

THE EXPERIMENTAL PRODUCTION OF CARDIOSPASM IN DOGS

by

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THE EXPERIMENTAL PRODUCTION OF CARDIOSPASM IN DOGS

"Cardiospasm," as defined by Sturtevant (1), "is the common name for a condition in which, without demonstrable obstructive pathological change, and usually without pain, food does not pass readily from the esophagus into the stomach, but is held in the esophagus, which, in the majority of cases, undergoes dilatation, sometimes extreme." Other terms more or less synonymous are achalasia, oesophagectasia, oesophageal dilatation without stricture, phrenospasm, megaesophagus, and preventriculosis. An early description of the disorder to which Major has called attention occurs in the *Pharmaceutice rationalis* published by Thomas Willis in 1672. "No less will a very rare case of a certain man of Oxford show an almost perpetual vomiting to be stirred up by the shutting off of the left orifice. A strong man, and otherwise healthful enough, labouring for a long time with often vomiting, he was wont, very often, though not always, presently to cast up whatsoever he had eaten. At length the disease having overcome all remedies, he was brought into that condition, that growing hungry he would eat until the esophagus filled up to the throat, in the meantime nothing sliding down into the ventricle, he cast up raw (or crude) whatsoever he had taken in; when that no medicine could help and he

languished away for hunger, and every day was in danger of death, I prepared an instrument for him like a rod, of a whale bone, with a little round button of sponge fixed to the top of it; the sick man having taken down meat and drink into his throat, presently putting this down in the esophagus, he did thrust down in the ventricle, its orifice being opened, the food which otherwise would have come back again; and by this means he hath daily taken his substance for fifteen years and doth use yet the same machine, and is yet alive and well who would otherwise perish for want of food. Without doubt in this case the mouth of the stomach being always closed, either by a tumor or palsie, nothing could be admitted into the ventricle unless it were violently opened."

Since the time of Willis, instances of this condition have been reported in increasing numbers. Purton (2) described one case in 1821, Rokitsanski (3) reported three in 1840, Zenker and von Ziemssen (4) analyzed 17 cases in 1878, Geppert (5) referred to 140 in 1900, von Mikulicz (6) referred to 100 cases in 1904, and Plummer and Vinson (7) reported 301 cases from the Mayo clinic in 1921.

While the disease is being diagnosed with increasing frequency, its pathogenesis is not yet established. Necropsy findings have pointed toward a neurogenic origin of the disorder. Heyrovsky (8) noted vagus neuritis in some cases of cardiospasm. Loeper and Forestier (9) cited ascending invasion of the vagus by tumor cells as a possible cause. A loss of ganglion cells from the myenteric plexus has been described by Hurst and Rake (10), Stokes (11), Cameron (12), Beattie (13), Mosher and McGregor (14), Lendrum (15), and Hara (16). Hurst (17) has been eager to advance the concept that there is no true spasm, but rather an

achalasia or failure of normal relaxation at the cardia.

Animal experimentation sheds further light on the problem. In 1907 Cannon (18) noted that cats bilaterally vagotomized suffered from esophageal obstruction in some cases lasting for several days and in others persisting indefinitely. Of the latter he remarks, "The esophagus in these cases suffered a marked dilatation and became filled with food which fermented." Cannon and Lieb (19) in 1912 reported receptive relaxation of the cardia in response to a swallowed bolus. They observed that the cardiac end of the stomach began to relax before a peristaltic wave in the esophagus had time to reach the stomach. They concluded that the relaxation is controlled reflexly by the vagus, since bilateral vagotomy in the neck abolished the reflex. Knight (20), using cats, was able to reproduce the X-ray appearance of achlasia of the cardiac sphincter by complete bilateral vagotomy in the thorax. Zeller and Burget (21), using the balloon method of studying the effects of various nerve lesions on the cardia of unesthetized dogs, subjected nine dogs to bilateral vagotomy in the thorax and in none of these dogs did they observe loss of tonus or failure of relaxation in the cardia. In explanation they state: "Either section of the vagi in the thorax leaves connection along the esophageal wall with the vagus above the section that is effective in carrying out the reflex (long vagus fibers), or the dog has a myenteric plexus in the esophagus with which the vagus above the section makes contact and by which it relays impulses to the cardia." It would seem possible that the remaining pathways which these authors postulate could be interrupted by an operation which would

encircle the esophagus above the diaphragm and cut through all external layers down to the submucosa. It is the purpose of this paper to explain how that problem was attacked and to discuss the results obtained.

Since anesthetics might interfere with the reflexes under study, a modification of the method outlined by Burget and Zeller (22) for recording motility in unanesthetized dogs was used. To facilitate the passage of tubes down the esophagus without evoking the gag reflex the dogs were subjected to preliminary esophagostomy. Under aseptic conditions, using nembutal anesthesia, a midline incision was made below the cricoid cartilage, the ribbon muscles were separated in the midline, and the esophagus was brought to the exterior. A five centimeter incision was made along the outer layer of the esophagus and this layer was sutured to the subcutaneous fascia. An incision almost as long was made through the underlying esophageal muscle and it was also sutured to the subcutaneous fascia. Finally the lumen of the esophagus was entered by the last incision and the mucosa was sutured to the skin. The animals suffer little inconvenience from this operation, and lose surprisingly little food through the opening. These dogs do not regurgitate food.

A few days after the esophagostomy was performed the training of the dogs was begun. They became accustomed to lying quietly on a table while balloons were passed into the esophagus and motility records were made. A balloon 5 cm. long filled with soft sponge rubber to a diameter of 12 mm. was attached to a F18 soft rubber

catheter and passed down the esophagus until it met the moderate resistance of the cardia. A mark was made on the catheter where it emerged from the esophageal opening, and the balloon was kept in that position. A second rubber balloon about 4 cm. long was attached to a F9 soft rubber catheter and passed down the esophagus to lie about 5 cm. above the first. A third balloon of similar size and also attached to a F9 soft rubber catheter was made to lie about 5 cm. above the second. The lower two balloons were connected to sensitive Becker tambours. The uppermost, or stimulating, balloon was connected by a T tube with a rubber bulb used for distension and to a mercury manometer for recording pressures used. Records obtained after simple esophagostomy show that moderate distension of the uppermost balloon results in an almost immediate relaxation in the region of the cardia, which relaxation precedes the interception of a peristaltic wave by the middle balloon.

When the dogs were well trained the interruption of nerve pathways in the thorax was undertaken. Under aseptic conditions, with nembutal anesthesia, and artificial respiration by tracheal cannula, the chest was entered on the left side--usually a section of the sixth or seventh rib was removed--both vagi and the communicating branch were sectioned about 4 cm. above the diaphragm, and the outer coats of the esophagus were cut along its entire circumference at this level, laying bare a band of white submucosa 1 cm. wide. In five dogs this procedure was varied by doing the operation in two stages, first girdling the esophagus and noting the effect on cardiac relaxation, and then entering the chest a few weeks later to cut the vagi. In one dog the denuded submucosa was painted with cotton pads soaked in liquified

phenol. The phenol was sponged off with alcohol followed by water a minute later.

After the nerve pathways were interrupted the dogs were observed to determine whether or not they had difficulty in swallowing food, and repeated motility studies were made to detect receptive relaxation to the cardia. Among the results obtained it should be noted that in the studies made upon the five dogs after circling the esophagus without cutting the vagi there was no evidence of difficulty in swallowing, and receptive relaxation was in no way interfered with.

The twelve dogs may be divided into four groups on the basis of the results obtained after the vagi were cut and the esophagus was girdled. In the first group were five dogs showing no evidence of receptive relaxation of the cardia and manifesting extreme difficulty in swallowing. Any one of these dogs, given half a can of food, would bolt it down, immediately begin to strain and stretch his neck, make swallowing movements, and soon return practically all of the food as a mucus coated, sausage shaped mass. The regurgitated food would not change the color of blue litmus paper. The dog would persist in his efforts to down the food, and might by dozens of attempts gradually dispose of half a can of food within ten minutes. All of the dogs of the first group showed marked loss of weight in the course of the experiment.

The second group includes three dogs that regurgitated food like the first group, but, unlike the first group, these dogs sometimes showed receptive relaxation of the cardia. Two of the dogs only rarely exhibited relaxation in the course of dozens of recordings, and

then the relaxation was slight and in response to strong stimulation. The third dog showed post-operative relaxation indistinguishable from that recorded before the operation, which is more difficult to explain in view of the fact that he suffered a marked loss of weight.

The third group consisted of two dogs that experienced great difficulty in swallowing, but would not lie still so that satisfactory motility studies could be made post-operatively. One of these dogs had been hard to train for his normal tracings, while the other was unique in that following the operation he would set up an uncontrollable howling as soon as he was placed on the table. The latter, by the way, was the dog whose submucosa had been daubed with liquified phenol. None of the dogs had more trouble swallowing than did these two, and both of them suffered a rapid loss of weight.

In the fourth group were two dogs who died of perforation or rupture of the esophagus within three days of the second operation.

Post mortem examination of the dogs in group four showed nothing but esophageal rupture and mediastinitis. One of the dogs in group one died on the thirteenth post-operative day, and was found to have hemorrhages into the stomach and small intestine. In this dog and in other dogs sacrificed at intervals of from thirty-four to eighty-four days post-operatively the esophagus showed no signs of inflammation, dilatation, or constriction. Neither of the dogs in group three showed an esophagitis to account for their apparent distress. It was possible in every case to pass one or two fingers through the cardiac orifice of the stomach. The absence of esophageal dilatation might be due to the relatively short duration of the experi-

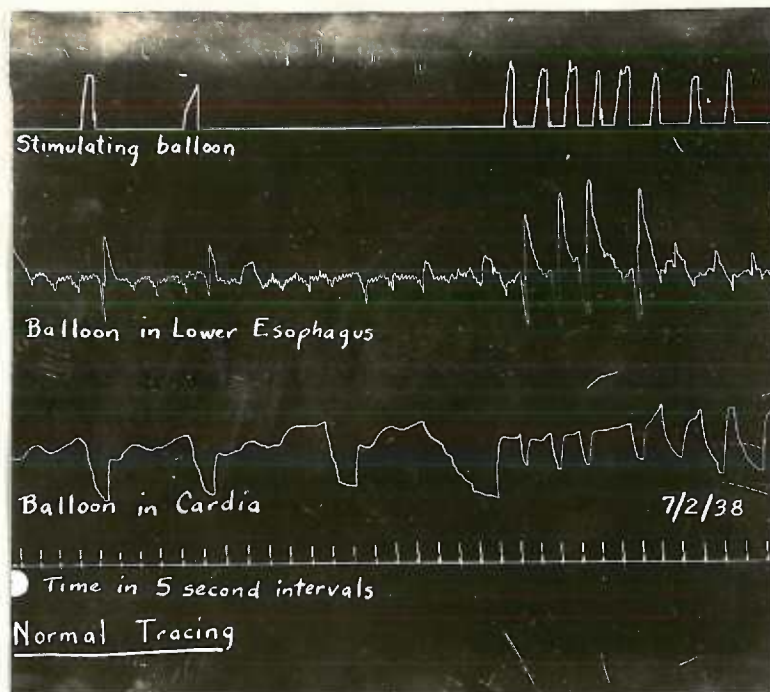
mentally produced disorder in these animals.

In summary it may be stated that a method is described by which the clinical picture of acute cardiospasm is reproduced in dogs. In the majority of cases the regurgitation of food can be shown to be accompanied by a failure of receptive relaxation at the cardiac orifice of the stomach. Since neither bilateral vagotomy in the thorax as performed by Zeller and Burget nor girdling the esophagus above the diaphragm is sufficient in itself to produce these results, it may be inferred that some but not all of the fibers responsible for receptive relaxation of the cardia course downward within the muscle coats of the dog's esophagus.

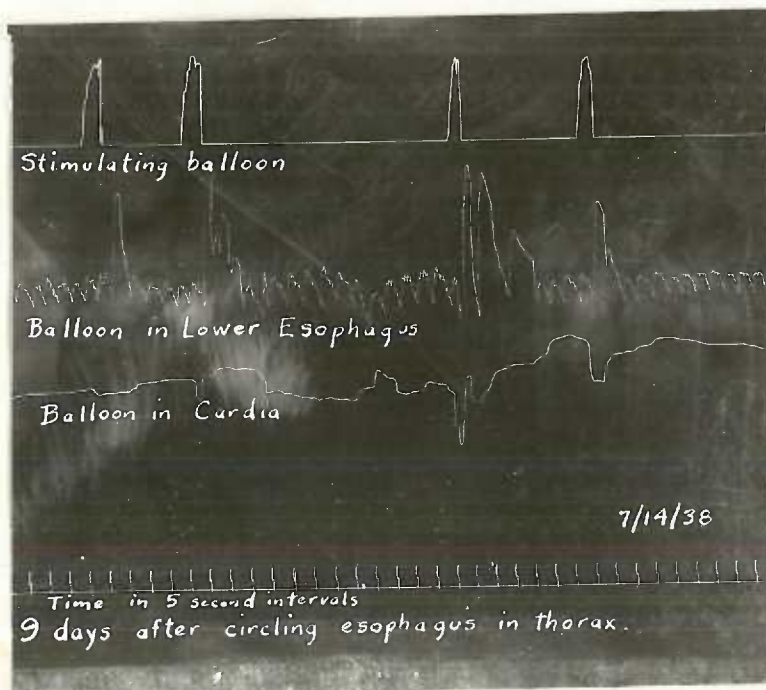
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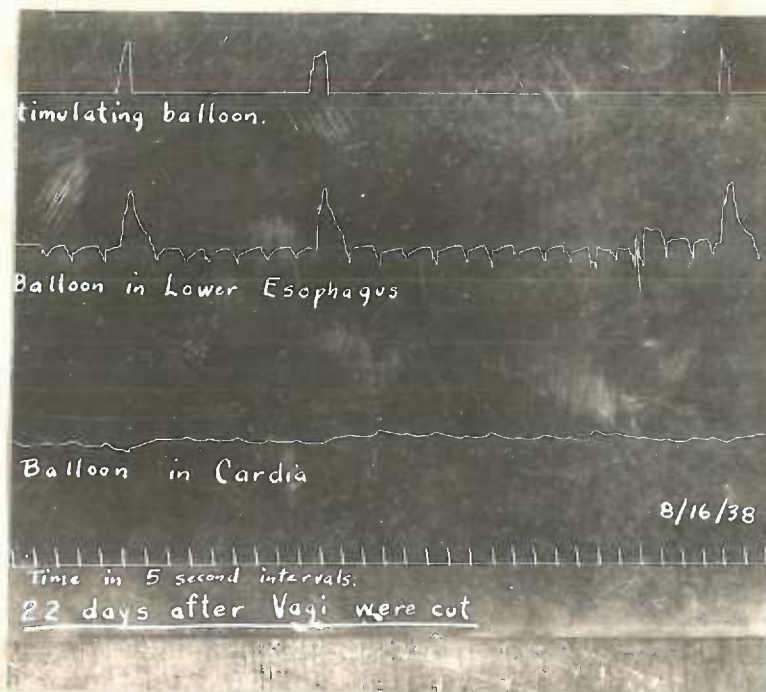
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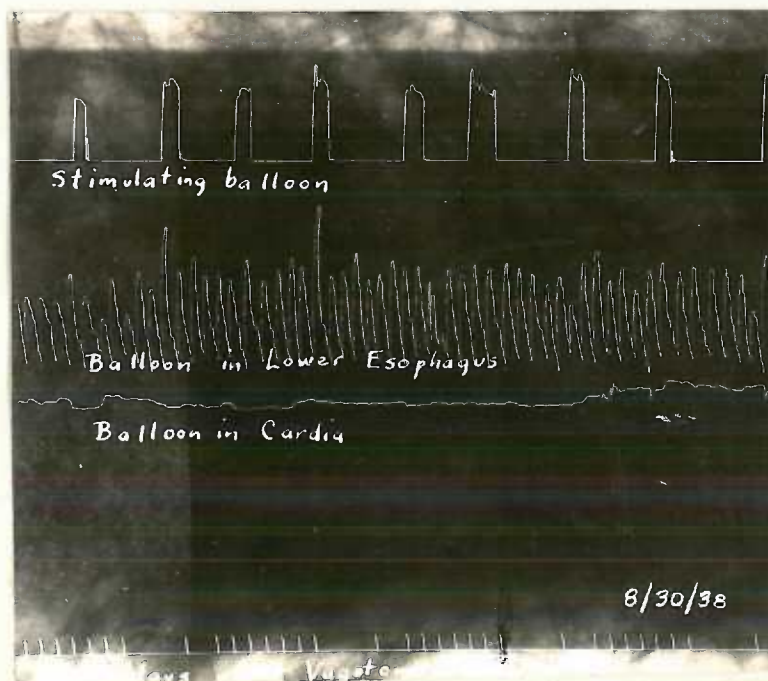
Record showing receptive relaxation of the cardia
in the normal dog.



Record showing receptive relaxation after circling
the esophagus with vagi left intact.



Record showing absence of receptive relaxation
in dog with esophagus circled and vagi cut.



Record showing absence of receptive relaxation
36 days after operation.

AN ABSTRACT OF THE THESIS OF

Jack W. Grondahl for the degree of Master of Science in Physiology.

Date of receiving this degree: June 4, 1939

Title: The Experimental Production of Cardiospasm in Dogs.

Approved: _____

N. F. Harvey

Cardiospasm may be defined as a condition in which, in the absence of anatomic obstruction, food does not pass readily into the stomach. An early clinical description is that given by Thomas Willis in 1672. The disorder is being diagnosed with increasing frequency, but the pathogenesis is not yet established. Necropsy findings suggest a neurogenic basis for the disease. Inflammatory and generative changes have been found in the vagi, and many investigators report a diminution in the number of ganglion cells in the myenteric plexus of the lower esophagus.

Turning to animal experimentation, Cannon has noted that the cardiac orifice of the stomach normally relaxes in anticipation of the propulsion of a bolus of food down the esophagus. This receptive relaxation is abolished in cats by cutting the vagi in the neck. Knight has also abolished relaxation of the cardia in cats by complete bilateral vagotomy in the thorax, reproducing the X-ray appearance of cardiospasm in these animals. Zeller and Burget performed bilateral thoracic vagotomy in nine dogs, but subsequent motility studies by the balloon method failed to show loss of tonus or of receptive relaxation in the cardia. They suggested that other nerve pathways might exist in the esophageal wall. The present study is directed toward investigating that possibility.

In twelve dogs the vagi were cut in the thorax and an encirclement of the esophagus was performed 4 cm. above the diaphragm. In this operation the serosal and muscular coats were cut through in the entire circumference of the esophagus and a 1 cm. band of submucosa was laid bare. Balloon studies of motility recorded after the encircling operation without vagotomy showed that by itself this did not interfere with receptive relaxation at the cardia, and produced no obstruction to the passage of food into the stomach. Results after combined girdling of the esophagus and section of the vagi were as follows:

Group I	5 dogs.	Regurgitation of food. No receptive relaxation.
Group II	3 dogs.	Regurgitation of food. Relaxation rarely exhibited.
Group III	2 dogs.	Regurgitation. Too restless for satisfactory motility studies.
Group IV	2 dogs.	Died of esophageal rupture within three days of operation.

In summary it may be stated that an operation is described by which the clinical picture of cardiospasm is reproduced in dogs. In the majority of cases the regurgitation of food can be shown to be accompanied by a failure of receptive relaxation at the cardiac orifice of the stomach. Since neither bilateral vagotomy in the thorax nor girdling the esophagus above the diaphragm is sufficient in itself to produce those results, it may be inferred that some, but not all, of the fibers responsible for receptive relaxation of the cardia course downward within the muscle coats of the dog's lower esophagus.