THE EFFECT OF DISTENTION OF THE JEJUNUM UPON TONICITY OF THE CARDIA OF THE DOG

by

MERLE PENNINGTON

A Thesis

Presented to the Department of Physiology
and the Graduate Division of the University of Oregon Medical School
in partial fulfillment
of the requirements for the degree of
Master of Science

August 1944

APPROVED:

[redacted]

[redacted]

of the Medical School

Sept 5, 1944

THE EFFECT OF DISTENTION OF THE JEJUNUM
UPON THE TONICITY OF THE
CARDIA OF THE DOG

Introduction:

Much of our knowledge of the control of gastro-intestinal motility has been gained from studies of the effect of distention of one of its parts upon the state of activity of another. Thus dilatation of the stomach results in reflexly produced contraction of the colon, and dilatation of the anal sphincter results in inhibition of the small intestine. Likewise, distention of a segment of small intestine will inhibit another segment of small intestine and pressure within the duodenum will slow gastric emptying. The nervous pathways for these reflexes in many cases have been well demonstrated.

Vomiting is usually a prominent symptom in a patient having an intestinal obstruction. The intestinal obstruction is practically always accompanied by distention of loops of bowel and in mechanical obstruction the high pitched auscultatory sounds and the hyper-peristalsis could well indicate an increased pressure within the lumen of the intestine. Relaxation of the cardia has been considered an essential part of the act of vomiting. On the other hand however, not uncommonly one encounters in these patients, signs which suggest some element of cardiospasm, such as difficulty in swallowing and distention of the stomach with air and liquids.

In view of the fact that vomiting is so commonly a symptom of gastrointestinal disease, and in view of the opposing theories as to the presence and role of the cardia, it was thought advisable to undertake an experimental study of this region in an attempt to determine how it acts normally and its response, if any, to distention of the upper portion of the small bowel. It would seem that methods of study similar to those which have elucidated the problems referred to above as largely solved, might be applied to the question of the influence of intestinal distention on the activity of the cardiac sphincter. The present study is designed to demonstrate the influence of distention of an intestinal segment on the relaxation of the cardia which occurs normally following an esophageal peristaltic wave, and on the resting tonus of the sphincter. Remembering that the microscopic anatomy of the dog's esophagus differs somewhat from that in man, and that the vertebral axes are different, it is easily realized that the mechanisms described are not necessarily applicable to similar situations in the human. None the less, it was thought that the results obtained could be interpreted as lending some evidence that might be of value in understanding the role of the cardia in man.

Anatomy:

The lower end of the esophagus pierces the diaphragm and ends, after a very short abdominal segment, in the stomach. The muscular ring encircling the lower end of the esophagus is commonly known as the cardiac sphincter although the thickness of the muscle in this region is scarcely greater than that in the rest of the tube, especially in man. Histology of this region reveals, from without inwards, five layers: (1) the fibrous areolar or connective tissue coat separating the esophagus from neighboring structures, (2) the outer longitudinal muscular layer continuous above and below with a similar layer in esophagus and stomach respectively, (3) the inner circular muscular layer, likewise continuous above and below, (4) the submucous layer, and (5) the mucous membrane, showing abrupt transition from the stratified squamous of the esophagus to the columnar epithelium of the stomach. The two muscular layers are united by a thin septum of areolar connective tissue which contains a coarse-meshed nerve plexus composed mainly of unmyelinated fibers at whose intersections are numerous small sympathetic ganglia, the myenteric (Auerbach's) plexus and ganglia. The submucous layer contains a similar system of nerves, the submucous (Meissner's) plexus and ganglia.

Sphincter:

The existence of a true anatomical sphincter has been questioned by many workers since Mathew Baillie in 1807 first described one, though such a sphincter is easily demonstrated in many of the lower animals. Keith (1) pointed out in 1910 in specially prepared specimens that a true esophageal sphincter does exist in the wall of the esophagus at or about the level of the diaphragm, but entirely independent of it, and not at the anatomical cardia. Chevalier Jackson (2) in 1922 concluded, as had many before him as early as the first of the century, that there is no true sphincter but that the normal closure of the esophagus at this level is maintained by the tonicity of the fibers of the diaphragm which encircle the esophagus. This now seems improbable because by x-ray, the sphincter is generally situated one to two centimeters below the level of the diaphragm. Mosher and MacGregor,(3) in 1928, attributed most of the sphincteric action to the kinking and twisting of the esophagus as it enters the stomach. Feldman and Morrison (4), in 1934, after paralysis of both sides of the diaphragm observed the course of the esophagus and could demonstrate no kinks or twists under the fluoroscope and in other experimental studies. They agree with Keith that there is a true cardiac sphincter. Thus perhaps from an anatomic as well as from a physiologic standpoint we should speak of a "region of the cardia", implying some sort of sphincteric action, rather than of the "cardiac sphincter".

Nervous Control:

The nervous supply of the lower esophagus and cardia, like the rest of the intestinal tract, may be divided into two sets. The vagal plexus closely invests the lower two-thirds of the esophagus and numerous twigs of this plexus can be seen to enter its walls. Slender sympathetic filaments from the inferior cervical and thoracic sympathetic ganglia travel along with the intercostal vessels, but they are too small and delicate to trace for any distance. Thus there is probably a very scanty sympathetic supply directly from the adjacent ganglia. Sympathetic fibers, however, do enter and travel with the vagi from the cervical sympathetics. Sympathetics also enter this region by way of the coeliac plexus from which they may travel in company with the left gastric artery and along the cardio-esophageal branches.

Role of the Vagi:

The nervous control of the cardia is subject to debate. In 1889, Openchowski (5) (6) described the vagus as the "dilator nerve of the cardia" and showed that contraction or relaxation could be obtained on stimulation of this nerve. He suggested that the response was associated with the frequency and strength of the stimulus. Courtade and Guyon (7) obtained on all occasions a motor effect on the longitudinal fibers of the cardia and variable effects on the circular fibres as the result of vagal stimulation. Langley (8), working with curarised rabbits in which the esophagus was filled with water, found that an injection of atropine preceding vagal stimulation was necessary before a dilating response could be elicited. He then frequently noted relaxation of the lower part of the esophagus, cardia, and entire fundic end of the stomach, especially if the original tonus was high. When no atropine was administered, the vagal stimulation sometimes caused an increased tonus of this region. He therefore concluded that the vagus nerve carried both motor and inhibitory fibers to the cardia. May (9), working with cats, dogs, rabbits, and monkeys, obtained a relaxation of the cardia followed by a slow increase in tonus on some occasions, but on others, a purely motor response resulted. Klee (10) (11), in x-ray studies on dogs and decapitate cats, found that the cardia remained closed after vagal section, and furthermore, central vagal stimulation could produce typical vomiting. The efferents of this reflex were thought to be carried in the splanchnics. Koennecke (12) obtained closure of the cardia on vagal stimulation as observed by x-ray studies on chronic experiments, while Meltzer and Auer (13) reported a dilatation followed by a contraction. Carlson, Boyd and Pearcy (14) in a well controlled study found that the vagus exerts both motor and inhibitor control over the cardia. They suggested that the type of response is dependent upon the original tonus. Caballero (15), on the basis of studies employing the esophagoscope, states that the so-called 'cardiac sphincter' is merely a valve against regurgitation, does not present the characteristics of a sphincter, and that it is uninfluenced by nerve stimulation.

Role of the Sympathetics:

The sympathetics in this region have not been adequately studied. The concept put forward by Gaskell, that the splanchnic nerves are purely inhibitory has been allowed to pass almost unchallenged. Langley reported that epinephrine inhibited the cardiac sphincter in the rabbit and he therefore concluded that the sympathetic influence would be one of inhibition. Carlson, Boyd and Pearcy, (14) on the other hand, observed that splanchnic stimulation caused both motor and inhibitor effects on the cardia of the cat, motor effects in the dog, and inhibitor effects in the rabbit. May (9), in opposition to all previous observers, failed to find, on stimulation of the splanchnics, any direct influence on the stomach. He reproduced in an excised stomach, the complete picture of movements observed by Cannon (16) in normal animals and thus concluded that the local nervous mechanisms were sufficient for all coordinated movements.

Reflex vomiting:

The relationship of motility and distention of the small bowel upon the mechanics of the stomach has long been of interest. It is generally stated that distention of the small bowel will result in vomiting, the classical example cited being intestinal obstruction. Although vomiting may be initiated in many ways, certain reflexogenic zones are much more potent in this regard than are others. Parenteral foci for initiating vomiting are many and will not be discussed here. The vomiting reflex may be initiated with varying degrees of ease by localized distention throughout the enteric canal from the sensitive pharynx to the relatively insensitive anal canal. It is apparently true that reflexes from the bowel are more effective in producing emesis than are reflexes from the stomach as suggested by animal experimentation and by the fact that vomiting is often absent in cases of gastric ulcer and carcinoma (without obstruction), while it is often profuse with perforating duodenal ulcer, acute appendicitis, and intestinal obstruction. Goldberg (17) found in dogs, that distention of a pouch of the pars pylorica would produce vomiting while distention of the fundus was without effect. Burget, Moore and Lloyd (18) closed off segments of colon in dogs and found that distention of the segment sometimes caused vomiting.

Vomiting is a complex mechanism requiring close integration of a number of systems of the body. Regurgitation, on the other hand, is a simple process seen in many of the lower animals. It can be demonstrated in the frog with its abdomen open, and there, is apparently brought about entirely by reverse peristalsis in the stomach. Regurgitation occurs in the infants more often than vomiting, and regurgitation or "rumination" in older children and adults is a well known entity. Probably, as Alvarez states, "there are gradations between this type of regurgitation and true vomiting, with varying degrees of assistance on the part of the voluntary muscles." On the other hand, the importance of skeletal muscles in the process is well known. The classic experiment of Magendie in which a pig's bladder was substituted for a stomach unfortunately created more confusion than clarification, inasmuch as the cardia was left intact. But at least it demonstrated that the role of the abdominal muscles must be dealt with in any explanation of vomiting. Eggleston and Hatcher (19) removed the digestive tract from dogs from the cardia to anus, and demonstrated typical retching, with some regurgitation from the esophagus following the administration of various emetics. Cannon (20) described what he saw under the fluoroscope after giving apomorphine to cats and his findings have been largely verified and accepted. "The first change is total inhibition of the cardiac end of the stomach, which becomes a perfectly flaccid bag. This is followed, when apomorphine has been given, by several deep contractions that sweep from the mid-region of the organ towards the pylorus, each of which stops as a deep ring at the beginning of the vestibule, while a slighter wave continues. Finally, in all cases, a strong contraction at the anuglar incisure completely divides the gastric cavity into two parts. Although waves continue running over the vestibule, the body of the stomach and cardiac sac are fully relaxed. Now a simultaneous jerk of the diaphragm and the muscles of the abdominal wall shoots the contents out through the relaxed cardia. As these jerks are repeated, the gastric wall seems to tighten around the remnant of contents. Once during emesis I saw an antiperistaltic constriction start at the pylorus and run back over the vestibule, completely obliterating the cavity, but stopping at the angular incisure. In the process of ridding the gastric mucosa of irritants, therefore, the stomach plays a relatively passive role."

Openchowski (5) (6), in 1889, found that vomiting could be produced in the dog by electrical stimulation or pinching of the uterus, the wall of the urinary bladder, the wall of the intestine, or by direct simulation of the splanchnic nerves. He considered the vagus to contain the efferent limb of the reflex as far as dilation of the cardia was concerned. Carlson, Boyd and Pearcy (14), in 1922, obtained only a motor effect upon the cardia as a result of splanchnic stimulation in the dog, and variable effect in the cat. But at any rate it has been accepted for years that stimulation of numerous bodily organs including the intestine does produce vomiting. Relaxation of the cardia has been assumed as one of the essential parts of the vomiting act.

This paper represents an attempt to demonstrate the effect of intestinal distention on the tonus of the cardiac sphincter and on the relaxation of this sphincter which normally occurs during the act of swallowing.

Procedure:

In this series of experiments dogs were used exclusively. Records were obtained from four dogs over a period of three months. To eliminate the interference with reflexes under study due to anesthetics, a modification and extension of the method outlined by Burget and Zeller (21) for recording motility in the unanesthetised dog was used. Under intravenous nembutal anesthesia, the abdomen was opened by a high left rectus incision. The upper jejunum was identified and a seven to ten centimeter segment having a suitable blood supply was clamped and resected. The continuity of the gut was restored by the closed end-to-end anastomosis described by Martzloff and Burget (22). The proximal end of the resected segment was closed by inversion and then purse stringed. The distal end was brought to the surface through the original incision and sutured to the peritoneum, muscle and skin in separate layers as the rest of the incision was being closed in three layers; or the distal end was brought out through a stab wound and sutured to peritoneum, deep fascia, and skin and the abdomen closed as above.

About one week after the first operation, the dogs were subjected to esophagostomy in order to facilitate the passage of tubes down the esophagus without evoking a gag reflex. Under intravenous nembutal anesthetic, a midline incision was made about two to three centimeters below the cricoid cartilage. The ribbon muscles were separated in the midline and the esophagus brought around the trachea and to the exterior. The outer layer of the esophagus was sutured to the fascia covering the muscles in the form of an elipse about four centimeters long in the axis of the esophagus by six or seven millimeters across in its widest part. The outer layer of the esophagus was opened the full length of the elipse and the subcutaneous tissues sutured to the esophageal musculature just within the original line of sutures. The lumen of the esophagus was entered and the mucosa sutured to the skin. No animals died of mediastinal infection. No special post-operative care was given, the animals suffer little inconvenience from the fistula, and they are able to swallow liquids and solids with suprisingly little loss of food.

About a week after the esophagostomy was performed, the training of the dogs was begun. They were trained to lie quietly on a table with the balloons in position while motility records were being made. Three balloons were in place and tracings made on a smoked drum simultaneoulsy. The upper balloon was a two centimeter segment of condom tied over a rather rigid 14 Fr. catheter and inserted about four or five centimeters into the esophageal fistula and tied in place. It was attached to a mercury manometer. The balloon for recording cardiac activity consisted of a three centimeter segment of condom enclosing soft sponge rubber on the end of a 16 Fr. catheter. The soft sponge rubber served the purpose of keeping the balloon open and sensitive to decreases as well as increases in pressure, and helped to keep the cardiac balloon in proper position. The sponge rubber was fashioned with sharp scissors, was three centimeters long, one centimeter in diameter, and tapered slightly at both ends. The catheter occupied completely the long axis of the balloon. After insertion it was tied in place at the esophageal fistula and was attached to a sensitive Becker tambour. This caused no discomfort to the dog and did not initiate secondary esophageal peristalsis after the first two or three insertions in the training period. A four centimeter condom balloon was placed over soft rubber tubing, tied in place and attached to a mercury manometer for recording motility in the loop of jejunum brought to the surface in the first operation. In addition, time was recorded in ten second intervals by an electric timing clock and a signal magnet.

In making a recording, the cardiac balloon was first passed through the esophageal fistula and down the esophagus until it met the moderate resistance of the cardia. About one centimeter more of catheter was allowed to enter the fistula and then the catheter was marked at its point of emergence and tied in place. About three cubic centimeters of air were introduced through a Y connection into the tubing connecting the cardiac balloon with the Becker Tambour. Next the upper esophageal balloon was introduced and tied in position four or five centimeters below the fistula and water admitted to the recording system through a Y connection until the mercury manometer was at zero pressure. This same Y connection was used later for introducing ten cubic centimeters of water into the balloon to initiate a peristaltic wave down the esophagus. The third balloon was placed in the jejunal loop and three to five cubic centimeters of water introduced depending upon the strength of motility of the loop. A Y-connection in this system allowed for increasing the intraluminal pressure in the jejunum to determine the effect of this on the cardia.

The passage of the cardiac balloon is accompanied by one to three peristaltic waves in the esophagus. Between these, the catheter may be pushed down or pulled up the esophagus with ease. The increased tone at the cardia can be readily felt although the peristaltic waves mentioned above tend to force the balloon through the cardia into the stomach. If the balloon is allowed to enter the stomach and is then withdrawn there is felt the rather marked resistance of the cardia to penetration from below. This is suddenly released as the balloon slips into the esophagus. The position of the cardiac balloon may be checked also by noting the record of tonus and motility. If the balloon is in the stomach, no motility and low tonus are present, or wide swings at 30 to 60 second intervals and far greater than any other recorded from this region are seen. If, on the other hand, the balloon is even slightly too high, typical lower esophageal activity is seen. This consists of very strong, rapidly repeated peristaltic waves, from three to fifteen or more in number depending upon the dog, its stage in training, gastric motility and other unknown factors. After this the activity subsides and only respiratory movements are recorded. Thirdly it was assumed that the correct position for the cardiac balloon had been reached when a typical tonus change was obtained after stimulating the upper esophagus by means of distending the upper balloon. It was noted in these experiments, as did also Carlson, Boyd and Pearcy (14), that the tonus of the cardia roughly parallels that of the empty stomach of the dog. In fact it was soon found that tonus changes in the cardia were so great in some dogs at times when hunger contractions were prominent that recordings could not be taken and a time had to be chosen when the gastric motility was lessened.

Discussion of Results:

With the preparations and apparatus as described previously, it is readily apparent that the tone in the cardiac sphincter is greater than in either the stomach or esophagus. As mentioned before, the tonus of this sphincter roughly parallels that of the stomach as pointed out by Carlson, Boyd and Pearcy (14) and as verified by Zeller (23) in 1936. Cannon and Lieb (24) in 1911 using an esophageal fistula preparation showed a similar corelation with respect to the receptive relaxation of the fundic end of the stomach upon the introduction of liquids into the stomach. Furthermore the tonus of the cardia and the relaxation seen as a part of the act of deglutition is entirely independent of the activity of the diaphragm. Minute respiratory excursions can be seen on most tracings taken at the cardia (Fig. 1) but their order of magnitude and time interval are so much less than the tonus changes dealt with in this work that it is unlikely that the diaphragm has much to do with the active sphincteric action of this structure, despite the claims of such workers as Jackson (2), Caballero (15), and Fulde (25). When the dog swallowed spontaneously or when ten cubic centimeters of water were injected fairly rapidly into the upper esophageal balloon and then withdrawn (Fig. 1) the cardia relaxed in from one to four seconds while the peristaltic wave was still high in the esophagus. The maximum relaxation was reached in five to ten seconds or at about the time that the peristaltic wave had reached the cardia. Following relaxation, there was a rise in tonus which soon fell to normal and probably represents the contracting ring of the wave passing through the sphincter.

Intestinal motility varies from dog to dog and from time to time in the same dog. It was found to be constant and of large amplitude without superimposed periodic increases in pressure in only one dog. The others exhibited the more typical variations in amplitude, but at no time was there observed a relaxation of the cardia in response to these spontaneous increases in pressure. On two or three occasions, there was noted relaxation of the cardia similar to that produced by intestinal distention without any apparent reason. It is probable that there are other foci from which reflex cardiac relaxation can be elicited.

After recording several typical responses of the cardia to stimulation of the esophagus by distention of the upper balloon, the intestinal balloon was distended sharply with from four to seven cubic centimeters of water. The amount of water used depended upon the response of the dog, an attempt being made to avoid producing evidence of pain. The pressure was maintained for from one to three seconds and then withdrawn. Variations of this procedure were tried in which pressure was maintained for ten seconds and again in which pressure was alternately raised and lowered in quick succession four or five times. Niether of these latter two variations seemed to alter the result obtained by the first method. The amount of water necessary to elicit the reflex varied from dog to dog and from time to time in the same animal. The only determinable factor influencing this amount was the original pressure within the balloon. When this pressure was high, the amount of injected water necessary to elicit cardiac relaxation was materially reduced. (Fig. 3) Thus the original tonus of the segment of intestine probably determines to a great extent the sensitivity of this reflex. It usually was found that relaxation of the cardia would not occur with the first two to seven distentions of the intestinal balloon in any experiment, but subsequent distentions with the same volume of water would produce first only slight, or questionable decrease in tonus, and then unmistakable relaxations of the cardiac sphincter. (Fig. 2) Once the correct amount of distention had been determined and the loop had been "sensitised" by preliminary distentions, the reflex relaxation of the cardia could be elicited nearly every time.

The decrease in tonus of the cardia as a result of intestinal distention was nearly always at least half as great as that obtained as a part of the act of deglutition and often approached the amplitude of the latter. The relaxation occurred in from two to five seconds, was maximal in three to seven seconds more and the tonus was back to normal in fifteen to thirty seconds on most occasions although exceptions to this will be pointed out later. Most of these relaxations failed to show the marked rise above the normal tonus level seen in the complexes resulting from a spontaneous swallow or esophageal distention. (Fig. 3) This is further evidence that the increased tonus in the latter is due to the passage of the peristaltic wave through the cardiac sphincter.

a condition which presumably would not occur in the absence of a contraction wave passing down the esophagus.

No evidence of discomfort or nausea was noted in the dogs at any time as a result of simple distention of the intestinal balloon with small amounts of water and at low pressures. When the pressure had been increased by retaining four or five cubic centimeters of water in the balloon, subsequent distentions resulted in a stretching movement of the animal which distorted the record due to a sharp upward deflection of the lever from the cardiac balloon. With further increases of pressure up to 80 or 90 millimeters of mercury the dogs showed evidences of nausea and would eventually vomit if this pressure was maintained. Interesting in this respect was the production of prolonged relaxation of the cardia (Fig. 4) of about 60 seconds duration preceding and accompanying signs of nausea in an animal in which the intestinal balloon was distended to the extent of 60 millimeters of mercury and again to 80 millimeters of mercury.

Next the question arose as to whether there was any evidence of spasm of the cardia as a result of intestinal distention. The pressure in the intestinal balloon was increased in steps of ten to thirty millimeters of mercury by the introduction of three to five cubic centimeters of water at a time. Between each increase in pressure the upper esophageal balloon was inflated two or more times, initiating a swallow reflex. In nearly all cases (Fig.5) the cardia responded with a typical relaxation-contraction pattern upon inflation of the esophageal balloon even with pressures within the intestine as high as 80 to 90 millimeters of mercury. In only one record was there any suggestion of spasm. In this, the intestinal distention had been increased to 30 to 40 millimeters of mercury without any signs of nausea. Then a spontaneous swallow and three distentions of the esophageal balloon in succession had either questionable or no effect on the tonus of the cardia. The pressure in the intestinal balloon was then brought to zero at which time esophageal distention produced its typical tonus change at the cardia. These procedures were repeated on the same animal subsequently with no evidence of cardiospasm. The atypical results could have been due to the slipping of the cardiac balloon partially into the stomach although no evidence of this was noted at the time. Thus, cardiospasm in the dog probably occurs rarely or not at all as a result of intestinal distention.

That intestinal obstruction is capable of provoking vomiting is common knowledge. Likewise cardiac relaxation has been assumed to accompany the vomiting act. These experiments indicate that cardiac relaxation may occur in the dog with mild intestinal distention without accompanying signs of nausea or other distress. The time period between intestinal distention and cardiac relaxation necessitates the assumption that this is a reflex carried over nervous pathways. No attempt has been made to elucidate these pathways. The surgical procedure of disrupting the continuity of the gut eliminates the possibility of this being a local reflex. Further experimentation should reveal the pathways involved.

Whether this reflex could be elicited with greater ease and less pressure if a longer segment of intestine were distended is another interesting question. Work being done by Peterson (26) on the intestino-intestinal reflex suggests that stimuli arising from several points along the intestine may have an additive effect.

There is no evidence from these experiments that cardiospasm can be produced by intestinal distention. It is, however, possible that conditions more nearly resembling clinical intestinal obstruction could be shown to produce spasm of that sphincter.

Summary and Conclusions:

Experiments were undertaken to study the effect of distention of a segment of intestine upon the tonus of the cardiac sphincter and upon the relaxation reflex occurring in that sphincter resulting from oesophageal distention. It was found that distention of an intestinal segment does produce a drop in tonus of the cardiac sphincter without accompanying signs of nausea or other distress. It was also found that distention of an intestinal segment does not obliterate the relaxation of the cardia which accompanies oesophageal distention or as occurs as part of the act of swallowing.

BIBLIOGRAPHY

(1) Keith, A., "Constrictions and Occlusions of the Alimentary Tract of Congenital or Obscure Origin." Brit. Med. Journ., I;301, (1910)

(2) Jackson, C., "The Diaphragmatic Pinchcock in So-called 'Cardiospasm'". Laryngoscope, XXXII;139, (1922)

(3) Mosher, H. P. and MacGregor, G. W., "A Study of the Lower End of the Esophagus." Tran. Am. Laryng., Rhin., and Otol. Soc., XXXIV;294, (1928)

(4) Feldman, M. and Morrison, S., "An Experimental Study of the Lower End of the Esophagus." Amer. J. Dig. Dis. and Nutr., I;471, (1934)

(5) Openchowski, T. "Über die nervösen Vorrichtungen des Magens." Zentr. f. Physiol., III;1-10, (1889)

(6) Openchowski, T. "Über die gesammte Innervation des Magens." Deutsche med. Wchnschr., XV;717, (1889)

(7) Courtade, D. and Guyon, J. F., Journ. de physiol. et path. gen., I;38, (1899) Quoted from McSwiney, B. A., "Innervation of the Stomach." Physiol. Rev., XI;478, (1931)

(8) Langley, J. N., "On Inhibitory Fibers in the Vagus for the Ends of the Esophagus and Stomach." J. Physiol., XXIII;407, (1898)

(9) May, W. P., "The Innervation of the Sphincters and Musculature of the Stomach." J. Physiol., XXXI;260, (1904)

(10) Klee, P. "Der Einfluss der Vagusreizung auf den Ablauf der Verdauungsbewegungen." Pfluger's Arch. fur Physiol., CXLV;557, (1912)

(11) Klee, P. "Zur pathologischen Physiologie des Mageninnervation." Deutsche Arch. Klin. Med., CXXVIII;204, (1919) Quoted from Physiol. Abstracts.

(12) Koennecke, W., "Experimentelle Innervationsstörungen am Magen und Darm." Zeitschr. f. d. ges. Exper. med., XXVIII;384, (1922)

(13) Meltzer, S. J. and Auer, J., "Vagus Reflexes upon the Esophagus and Cardia." Brit. Med. Journ., II;1806, (1906)

(14) Carlson, A. J., Boyd, T. E. and Pearcy, J. F., "The Innervation of the Cardia and Lower Esophagus in Mammals." Am. J. Physiol., LXI;14-41, (1922)

(15) Caballero, R. V., "Étude expérimentale de la Fermeture de l'extrémité inférieure de l'oesophage." Compte rend. soc. biol., LXXXVIII;12, (1923)

(16) Cannon, W. B. "The Movements of the Stomach Studied by Means of the Rontgen Rays." Amer. J. Physiol., I;359, (1898)

(17) Goldberg, S. L., "The Afferent Paths of Nerves Involved in the Vomiting Reflex Induced by Distention of an Isolated Pyloric Pouch." Am. J. Physiol., XCIX;156, (1931)

(18) Burget, G. E., Moore, P. H. and Lloyd, R. W., "Absorption of Glucose by Chronic Loops of Colon." Am. J. Physiol., CV;187, (1933)

(19) Eggleston, C. and Hatcher, R. A., "The Seat of the Emetic Action of Various Drugs." J. Pharm. and Exper. Therap., VII;225, (1915)

(20) Cannon, W. B., "The Mechanical Factors of Digestion." New York, E. Arnold, pg. 57, (1911)

(21) Burget, G. E. and Zeller, W. E., "A Study of the Cardia in Unanaesthetized Dogs." Proc. Soc. Exper. Biol. and Med., XXXIV;433, (1936)

(22) Martzloff, K. H. and Burget, G. E., "The Closed Intestinal Loop." Arch. of Surg., XXIII;26, (1931)

(23) Zeller, W. E., "Studies on the Cardia." A Thesis for M. S. Degree, U. of O. Medical School (1936)

(24) Cannon, W. B. and Lieb, C. W., "The Receptive Relaxation of the Stomach." Am. J. Physiol., XXIX;267, (1911)

(25) Fulde, E., "Experimentelle Störungen der Kardiafunktion." Arch. f. Klin. Chir., CLXXX;540, (1934)

(26) Peterson, C. G., Work in progress on the intestino-intestinal reflex. Personal communication.

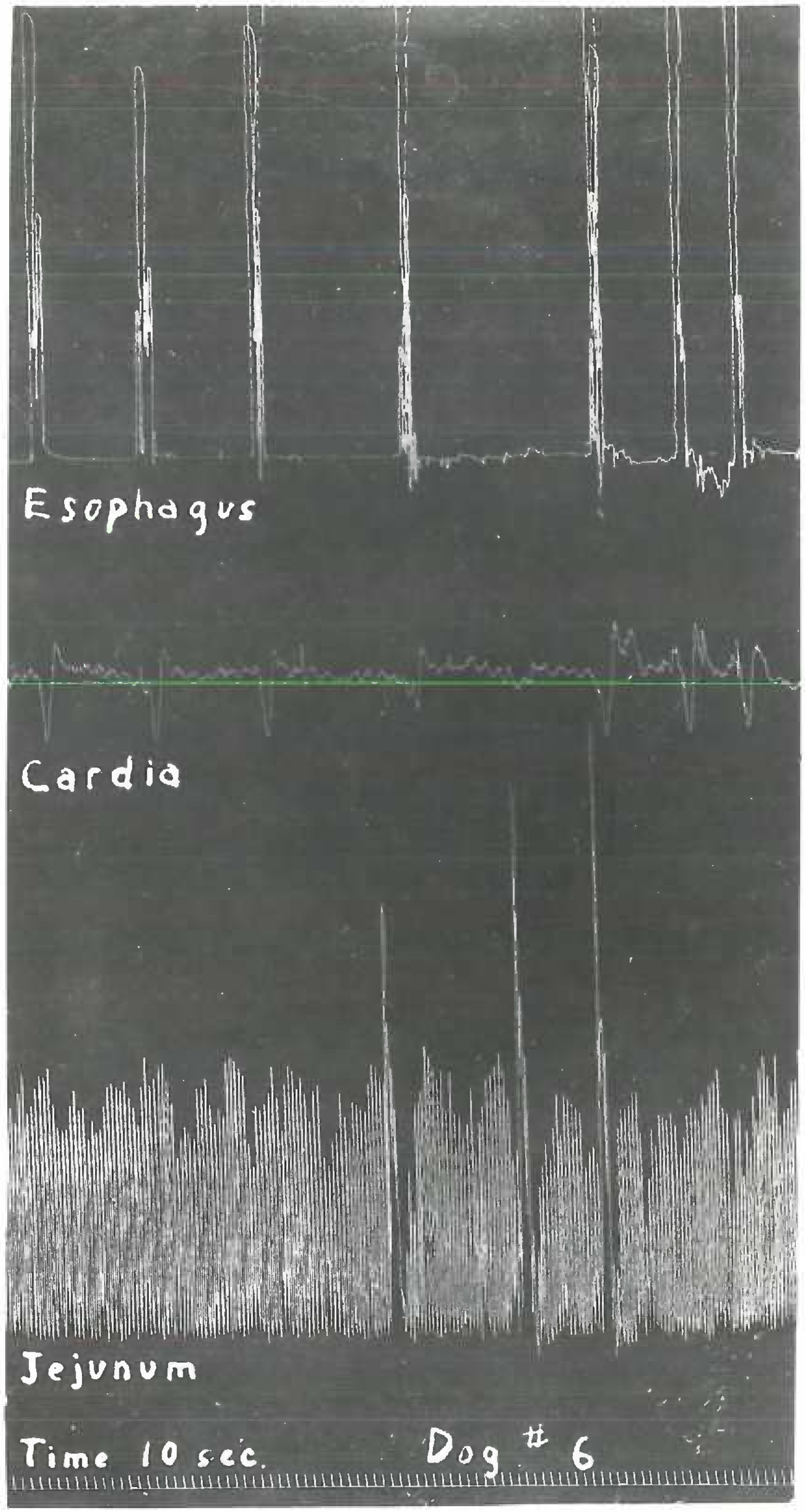

Fig. 1. Respiratory movements at the cardia. Typical relaxation-contraction pattern of the cardia in response to distention of the esophageal balloon.

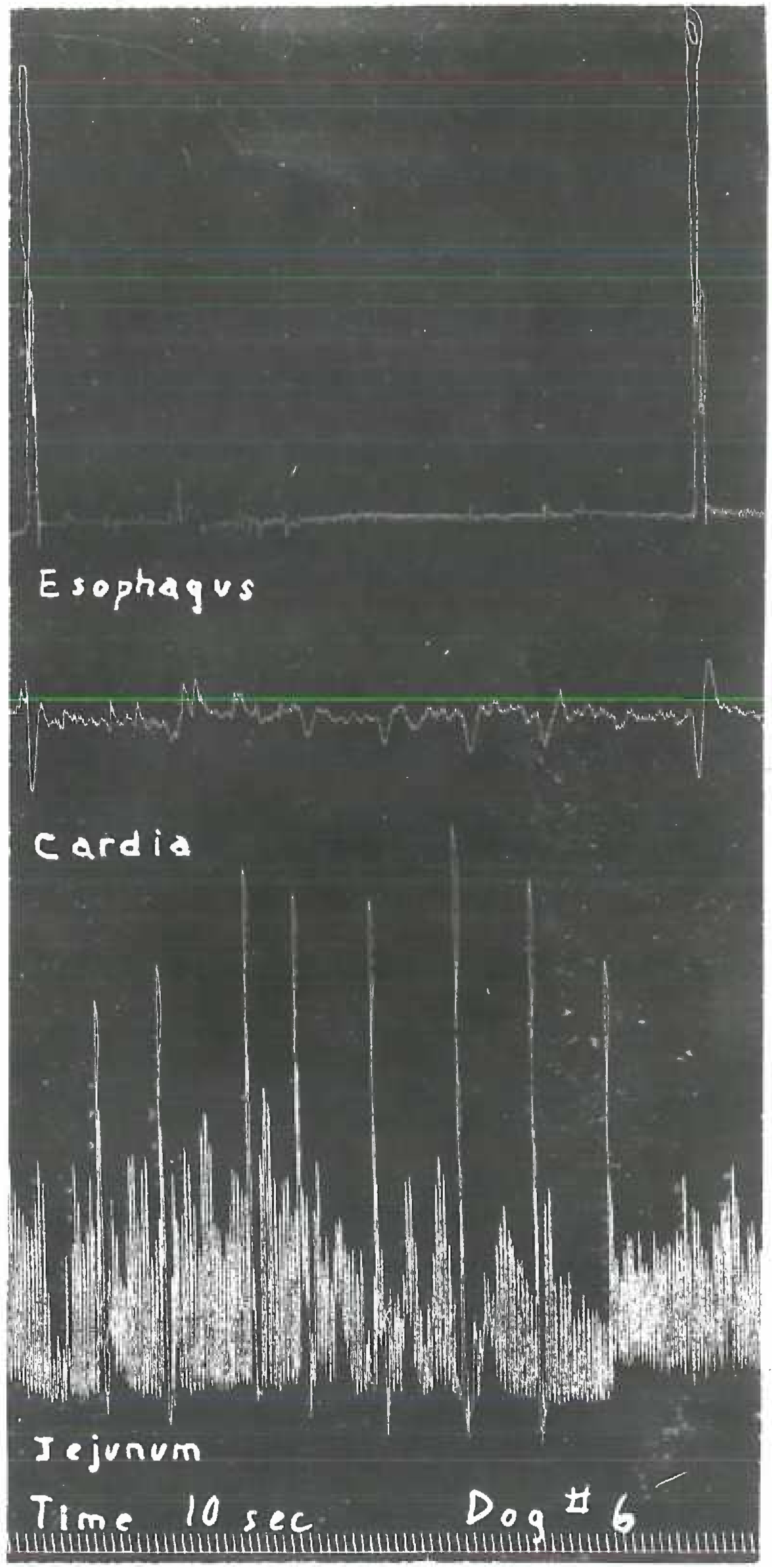

Fig. 2. Intestinal balloon distended with 6 cc. of water each time showing gradual "sensitization" of the reflex.

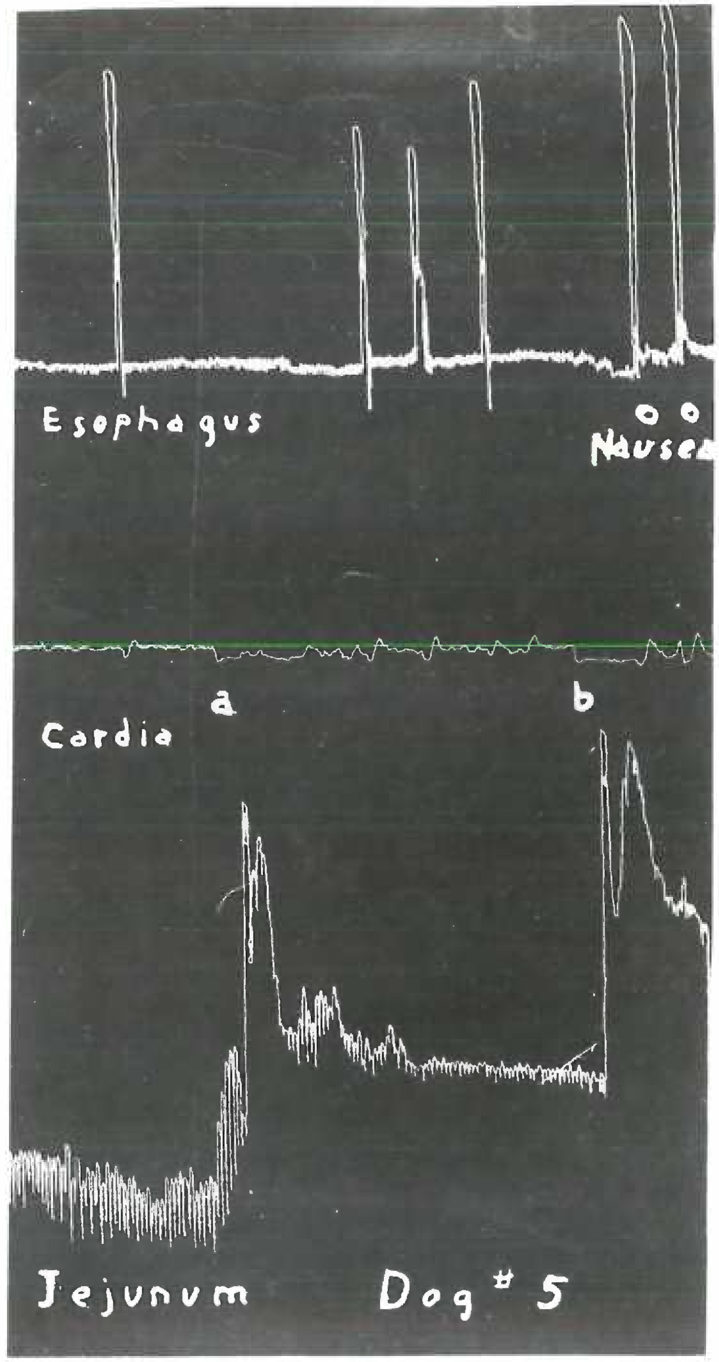

Fig. 4. Prolonged relaxation of the cardia at 'a' with intestinal pressure at 60 mm. of Hg. and at 'b' with intestinal pressure at 80 mm. of Hg. Signs of nausea occurred shortly after cardiac relaxation at 'b'.

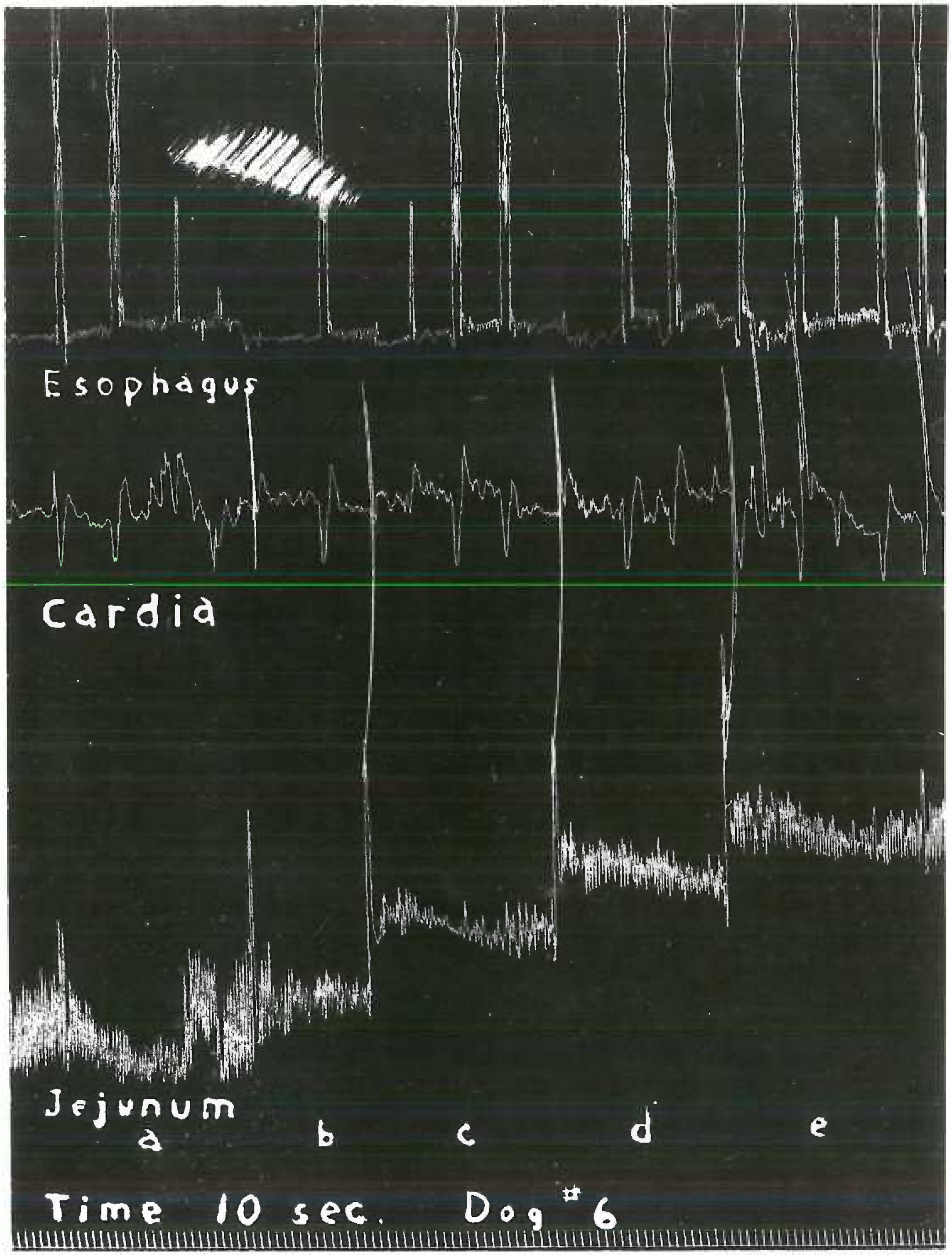

Fig. 5. Typical cardiac relaxation-contraction pattern in response to esophageal distention despite gradually increased pressure within the intestinal segment. Pressure at a=30 to 50 mm. of Hg.; at b=40 to 50 mm. of Hg.; at c=60 to 70 mm. of Hg.; at d=70 to 80 mm. of Hg.; and at e=80 to 90 mm. of Hg. (Wide swings on cardiac record are due to stretching movement of dog.)