogs, establishing a large gradient of motor activity from the antrum to the duodenum. This was not apparent following pyloroplasty.

D. Heineke-Mikulicz Pyloroplasty - Electric Activity

1. Control dog

Electric activity from the terminal antrum and duodenal cap was analyzed from one normal dog. The antral

Figure 25. Examples of circular muscle contractile activity from the canine gastric body and antrum and the duodenum following administration of metoclopramide (2 mg/Kg iv) during the digestive state. The upper panel shows the pattern from a normal dog. The lower panel shows the pattern from a dog following Heineke-Mikulicz pyloroplasty. The numbers on the left of each panel refer to the positions of the force transducers shown in Figure 1. Vertical bars on the right of each panel represent the calibration of the force transducers. Time is given by the horizontal bar at the top.

Figure 25

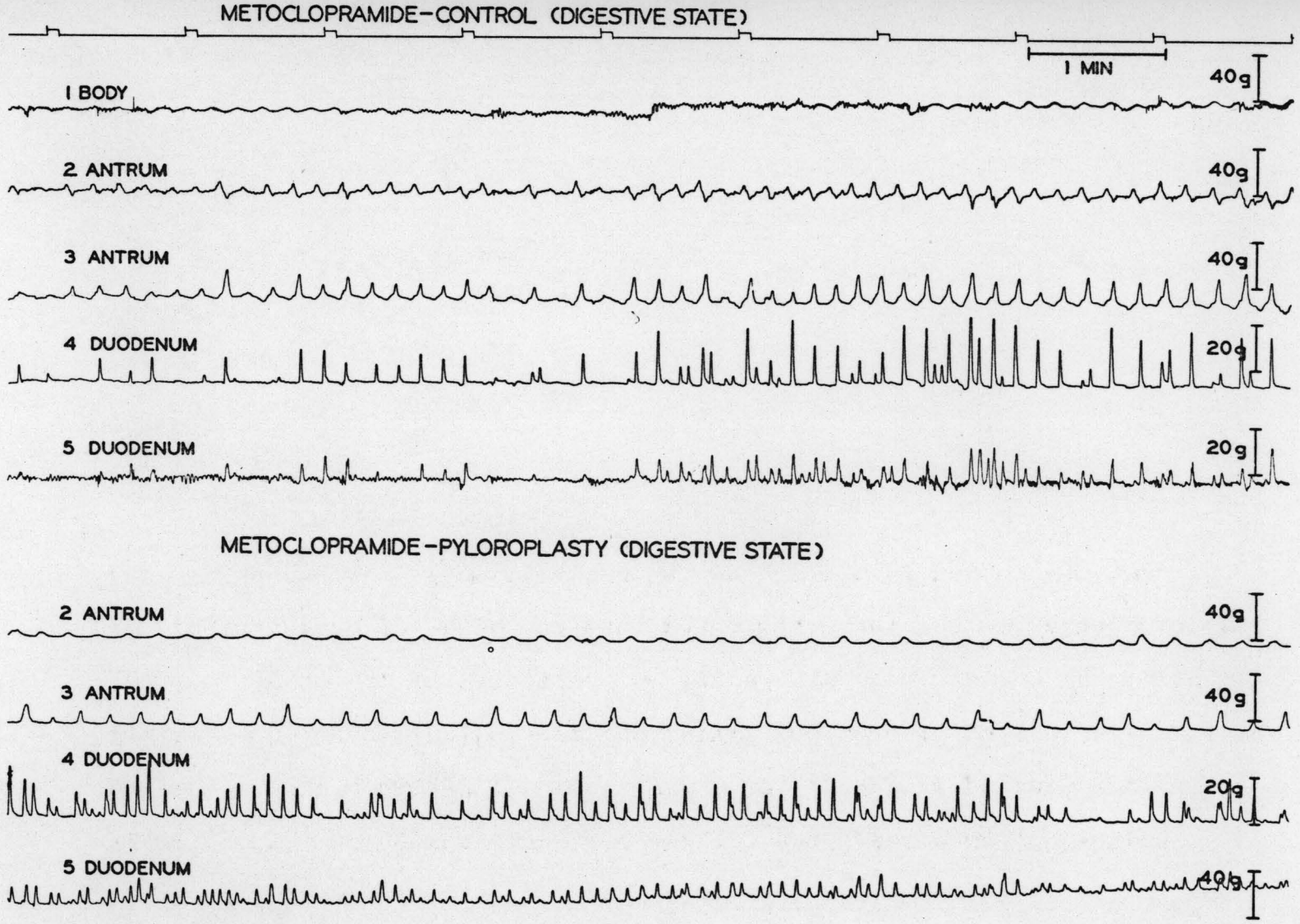
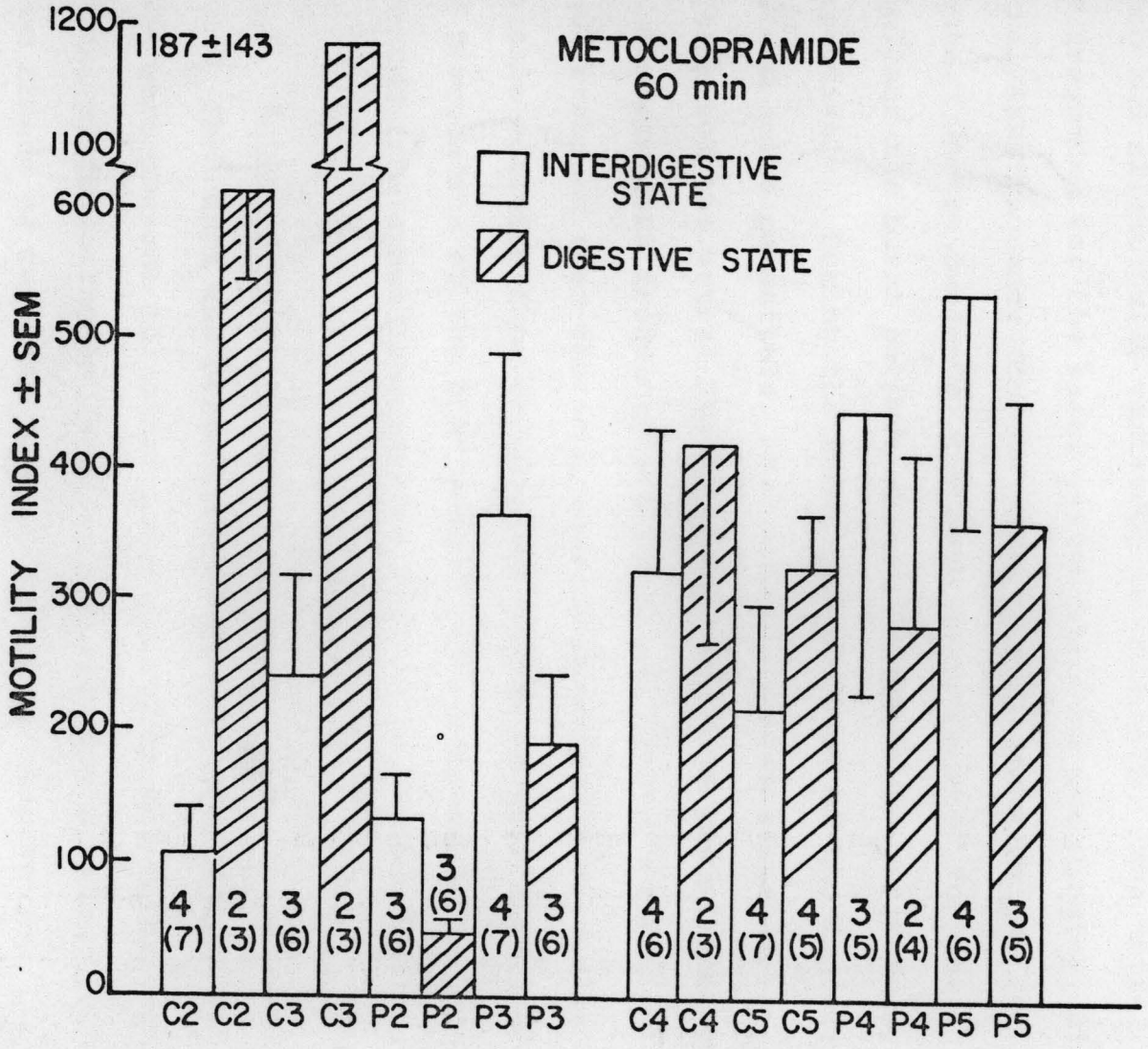

METOCLOPRAMIDE-CONTROL (DIGESTIVE STATE)
1 MIN
1 BODY
40g
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
20g
METOCLOPRAMIDE-PYLOROPLASTY (DIGESTIVE STATE)
2 ANTRUM
40g
3 ANTRUM
40g
4 DUODENUM
20g
5 DUODENUM
40g

Figure 26. Circular muscle contractile activity of the antrum and duodenum expressed as motility index (MI) ± SEM for the metoclopramide responses in the interdigestive and digestive states. The letters and numbers on the abscissa refer to the positions of the force transducers shown in Figure 1. The numbers within the columns are described in Figure 13.

Figure 26


METOCLOPRAMIDE
60 min
INTERDIGESTIVE STATE
DIGESTIVE STATE
MOTILITY INDEX ± SEM
1187±143
1200
1100
600
500
400
300
200
100
0
4 (7)
2 (3)
3 (6)
2 (3)
3 (6)
3 (6)
4 (7)
3 (6)
4 (6)
2 (3)
4 (7)
4 (5)
3 (5)
2 (4)
4 (6)
3 (5)
C2 C2 C3 C3 P2 P2 P3 P3 C4 C4 C5 C5 P4 P4 P5 P5

BER and the duodenal BER were recorded during the basal and burst periods of the interdigestive state and following administration of bethanechol. As has been described, the BER from both organs was an omnipresent rhythmic phenomenon which had slight daily variation in frequency. The antral BER frequency for the basal period was 5.43 per minute. The antral BER frequency for the burst period was 4.21 per minute. On the duodenum, the mean BER frequency for the basal and the burst periods was 19.09 and 18.24 per minute, respectively. During the burst period 93.3% of the duodenal BER had spike potentials. Following administration of bethanechol the antral BER frequency was 4.78 per minute and the duodenal BER frequency was 18.40 per minute. These results showed that the technique of chronically recording electric activity from the dog was viable in this laboratory. The frequencies of the BER recorded were comparable to those reported from other laboratories.

2. Interdigestive state

The basal and burst periods of the interdigestive state were present following pyloroplasty in all three dogs. Generally, following an 18 hour fast each dog's stomach had to be rinsed of residual food particles to observe the basal-burst sequence. Often when this was performed the rinse solution returned yellow-green in color. This was assumed to be bile, either present in the stomach or aspirated through the GDJ at the time of rinsing. An example

of an interdigestive burst period is shown in Figure 27 from dog 3. The burst was most easily identified by a continuous pattern of spike potentials on the duodenum. The counterpart to the segments of duodenal inhibition recorded with force transducers appeared on the electric recordings as 1-3 duodenal BERs without spike potentials (note electrodes 4-6, center of Figure). During the burst period the antral BER had a variable period (also apparent in Figure 27) which generally was 11-15 seconds long, but occasionally was as long as 30 seconds. It was difficult to establish what wave form on the antrum correlated with contractions on that organ. When the frequency of the BER was calculated during a burst period for dog 2, the antral frequency was 4.61 per minute and the duodenal frequency was 19.37 per minute with 93.8% spike potentials.

The period between two burst periods of continuous duodenal spike potentials was referred to as the basal period. This was a quiescent period, essentially without the presence of spike potentials. It was also during this period that the greatest abnormalities in the antral BER were observed. Segments of antral arrhythmias were noted in all three dogs with the most altered BERs being found in dog 1 and dog 2. Both of these dogs displayed spontaneous tachygastria as well as arrhythmias from the terminal antrum during the basal period. Examples of these arrhythmias and tachygastria are shown in Figure 28. The top panel shows a variety of arrhythmias recorded from dog 2. These can occur

Figure 27. Example of electric activity from the canine antrum and duodenum following Heineke-Mikulicz pyloroplasty. The pattern from a burst period of the interdigestive state is shown. The numbers on the left of each tracing refer to the positions of the electrodes shown in Figure 4. Vertical bars on the right of each tracing represent calibration of the electrical signal in millivolts (mv). Time is given by the horizontal bar at the top. Small vertical deflections in the tracings represent EKG artifact.

Figure 27

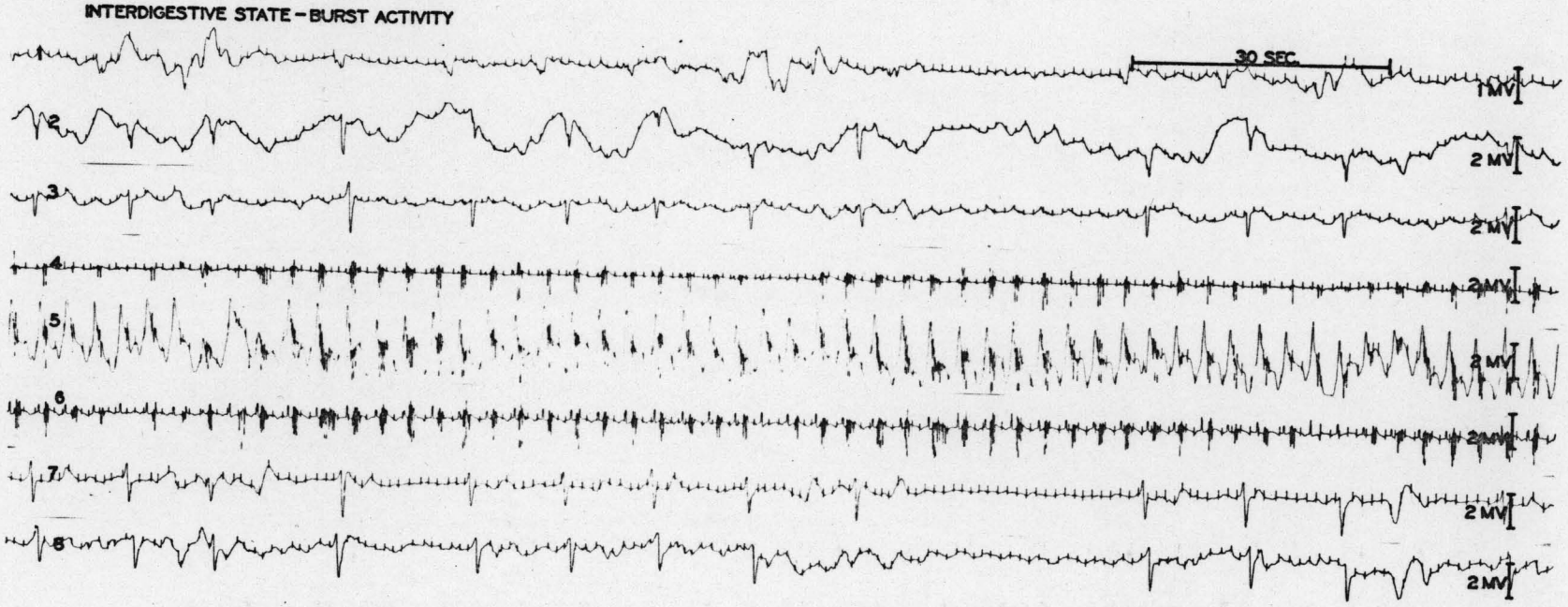
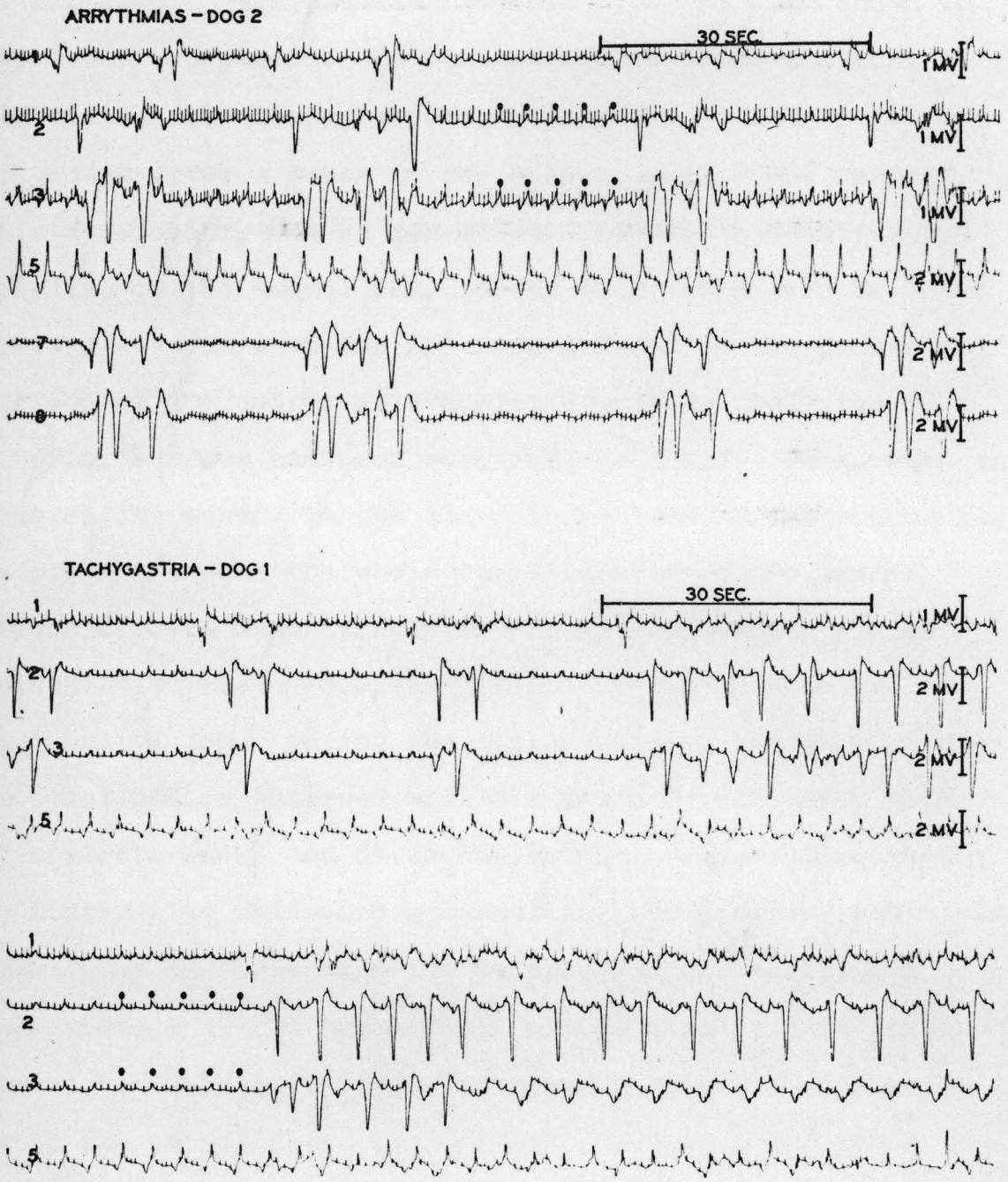

INTERDIGESTIVE STATE - BURST ACTIVITY
30 SEC.
1 MV
2 MV
2 MV
2 MV
2 MV
2 MV
2 MV
2 MV
1
2
3
4
5
6
7
8

Figure 28. Examples of abnormalities in the electric activity from the canine antrum following Heineke-Mikulicz pyloroplasty. Records were taken from the basal period of the interdigestive state. The upper panel shows arrhythmias recorded from dog 2. The lower two panels show a continuous tracing with tachygastria from dog 1. The black dots indicate the duodenal signal recorded from antral electrodes. The numbers on the left of each panel and the calibration bars on the right and at the top are described in Figure 27.

Figure 28


ARRYTHMIAS – DOG 2
30 SEC.
1 MV
1 MV
1 MV
2 MV
2 MV
2 MV
TACHYGASTRIA – DOG 1
30 SEC.
1 MV
2 MV
2 MV
2 MV

as coupled beats (bigeminy) or as three, four, or a group of potentials followed by a pause when the BER does not occur as expected. Tachygastria recorded from dog 1 is shown in the lower two panels. Following a pause after a series of bigeminies, the tachygastria begins in the middle panel and continues after a pause in the bottom panel. The rate of this abnormality was 12 per minute, between a doubling and tripling of the normal BER. As is shown in Figure 28 (top) these alterations in the BER were present on the posterior surface of the antrum (electrodes 7 and 8). Only the anterior surface had been surgically altered. Thus, when an abnormality occurs in the electric pattern of the antrum it is present around the whole circumference of the organ. Figure 28 also demonstrates an abnormality caused by the Heineke-Mikulicz pyloroplasty which was never observed in the control dog. During the pauses between arrhythmias the duodenal BER is observed (cf. electrode 5 with black dots over electrodes 2 and 3) in the antrum. Closer observation indicated that following pyloroplasty the duodenal BER could usually be recorded from the terminal antral electrodes (positions 2 and 3) between all antral BERs. It is possible therefore that an electric influence from the duodenum may alter the antral electric activity. Whatever the cause, it is apparent that following pyloroplasty the hypomuscular segment has been altered to the extent that the duodenal BER can be recorded in the antrum and antral arrhythmias occur spontaneously during the basal period of the interdigestive

state.

3. Digestive state

The digestive state was characterized by a regular BER on the antrum and duodenum with intermittent spike potentials apparent on the duodenum. As shown in Figure 29, when dog 1 was fed 200 g of canned food between the arrows, antral tachygastria returned to normal BER before the dog had finished eating the food. Thus, food in the stomach was an adequate stimulus to prevent the spontaneous occurrence of abnormal antral BER. This was true for all three dogs with pyloroplasty. When the frequency of the BER was calculated 30-35 minutes after feeding dog 2, the antral frequency was 4.86 per minute and the duodenal frequency was 19.00 per minute with 46.3% spike potentials.

4. Citrate-fat test meal

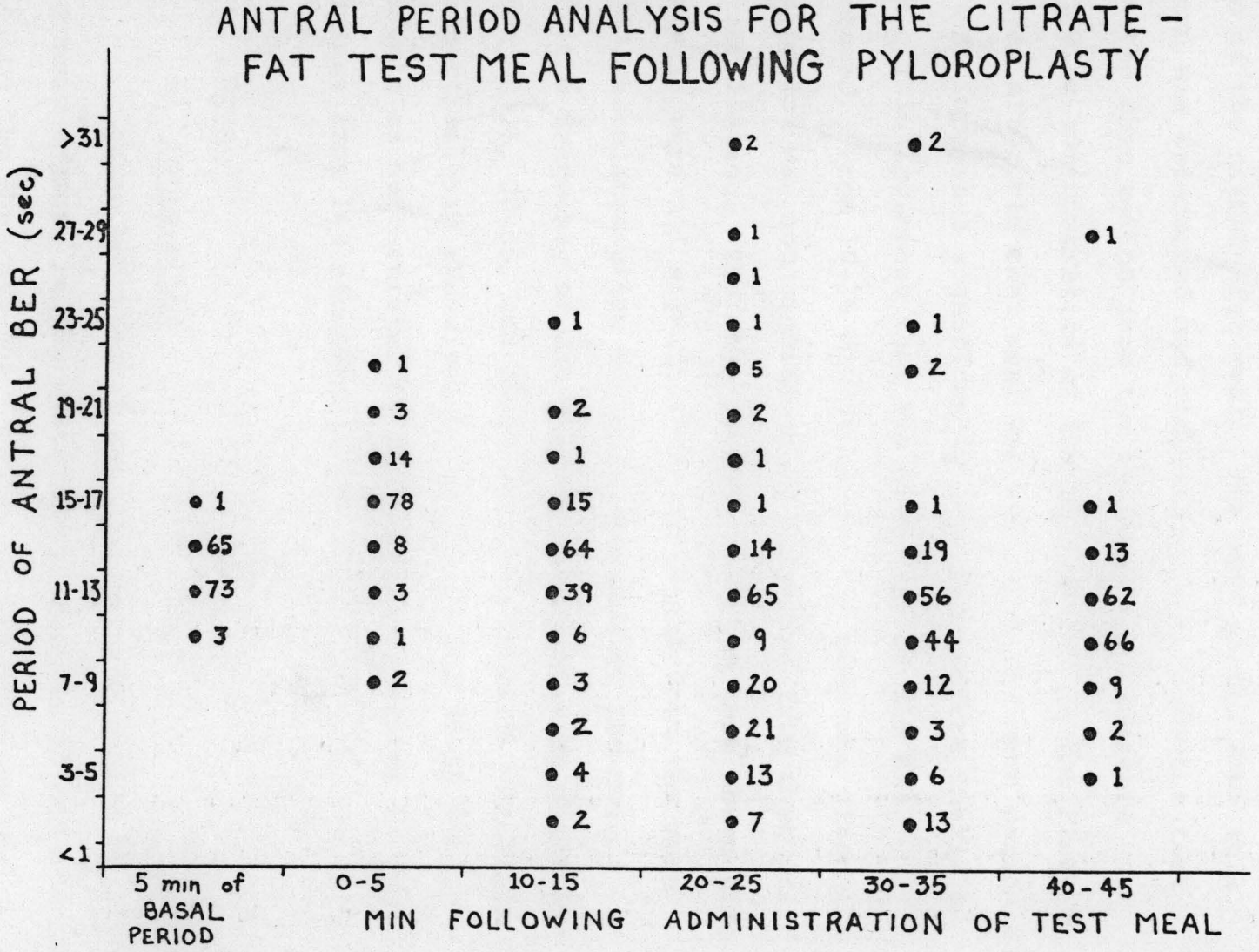
Following administration of the 300 ml citrate-fat test meal, arrhythmias became apparent after the first 5 to 10 minutes. Since the period of the BER appeared to be variable throughout the time the test meal was present in each dog's stomach a detailed analysis was performed. The period of the BER was measured for 5 minute segments in each of the three dogs. For each segment the results were placed in groupings as described in the Methods. The total number of periods measured for all dogs was pooled and the results are depicted graphically in Figure 30. The first column

Figure 29. Effect of feeding on the abnormal electric activity of the canine antrum following Heineke-Mikulicz pyloroplasty. 200 g of canned dog food was presented to the animal during a period of tachygastria. The dog ate the food between the arrows. The numbers on the left of each tracing and the calibration bars on the right and at the top are described in Figure 27.

Figure 29

Figure 30. Antral period analysis for the citrate-fat test meal following Heineke-Mikulicz pyloroplasty. The period of the BER is shown on the ordinate in 2-second groupings. The time intervals subjected to analysis are shown on the abscissa. The first time interval was taken from a basal period in the interdigestive state without arrhythmias. The remaining intervals represent the time following administration of the citrate-fat test meal. A black circle on the figure indicates a period recorded in that 2-second grouping. The numbers next to the black circles show the total number of periods in a grouping for two experiments in each of three dogs (i.e., each number is the total number of periods in that grouping for six experiments).

Figure 30


ANTRAL PERIOD ANALYSIS FOR THE CITRATE - FAT TEST MEAL FOLLOWING PYLOROPLASTY
PERIOD OF ANTRAL BER (sec)
>31
27-29
23-25
19-21
15-17
11-13
7-9
3-5
<1
5 min of BASAL PERIOD
0-5
10-15
20-25
30-35
40-45
MIN FOLLOWING ADMINISTRATION OF TEST MEAL

shows the periodicity of the BER for the group of dogs taken from a basal period without arrhythmias before administration of the citrate-fat meal. The mean period from this column was determined and compared by the Student t-test with the mean period from the various time intervals following administration of the test meal. In the first 5 minutes after the test meal was instilled the mean period of the BER increased significantly over that before instillation. This indicates that the frequency of the BER decreased. From 10-15 minutes after the meal was given the mean period was not significantly different from that prior to instillation. The mean periods from the last three time intervals were all significantly decreased from the mean period calculated prior to administration of the meal. Thus, the frequency of the BER was increased significantly in the 20-25, 30-35, and 40-45 minute intervals. Arrhythmias were particularly prevalent in the 20-25 and 30-35 minute intervals as demonstrated by the number of periods in the groupings from 1-9 seconds.

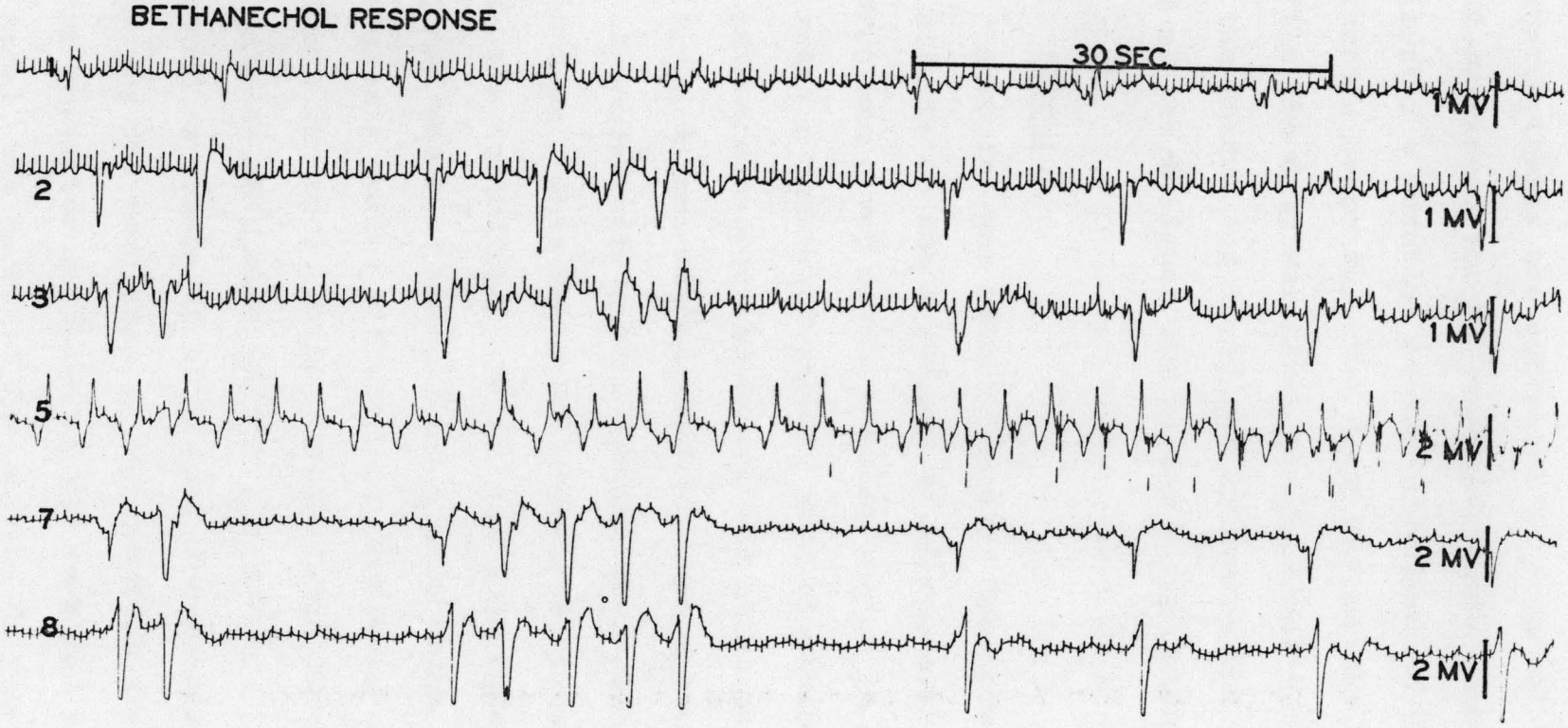
5. Drugs

a) Bethanechol

When bethanechol was administered during an arrhythmic segment in the interdigestive state it effectively inhibited the abnormal BER. Figure 31 demonstrates the response in dog 2 to bethanechol. As the drug takes effect spike potentials appear on the duodenum (electrode 5) and

Figure 31. Effect of bethanechol administration (0.1 mg/Kg sc) on the abnormal electrical activity of the canine antrum following Heineke-Mikulicz pyloroplasty. Bethanechol response begins with the initiation of spike potentials on electrode 5. The numbers on the left of each tracing and the calibration bars on the right and at the top are described in Figure 27.

Figure 31



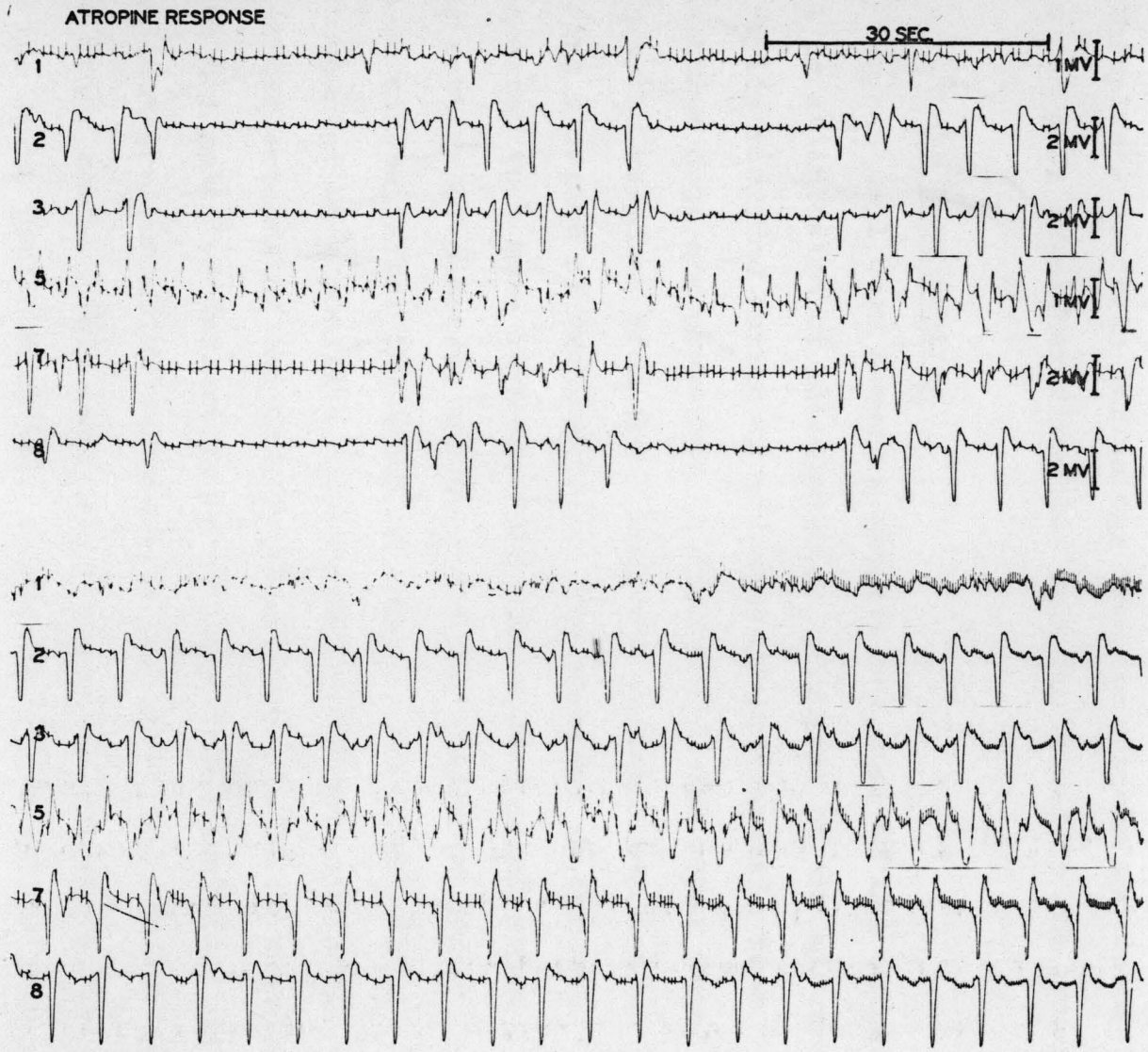
the antral arrhythmias are converted to a normal BER. The regular BER persisted for at least two hours (the length of the experiment), a duration longer than that of the bethanechol contractile response. The frequency of the BER 10-15 minutes after the drug was given to dog 2 was 4.82 per minute in the antrum and 19.30 per minute in the duodenum with 96.9% of the duodenal BER having spike potentials.

b) Atropine

Atropine was administered to the three dogs to study its effects on the incidence of antral arrhythmias. When the drug was given during a burst period in the interdigestive state a number of effects were observed. First, the spike potentials observed during the burst period were abolished and a normal BER was found on the antrum and duodenum. A second effect observed was an increased heart rate in the dogs. This was readily observed from the EKG artifact in the recordings. Third, the most important effect was the onset of antral arrhythmias which lasted for varying intervals during a three hour recording session. In one experiment in dog 3, antral tachygastria occurred which lasted 50 minutes at a rate of 11.5 per minute. A portion of this record is presented in Figure 32 demonstrating the abnormality and the fact that it was recorded from the anterior and posterior surfaces of the terminal antrum. In the upper panel, the duodenal BER appears during the pauses between arrhythmias on the antrum. In addition, during the

Figure 32. Effect of atropine on the electrical activity of the canine antrum and duodenum following Heineke-Mikulicz pyloroplasty. Atropine (1 mg) was administered during a burst period in the interdigestive state. The two panels shown are continuous, beginning 10 minutes after the drug was injected subcutaneously. The numbers on the left of each panel and the calibration bars on the right and at the top are described in Figure 27.

Figure 32



arrhythmias in the upper panel and the tachygastria in the lower panel, the antral BER can be seen propagating into the duodenum (cf. the waveform from electrode 5 during the antral pauses and during tachygastria). It appears that following pyloroplasty electric influences from the antrum and duodenum can pass in either direction from one organ to the other.

c) Pentagastrin

All dogs showed a similar response of the antral BER to an infusion of pentagastrin. Examples of the electric activity recorded during an infusion of pentagastrin from the three dogs are presented in Figure 33. The upper panel shows the response from dog 1 when the infusion was begun during a period of tachygastria. The abnormal rhythm was converted to a more rhythmic BER. The middle panel shows the pattern of electric activity for the antrum of dog 2, 18-20 minutes after the infusion began. Since each BER is accompanied by a positive deflection between the two negative deflections of the BER (see electrode 3), it is assumed that the positive deflection is the electrical correlate of the contractions which pentagastrin was shown to initiate in the motor study. This secondary deflection is also apparent in the lower panel which is a segment of record taken from dog 3, 18-20 minutes after the infusion began. This deflection appears best in the record from electrode 7.

When the frequency of the BER was determined following pentagastrin administration, it appeared to be increased in

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Figure 33. Effect of pentagastrin on the electrical activity of the canine antrum and duodenum following Heineke-Mikulicz pyloroplasty. The upper panel shows the effect when the infusion (1 μg/min) was started during a period of arrhythmias in dog 1. The middle panel from dog 2 and the lower panel from dog 3 show the effect on the antrum after 20 minutes of drug infusion. The numbers on the left of each panel and the calibration bars on the right and at the top are described in Figure 27.

Figure 33

PENTAGASTRIN RESPONSE – DOG 1
30 SEC
1
30 SEC
1 MV
2
2 MV
5
2 MV
7
2 MV
8
2 MV
DOG 2
30 SEC
2
1 MV
3
1 MV
7
2 MV
DOG 3
30 SEC
2
2 MV
3
2 MV
7
2 MV

both the antrum and duodenum when compared with the frequency in the digestive state or in the burst period of the interdigestive state. The antral BER frequency from dog 2 was 5.80 per minute, 10-15 minutes after the infusion began. The frequency of the duodenal BER was 22.04 per minute during the same interval.

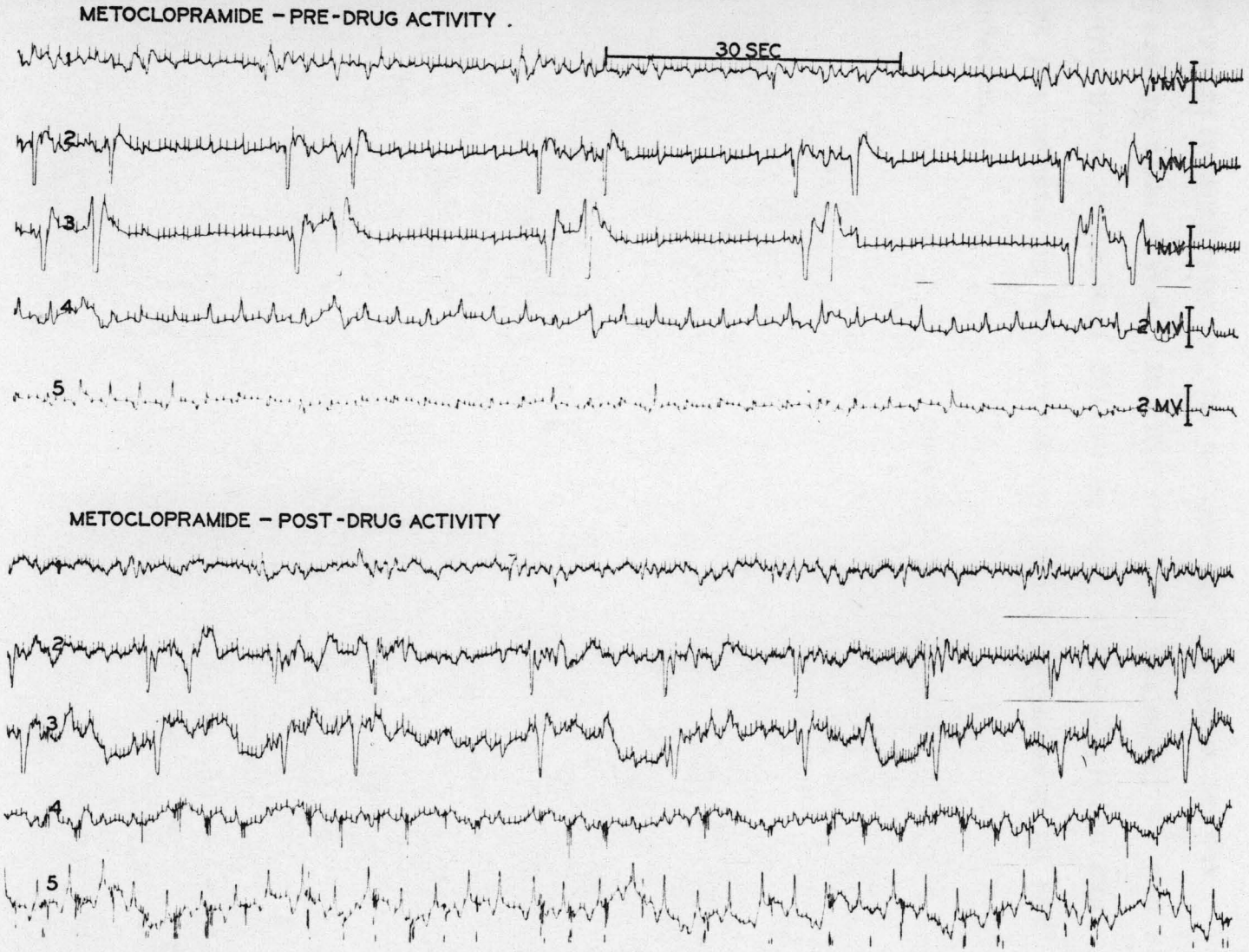
It is interesting to note in the bottom panel of Figure 33 that the BER appears almost simultaneously at electrodes 2, 3 and 7. The distances of these electrodes from the suture line on the anterior surface and the GDJ on the posterior surface were measured at autopsy. Electrodes 2 and 3 were 0.5 cm from the suture line and electrode 7 was 2.0 cm from the GDJ. The smooth muscle at each of these positions appears to generate its cyclic change in electric potential at the same time.

d) Metoclopramide

Metoclopramide was also capable of "normalizing" the BER. Figure 34 presents two segments of record from dog 2. The upper panel shows the pattern of spontaneous arrhythmias which were found in the basal period of the interdigestive state 2-4 minutes before the drug was given. The lower panel shows the response to metoclopramide 2-4 minutes after the drug was injected intravenously. Antral arrhythmias are replaced by a more regular BER. Also, spike potentials appear on the duodenum (electrodes 4 and 5) in response to metoclopramide. This agrees with the study of

Figure 34. Effect of metoclopramide (2 mg/Kg iv) on the electrical activity of the canine antrum and duodenum following Heineke-Mikulicz pyloroplasty. The upper panel demonstrates arrhythmias in the antral electrical pattern present 2-4 minutes before the drug was given. The lower panel shows the electrical activity 2-4 minutes after drug administration. The coupled arrhythmic beats present in the upper panel are not observed in the lower panel. Spike potentials are present on the duodenal electrodes in the lower panel. The numbers on the left of each panel and the calibration bars on the right and at the top are described in Figure 27.

Figure 34


METOCLOPRAMIDE – PRE-DRUG ACTIVITY .
30 SEC
1 MV
2
1 MV
3
1 MV
4
2 MV
5
2 MV
METOCLOPRAMIDE – POST-DRUG ACTIVITY
2
3
4
5

the motor activity following Heineke-Mikulicz pyloroplasty which showed that metoclopramide stimulated circular muscle contractile activity in the antrum and duodenum in the interdigestive state. In this dog, the frequency of the BER in the first 5 minutes following drug administration was 4.85 per minute on the antrum and 18.60 per minute on the duodenum.

DISCUSSION

A. Vagotomy and Pyloroplasty Procedures

The motor coordination of the antral-duodenal area was minimally altered by parietal cell vagotomy with or without pyloroplasty. This is in agreement with the work of Walker and associates (1974) following parietal cell vagotomy alone in dogs maintained on solid food. In contrast, Walker showed that dogs with a truncal vagotomy, maintained on a diet of solid laboratory chow, had reduced motor activity of the antrum and duodenum. His animals did not exhibit the characteristic basal, burst sequence of the interdigestive state. Instead, a continuous pattern of antral activity which was uncoordinated with the duodenal activity was present. This type of antral motor activity is characteristic of a recently fed animal and may be indicative of retention of solid food. In the early part of the present study animals with truncal vagotomy did not demonstrate "normal" motor patterns and were a maintenance problem. Both situations were alleviated by placing the animals on a liquid, nutritionally balanced diet. When this was done basal, burst sequences in the interdigestive state were observed. This, however, was not as consistent a finding as following parietal cell vagotomy. The contractile activity after truncal vagotomy appeared to be reduced.

Motor patterns of the antral-duodenal area have not been previously characterized for truncal vagotomy with

Heineke-Mikulicz pyloroplasty. The obstructive nature of the truncal vagotomy procedure with regard to solid food was diminished by the addition of a Heineke-Mikulicz pyloroplasty. This supports the hypothesis of Dragstedt that a secondary surgical procedure is necessary to relieve gastric stasis resulting from truncal vagotomy alone (Dragstedt et al., 1949). Unfortunately, the benefit of relieved gastric retention may be accompanied by the addition of other side-effects when pyloroplasty is performed (e.g., Goligher et al., 1972), although none were apparent in these experiments.

The present experiments lend support to the hypothesis of Dozois et al. (1971) that there is a differential handling of solid and liquid meals by the stomach. In spite of the retention of solid food in the dogs with truncal vagotomy, they were able to empty a liquid diet. Dogs are also capable of emptying liquid test meals in a normal manner following truncal vagotomy with or without pyloroplasty (Springfield et al., 1974). Retention of solid food may cause the gastric smooth muscle to be stretched, possibly to the point where contractions are less efficient, as has been suggested by Nelson and co-workers (1967). Even if this is the case, the contractions still allow liquids to empty in a normal manner. A flaccid bowel may be capable of moving liquid substances since it would have less resistance to flow and tend not to slow transit. The ability of a hypomotile bowel to transport liquids has been demonstrated

to be present in the colon during diarrhea (Connell, 1962).

The vagotomy and pyloroplasty procedures did not alter the cholinergic receptor stimulating properties of bethanechol. Bethanechol stimulated circular muscle contractile activity in the antrum and the duodenum. A characteristic response was observed following bethanechol administration in the interdigestive state or after instillation of the citrate-fat test meal. No explanation is available for the greater motility index found for the parietal cell vagotomy with pyloroplasty condition challenged with bethanechol alone.

Insulin exerts its action on gastrointestinal smooth muscle through a central vagal mechanism. An intact antral innervation was evident by the ability of insulin to stimulate this organ in animals with parietal cell vagotomy. The absence of an insulin response in dogs with truncal vagotomy confirms that the antrum was denervated in these dogs. In contrast, no significant differences in motor activity among the four surgical conditions were observed on the duodenum. The basic reason for this appears to be the ability of insulin to stimulate circular muscle contractility in the duodenum of dogs with truncal vagotomy shortly after injection. It is not known whether this is a direct or an indirect response to the drug. Thus, in addition to its classical central vagal mechanism, insulin appears to have a peripheral mechanism of stimulation on the duodenum.

In dogs and man liquid test meals tend to empty in an

exponential manner (Weisbrodt et al., 1969; Hunt and Knox, 1968). The concept advanced by Weisbrodt to explain the antral-duodenal contractile activity involved in gastric emptying is that the accompanying motility is characterized by a certain ratio or gradient of activity between the antrum and duodenum. With high antral and low duodenal activity, as in the case of the citrate test meal, the rate of emptying is relatively fast. A decrease in the antral-duodenal motor gradient, as in the case of the citrate-fat test meal, results in slower emptying. These types of motor gradients were observed with the citrate and citrate-fat test meals following either vagotomy procedure with or without pyloroplasty. The two drugs used in this study, bethanechol and insulin, are known to enhance stomach emptying (Weddle et al., 1974; Springfield et al., in press). Both drugs initiated relatively high antral, low duodenal contractile activity adding further support to Weisbrodt's concept.

The motility ratio may also be related to the resistance of flow in the lumen. Bowel resistance is related to contractile activity. If it is assumed that intraluminal contents move from an area of high motor activity to an area of lesser motor activity, then rapid flow occurs when bowel resistance is low. Thus, the citrate test meal initiates high antral and low duodenal activity, low duodenal resistance, and consequently a rapid rate of gastric emptying. In contrast, the citrate-fat test meal initiates relatively

greater duodenal contractility (i.e., a small motility ratio), increased duodenal resistance, and slower emptying.

With both test meals a motility ratio is present which allows material to move from the stomach into the duodenum. This seems to occur similarly following any of the vagotomy and pyloroplasty procedures studied in the present experiments. Thus, the motor coordination involved in the gastric emptying of liquid test meals does not appear to be substantially affected by either the denervation of the body of the stomach or of the whole stomach. Altering the normal anatomy of the GDJ with pyloroplasty also appears to have little effect on the coordinated emptying of liquid test meals following either vagotomy procedure. As has been mentioned, truncal vagotomy seriously disrupted the motor coordination involved in the emptying of solid food. It is apparent that the antrum must be innervated for normal motor coordination of the emptying of solids to take place.

B. Heineke-Mikulicz Pyloroplasty - Gastric Emptying

Few definitive studies exist concerning the effects of pyloroplasty alone on motility or gastric emptying. Finney pyloroplasty alone results in uncoordinated antral-duodenal activity and delayed emptying of solids (Ludwick et al., 1969; Ludwick et al., 1970). Ludwick's work also showed Finney pyloroplasty to be obstructive to the emptying of liquid test meals. He and his associates concluded that pyloroplasties alone do not enhance the emptying of liquid

test meals for at least 3 months following surgery. When the stomach emptying of the citrate-fat liquid test meal was studied following parietal cell vagotomy, a Heineke-Mikulicz pyloroplasty tended to delay the rate of emptying (Weddle et al., 1974). Furthermore, the addition of a Heineke-Mikulicz pyloroplasty to the parietal cell vagotomy significantly increased the levels of peripheral venous serum gastrin (Weddle et al., 1974). Since gastrin has been demonstrated to delay gastric emptying (Dozois and Kelly, 1971), pyloroplasty may actually delay emptying through this mechanism.

The present study shows that Heineke-Mikulicz pyloroplasty alone enhances the emptying of the citrate-fat test meal. This is in contrast to the results of Ludwick which demonstrated that after Finney pyloroplasty, dogs tended to retain the citrate-fat test meal. Thus, their tentative conclusion about the obstructive nature of pyloroplasties does not hold in regard to the emptying of liquids following Heineke-Mikulicz pyloroplasty.

A number of clinical reports demonstrate more rapid gastric emptying following vagotomy procedures including a pyloroplasty than after vagotomy alone. This was true when patients with selective vagotomy and pyloroplasty were compared with patients with parietal cell vagotomy alone (Madsen et al., 1973), or when patients with either selective vagotomy or parietal cell vagotomy were compared with those having a similar vagotomy procedure and a Weinberg pyloroplasty (Clarke and Alexander-Williams, 1973). Humphrey and

Wilkinson (1972) found that emptying of a hypertonic glucose test meal was enhanced in patients with truncal or selective vagotomy and pyloroplasty when compared with an unoperated control group. Cobb and co-workers (1971) have demonstrated an extremely rapid initial emptying of liquids in patients with truncal vagotomy and pyloroplasty. They noted that the patients with the most rapid initial emptying were those who also complained of dumping. Humphrey and Wilkinson (1972) had also associated experimentally induced dumping with rapid gastric emptying and pyloroplasty.

Having found a significant incidence of dumping in patients with pyloroplasty alone, Douglas and Duthie (1972) concluded that the effects of pyloroplasty on gastric emptying were similar to the effects of vagotomy and pyloroplasty together. The present results support the suggestion of the above authors that enhanced gastric emptying is associated with pyloroplasty, in this case, Heineke-Mikulicz pyloroplasty. Whether this enhanced emptying can lead to the dumping syndrome is unknown. The results of these experiments showed an enhancement of approximately 15% after 45 minutes. The initial emptying was not measured. This degree of enhancement may not be sufficient to create dumping. Clearly, more data are needed concerning the effects of pyloroplasty on the complete emptying picture of a variety of liquid test meals and of solid food before it is certain that pyloroplasty leads to dumping.

In 1934, Gianturco studied the emptying of small

volumes of various liquids mixed with barium in normal cats and in cats with pyloroplasty. His results led him to conclude that little change occurred in the pattern of emptying between these two groups of animals. Nevertheless, his data reveal a somewhat faster interval for the complete emptying of oils in cats with pyloroplasty than in normal cats. The present results are obtained with a method which is more precise than Gianturco's roentgenographic method. Although the present method is essentially a point analysis and cannot give information about the overall pattern of emptying, it is clear that the amount of citrate-fat remaining in the stomachs of the dogs studied was less at the point measured after pyloroplasty than before. This result indicates that the normal anatomical relationship of the GDJ has some importance in the coordination of the gastric emptying of the citrate-fat test meal. The Heineke-Miķulicz pyloroplasty must alter the gradient of motor activity between the antrum and duodenum set up by the citrate-fat test meal. This could be by a limiting of the effect of fat on duodenal receptors and a decrease in duodenal contractile activity or by an increase in antral circular muscle contractile activity.

C. Heineke-Mikulicz Pyloroplasty - Motor Activity

Several clinical studies propose that a pyloroplasty is an unnecessary adjunct to parietal cell vagotomy for uncomplicated duodenal ulcer (Johnston and Wilkinson, 1970; Amdrup and Jensen, 1970; Imperati et al., 1972; Grassi et al.,

1973). The reasons given for this contention were that the mechanisms controlling normal emptying would remain in effect if pyloroplasty was avoided. Implicit in such a statement is the idea that pyloroplasty alters normal motor coordination at the antral-duodenal segment. This speculation is supported by only a few studies of gastric emptying following pyloroplasty alone. No studies have been reported in which circular muscle contractile activity has been monitored following Heineke-Mikulicz pyloroplasty.

The present experiments demonstrate that Heineke-Mikulicz pyloroplasty is capable of altering normal patterns of circular muscle contractile activity during the interdigestive state. In both preburst activity and during the burst period antralization of the duodenum was observed. In the one dog with pyloroplasty in which this phenomenon mainly occurred the normal segments of duodenal inhibition during the burst period were replaced by antral-like contractions. During the preburst activity the duodenal cap showed large amplitude contractions occurring almost simultaneously with antral contractions. A similar pattern of contractile activity was found by Ludwick and co-workers (1969) after Finney pyloroplasty and postulated to affect efficient gastric emptying. Taken together these results demonstrate that by altering the normal anatomical location of the GDJ pyloroplasties impair one of the normal physiological reflexes at work during the interdigestive state.

The analysis of motility indices for the burst period

on the antrum did not show any significant alteration of the contractile pattern following pyloroplasty. In both the control group and pyloroplasty group of dogs there was greater motor activity in the terminal antrum as compared to the orad antrum.

In the digestive state one of the dogs with pyloroplasty again demonstrated antralization of duodenal cap contractile activity. This phenomenon was most apparent immediately after feeding the animal, but it could be detected later in the digestive state as well. The duodenal cap appeared to contract simultaneously with the terminal antrum. Although intraluminal activity was not monitored, it is a reasonable assumption that circular muscle contractions in the narrowed terminal antrum and duodenum increase resistance to flow and may occlude the lumen altogether. It is therefore postulated that antralization of the duodenum increases resistance to flow since a larger segment than normal is contracted at the same time. This may be of little effect on the emptying of liquids since as shown above pyloroplasty enhances the emptying of citrate-fat. On the other hand, such a pattern of contractile activity may change the emptying characteristics of solid food. This is supported by Ludwick's finding of gastric retention following Finney pyloroplasty (Ludwick et al., 1969) and by the repeated observation in the present experiments of food residue in the stomachs of dogs with pyloroplasty after 18 hours or more of fasting.

The possibility that pyloroplasty delays emptying of solids receives some further support from the analysis of the motility index in the digestive state. In the control group of dogs a trend exists for greater motor activity in the terminal antrum than in the orad antrum. This trend is significant in the dogs with pyloroplasty and further analysis showed both the number of terminal antral contractions and the force of these contractions to be greater than those in the orad antrum. Carlson et al. (1966) have demonstrated that the main function of the terminal antral contraction is retropulsion. Thus, it would appear from this analysis that motor activity measured in the antrum of dogs with pyloroplasty during the digestive state would result in retropulsion of intraluminal contents. This may be a greater effect in dogs with pyloroplasty than in control dogs. A second important factor involved in the motor activity of dogs with pyloroplasty is that there was a significantly greater number of contractions in the hour analyzed in the duodenum (caudad to cap) of these dogs than in the control animals. If, indeed, circular muscle activity of the duodenum can provide a resistance to intraluminal movement, this difference may contribute to any delay in the emptying of solids observed in the pyloroplasty group of dogs. Confirmation of such speculation awaits improved technology in the measurement of gastric emptying and transit of solid food.

In the study of the gastric emptying of the citrate-fat test meal discussed above, pyloroplasty was shown to enhance

the emptying of that test meal. When antral and duodenal circular muscle contractile activity was monitored in the presence of citrate-fat no significant differences were found between the two test groups on either organ. Citrate-fat appeared to stimulate duodenal contractile activity in both groups and showed little effect on the antrum. This is the typical response to citrate-fat as described by others. One important trend appeared in the pyloroplasty group of dogs which may have played some part in the enhanced emptying. Since all dogs did not show significantly enhanced emptying when it was measured and the MI was a parameter with large variability, it is not surprising that this trend did not reach the level of statistical significance. As shown by the motility index data, the terminal antrum of the pyloroplasty dogs had greater motor activity in the presence of the test meal than the orad antrum or the terminal antrum of the control dogs. Since gastric emptying was not studied in these dogs it can only be speculated that such a contractile pattern might be responsible for a sufficient change in the antral-duodenal motor gradient to effectively propel more of the citrate-fat test meal into the small bowel.

Qualitatively and quantitatively the smooth muscle stimulation following bethanechol was the same in dogs with or without pyloroplasty. Thus, pyloroplasty does not affect the antral or the duodenal cholinergic receptors. This same conclusion was drawn following the vagotomy and pyloroplasty

procedures discussed earlier. In that study, a gradient of motor activity was present as shown by the MI ratios which were calculated. In the present study of pyloroplasty alone a gradient from antrum to duodenum was not apparent in the analysis of motility index for bethanechol. This was also the case in the control dogs. Throughout these experiments the observation was made that the antrum was stimulated for a shorter duration and to a lesser degree than the antrum of the dogs with PCV or TV with or without pyloroplasty. Even though the control records and those for dogs with pyloroplasty were analyzed for 30 minutes instead of 60 minutes (the time period used in the previous study) a gradient of activity from antrum to duodenum was not found. Since the importance of motor gradients in the interdigestive state has not been stressed, this result does not detract from the motor gradient found for bethanechol in the earlier study when a test meal was present in each dog's stomach. It is possible that such a motor gradient might have been seen in the experiments following Heineke-Mikulicz pyloroplasty if bethanechol had been examined in the digestive state.

Both Dozois and Kelly (1971) and Cooke et al. (1972) have demonstrated delayed emptying of liquid test meals in dogs intravenously infused with pentagastrin. The work of Cooke and associates further showed that pentagastrin increased the motility index on the antrum of their dogs indicating an increase in the frequency and amplitude of contractions. Since Weisbrodt et al. (1969) had previously

shown a shallow gradient of activity from antrum to duodenum with test meals which empty relatively slowly, the results of Cooke *et al.* presented an enigma. This caused Cooke to suggest that pentagastrin may delay emptying by working at a site other than the antrum. This suggestion serves only to confuse the issue and avoids a further investigation of pentagastrin's effects on the antrum. These effects may actually be the reason why pentagastrin delays emptying since increased antral intraluminal pressure and increased per cent motor activity have also been demonstrated in man (Kwong *et al.*, 1971) and Szurszewski (1974) has provided evidence *in vitro* that pentagastrin has a direct action on canine antral smooth muscle. The question which needs to be answered is how does the increased antral contractile activity and intraluminal pressure produced by pentagastrin result in delayed emptying of liquids.

The present results with infusions of pentagastrin in normal dogs and dogs with pyloroplasty demonstrate a pattern of antral circular muscle contractile activity which could be responsible for pentagastrin's emptying response. With two extraluminal force transducers on the antrum of these dogs (Cooke's group apparently only analyzed records from one antral force transducer) a differential stimulation to pentagastrin was recorded. Pentagastrin consistently produced a greater amplitude response from the terminal antrum than from the orad antrum. In both the control group of dogs and in dogs with pyloroplasty the difference in the

motility index between the terminal antrum and the orad antrum was significant. Furthermore, as shown in Figures 22 and 23, when pentagastrin is administered in a basal period of the interdigestive state its effect is primarily a stimulation of the antrum with only a minimal contractile response on the duodenal cap or from the duodenum caudad to the cap. Figure 22 also shows that following pyloroplasty one of the dogs had antralization of the duodenal cap during the pentagastrin infusion. This appeared to be the only difference in the response to pentagastrin between the control and pyloroplasty groups of dogs. In general, pentagastrin produced a similar response on the antrum in all dogs.

It would appear from these results that pentagastrin has the potential to differentially stimulate the terminal antrum over the orad antrum. In contrast, pentagastrin does not appear to stimulate the duodenum. Although it is understood that emptying studies will need to be performed in conjunction with studies using force transducers and possibly cineradiography for confirmation, the following hypothesis is offered to explain pentagastrin's enigmatic effects. It is proposed that the delayed emptying of liquids caused by pentagastrin administration is due to essentially an increase in the retropulsive properties of the antral musculature. The rapid frequency of antral contractions and the greater amplitude of contractions in the terminal antrum set the stage for increased resistance to flow into the small bowel and increased retropulsion of antral contents.

This does not negate the theory of antral-duodenal motor ratios being responsible for gastric emptying, but simply adds a corollary. In addition to antral-duodenal motor gradients, antral-antral motor gradients are also involved in regulating gastric emptying of liquids. It is already well documented that antral-antral motor gradients (the TAC of Carlson et al., 1966) result in the regulated emptying of solid foods by causing retropulsion.

Metoclopramide was first studied by the French in the early 1960's for its anti-emetic properties. Jacoby and Brodie (1967) later demonstrated that the drug increased gastric emptying in rats and monkeys and stimulated contractile activity of the antrum and duodenum of unanesthetized dogs. These workers suggested that metoclopramide acts through peripheral, possibly cholinergic, mechanisms to stimulate motor activity. Clinically, metoclopramide has been shown to enhance gastric emptying and small bowel transit time of barium (James and Hume, 1968; Howarth et al., 1969; Howells et al., 1971). Intraluminal pressure studies in the anesthetized dog (Johnson, 1971a) and in man (Eisner, 1971) demonstrated the ability of metoclopramide to increase the strength of antral and duodenal contractions (increased intraluminal pressure) as well as create a more regular duodenal pattern of activity. These effects in man were confirmed by Johnson (1971b) who also showed that the motor response to metoclopramide appeared to depend on the pattern of contractile activity existing when the drug was

administered. A minimal amount of contractile activity recorded prior to the drug became enhanced. When no activity was present before metoclopramide was given, the drug did not produce any appreciable stimulation. In a more recent study Johnson (1973) has elaborated his concept of gastroduodenal synchronization or "linkage" to account for the enhanced gastric emptying seen by others. Enhanced emptying according to Johnson would take place when duodenal contractions regularly follow antral contractions or are linked by metoclopramide. This is simply an extension of the concept of antral-duodenal motor gradients which attempts to emphasize an increase in propulsion with metoclopramide enhanced emptying.

The results with extraluminal force transducers in the present study confirm those of Jacoby and Brodie. In the interdigestive state metoclopramide stimulated both antral and duodenal circular muscle contractile activity. Control dogs and dogs with pyloroplasty showed a variable response to metoclopramide in the interdigestive state. Since the drug was injected in a basal period in all dogs the pre-existing contractile pattern may not be as important in determining the response to metoclopramide as the state of the gastrointestinal smooth muscle itself (which could not be measured).

In the digestive state metoclopramide appeared to enhance the contractile activity of the antrum and duodenum in both groups of dogs. This effect has previously been

observed in normal dogs implanted with mercury column strain gauges (Kelly, 1973). Kelly postulates that metoclopramide stimulates propulsive antral motor activity eliminating an initial phase of retropulsive, mixing activity. The analysis of motility index data from the present study provides some support for Kelly's hypothesis.

Although the number of control dogs studied was small, metoclopramide produced a striking effect on the gradient of antral-duodenal activity in the digestive state in these animals. The relative amounts of motor activity from antrum to duodenum are much greater in the antrum during the digestive state, and this type of pattern may be responsible for increased propulsion or enhanced emptying. Like the control dogs, dogs with pyloroplasty do not have a steep gradient of activity between the antrum and duodenum in the interdigestive state. Interestingly, in the digestive state, dogs with pyloroplasty have significantly less antral motor activity following metoclopramide than control dogs. The steep gradient observed in the control animals was not found in the analysis of motility index for the pyloroplasty group. This result suggests that in dogs following pyloroplasty metoclopramide is not capable of enhancing antral contractile activity in the digestive state. The antral motility index for the pyloroplasty group of dogs was found to be the same when food is given alone or with metoclopramide. Pyloroplasty may have inhibited the ability of metoclopramide to produce a steep antral-duodenal motor gradient and enhance

emptying.

D. Heineke-Mikulicz Pyloroplasty - Electric Activity

The present study clearly demonstrates that Heineke-Mikulicz pyloroplasty disrupts the electrical characteristics of the antral-duodenal segment. During the burst periods of the interdigestive state the rhythmicity of the antral BER was affected and during the basal periods of the interdigestive state a variety of arrhythmias were consistently observed on the antrum. These abnormalities were apparent as rapid BER cycles ranging from bigeminy to tachygastria. Electrical correlates of contractions were not observed on the antrum during arrhythmic intervals. The rapid BER cycles interrupted the propagation of the normal BER such that sometimes the abnormal activity appeared to be propagated in the orad direction. In the vocabulary of the relaxation oscillator model of gastrointestinal electric activity (e.g., Sarna et al., 1971), the oscillators became uncoupled, were no longer phase-locked and occasionally showed reversal of the direction of phase-lag in the antrum. During tachygastria, oscillators on the terminal antrum were often phase-locked with an aboral phase-lag but were completely uncoupled from the oscillators of the orad antrum. The dominant oscillator appeared to be located in the terminal antrum during all arrhythmias.

The spontaneous arrhythmias observed following pyloroplasty were removed by feeding solid food to the animals.

Antral tachygastria was inhibited in less than 30 seconds after one of the dogs began to eat. This response suggests two possible mechanisms which might normally prevent the occurrence of abnormal pacemakers. Since food stimulates gastrin release and the vagus is stimulated by feeding, abnormal pacemakers may be held in check by hormonal or cholinergic activity. The latter suggestion would agree with others (Nelson et al., 1967; Kelly and Code, 1969) who showed that arrhythmias occurred following truncal vagotomy in dogs.

In their study of spontaneous arrhythmias in normal dogs, Code and Marlett (1974) showed that ingestion of water or milk could interrupt antral arrhythmias or tachygastria. These authors contend that abnormal electric activity does not occur when spike potentials (contractions) appear on the antrum. After the ingestion of a citrate-fat test meal, the dogs in the present study showed a reduced incidence of abnormal electric activity for approximately 5 minutes. As shown by the antral period analysis for citrate-fat, the variability of the periodicity (increased arrhythmias) increased after the first 10 minutes following ingestion of the meal. Since the $T_{1/2}$ for citrate-fat is approximately 50 minutes, these results demonstrate that arrhythmias can occur in the antrum when greater than 150 ml of liquid is present in the stomach. This does not contradict Code's and Marlett's observation concerning antral contractile activity since citrate-fat is known to cause little stimulation of

the antrum.

The antral period analysis was also used to calculate the frequency of the BER at various time intervals during the citrate-fat experiments. These results showed that the frequency was increased during the first 5 minutes, returned to normal 10-15 minutes after instillation of the meal, and became significantly faster after the meal had been present for at least 20 minutes. This result confirms in animals the same finding in man (Duthie et al., 1971) for citrate-fat. The reason for this pattern of electric activity is not clear, but may be due to an initial decrease in propagation velocity and BER frequency due to distention, followed by a later increase in BER frequency accompanying an hormonal influence on gastric emptying. This speculation is supported by the work of Dozois and Kelly (1971) who showed a decrease in antral BER frequency and propagation velocity following instillation of a 500 ml saline test meal as well as an increase in BER frequency to exogenously administered pentagastrin.

If a period of antral arrhythmias or tachygastria were continuous while food was present in the stomach, it is quite possible that gastric emptying would be impaired. Since these results show that antral oscillators can be uncoupled from more oral gastric oscillators and phase-lag can be in the oral direction, it is interesting to speculate what effects arrhythmias could have on gastric emptying. Such abnormal activity might result in weakened propulsive

activity and delayed emptying. This speculation has received support from patients with chronic atrophic gastritis, antral arrhythmias and delayed emptying (Barbara et al., 1974). In addition, Sarna and co-workers (1973) have provided evidence from the stimulation of the BER with antral electrodes that contractile activity could be in the oral direction accompanying the stimulated BER and that the emptying of liquids and solids was thereby delayed.

Pharmacological evidence indicates that abnormal electric activity from the antrum may be associated with decreased activity in the cholinergic nervous system. Whenever bethanechol was administered during arrhythmic activity it consistently returned the electric pattern to that of the normal BER with apparent phase-lock and aboral phase-lag. When atropine was administered to these dogs during a burst period in the interdigestive state (a period which usually was without arrhythmias) it abolished all spike potentials and abnormal electric activity was periodically recorded from the terminal antrum. Since atropine can reduce the absolute refractory state in the antrum but not the corpus (Sarna and Daniel, 1974), it is not surprising that arrhythmias occurred in the presence of this drug.

These results suggest that abnormal electric activity can be corrected with cholinergic agonists such as bethanechol. This provides a reason for the use of cholinergic drugs clinically to treat patients after surgery. The experiments with atropine suggest that a contributing factor

to spontaneously occurring arrhythmias is a decrease of acetylcholine at the muscarinic receptor. The role of the adrenergic nervous system in the production of arrhythmias was not investigated. Daniel (1965) has suggested that a sympathetic dominance pattern is operative in the production of arrhythmias with intra-arterial epinephrine in the anesthetized dog. Such a mechanism is consistent with the present finding, but further work is needed.

Metoclopramide was generally found to correct abnormal electric activity. It increased the incidence of spike potentials on the antrum and duodenum and consequently decreased antral arrhythmias. The mechanism of action of metoclopramide is currently under investigation. The drug is known to increase the response of the isolated guinea-pig colon to acetylcholine (Beani et al., 1970) and was postulated to inhibit non-adrenergic, non-cholinergic inhibitory neurons. More recent work with the guinea-pig ileum (Fontaine and Reuse, 1973) suggests that metoclopramide sensitizes cholinergic receptors indirectly. Fontaine and Reuse postulate that metoclopramide acts by releasing 5-hydroxytryptamine. Since metoclopramide appears to act indirectly on the cholinergic muscarinic receptor, it is not surprising that this drug could correct arrhythmic electric activity in light of the experiments with bethanechol.

Experiments with extraluminal force transducers showed that pentagastrin stimulated circular muscle contractile activity in the terminal antrum. The results with

chronically implanted electrodes showed that pentagastrin produced a regular BER with a frequency of nearly 6 cycles per minute. Since this was the same as the contractile rate measured with force transducers, it is assumed that each BER was accompanied by spike potentials. In all dogs this was found to be a positive deflection between two waves of the BER. Such a pattern of electric activity must represent a fusion of numerous spike potentials. Others have observed spike potentials fuse into a negative deflection between two waves of the BER (Kelly et al., 1969). The electric responses to pentagastrin in the present experiments are similar to those in Kelly's original work with the hormone (Kelly, 1970). It appears that pyloroplasty does not affect the electric response typically seen with pentagastrin. Moreover, pentagastrin is capable of correcting antral arrhythmias present prior to its administration. Since pentagastrin is known to delay emptying of liquid meals, bethanechol would seem to be a better drug of choice for the relief of abnormal antral electric activity.

In their original study of the electric activity of the GDJ in dogs with exteriorized antral-duodenal segments, Bass, Code, and Lambert (1961b) found the GDJ to be characterized by an attenuation of the BER and spike potentials. Their work demonstrated that the hypomuscular segment was 1.0-1.5 cm wide and they appropriately called this segment the "insulatory zone". The electric properties of the antrum and duodenum appeared to be separated by the GDJ

suggesting that the coordination between the two organs was not by a myogenic link. In contrast to this study, work with the isolated cat antral-duodenal segment (Bortoff and Weg, 1965) and in situ studies in cats, dogs, rhesus monkeys, and baboons (Bortoff and Davis, 1968) demonstrated a transmission of the BER from the antrum to the duodenum. Bortoff concluded from these experiments that the mechanism of antral-duodenal motor coordination was by the myogenic spead of the BER from the first organ to the second. In the first study the isolated segment was opened lengthwise and pinned down in a bath. In the second study all the animals were anesthetized and their abdomens were filled with Tyrode solution or with mineral oil. It is difficult to determine what relationship these results have to the healthy unanesthetized animal. When chronic electrodes were implanted in dogs and recordings were made in the unanesthetized state, Bass again was able to demonstrate that the GDJ was an area with attenuated electric activity (McCoy and Bass, 1963).

Daniel studied the reflex responses to distention of the gastric body and the duodenum on the mechanical and electric properties of the antrum and duodenum (Daniel and Wiebe, 1966). Gastric distention inhibited duodenal spike potentials and contractile activity. This reflex was inhibited by reserpine pretreatment, but not by bilateral cervical vagotomy or by section at the GDJ. Duodenal distention resulted in a delayed (15 second) decrease in antral BER frequency. This response was inhibited by reserpine

pretreatment and by vagotomy, but not in some of the experiments with section of the GDJ. Daniel and Wiebe concluded that an intramural conduction pathway was not involved in these reflexes.

A thorough study of the correlation of electrical events in the antrum and duodenum was performed by Allen et al. (1964). Recordings from chronically implanted electrodes were analyzed by a cross-correlation technique for the interdigestive and digestive states. No temporal relationship was found at any time between the antral and the duodenal BER. In the digestive state a correlation was observed between the antral BER and the spike potentials in the duodenum. Since this correlation existed only in the presence of food, the authors suggested that antral-duodenal coordination was due to the passage of chyme through the GDJ to the duodenum, or to conduction of impulses along Auerbach's plexus across the GDJ. Atanassova (1969a) has presented evidence using chronic electrodes that during times of increased contractile activity there is a correlation between the spike potentials of the antrum and those of the duodenum, and that the GDJ must be intact for this response to be seen. She has also suggested a role for the myenteric plexus in the coordination of the antral-duodenal segment of the anesthetized dog (Atanassova, 1969b). There seems to be general agreement that antral-duodenal coordination exists in the digestive state. Just what mechanisms come into play once food passes across the GDJ are not clear.

The present results suggest that an intact GDJ is important for normal electric activity to take place in the antral-duodenal segment. By surgically altering the GDJ with Heineke-Mikulicz pyloroplasty, uncharacteristic arrhythmic activity occurs. The juxtaposition of antral and duodenal smooth muscle at the suture line of the pyloroplasty allows the spread of antral and duodenal BER into either organ. Figure 28 clearly shows the presence of the duodenal BER at positions at least 5 mm orad to the pyloroplasty suture line and in some instances as far orad as 2 cm. Hermon-Taylor and Code (1971) have demonstrated that the duodenal pacemaker, the site with the greatest intrinsic BER frequency, is located in the first 5 or 6 mm of the duodenum. In their experiments a chronic recording electrode was also placed 1 to 2 cm orad to the GDJ. At no time did they observe propagation of the duodenal BER into the antrum of dogs with a normal GDJ. The present results appear to be the first demonstration of such a phenomenon.

The presence of the duodenal BER in the antrum suggests that duodenal oscillators with an intrinsically greater frequency can influence terminal antral oscillators following pyloroplasty. The duodenal oscillators may enhance the frequency of the antral oscillators resulting in arrhythmias or tachygastria. This is consistent with the observations that the antrum is more excitable than the corpus (has a smaller rheobase and a briefer chronaxie) (Kelly, 1974), and that the absolute refractory state is shorter in the antrum than

in the corpus (Sarna and Daniel, 1974). The terminal antrum becomes uncoupled from the gastric pacemaker and falls under the influence of the oscillator with the greatest frequency (the duodenal oscillator). Since the frequency of the antral oscillator is limited by the refractoriness properties and excitability of the antral smooth muscle, the influence of the dominant duodenal oscillator is to raise the frequency in the antrum to its maximum rather than to duodenal frequencies. The apparent result is an ectopic antral pacemaker. The origin of the pacemaker was not defined by the present experiments, but arrhythmias could be recorded 2 to 3 cm from the GDJ on the posterior surface of the antrum. Whether the abnormal electric activity occurred simultaneously on the anterior and posterior surfaces of the antrum or spread from one surface to the other could not be determined by these experiments.

The electric properties of the duodenum are also affected following pyloroplasty. Figure 32 demonstrates that during periods of arrhythmia and tachygastria the rapid frequency of the antral BER was superimposed on the duodenal BER recorded 0.5-1.0 cm caudad to the suture line. The antral BER in these instances appeared to be propagated into the duodenum with an aboral phase-lag. This phenomenon was not observed in the single control animal used in these experiments or in previous work with the chronically implanted unanesthetized dog (McCoy and Bass, 1963).

These results support the concept of an electric

insulator at the GDJ (Bass et al., 1961b). When the insulatory zone was surgically altered electric events characteristic of the duodenum were observed in the antrum and vice-versa. The normal anatomical arrangement of a hypomuscular zone between the terminal antrum and the duodenum would appear to separate the electric activity between these two organs. Pyloroplasty appears to allow myogenic spread of the duodenal BER into the antrum which may influence the normal orderly process of cyclic depolarizations of the antral smooth muscle. With the antral and duodenal muscle coats apposed, antral arrhythmias occur spontaneously. This type of electric pattern may affect contractile activity and alter the normal motor coordination between the antrum and duodenum. The present results suggest that a myogenic link between the antrum and duodenum is not the mechanism of coordination between the two organs but a possible mechanism of uncoordination.

The extent of the effect of pyloroplasty on the myenteric plexus was not examined in these experiments. If pyloroplasty permanently severed neural connections to any portion of the antral-duodenal segment, such a denervation might be partially responsible for the abnormal electrical properties observed in these experiments. Thus, it remains to be found whether the mechanism of motor coordination between the antrum and duodenum is due to conduction across the GDJ in Auerbach's plexus, or to a pattern of events set into play by the passage of intraluminal contents from the

antrum to the duodenum. Code (1970) has suggested that a "mystique hovers over the region," but continuous research will undoubtedly unfold the mystery.

CONCLUSIONS

A. Vagotomy and Pyloroplasty Procedures

1. Parietal cell vagotomy (PCV)

   a. Interdigestive state motor coordination was minimally altered by PCV.

   b. Bethanechol stimulated antral and duodenal contractile activity after PCV.

   c. Insulin stimulated antral contractile activity after PCV.

   d. PCV does not appear to affect the emptying of solids or liquids.

2. Truncal vagotomy (TV)

   a. Animals with TV retained solid food. This gastric retention was alleviated by a liquid diet.

   b. The pattern of interdigestive state motor coordination was apparent after TV, but the contractile activity was somewhat reduced.

   c. Bethanechol stimulated antral and duodenal contractile activity after TV.

   d. After TV insulin did not stimulate antral contractile activity but did stimulate duodenal contractile activity.

   e. TV does not appear to affect the emptying of liquids.

3. Pyloroplasty

   a. Following pyloroplasty the interdigestive state motor coordination, the effects of liquid test meals, and of bethanechol and insulin remained the same as after the vagotomy procedures alone.

   b. Pyloroplasty alleviated the gastric retention due to truncal vagotomy.

B. Heineke-Mikulicz Pyloroplasty - Gastric Emptying

1. Heineke-Mikulicz pyloroplasty enhances the emptying of the citrate-fat liquid test meal.

2. Unlike the Finney pyloroplasty, the Heineke-Mikulicz pyloroplasty is not obstructive to liquids.

3. The normal anatomical relationship at the GDJ is important for normal emptying of liquids.

4. It is speculated that pyloroplasty alters the motor gradient seen in normal animals after administration of a citrate-fat test meal.

5. Enhanced emptying after Heineke-Mikulicz pyloroplasty could be a factor in the dumping syndrome observed clinically.

C. Heineke-Mikulicz Pyloroplasty - Motor Activity

1. Heineke-Mikulicz pyloroplasty can alter the motor coordination during a burst period in the interdigestive state. The phenomenon observed has been called "antralization of the duodenum."

2. This result confirms that pyloroplasties impair the duodenal inhibitory reflex observed during burst

periods in the interdigestive state.

3. Following pyloroplasty, antralization of the duodenum was also observed in the digestive state.
4. It is postulated that during antralization of the duodenum, the antral-duodenal segment contracts all at one time, increasing the resistance to intraluminal flow. This may affect the gastric emptying of solids.
5. Following pyloroplasty, a greater MI is present in the terminal antrum than in the orad antrum during the digestive state. This gradient may lead to more retropulsion and delayed emptying of solids.
6. In contrast, the tendency of the terminal antrum to have a greater MI after pyloroplasty may increase the antral-duodenal motor gradient and propel more citrate-fat into the small bowel.
7. When canned food was fed to control dogs and dogs with pyloroplasty a greater number of contractions was present in the duodenum (caudad to the cap) in the pyloroplasty group. This contractile activity may increase the resistance to intraluminal flow and slow the gastric emptying of the solid meal.
8. Pyloroplasty does not affect the antral-duodenal contractile response to bethanechol.
9. In all dogs, pentagastrin stimulated greater contractile activity in the terminal antrum than in the orad antrum.

10. It is hypothesized that the differential stimulation of antral motor activity by pentagastrin increases retropulsion and is responsible for the delayed emptying observed with this drug.
11. Metoclopramide stimulated antral and duodenal circular muscle contractile activity in the interdigestive state of all dogs. This response is variable and may depend on the state of the smooth muscle before the drug is administered.
12. Metoclopramide produces a steep antral-duodenal motor gradient in the digestive state of control dogs. It is speculated that this gradient is responsible for the enhanced gastric emptying observed with metoclopramide.
13. After pyloroplasty, metoclopramide does not produce a steep antral-duodenal motor gradient in the digestive state. It is speculated that following pyloroplasty metoclopramide does not enhance gastric emptying.

D. Heineke-Mikulicz Pyloroplasty - Electric Activity

1. Heineke-Mikulicz pyloroplasty alters the BER of the antrum. The abnormalities in the electric pattern are called arrhythmias and tachygastria.
2. Arrhythmias interrupt the propagation of the normal gastric BER.
3. According to the relaxation oscillator model, terminal antral oscillators become uncoupled from more

orad antral oscillators. Terminal antral oscillators can be phase-locked with an aboral phase-lag during arrhythmias. An oral phase-lag may also be present.

4. Feeding the dogs corrected abnormal electric activity.
5. Arrhythmias occurred within 10 minutes after instillation of the citrate-fat test meal - a time when more than 150 ml was present in the stomach.
6. Citrate-fat significantly slowed the antral BER frequency during the first 5 minutes after instillation and significantly increased the frequency 20 to 45 minutes after instillation.
7. It is proposed that citrate-fat slows the BER frequency by distending the antrum and later enhances the BER frequency through an hormonal influence.
8. It is hypothesized that arrhythmias can lead to weakened propulsive activity and delayed emptying if phase-lag is continuously in the oral direction.
9. Bethanechol corrected arrhythmias.
10. Abnormal electric activity was apparent in the antrum after atropine administration.
11. Arrhythmic antral electric patterns are postulated to be associated with a decrease in activity of the cholinergic nervous system, especially at the muscarinic receptor. Arrhythmias can be corrected with cholinergic agonists.

12. Metoclopramide corrected arrhythmias. This result supports the speculation of an association between arrhythmias and cholinergic activity since metoclopramide appears to act indirectly at the muscarinic receptor.
13. The electrical response to pentagastrin appears to be similar in control dogs and dogs with pyloroplasty.
14. Pentagastrin corrected arrhythmias.
15. Following pyloroplasty, duodenal oscillators appear to become dominant, affect terminal antral oscillators and uncouple the antral BER. This results in apparent antral pacemaker activity.
16. It is hypothesized that the GDJ is an electric insulator which is necessary for normal antral and duodenal electric activity. Pyloroplasty alters the GDJ and allows the abnormal myogenic spread of the BER in either direction.

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