

III-D and Table III-E showed similar precipitation zone indicating that the removal of normal tissue antibodies did not remove the antibodies necessary to precipitate the common antigen or antigens found in mouse mammary cancer and normal mammary gland tissues containing the agent.

Summary. The data presented in this report describe a precipitin test for mouse tissues containing the milk agent. Antiserum produced in rabbits against mouse mammary cancer reacts in high titre with tissues containing the cancer agent and in low titre with tissues lacking the agent. Antiserum prepared against normal mammary gland tissues abundant with milk agent will precipitate mam-

mary cancer antigen in high serum dilutions. Antiserum prepared against normal mammary gland tissues lacking the agent will precipitate mammary cancer antigen in low serum dilutions. Precipitin-adsorption reactions show that the removal of antibodies against mammary gland tissues without the agent in mouse mammary cancer antiserum will not remove antibodies which react with the common antigen or antigens found in mouse mammary cancer and mouse mammary gland tissues containing the milk agent.

The authors are indebted to Dr. J. J. Bittner of the University of Minnesota for generously supplying the mice and advising as to the strains of mice that should be used in this investigation.

16424

The Effect of Phrenicotomy on Gastrointestinal Mechanisms.*

NELSON C. JEFFERSON AND H. NECHELES.

From the Department of Gastro-Intestinal Research, Medical Research Institute of Michael Reese Hospital and the Department of Surgery, Provident Hospital, Chicago, Ill.

A number of observations point to a functional relationship between left diaphragm and stomach. Sauerbruch¹ has described a gastro-cardiac symptom complex after exeresis of the left phrenic nerve, consisting of cardiovascular and gastro-intestinal disturbances, caused by changes in the gastro-intestinal tract. One factor was considered to be the pressure exerted by the stomach on the left cup of the diaphragm, resulting in displacement of the heart and large vessels. Bradycardia and premature systoles were ascribed to vagal stimulation, but occasionally, tachycardia and vertigo were observed. Frequently anxiety, epigastric distress, lack of appetite, pallor, nausea, vomiting and eructations occurred,² which were relieved by removing the subdiaphragmatic accumulation of air.³ The

latter did not seem to be due so much to swallowing of air, as to inability to belch it up. This symptom complex has been named "Roemheld's Syndrome."

Joannides³ found that he could induce prompt contractions of the stomach by having the patient take deep breaths. This he ascribed to be due in part to the intermittent increase and decrease of intragastric pressure, induced by the contractions of the diaphragm. Joannides stated that cardiospasm may be an exaggeration of the normal contractions of the diaphragmatic pillars, and that partial contraction and relaxation of the diaphragm plays a role in belching.

Rickers⁴ reported 2 cases of left side phrenic exeresis for tuberculosis, which developed the gastro-cardiac symptom complex.

* Aided by a grant from the Isaac and Kate Meyer Fund. The Department is in part supported by the Michael Reese Research Foundation.

¹ Quoted by Roemheld, L., *Munch. Med. Wchnschr.*, 1928, **75**, 1872.

² Noack, R., *Beitr. z. Klin. d. Tuberk.*, 1933, **82**, 397.

³ Joannides, M., *Arch. Int. Med.*, 1929, **44**, 856.

⁴ Rickers, L., *Beitr. z. Klin. d. Tuberk.*, 1933, **83**, 175.

X-ray studies revealed an elevation of the cupula of the diaphragm to the level of the fourth costal cartilage; the stomach extended perpendicularly downward, with a large gas bubble in the fundus. The pylorus was bent acutely to the right. Barium was found in the small intestine immediately after ingestion.

Noack² commented that the gastro-cardiac symptom complex after phrenic exeresis may be due in part to tearing and trauma of sympathetic fibers during the operative procedure. Reactivation of the diaphragm was observed 1½ to 2 years after phrenic exeresis and he assumed that, in addition to the phrenic nerves, the diaphragm was supplied by the 12th dorsal and by sympathetic nerves. In cases of left side phrenic exeresis the intestines were found to be pushed up, and a large gas bubble was seen in the stomach. The stomach was high, vertical, and had a rectangular kink at the pylorus, which was said to explain its rapid emptying. Food appeared to drop into the duodenum without staying in the stomach.

Gavazzeni⁵ studied 2 patients before and after left side phrenic exeresis. Postoperatively, marked hypokinesia and decreased tonus of the stomach and a lack of gastric contractions after rapid respirations were observed. From these observations one could assume a slow rather than a rapid rate of emptying of the stomach.

Belbenoit⁶ stated that complete and permanent cure of the gastro-cardiac symptom complex, if such should follow left side phrenic exeresis, may be obtained by pneumoperitoneum.

The nausea and vomiting present in cases of diaphragmatic hernia were decreased or abolished in a number of instances by left side phrenicotomy.⁷⁻¹¹ This probably has

little to do with the gastro-cardiac symptom complex, and may be due mainly to afferent reflexes from diaphragm and stomach.

It is seen that the reports on left side phrenicotomy in relation to the stomach lack controlled data, and that most of the observations were complicated by such diseases as pulmonary tuberculosis or hiatus hernia. No adequately controlled work in normal human or animals was found.

Experiments. The effect of left side phrenicotomy was studied in the dog. In normal healthy animals, gastric emptying time was estimated according to the technique of Kozoll and Necheles.¹² Dogs, kept on a standard diet, were starved for 24 hours before fluoroscopy. Then they were fed a mixture of one pound of commercial dog food, mixed well with 70 g of barium sulfate and 150 cc water. They were fluoroscoped 15 minutes after feeding and thereafter every hour, until complete emptying of the stomach. Fluoroscopies were done at weekly and bi-weekly intervals. Left side phrenicotomy or vagotomy was performed aseptically under sodium pentobarbital anesthesia by the supradiaphragmatic approach. Following surgery, fluoroscopies were performed at weekly intervals as soon as the animals had recovered (5-6 days).

Results. In 4 dogs, following left side phrenicotomy, gastric emptying time decreased uniformly from an average of 6.3 hours to 4.3 hours. Fluoroscopically, gastric dilatation and hypotonia was observed and, after feeding, a relatively large gas bubble was seen

TABLE I.
Gastric Emptying Time in Hours.

Dog No.	Normal controls		Following left phrenicotomy	
	variation	Avg	variation	Avg
1	8,6	7	4,3,3,2	3
2	6,6,5	5.6	5,4,5,3,6	4.6
3	6,7,7,6,7,7	6.6	6,5,5,5,5,4	5.0
4	5,6,6,6,6,7	6.0	6,3,3,5,5,3	4.1

⁵ Gavazzeni, M., *Il Policlinico* (sezione pratica), 1935, **42**, 1343.

⁶ Belbenoit, S., *La Presse Méd.*, 1945, **53**, 88.

⁷ Eisen, D., *Can. Med. Assn. J.*, 1938, **39**, 207.

⁸ Ohler, W. R., and Ritvo, M., *New Eng. J. Med.*, 1943, **229**, 191.

⁹ Trueman, K. R., *Can. Med. Assn. J.*, 1947, **56**, 149.

¹⁰ Harrington, S. W., *J.A.M.A.*, 1933, **101**, 987.

¹¹ Harrington, S. W., *West J. Surg., Obst., Gyne.*, 1936, **44**, 255.

¹² Kozoll, D. D., and Necheles, H., *Surg.*, 1942, **2**, 360.

regularly in the fundus of the stomach. Yet, the barium emptied rapidly and was puddled in a moderately contracted small intestine. (Table I).

Since phrenicotomy shortened gastric emptying time considerably, its effect on the gastric retention following double vagotomy was tested. In 2 control dogs, following bilateral supradiaphragmatic vagotomy at the level of the hilus, gastric and esophageal atony with marked gaseous distention of stomach and intestine was observed. These dogs had a 24-hour gastric retention for 4 and 5 weeks respectively, during which time they vomited or regurgitated food and frothy mucoid gastric juice frequently, often intermittently, for periods of hours.

In 2 other dogs, following simultaneous bilateral supradiaphragmatic vagotomy and left side phrenicotomy, gastric atony, distention, and a large gas bubble in the gastric fundus were noted. However, no vomiting

occurred, and little or no gas was observed in the stomach or intestine. The stomach appeared sausage shaped. A 24-hour gastric retention persisted for 3 weeks in both dogs. The animals did not appear sick, in contrast to the 2 dogs with vagotomy only. The striking differences between the above 2 groups of animals are demonstrated in Fig. 1 and 2. The x-ray films were taken 6 hours after feeding and 25 days after operation.

Discussion. A gastro-cardiac symptom complex following phrenic exeresis has been described by earlier authors. However, the gastro-intestinal symptoms of this complex, namely eructations, nausea, and vomiting were not noted by us in the dog. The gastro-cardiac symptom complex of phrenic exeresis in the neck may well be due to trauma to and avulsion of sympathetic fibers when the roots of the left phrenic nerve are pulled at or torn.

It has been explained by Noack² that the rapid emptying time following interruption

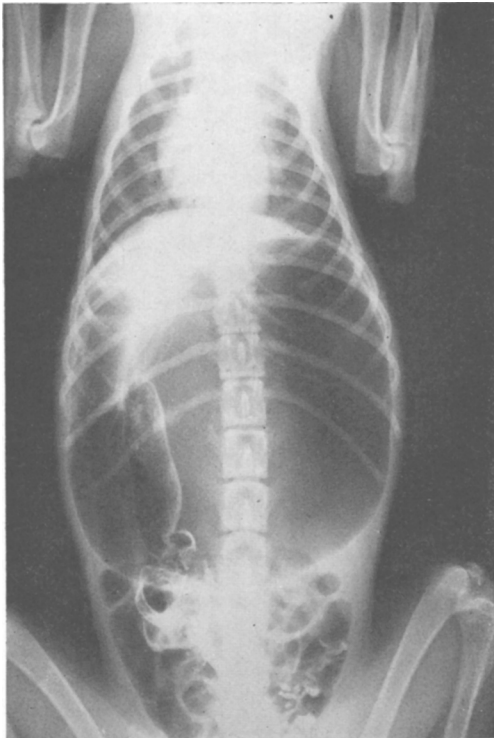


Fig. 1.

Bilateral supradiaphragmatic vagotomy, 25 days after vagotomy, 6 hours after feeding. Anterior-posterior view.

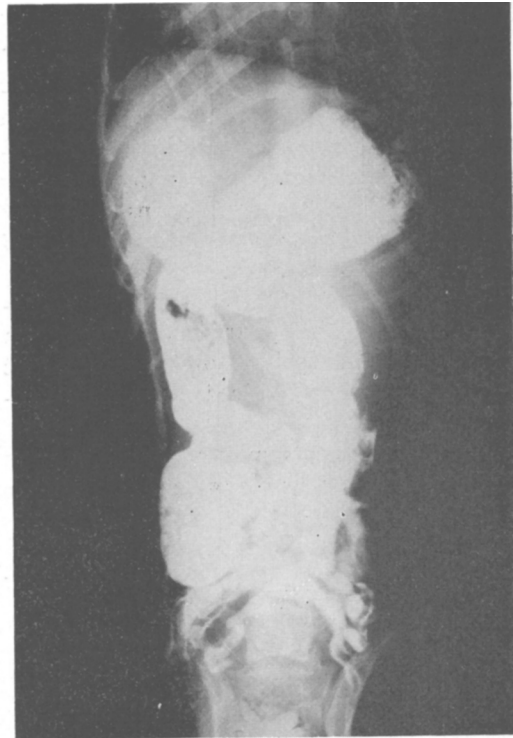


Fig. 2.

Bilateral supradiaphragmatic vagotomy plus left phrenicotomy, 25 days after operation, 6 hours after feeding. Anterior-posterior view.

of the left phrenic nerve may be associated with the mechanical elevation of the stomach, which leads to dumping of the food into the duodenum. Surprisingly, a similar rapidity of gastric emptying is seen in the dog, which does not assume the up-right position of the human. After phrenicotomy the stomach in the dog was ballooned, and hypotonia and hypokinesia were apparent, but there was never any vomiting. The small intestine appeared moderately contracted, with puddling of barium. Although a relatively large gas bubble was present in the fundus of the stomach after phrenicotomy, no or very little gas appeared in the intestine.

Following bilateral supradiaphragmatic vagotomy, there was much gas in the stomach and intestines and severe vomiting of frothy mucoid material was present, and the dogs appeared to be quite ill.

When the left phrenic nerve and both vagi were cut at the same time, there was no vomiting and the animals did not appear to be ill at any time postoperatively.

While left side phrenicotomy, performed in addition to bilateral vagotomy, does not relieve the retention and loss of tone of the stomach which follows bilateral supradiaphragmatic vagotomy only, yet, a number of disturbing complications of vagotomy such as gaseous distention and vomiting were not observed. It is possible that in case of atony of the stomach the pumping action of the left diaphragm forces air into the stomach, which cannot escape through the cardia, and part of which enters the intestine. Achalasia of the cardia may be present following supradia-

phragmatic vagotomy and may be a factor in the retention of air in the stomach. Paralysis of the left diaphragm by phrenicotomy may abolish the pumping of air into the stomach and, by stretching the stomach forward, may facilitate escape of air through the esophagus.

Discrepancies in the clinical reports on gastro-intestinal effects of interruption of the left phrenic nerve may be due in part to the fact that the patients were suffering from advanced tuberculosis of the lungs, possibly also from intestinal tuberculosis. Furthermore, the method of interruption of the phrenic nerve is important, whether it was crushed, cut, or avulsed. In cases of avulsion or exeresis in the neck, sympathetic fibers may have been disturbed, thereby accounting for additional symptoms.

We do not propose left side phrenicotomy in cases of gastric atony and retention, but merely want to bring to attention some of the relations between the diaphragm and the gastro-intestinal system.

Summary. Section of the left phrenic nerve is followed by gastric hypotonia and hypokinesia and the presence of a large gas bubble in the fundus of the stomach. Gastric emptying time is shortened considerably. The barium appears to puddle in a moderately contracted intestine. There were no symptoms observed which could be associated with the so-called gastro-cardiac symptom complex. When phrenicotomy is done simultaneously with vagotomy, the vomiting and the gaseous distention of the gastro-intestinal tract associated with bilateral supradiaphragmatic vagotomy only, are not seen.

16425 P

Relation Between Resting and Action Potential in the Frog Eye.*

VERNER J. WULFF.

From the Department of Zoology and Physiology, University of Illinois, Urbana, Ill.

It has been observed that the magnitude (b-wave) of the action potential elicited from

the excised frog eyeball in response to a light stimulus varies with the magnitude of the resting potential,¹ other conditions remaining

* This investigation was supported by a grant from the Research Board of the University of Illinois.

¹Therman, P. O., *Acta Societatis Fennicae, N.S.B.*, 1938, **2**, No. 1.