STUDIES ON THE CARDIA

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Introduction:

The oesophagus is a narrow muscular tube extending from the crico-pharyngeus muscle to the cardiac portion of the stomach. Histologically, it consists of five layers. From without inwards, there are: (1) the fibrous areolar or connective tissue coat separating the oesophagus from neighboring structures, allowing it to distend, but not having the character of a well-marked fascial plane; (2) the outer longitudinal muscular layer; (3) the inner circular muscular layer; (4) the submucous layer and (5) the mucous membrane. It should be noted that the muscle coats in the upper third of the oesophagus in man and the cat contain considerable striated muscle continuous with the pharyngeal muscles while the remainder of the organ consists of plain muscle only. In the dog, striated muscle is found throughout the whole length of the gullet, resulting not so much in a difference in function as in a difference in time relations for the wave to traverse this portion of the tract. The mucous membrane is lined with stratified squamous epithelium into which papillae from the corium project. There is a sharp transition from this type of epithelium to the columnar epithelium in the stomach at the oesophageo-gastric junction.

Physiologically there are three main points of narrowing: (1) at the cricoid cartilage, (2) at the level of the left bronchus, and (3) at the level of the diaphragm where the cardiac sphincter is located.

The sphincter formed by the crico-pharyngeus muscle which closes the upper end of the oesophagus at rest, relaxes and permits the food to enter the oesophagus as a result of the act of swallowing. The bolus is then carried rapidly down the oesophagus by a peristaltic wave, through the slight narrowing at the level of the left bronchus and down to the cardia where there is a momentary pause. The cardia then undergoes an active relaxation on the arrival of the peristaltic wave at the lower end of the oesophagus in accordance with the Bayliss and Starling law of peristalsis, according to which a wave of relaxation precedes the wave of contraction. As soon as the food enters the stomach, the sphincter once more closes. It is with the activity of the cardiac sphincter that this paper is primarily concerned.

Anatomical Sphincter.

The existence of a true anatomical sphincter has been disputed since one was described by Mathew Baillie in 1807. Chevalier Jackson[1] concludes that there is no sphincter but that the normal closure of the oesophagus at this level is maintained by the tonicity of the fibers of the diaphragm which encircle the oesophagus. Mosher and MacGregor[2] attribute most of the sphincteric action to the kinking and twisting of the oesophagus as it enters the stomach. Keith[3], however, pointed out in 1910 in specially prepared specimens that a true oesophageal sphincter does exist in the wall of the oesophagus at or about the level of the diaphragm but entirely independent of it, and not at the anatomical cardia. Feldman and Morrison[4] in 1934 after paralysis of both sides of the diaphragm observed the course of the oesophagus and could demonstrate no kinks or twists under the fluoroscope and in other experimental studies. They too agree with Keith that there is a true cardiac sphincter.

Nerve Supply.

The oesophagus, like the rest of the intestinal tract, is supplied with two sets of nerves. The vagal plexus closely invests the lower two-thirds of the oesophagus and numerous twigs of this plexus can be seen to enter its walls. Slender sympathetic filaments from the inferior cervical and thoracic sympathetic ganglion travel along with the intercostal vessels, but they are too small and delicate to trace beyond the front of the vertebral column and the aorta. It is unlikely that the oesophagus receives other than a very scanty sympathetic supply directly from the adjacent ganglia. Sympathetic fibers, however, do reach the oesophagus from above having entered the vagi from the cervical sympathetic chain. The other route by which sympathetic fibers may reach the region of the cardia is by way of the coeliac plexus from which they may travel in company with the left gastric artery and along the cardio-oesophageal branch.

The act of swallowing is performed mainly under the influence of the parasympathetic portion of the visceral nervous system. The physiological processes which take place on sympathetic stimulation are a diminished flow of saliva, an inhibition of peristalsis, and a spasmodic contraction of the upper and lower sphincters of the oesophagus. The effects of deglutition on stimulation of the parasympathetic system are an increased flow of saliva, peristalsis of the oesophagus, and relaxation of the sphincters. This relaxation is brought about first by the direct action of the longitudinal fibers, and secondly by a diminution in the tone of the sphincteric fibers—an inhibitory reflex initiated by the act of swallowing.

It follows, therefore, that any disturbance of this reflex relaxation mechanism would result in an obstruction to the passage of food from the oesophagus to the stomach; this in turn would bring about hypertrophy and dilatation of that part of the oesophagus lying above the obstruction. Before the middle of the 19th century, when this condition of the oesophagus was seen at autopsy, it was given the name of "idiopathic dilatation of the oesophagus" or "primary and essential dilatation". In 1882, Mikulicz [5] suggested that the condition might be due to a spasm of the cardia, which spasm naturally was associated with hypertrophy and hypertonicity of the sphincter with blockage to the flow of material through it. The oesophagus then dilates as a result of its failure to overcome the increased resistance. His term, "cardiospasm", then replaced the earlier designations of "idiopathic or essential dilatation" until the first quarter of the twentieth century. In 1913, Hurst [6] found hypertrophy and dilatation in the oesophagus above but no hypertrophy or hypertonicity in the sphincter itself since he was able to pass a balloon filled with mercury easily through the cardia in one of these patients without being able to detect with the hand which held the bougie when it passed from the oesophagus into the stomach. Histologically, he found well marked inflammatory and degenerative changes in the neighborhood of the sphincter involving the whole of the nerve plexus. On the basis of these findings his theory was diametrically opposed to that of Mikulicz in that failure to relax normally, and not spasm, was believed to be the cause of the condition. An obstruction to the normal flow would follow in either condition. Sir Cooper Perry coined the word, "achalasia" from the Greek since it seemed that the word, "cardiospasm" and the erroneous idea it conveyed would never be discarded unless some less cumbersome expression than "absence of relaxation" was devised. Chevalier Jackson[1] considers the normal close of the oesophagus at this level to be effected by the tonicity of the fibers of the diaphragm which encircle the oesophagus, and refers to an obstruction at the cardia as "hiatal oesophagismus".

Another explanation for the obstruction at the lower end of the oesophagus is advocated by Mosher[7]. In a clinical review of disturbances of the oesophagus and cardia, he feels that spasm plays but a minor role in "cardiospasm". The essential thing is fibrosis of the terminal portion of the oesophagus in the region of the crural canal, secondary to infectious ulcers or erosion which may have produced temporary cardiospasm. His explanation is strengthened by the number of "so-called cures" following only one or two mechanical dilatations of the cardia.

In view of the fact that an obstruction at the cardia is not uncommonly seen clinically, whatever the cause might be, and in view of the opposing theories, it was thought advisable to undertake an experimental study of this part of the oesophagus in an effort to throw light on how it acts normally and how it acts following sectioning of various extrinsic nerves supplying the area. Dogs were used exclusively, other animals being too small for the type of experiment used; and although the microscopic anatomic relationships are not exactly the same, it was thought that the results obtained could be interpreted as lending some evidence that might be of value in understanding cardia disfunction in man.

II. Procedure:

Oesophageal fistulae were made in the neck about one inch below the level of the cricoid cartilage. Under aseptic technique a midline incision was made in the neck, the ribbon muscles separated from the deeper tissues and pulled up to the left of the trachea. Care was taken to prevent injury to the recurrent laryngeal nerve. The walls of the oesophagus were then sutured separately to the fascia overlying the ribbon muscles and to the skin before the gullet was opened, and the lumen of the oesophagus exposed. No special post-operative care was necessary, and the animals were able to swallow liquids and solids with a minimum of leakage from the fistula.

Gastric fistulae were made in the dogs about a week following the first operation. Under ether anesthesia, the abdomen was opened by a high right rectus incision. A segment of jejunum or ileum about seven or eight centimeters long which had a suitable blood supply was resected. The distal end was anastamosed to an opening made in the anterior wall of the fundus of the stomach. The proximal end was brought to the surface through the original incision and sutured to the peritoneum, muscle and skin in separate layers. The continuity of the gut was restored by the closed end-to-end anastomosis as described by Martzloff and Burget.[31] The abdomen was closed in three layers using plain #2 catgut for peritoneum and muscle, and linen for the skin.

The advantage of this type of fistula over the usual gastrostomy opening is evident. Since the direction of peristalsis is from outside inward, any material which is forced in to the segment of gut as a result of increased intragastric pressure is immediately propelled back into the stomach. No leakage of gastric juice from the fistula occurs, and therefore there is no skin irritation. It is unnecessary to plug the opening and special post-operative care is unnecessary.

These fistulae were used as a means for placing balloons at different levels in the oesophagus and stomach and recording the activity following peristalsis produced either as a result of a swallow or distension of the oesophagus. At first, three rubber condom balloons were used for recording; one placed in the stomach through the gastric fistula; a second placed in the cardia through the oesophageal fistula, and a third in the upper oesophagus. The stomach balloon was rather large and connected by means of a rubber tubing to a chloroform manometer. The balloon for recording cardiac activity consisted of a balloon about 3 cm. long on the end of a rather rigid catheter which ran completely through the balloon, so that its position in the cardiac sphincter could be accurately maintained by the operator. To keep the balloon open and sensitive to decreases in pressure as well as to increases, soft sponge rubber was used on the end of the catheter under the rubber balloon. It was about 2.5 cm. long and has a diameter of about 1 cm., tapering at both ends. This produced a balloon which was sufficiently large to record relaxations as well as contractions and yet small enough so that it produced no discomfort and did not initiate secondary oesophageal peristalsis. It was connected to a sensitive tambour. The upper oesophageal balloon was small, 3 cm. long, connected by a T-tube with another tambour. It was possible then for the operator to blow through one limb of the T-tube, inflate this balloon, and initiate a peristaltic wave in the oesophagus;

at the same time, the moment of inflation and the effect of the initiated wave on the two lower balloons were recorded on a slowly moving smoked drum.

A second set-up differs only in that an additional balloon was used to record the activity immediately above the cardia. The upper balloon for stimulation was not now connected with a tambour, the points of stimulation or inflation being indicated by a signal key.

Beginning about one week after the gastric fistula was made, and at intervals following that, records were taken. The dogs were trained to lie quietly on a table with the balloons in position while the experiments were being run. Sufficient records were taken on each dog to establish a normal before any nerve lesions were made. As early as possible after the nerve sections, tracings were again taken, and at frequent enough intervals to follow the progress of the condition resulting from such lesions. All nerve lesions were checked at autopsy to make sure that the section was complete. The different nerve lesions made were the following:

1. Single vagotomy in the neck.
2. Double vagotomy in the neck.
3. Double vagotomy in the thorax, about one inch above diaphragm
4. Double vagotomy in the thorax plus single vagotomy in neck.
5. Sympathectomy in abdomen by cutting the cardio-oesophageal branches of the left gastric artery.
6. Splanchnicectomy in the thorax.
7. Sympathectomy plus double vagotomy in thorax.
8. Splanchnicectomy plus double vagotomy in the thorax.

In some instances two or three of these procedures were carried out on a single dog, the effects of each being studied in the intervals between operations.

III. Findings on the normal animal:

In the normal animal with the first set-up as described earlier, the tone in the cardiac sphincter is definitely greater than in either the stomach or the oesophagus. When the cardiac balloon is lowered into position, the operator can definitely determine when the cardia is passed. On pulling back from the stomach into the lower oesophagus one meets a definite resistance which is suddenly released as the balloon passes through the cardiac sphincter. The tonus of the cardia runs almost parallel with the tonus and hunger contractions of the empty stomach, although a times, marked contractions may be seen in the stomach with little or no effect on the cardia. Following an act of deglutition, the cardia and stomach are seen to begin relaxation almost immediately while the peristaltic wave is still high in the oesophagus. The height of relaxation is reached at about the time the wave reaches the cardia. Following the relaxation, there is a temporary rise in tonus which is probably the contracting ring of the peristaltic wave passing through the sphincter. Exactly the same results are seen on inflation of the balloon in the upper part of the oesophagus. Secondary peristaltic waves originate at the point of distension in an attempt to sweep the obstructing bolus into the stomach. There is an immediate fall in tonus in both cardia and stomach, especially the former; and this fall in tonus is maintained as long as there is activity present in the oesophagus. When the oesophagus is no longer actively contracting, the tone of the cardia slowly returns, and usually shows this temporary rise above normal, after which the tone returns to the normal level (fig. 1).

There is a small section of oesophagus immediately above the diaphragm which in most of the dogs showed some relaxation after swallowing or after distension of the upper balloon, suggesting that the cardiac sphincter extends just slightly above the diaphragm. If the cardiac balloon is elevated only one centimeter above this point, however, typical lower oesophageal activity is seen, consisting of very strong rather prolonged secondary peristaltic waves, usually three to six in number depending upon the dog and the irritability of the oesophagus, after which the activity subsides and only respiratory movements are recorded (fig. 2).

An interesting observation was made in one instance where the cardiac balloon had been pulled into the lower oesophagus; the stomach was seen to relax in response to a peristaltic wave in the upper oesophagus, but this wave was not picked up by the cardiac balloon. As a result, an extra balloon was introduced into the oesophageal fistula to record the activity in that part of the oesophagus just above the cardia, the balloons in the cardia and stomach being unchanged. With this second arrangement a check could be made on the ultimate termination of the wave passing down the oesophagus. With very weak distension of the upper oesophageal balloon, secondary peristaltic waves are seen to originate at the balloon level and start to pass down the gullet. The cardia and stomach relax just as they do with the other arrangement, but no evidence of the wave having reached the lower oesophagus can be obtained. With stronger distension of the upper balloon, however, the waves traverse the whole length of the oesophagus and are definitely recorded as contractions on the lower oesophageal balloon, while the cardia and stomach relax as before. Note especially in figure 3 that when the upper balloon was distended for a considerable length of time, the tone in the cardia and stomach dropped and stayed down until the pressure in the distending balloon was released, and yet, no waves reached the lower oesophagus.

This relaxation in the cardia is absolutely independent of diaphragmatic activity as is seen in figure 3 since at the time this tracing was taken the dog was very hot and panting rapidly. It is inconceivable, after seeing such marked relaxation with the respiratory movements superimposed, to imagine that the diaphragm has much to do with the process, as has been claimed by Jackson[1], and recently by Fulde[8].

IV. Effects of Vagus Section:

1. Unilateral section of the vagus in the neck was performed on six dogs, three on the left side and three on the right. Tracings were taken as early as six hours after operation on some dogs. During the first 24 hours, the oesophagus is partially paralyzed, rather lax and atonic. Although some relaxation in the cardia can be elicited on distension of the oesophagus, the pressure in the balloon must be increased about three times as high as normally to initiate a response, and even then the relaxation is not very marked. However, within a few days the tone is regained and relaxation follows a swallow or distension of the oesophagus just as well as before the nerve section; the only difference being that the oesophagus is not quite as irritable and requires a slightly stronger stimulus to initiate a response. No differences in the type of response or the relative time relations before and after operation could be ascertained.

2. Section of both vagi in the neck was performed on three dogs with complete paralysis of the oesophagus. It was impossible to initiate a wave which would carry through the length of the oesophagus. If one was initiated high in the oesophagus, it seemed to run only as far as the level of the vagus section. In one dog, the oesophagus was so lax that the cardia balloon could not be placed in position before the diaphragm. This was not due to a cardiospasm, since a large more rigid catheter could be pushed easily through the cardia into the stomach, but because the balloon was fastened to a tubing which was not rigid enough to allow it to be forced straight down, and the walls of the oesophagus were too lax to direct it

down, allowing kinking and doubling of the tube to take place. In the other two dogs, however, the cardia balloon could be placed in position rather easily through the cardiac sphincter into the stomach if the end of the tube happened to strike the orifice directly, and could be pulled back into the oesophagus without feeling the tug or pull which was present before operation. However, if the end of the tube did not strike the opening, it would double upon itself due to the atonicity of the oesophageal walls.

In the second dog, the cardia did not regain its former tonus at any time. This dog was different from the other two in that during stomach feedings, which were necessitated by the oesophageal paralysis, as much as 380 cc. of milk or cereal could be injected into the stomach with very little being regurgitated through the oesophageal fistula or being lost through leakage from the gastric fistula. Nutrition was fairly well maintained in this dog for the first week, and the dog had normal stools. However, just as it happened in the first dog, some regurgitated food was apirated into the lungs, and the dog died of pneumonia on the fifteenth day. Post-mortem examination revealed besides the pneumonia, an oesophagus diffusely dilated and filled with air and a little fluid. The stomach was contracted rather tightly; the small and large bowel were slightly dilated, but otherwise normal in appearance. No areas of hemorrhage or ulceration were seen.

In the third dog, the oesophagus and cardia were paralysed and atonic on the first day after operation. On the second day, the cardia began to regain some of its tone, and the operator could easily detect by the feel and by the kymographic record when the balloon was pulled back through the sphincter into the oesophagus. By distending the stimulating balloon high in the oesophagus above the nerve section, one could see a series of secondary waves begin, but they died out almost immediately. They could not be picked up by another balloon placed only one inch below the distending balloon. Relaxation of the cardia or stomach was not seen in any of the records. By the third and fourth day, the tone in the cardiac sphincter had returned to such a state that it differed from the normal only in that the tug or pull felt in drawing the balloon through the sphincter into the lower oesophagus was not present as it had been before operation (fig. 4). This dog, like the first one, was very difficult to maintain since milk or cereal injected into the stomach by tube was almost immediately squirted out forcibly from the gastric fistula in interrupted spurts, showing that the stomach was very active and hypertonic. When the dog attempted to lap up this rejected food, there was noticed much regurgitation from the oesophageal fistula, presumptive evidence that the cardia was relaxing when the dog made repeated attempts at swallowing. On the fifth day, the dog was in a very poor condition, due to his inability to retain the food and to repeated attacks of vomiting in which the dog would bring up small amounts of bile-stained fluid. He was chloroformed and posted at once. The oesophagus was rather atonic and somewhat dilated. No evidence of spasm or obstruction was seen at the cardia; the stomach was small and tightly contracted; the small and large intestines were normal in appearance as seen grossly. On opening the gut, much hyperemia and superficial erosion and hemorrhage was seen extending from the stomach throughout the small intestine. Both vagi were found to have been sectioned just before passing into the thorax.

3. Six dogs were operated on with both vagi in the thorax being sectioned. The approach was made through the left side posteriorly between the eighth and ninth ribs. Under ether anesthesia, a small incision about 6 cm. long was made parallel with the ribs, the fibers of the latissimus dorsi muscles cut through and the intercostal muscles separated close to the upper border of the ninth rib. When the pleura was cut, a small rib-spreader was placed between the two ribs to hold them apart, the lung fell away and revealed both vagi, the left one anterior and the right one posterior to the oesophagus with the branch from the left one coming down to join the right one about one inch above the diaphragm. Both vagi and the connecting branch were grasped with hemostats and sections of nerve removed by cutting on either side of the clamps with scissors. The pleura and intercostal muscles were closed together with 00 plain catgut, the fibers of the latissimus dorsi re-approximated with gut and the skin closed with linen. The operation was done so quickly once the pleura was opened that it was found necessary to aid respiration with intratracheal insufflation. If the animal experienced marked respiratory difficulty during the operation, the thorax was temporarily closed by holding a sponge tightly over the incision until the forced respiratory movements subsided. The dogs withstood the operation well and tracings were taken on them the next day.

Double vagotomy low in the thorax seems to have no apparent effect on this relaxation mechanism in the cardia and stomach. No evidence of spasm or paralysis is seen in any of the dogs. It is impossible to detect any difference in the type or time relations of the relaxation as compared with the normal dog either immediately or as long as nine months after operation. This same interesting observation was made on three of these dogs as was seen in the normal, namely that relaxation occurred in the cardia and stomach on weak distension of the upper oesophageal balloon without being able to pick up a peristaltic wave in the lower oesophagus. Stronger distension produced a wave which was recorded by the lower oesophageal balloon, while the stomach and cardia relax as before.

In one dog, the vagi were cut as high in the thorax as possible and still being below the pulmonary and cardiac plexuses. The root of the lung prevents cutting the vagi higher than about 2.5 inches above the diaphragm. The tracings obtained from this dog following the lesion differed in no way from those taken before the operation or from those of the other dogs (fig. 5).

4. Three dogs had a combination of both vagi sectioned in the thorax and one cut in the neck with no apparent change in the type of activity in the cardia or stomach following peristalsis in the oesophagus. The only difference noted was that the oesophagus after this combination of lesions was not quite as irritable and required a stimulus about three times as strong as normally to initiate a response (fig. 6).

V. Effects of Section of the Sympathetic Supply:

The sympathetic supply to the cardia, as described by Knight and Adamson[9], was sectioned in two dogs. Through a left rectus incision, extending upwards as far as the xiphosternum and down to the umbilicus, the left gastric artery was exposed high up on the lesser curvature of the stomach. It was freed and ligated along with its vein. With artery forceps on the central end of the vessels acting as a retractor, a downward pull was made and the oesphageal branch of the artery made to stand out. This was dissected free along with a bundle of nerve tissue lying alongside and pulled over to the dog's right. The deep aspect of the left gastric artery was thus exposed and many strands of nerve tissue were found passing from the coeliac axis to the lower end of the oesophagus. These were all divided at their peripheral ends. Dissection was carried centrally until the left side of the coeliac axis was exposed. The last stage consisted of ligating the left gastric artery at its origin from the coeliac and so removing the segment of artery along with the mass of nerve tissue that had been dissected free. The abdomen was closed in the usual manner.

Tracings taken as early as 24 hours and as long as 8 months after operation revealed no apparent change from the normal in the activity of the cardia or stomach following peristalsis in the oesophagus. No immediate or late spasm or paralysis of the cardia was seen, nor was the tone of the cardiac sphincter appreciably altered. The same phenomenon of relaxation occurring in the cardia and stomach following distension of the upper oesophageal balloon with no evidence of the wave ever having reached the lower oesophagus was noted (fig. 7). In one dog, stenosis apparently due to cicatricial bands around the gastric opening of the fistula, made it difficult and, at times, impossible to insert the stomach balloon to record gastric activity; but this in no way interfered with the cardiac activity.

In order to determine whether the splanchnics had any control over this relaxation mechanism, splanchnicectomy in the thorax was done in one dog. Because of the anatomical location of the splanchnic nerves which make it impossible to reach both nerves from the one side and because we wished to avoid shocking the animal too much, this operation was performed in two stages. The right side of the thorax was entered first at the same level as has been described earlier in vagotomy, the splanchnic trunk was grasped through the pleura with a hemostat and its continuity interrupted by cutting on either side of the hemostat, taking care to avoid the intercostal arteries which cross at right angles under it. The chest was closed as before. Tracings taken 7 days later showed good relaxation in the cardia and stomach following peristalsis in the oesophagus above, indistinguishable from the normal (fig. 8). There was no evidence obtained from watching the dog eat and drink on the day after operation and on the following days that would lead one to think that there was any spasm or paralysis of the cardia. Nineteen days after the first operation, the left side of the thorax was opened, and the splanchnics on that side sectioned in a similar manner. There were no immediate or late signs of paralysis or spasm of the cardia. Relaxation in the cardia and stomach following oesophageal peristalsis, and typical lower oesophageal activity were present, with no change from the normal (fig. 8).

VI. Effects of Section of Both Vagi and Sympathetics:

Two dogs were prepared with a combination of lesions, one with double vagotomy in the thorax plus sympathectomy by cutting the cardio-oesophageal branch of the left gastric artery as described earlier; the other dog with double vagotomy in the thorax plus splanchnicectomy in the thorax.

In the first case, tracings taken 48 hours after operation showed the cardia and stomach to be relaxing perfectly in response to a distension of the oesophageal balloon. Gastric motility was somewhat reduced. Tracings taken up to 45 days later showed a return to normal gastric motility. The cardia and stomach continued to relax following initiation of a wave in the oesophagus, probably a little more marked in the cardia than in the stomach, and both of them probably not quite as well as before operation. However, even though the degree of relaxation was not as great after operation as before, the type and time relations were not altered as far as could be determined (fig. 9).

In the second dog with both vagi and splanchnics cut, tracings taken 24 hours after operation showed the oesophagus, cardia and stomach all to be rather atonic. It was very difficult to determine by feel at what level the cardia was, because the balloon passed very easily from the stomach through the cardiac sphincter into the oesophagus, regardless of diaphragmatic activity. There was some suggestion of relaxation in the cardia, but it was very poor (fig. 10). Three days post-operatively, the tone was gradually coming back into these structures, but it was still very poor in the cardia. Some relaxation in the cardia following oesophageal activity was noted. On the sixth day after operation, relaxation in the cardia was very good following distension of the upper oesophagus, but it was not as apparent in the stomach where the points of relaxation were superimposed on the regular rhythmic waves there. On the seventh day, with the improved set-up for recording, perfect relaxation in the cardia and stomach following a swallow or distension of the upper oesophagus was seen. One instance was noted where relaxation occurred in the cardia without the wave ever being recorded on the lower oesophageal balloon. Tracings taken up to three and a half months after operation revealed activity in the oesophagus, cardia and stomach which in no way could be distinguished from normals taken before nerve section (fig 10).

VII. Discussion:

In reviewing the literature and following the progress of the study of this part of the intestinal tract, we find that Reid[10], as early as 1839, noted in rabbits that stasis of food in the oesophagus was seen following vagus section in the neck. Many have agreed that this stasis was due to increased tonus of the cardiac sphincter followed later by dilatation of the oesophagus (Bernard[11], Kronecker and Meltzer[12], and Klee[13]). Kronecker and Meltzer[12], 1883, noted relaxation in the cardia following repeated acts of deglutition, but ascribed this to central inhibition of vagus motor tone to the cardia. Langley[14], 1898, working with curarised and atropinised rabbits, stimulated the vagi in the neck after filling the oesophagus with water and noted relaxation in the lower part of the oesphagus and cardia. When no atropine was administered, the vagus stimulation caused increased tonus of the cardia. He therefore concluded that the vagus nerve carried both motor and inhibitory fibers to the cardia. He later reported that adrenalin inhibited the cardiac sphincter in the rabbit.

Krehl[15], 1892, in chronic experiments reported that section of both vagi below the diaphragm in the dog left the oesophagus and cardia atonic or patulous. He determined the state of tonus by the resistance to the passage of a stomach tube into the oesophagus through the gastrostomy opening. Sinnhuber[16], 1903, working on four dogs, concluded that section of vagi above but close to the diaphragm renders the cardia atonic, while section of the vagi high in the neck leads to temporary hypertonicity of the cardia. If he is correct, it would seem that in the dog, the inhibitory fibers to the cardia leave the vagi at some distance above the diaphragm and pass down to the cardia in the wall of the oesophagus.

May[17], 1904, on cats, dogs, rabbits and monkeys, found that the vagi had both motor and inhibitory fibers to the cardia. As regards the splanchnics, he was in opposition to all previous observers, failing 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[18] in normal animals, showing that the apparently highly coordinated movements of the stomach depended on a local mechanism and did not require the interaction of the central nervous system.

Cannon[19] reported in 1907 that section of both vagi in the neck in the cat leads to an increased tonus of the cardia lasting several days, parallel with decreased tonus and peristalsis of the oesophagus. He based this conclusion on the observation that the peristalsis of the lower oesophagus frequently failed to force the food through the cardia and the increased resistance at the cardia to the passage of the stomach tube. In 1911,[20] while feeding meat to cats with chronic oesophageal fistulae, he observed "receptive relaxation" in the cardiac portion of the stomach. He noted that the stomach began to relax a considerable period before the wave had reached the cardia and made the statement,— "the vagus impulses anticipate the oesophageal needs by a good margin". Section of both vagi in the neck abolished this relaxation mechanism completely. He concluded that inhibition of gastric contraction which attended an emotional outbreak was due to impulses discharged by way of the splanchnics. Inhibition which follows deglutition is produced by way of the vagus nerves. In 1912,[21] in isolated segments of the digestive tract of cats, he confirmed the presence of a "myenteric reflex" in the oesophagus as well as in the stomach and intestine, an intrinsic arrangement whereby a stimulus causes a contraction above and a relaxation below the point of application. Pinching the oesophagus immediately above the recording ring caused relaxation, even in animals which had had both vagi sectioned in the neck several days previously.

Carlson, Boyd and Pearcy[22], 1922, using cats and dogs, in acute experiments and in animals provided with permanent and oesophageal fistulae studied the innervation of the cardia and lower end of the oesophagus. They were unable to demonstrate by stimulation of the thoracic sympathetic chain at different levels a sympathetic supply to the lower oesophagus and cardia other than that via the splanchnics. They found on stimulation of the splanchnic nerves in the thorax with the brain and spinal cord pithed, both motor and inhibitory efferents to the cardia and lower oesophagus in the cat. In the dog only motor action, in the rabbit only inhibitory action was demonstrated. These variations they ascribed to the condition of the tonus at the time of stimulation and concluded that the splanchnics, like the vagi, carry both motor and inhibitory efferents to the stomach, the effect of stimulating either one depending on the existing state of tonus. Under ether anesthesia, section of both vagi induced a spasm lasting 3 to 15 minutes, which they attributed to the irritation of the section itself. Vagus inhibitory and sympathetic motor and inhibitory action in the acute animal they found to be lost with the disappearance of Auerbach's plexus, and the change of the musculature to the striped variety. As a working hypothesis, the view is advanced that the visceral efferent nerve fibers are in reality afferents to the local but diffuse reflex nervous centers in the visceral organs.

Veach[23], 1926, in acute experiments on cats under chloralose or other anesthesia, found on distension of an oesophageal balloon a relaxation of the stomach accompanied by peristalsis of the lower end of the oesophagus. Bi-lateral vagotomy in the neck abolished this receptive relaxation, and he suggests that the myenteric plexus may not function under ordinary circumstances, between the parts of the alimentary canal involved.

M'Crea, McSwiney and Stopford[24], 1926, studied the effect of vagus section on motor activity of the stomach in dogs. They state that the pylorospasm described by Klee[15], Exner and others as immediate on vagus section are purely temporary and are no doubt due to the irritation of the nerve section. They are in accord with the view of Carlson et al[22], that the variable effects of vagus stimulation are related to the coexisting gastric tonus.

Brown Kelly[25], 1927, cut the vagi in the cervical region in cats. On giving opaque meals and studing the animal under the fluoroscope, he found a dilated oesophagus with what he termed a cardiospasm, in all cases. He suggests that the destruction of the nerve mechanism of Auerbach's plexus owing to chronic fibrosis and degenerative change may account for the loss of the normal muscular contraction and relaxation, and result in a greater tendency to abnormal reflex overaction of the circular fibers.

Alvarez, Hosoi, Overgard and Ascanio[26], 1929, studied the effects of degenerative section of the vagi and splanchnics in the intestinal tract of rabbits. They state that S. E. Johnson examined histologically segments of stomach and gut from some of his animals, which had nerve lesions more than three weeks before, and reported the same marked degeneration of the fibers in Auerbach's plexus that he had observed previously in dogs with the vagi cut.

Pierre[27], 1933, in the dog and the rabbit found that slight oesophageal distension of about 20 cm. of mercury was sufficient to start the peristaltic wave of deglutition and the carriage of a bolus in the tube to the stomach.

Knight,[28,29] in 1934 and 1935, has made rather extensive studies on the innervation of the oesophagus and cardiac sphincter in an attempt to obtain a rational basis for the surgical treatment of achalasia. Quoting Ken Kuro, Knight[28] states that previous work showed that section of the vagi in the neck in dogs resulted in a paralyzed dilated oesophagus and a contracted cardiac sphincter, and that section of the sympathetic fibers passing to the sphincter increased the ostruction which resulted at this region from bilateral vagectomy. Knight, using cats, found that vagal stimulation caused increased tonus and motility of the lower third of the oesophagus, which is composed of plain muscle. The tonus and motility were inhibited by sympathetic stimulation. Bilateral vagal section, if complete, reproduced the appearances of achalasia of the cardia. Simultaneous removal of the sympathetic fibers prevented the onset of this obstruction. When the obstruction developed it could be relieved by section of the sympathetic supply to the sphincter.

In the main, the degree of changes produced depended upon the level at which the vagi were divided and the time that had elapsed since the operation. In one animal with both vagi cut below the lung root, no obstruction at the cardia was noted by X-ray two weeks after operation. However, seven months after operation, the obstruction had increased sufficiently to produce vomiting. When the denervation was more extensive and designed to cut off all vagal fibers by division of the right vagus in the chest below the recurrent laryngeal, and the division of the nerve plexus on the surface of the oesophagus high in the thorax to interrupt these fibers descending in the plexus from the right recurrent laryngeal and division of the left vagus in the neck, then the obstruction at the cardia was so severe as to cause enormous dilatation of the oesophagus and death.

In looking back over the work of these men, it seems to me that the greatest criticism lies in the method employed in obtaining the information. Acute experiments in which the animal is anesthetised and more or less shocked by the surgical procedures are far from ideal for arriving at a conclusion of the physiological function of a structure such as the cardiac sphincter. The same objection may be applied in those cases in which the nerves are stimulated electrically. It is true, such electrical stimulation produces results which are capable of interpretation, but does the organ normally receive stimuli of this character and strength?

While our method for recording is not perfect, it nevertheless has overcome these two serious objections. Our method of stimulation of the oesophagus to initiate peristalsis is of somewhat the same character as that encountered normally when the animal swallows large pieces of food which may temporarily become lodged in the oesophagus. The objection might well be raised that the presence of the rubber tubes and balloons in the oesophagus could alter the irritability of the oesophagus, deform the wave as it passed down the oesophagus or initiate waves at their locations which would complicate the picture. However, the tubing is so small and the balloons of such a size, that they do not make the dog uncomfortable and have never been seen to serve as irritable foci where new waves might originate. Even persons who are trained and accustomed to the presence of a tube in the oesophagus experience no difficulty in swallowing liquids or solids.

Our results differ from previous work in several particulars. We have evidence in the normal animal that relaxation occurs in the cardia following distension of the upper oesophagus with no record of the wave having reached the lower oesophagus. It cannot be the result of a recording apparatus not sufficiently sensitive to record the wave since stronger stimulation gives rise to a wave which records perfectly on the lower oesophageal balloon. We have noted a small area extending just slightly above the diaphragm which relaxes in response to distension of the oesophagus suggesting that the cardiac sphincter extends partially above the diaphragm as well as below. That the diaphragm has very little to do with the relaxation mechanism, so ardently advocated by Jackson[1], is very plainly seen in the tracings. It would be rather diffuclt to conceive that the diaphragmatic fibers surrounding the lower oesophagus could relax over an extended period of time while the rest of the organ took part in respiratory movements, especially since there is but a single nerve supply to the diaphragm. As far as could be ascertained, the only nerve lesion which made any appreciable change in the response of the cardia to peristaltic waves elicited either by distension of the oesophagus or by the act of swallowing was section of both vagi in the neck. But there we have an animal which is not altogether suitable for this type of experimentation in that it was unable to initiate a peristaltic wave which would carry down to the stomach. It is possible that if one of the animals could have been maintained long enought for the oesophagus to regain some of its tone as sos tated by Cannon[19], one might well have obtained evidence of relaxation of the cardia after distension of the oesophagus. We have seen presumptive evidence of relaxation when regurgitation from the oesophageal fistula took place following gastric feeding when the animal attempted to swallow.

With the oesophagus atonic and completely paralyzed, a spasm of the cardia need not be assumed to produce dilatation of the oesophagus. A cardiac sphincter with normal tone could offer enough resistance to the passage of food into the stomach from an impotent oesophagus to produce the same result if no impulses came down to the oesphagus to cause it to relax, which may account for the dilatation reported by some workers.

Single vagotomy in the neck does not alter the type of response of the cardia except that it alters the sensitivity of the oesophagus, as one would expect if half of the afferent pathway were destroyed. Bilateral thoracic vagotomy seems to have no apparent effect on the relaxation mechanism of the cardia. Section of the splanchnics and sympathetic fibers on the left gastric artery had no effect on the response of the cardia and stomach to distension of the oesophagus. This is contrary to the results of those who found spasm or paralysis of the cardia.

An explanation for some of these phenomena, especially that one wherein the cardia relaxes in response to a distension of the oesphagus without the peristaltic wave reaching the lower oesophagus and the inability to alter this relaxation after certain nerve lesions as described above, is difficult. An adequate explanation must necessarily tread somewhat on the toes of the text-book theories of oesophageal activity. When Cannon[18] noted that the stomach began to relax a considerable period before the wave reached the cardia, he ascribed the activity as being under the control of the vagus and made the statement, "the vagus impulses anticipate the oesophageal needs by a good margin", but he failed to offer any explanation how the anticipation took place.

Let us assume that the center for deglutition consists of a series of "centers" in the medulla, each one connected to the next one in line and each one of these supplying a certain segment of oesophagus, through the vagus nerves. When the first one is stimulated, as in an act of deglutition, it fires off, so to speak, the lower ones in rapid succession and thus carries the peristaltic wave down to the stomach. Likewise any afferent impulse from some segment of the oesophagus could initiate a reflex at that level and this in turn initiate a reflex for the next lower level and so on. But we have seen the cardia begin to relax almost immediately when the wave is still high in the oesophagus. Therefore when an afferent impulse comes into one of these "centers", one or more efferent impulses reach the oesophagus at this level causing local activity of the oesophagus and almost immediate relaxation of the cardia. What pathway this latter impulse takes to reach the cardia is not known. It may pass through a long fiber directly to the cardia, or the inhibitory fibers may leave the vagi some distance above the diaphragm and below the point where we sectioned the vagi in the neck and travel to the cardia in the wall of the oesophagus, as suggested by Krehl[15]. One other and more probable possibility remains: it may be that the efferent impulse from the center in the medulla causes local oesophageal activity, which activity so acts on Auerbach's plexus at that level as to send an impulse directly to the cardia for relaxation. In favor of this last explanation is the result seen after cutting both vagi in the neck. It is possible to initiate what looks like a peristaltic wave high in the oesophagus, but this wave travels only to the level of the vagus section. Relaxation in the cardia does not occur. But at the upper part of the oesophagus in the dog, the musculature is almost purely striated and Auerbach's plexus is probably lacking. As Carlson[22] has found in acute experiments, "vagus inhibitory action thus seems to be lost with the disappearance of the Auerbach's plexus and the change of the muscle to the striped variety", which may explain our failure to obtain graphic evidence of relaxation in these dogs with the vagi cut in the neck. If one could find out exactly where Auerbach's plexus begins in the oesophagus, he could cut the vagi at this level or below and expect to get relaxation in the cardia even though no wave reached the lower oesophagus, section of the vagi of course cutting out all peristalsis below that level.

Reasoning thus, it is possible to understand that a very weak stimulus coming in from a certain segment of the oesophagus could be just strong enough to send out the efferent impulses to the cardia for relaxation and to that segment of the oesophagus for local contraction, but too weak to fire off the whole chain of centers, and therefore the peristaltic wave dies out before reaching the lower oesophagus. This explanation could account for our finding relaxation in the cardia with no wave reaching the lower oesophagus, whereas stronger stimuli carried the peristaltic wave to the stomach.

In the application of our findings to the mechanism of the clinical condition of achalasia or cardiospasm, it is seen that the cardia possesses an intrinsic nervous mechanism, which, although it is more or less under the controlling influence of the vagus and sympathetic nerves, is still capable of inducing relaxation in the cardia in response to a peristalsis of the oesophagus, independent of these extrinsic nerves. It is possible that hyperactivity of either the vagi or sympathetics could have a disturbing influence on this normal mechanism, and for which conditions, section of the overactive nerves would bring relief. However, in those conditions where there is a fibrosis of the terminal end of the oesophagus which restricts the normal opening of the spincter, the obstruction is mechanical; and we would not expect any favorable results from section of the extrinsic nerves. It is the cases in this latter group which are so greatly relieved by one or more mechanical stretchings of the sphincter. The third condition, or achalasia, which is a "failure to relax" instead of a spasm is due to degenerative changes in the Auerbach's cells around the sphincter, as had been pointed out by Hurst and Rake[30]. Since we have shown that the relaxation mechanism of the cardia is dependent upon an intact Auerbach's plexus, we might expect that any lesion which destroyed this plexus would also destroy the intrinsic nervous mechanism of the cardia and thus lead to a condition similar to achalasia.

VIII. Summary and conclusions:

A method of recording continuous cardia activity in unanesthetised animals is described. On the normal dog with all nerves intact, we have seen the cardiac sphincter relax in response to a peristaltic wave in the oesophagus, initiated either by a swallow or by distension of a balloon in the upper oesophagus. This same relaxation of the cardia occurs when the distension of the balloon is not great enough to produce a peristaltic wave which carries down to the lower end of the oesphagus. That the cardia possesses an intrinsic nervous mechanism which is dependent upon Auerbach's plexus and capable of activity in the absence of the vagal and sympathetic influences is shown in our inability to alter the character of the cardia relaxation after section of the extrinsic nerves. Single vagotomy in the neck, double vagotomy in the thorax, sympathectomy in the thorax and combinations of these lesions fail to alter appreciably the relaxation mechanism of the cardia. Double vagotomy in the neck results in a completely paralysed oesophagus in which peristalsis is not present. Relaxation of the cardia in this instance is not seen. A possible explanation for these phenomena is given.

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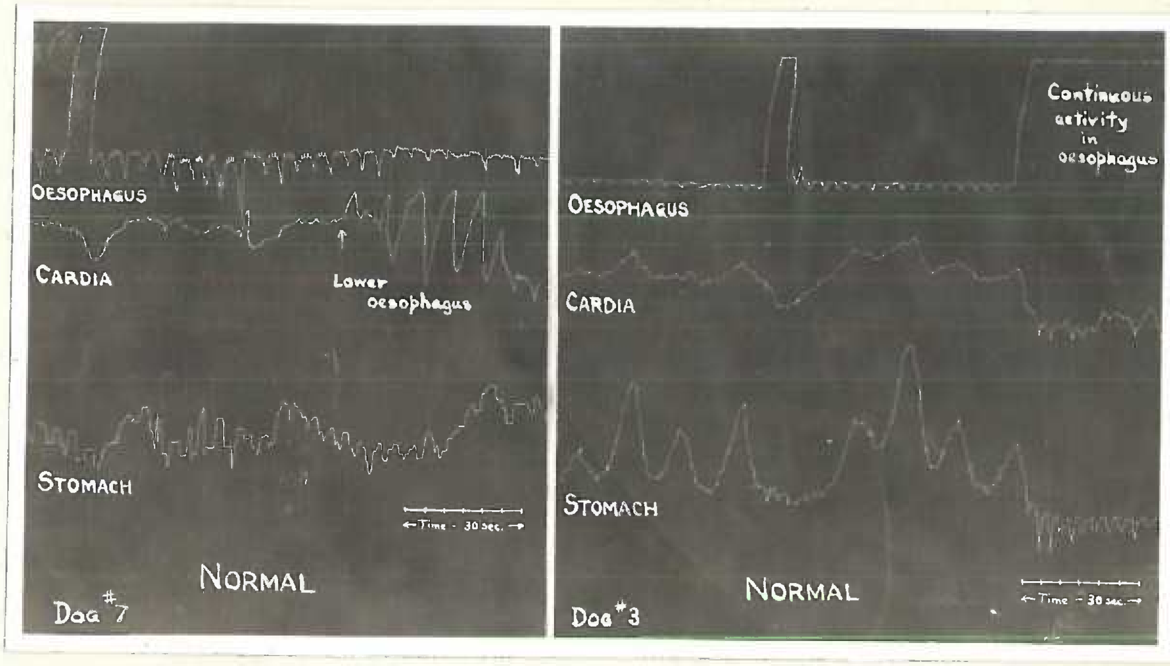
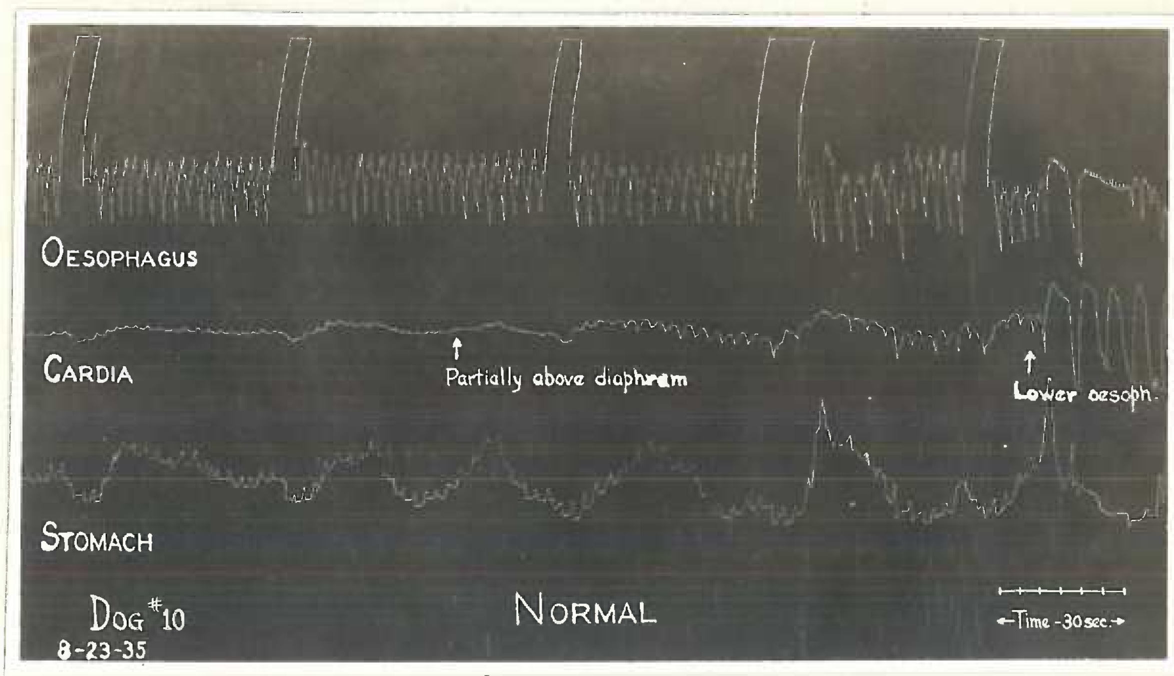
Fig. 1



OESOPHAGUS
CARDIA
Lower oesophagus
STOMACH
←Time - 30 sec.→
NORMAL
DOG #7
Continuous activity in oesophagus
OESOPHAGUS
CARDIA
STOMACH
NORMAL
←Time - 30 sec.→
DOG #3

Fig. 2



OESOPHAGUS
CARDIA
Partially above diaphram
Lower oesoph.
STOMACH
DOG #10
8-23-35
NORMAL
←Time -30 sec.→

Fig. 3

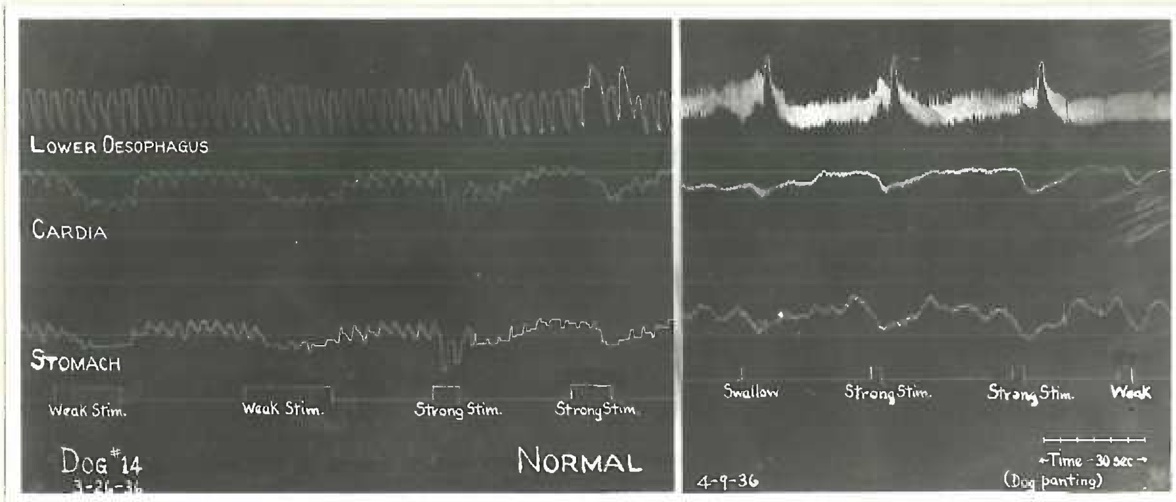

Lower Oesophagus
Cardia
Stomach
Weak Stim.
Weak Stim.
Strong Stim.
Strong Stim.
Dog #14
Normal
Swallow
Strong Stim.
Strong Stim.
Weak
4-9-36
←Time - 30 sec→
(Dog panting)

Fig. 4

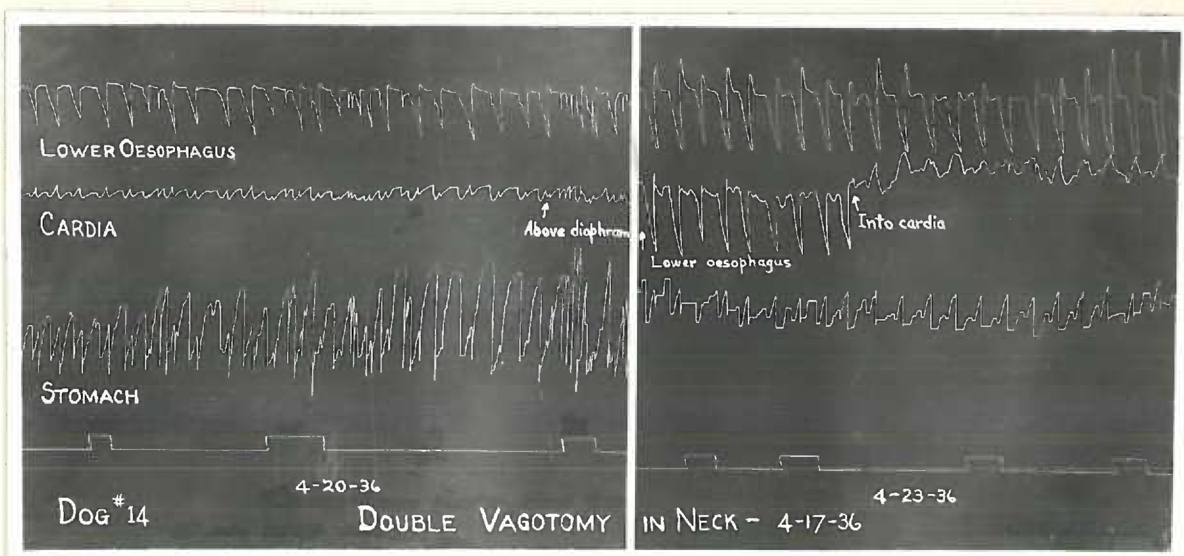
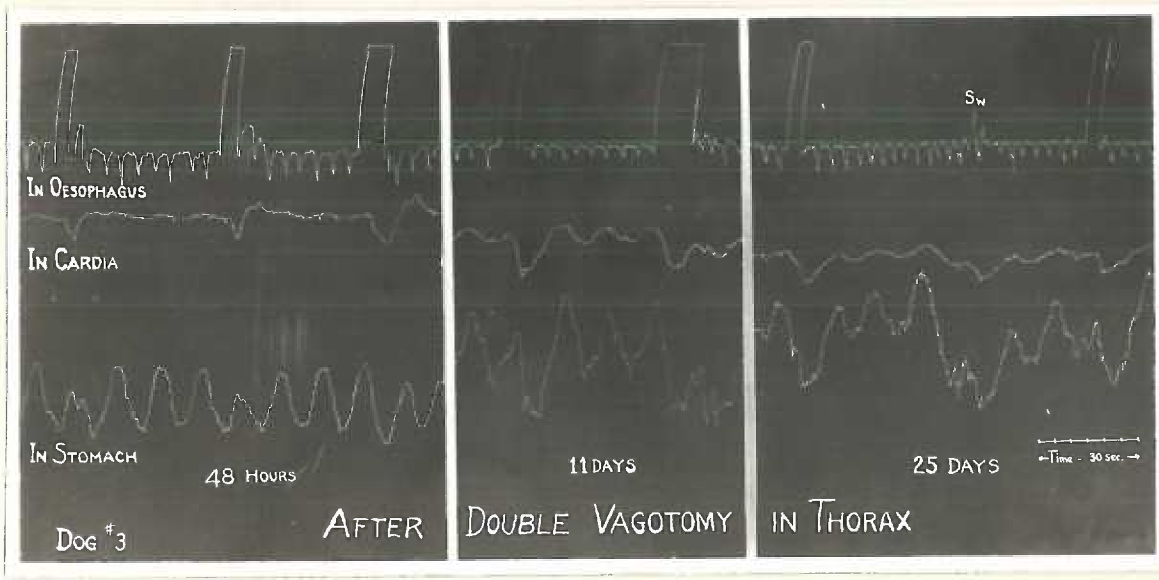
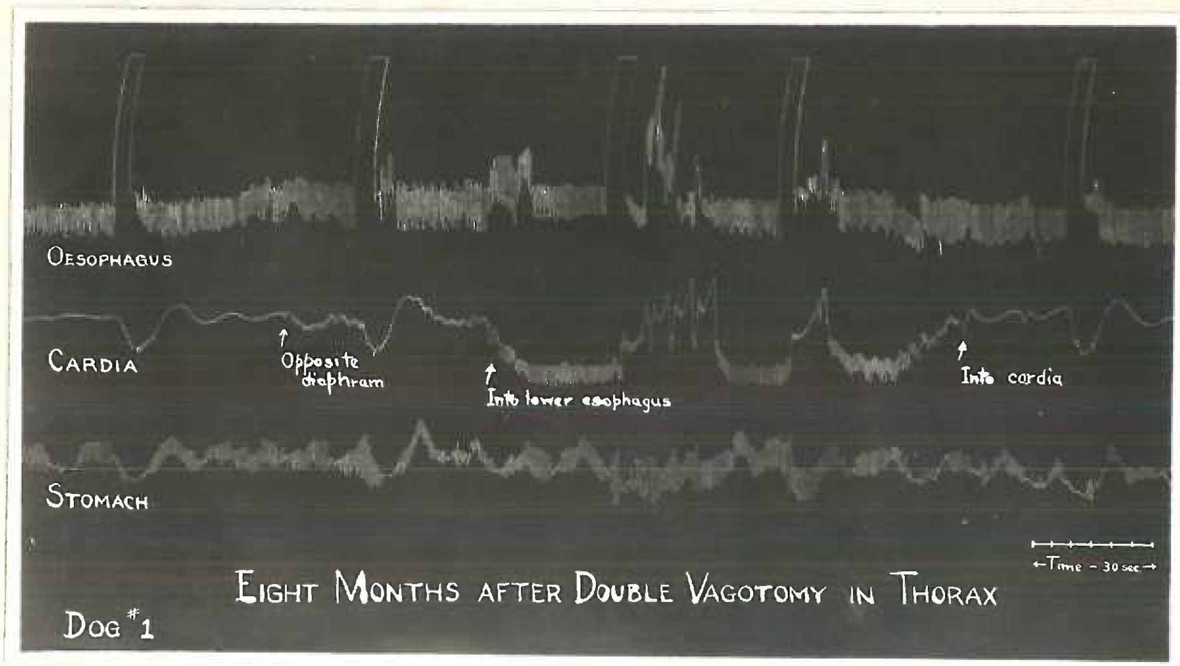

Lower Oesophagus
Cardia
Into cardia
Lower oesophagus
Stomach
4-20-36
Dog #14
Double Vagotomy in Neck - 4-17-36
4-23-36

Fig. 5 (a)



In Oesophagus
In Cardia
In Stomach
48 Hours
11 Days
25 Days
Sw
←Time - 30 sec.→
Dog #3
After Double Vagotomy in Thorax

Fig. 5 (b)



Oesophagus
Cardia
Opposite diaphram
Into lower esophagus
Into cardia
Stomach
←Time - 30 sec.→
Eight Months after Double Vagotomy in Thorax
Dog #1

Fig. 6

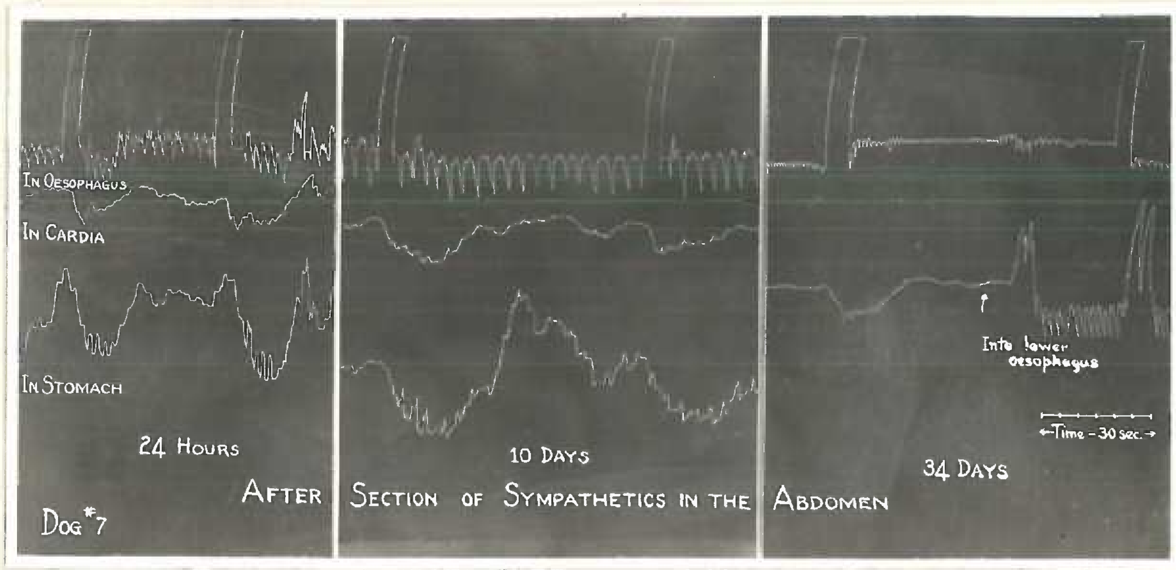

In Oesophagus
In Cardia
In Stomach
24 Hours
10 Days
34 Days
Into lower oesophagus
←Time - 30 sec.→
After Section of Sympathetics in the Abdomen
Dog #7

Fig. 7

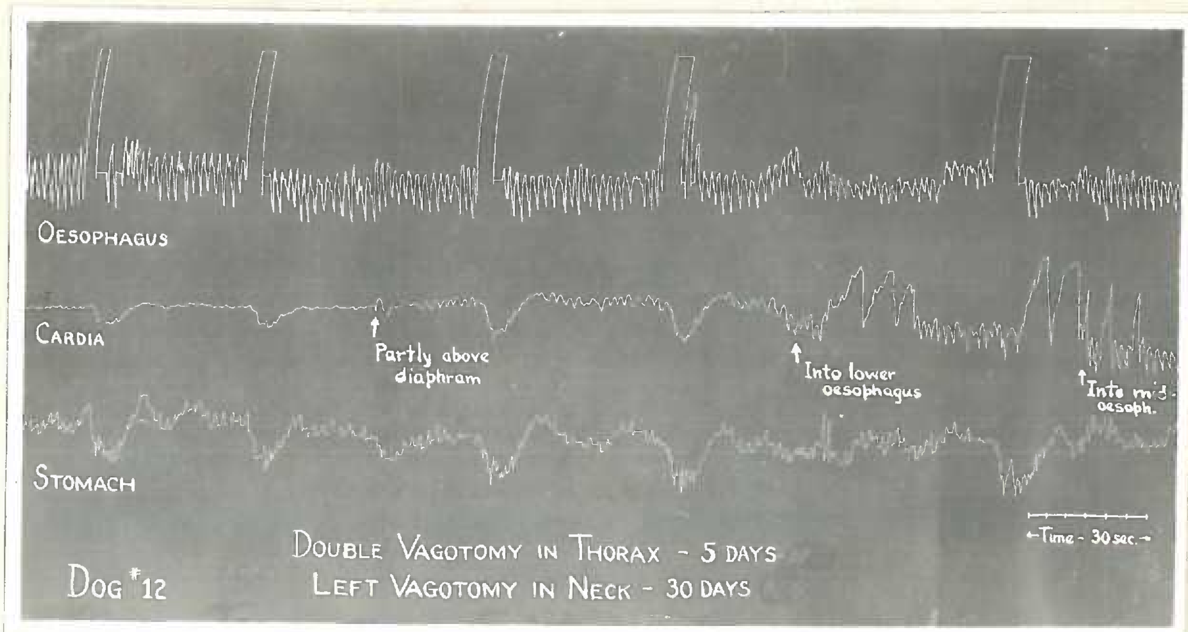

Oesophagus
Cardia
Partly above diaphram
Into lower oesophagus
Into mid-oesoph.
Stomach
←Time - 30 sec.→
Double Vagotomy in Thorax - 5 days
Left Vagotomy in Neck - 30 days
Dog #12

Fig. 8

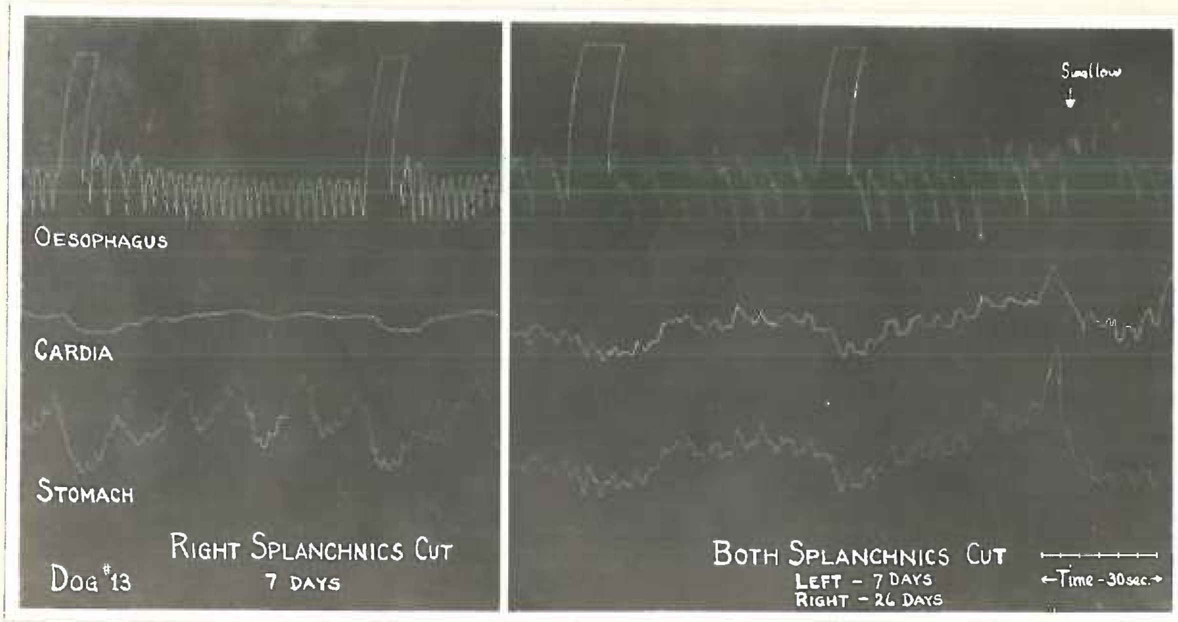

Swallow
Oesophagus
Cardia
Stomach
Dog #13
Right Splanchnics Cut
7 days
Both Splanchnics Cut
Left - 7 days
Right - 26 days
←Time - 30 sec.→

Fig. 9

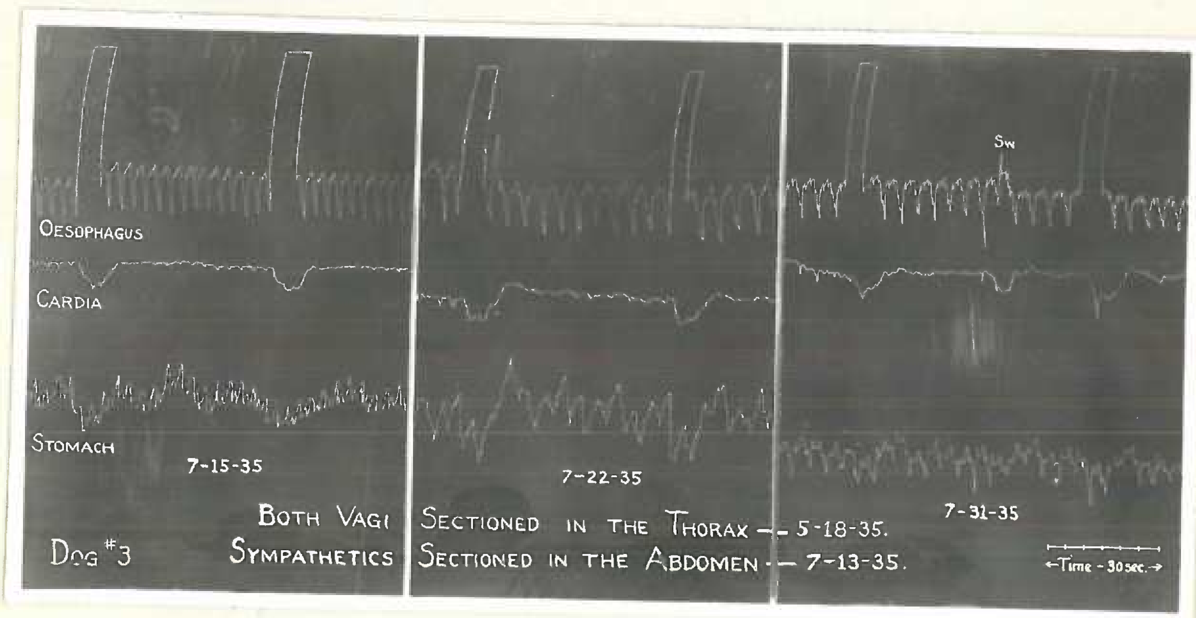

Sw
Oesophagus
Cardia
Stomach
7-15-35
7-22-35
7-31-35
Dog #3
Both Vagi Sectioned in the Thorax -- 5-18-35.
Sympathetics Sectioned in the Abdomen -- 7-13-35.
←Time - 30 sec.→

Fig. 10 (a)

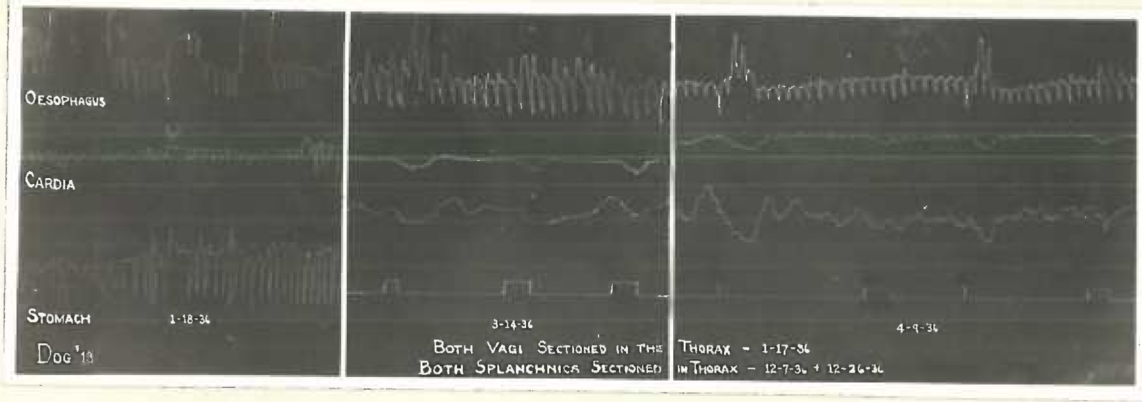
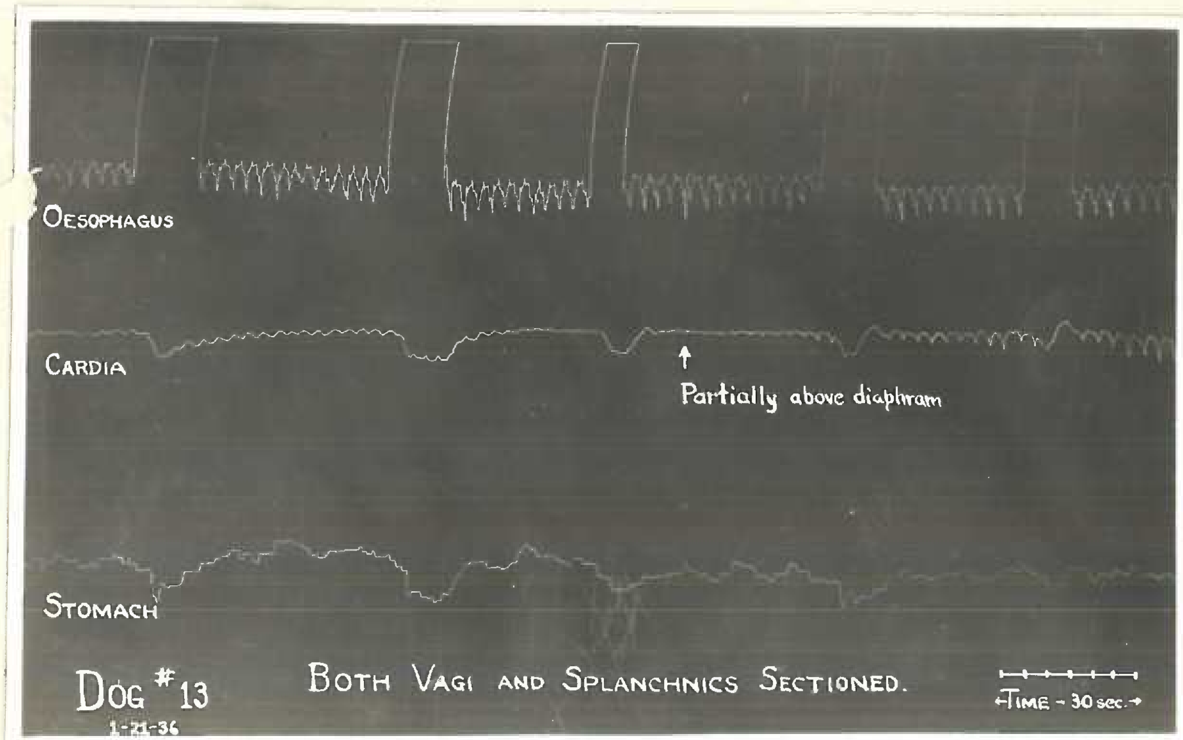


Fig. 10 (b)



There is a small section of oesophagus immediately above the diaphragm which in most of the dogs showed some relaxation after swallowing or after distension of the upper balloon, suggesting that the cardiac sphincter extends just slightly above the diaphragm. If the cardiac balloon is elevated only one centimeter above this point, however, typical lower oesophageal activity is seen, consisting of very strong rather prolonged secondary peristaltic waves, usually three to six in number depending upon the dog and the irritability of the oesophagus, after which the activity subsides and only respiratory movements are recorded (fig. 2).