

tagged phospholipid from the blood stream and the plasma lipid phosphorus level, the rate of utilization of phospholipid was calculated. It was observed in both normal and diabetic groups that the rate of utilization was roughly proportional to the plasma lipid phosphorus concentration. The absolute utilization of plasma phospholipid was slightly lower in the

diabetic group, but the proportion of plasma phospholipid utilized per hour was significantly higher in this group. Administration of insulin and sugar to diabetic dogs caused no significant change. Administration of raw pancreas to diabetic dogs increased the absolute utilization very markedly and the proportion utilized per hour only slightly.

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Effect of Celiac Ganglionectomy upon Experimental Peptic Ulcer Formation.*

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In a recent report,¹ we have investigated the effect on the gastrointestinal tract of complete excision of the celiac, superior, and inferior mesenteric ganglia. Extirpation of these ganglia removes essentially the postganglionic sympathetic fibers to the gastrointestinal tract from the stomach through the colon and results in a severe bloody diarrhea associated with typical appearing peptic ulcers in somewhat less than 50% of the dogs. These ulcers are located for the most part in the stomach or duodenum, but occasionally as far down as the terminal ileum or colon. Likewise, these ulcers often progress to hemorrhage or perforation. The question has been raised by ourselves as well as others as to whether these ulcers are an effect of the removal of the postganglionic sympathetic innervation or whether they develop as the consequence of a state of protein deficiency and emaciation which several investigators^{2,3} have shown to be often

associated with peptic ulcer in dogs.

This investigation was undertaken to appraise what specific effects, if any, complete excision of the postganglionic sympathetic innervation to the stomach and duodenum has upon susceptibility to gastroduodenal ulceration.

Experiment. Male and female dogs of medium size, previously dewormed and between the ages of 1½ to 5 years were used in these experiments. The animals were divided into 3 series as follows: Series I, dogs in which complete excision of the celiac ganglia was performed leaving undisturbed the vagi nerves and the superior and inferior mesenteric ganglia. This operation removes the postganglionic sympathetic innervation of the stomach, duodenum, and also that of the liver, spleen, and pancreas as well. Series II, consists of dogs in which in addition to complete excision of the celiac ganglia, the superior mesenteric ganglia were removed also. This operation removes the postganglionic sympathetic fibers to the stomach, duodenum, and small intestine. Series III consists of a control series of normal dogs of comparable age and size.

Operative procedure. For ganglionectomy intravenous nembutal anesthesia was used, sterile technic, and a midline abdominal in-

* Supported by a grant from the Surgical Study Section of the United States Public Health Service, the John and Mary R. Markle Foundation, and the Graduate School of the University of Minnesota.

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¹ Lillehei, C. W., Dixon, J. L., Friesen, S. R., and Wangenstein, O. H., *Proc. Soc. Exp. Biol. and Med.*, 1948, **68**.

² Weech, A. A., and Paige, B. H., *Am. J. Path.*, 1937, **13**, 249.

³ Keller, A. D., *Arch. Path.*, 1936, **21**, 127.

TABLE I.
Ulcer Production Following Celiac Ganglionectomy.
(30 mg histamine-base in beeswax intramuscularly daily.)

Dog No.	Wt, lb	Days postop. before hist. injections	No. of hist. inj.	Results
1	22	3	3	Died, perforated duodenal ulcers
2	32	3	2	Died, perforated duodenal ulcers, gastric ulcers
3	32	6	5	Died, perforated duodenal ulcer
4	27	41	5	Sacrificed, large gastric ulcer
5	27	45	5	Sacrificed, antral and duodenal ulcer
6	33	58	4	Sacrificed, moribund, 3 duodenal ulcers
7	38	64	3	Died, gastric ulcer, perforated duodenal ulcers
8	28½	108	5	Sacrificed, perforated duodenal ulcer, antral hemorrhages
9	46	165	5	Sacrificed, duodenal ulcers, antral hemorrhages
10	31	167	5	Sacrificed, multiple penetrating duodenal ulcers, antral hemorrhages
11	29½	181	5	Died, perforated duodenal ulcers
12	36	499	5	Sacrificed, penetrating duodenal ulcer, antral erosions
No. of dogs injected				12
No. of dogs with ulcer				12
No. of dogs with perforated ulcer				6

TABLE II.
Ulcer Production Following Celiac and Superior Mesenteric Ganglionectomy.
(30 mg histamine-base in beeswax intramuscularly daily.)

Dog No.	Wt, lb	Days postop. before hist. injections	No. of hist. inj.	Results
13	25	21	2	Died, multiple gastric erosions, severe esophageal ulceration
14	36	127	1	Died, perforated esophageal ulcers, erosion of mediastinal structures by gastric juice
15	34	210	4	Died, large (3 x 2 cm) perforated duodenal ulcer
No. of dogs injected				3
No. of dogs with ulcer				3
No. of dogs with perforated ulcer				2

cision. Upon entering the abdomen the stomach was retracted to the far right, exposing the celiac axis. The left semilunar ganglion may then be seen through the peritoneum and palpated as a firm flat button about ½ cm in diameter lying between the celiac artery and the left adrenal. The right semilunar ganglion lies deeper between the celiac artery and the vena cava. The removal of just the right and left semilunar ganglia fails to insure a complete deprivation of the sympathetic innervation to the stomach and duodenum. This observation is based on the fact that microscopic examination of serial sections along the celiac axis in such animals after a simple removal of the semilunar ganglia shows an abundance of ganglion cells remaining in smaller or larger groups along the vessel

wall. However, if the heavy bundles of nerve fibers which form a sheath around the celiac, hepatic, left gastric, and splenic arteries are removed in addition to the semilunar ganglia a much more complete sympathectomy is achieved. Therefore, in performing celiac ganglionectomy on these dogs we have followed this latter procedure of dissecting free and removing the ganglia and the heavy bundles of ensheathing nerve fibers from the celiac, splenic, hepatic, and left gastric arteries from the aorta to a point 7 to 8 cm distally. The ganglia and these nerve fibers are then removed in one piece leaving the vessel walls entirely clean. The same procedure was applied to the superior mesenteric artery in those dogs in which the superior mesenteric ganglia were removed.

TABLE III.
Production of Ulcer in Normal Dogs.
(30 mg histamine-base in beeswax daily.)
Control Series.

No. of dogs	No. histamine injections	No. dogs with	
		Ulcer	Erosion
21	5	2*	1

* No perforations.

Method of study. In the operated animals, a period following surgery varying from 3 days to 16½ months as indicated in Tables I and II was allowed to elapse before the daily injections of histamine-in-beeswax were begun as a stimulus to ulcer formation. The technic of preparing the histamine-in-beeswax mixture has been described in detail elsewhere.⁴ Histamine injections were not instituted on any animals that appeared sick. All animals in Series I, II, and III were given not more than 5 consecutive daily intramuscular injections of 30 mg of histamine-base-in-wax. Those animals not succumbing to ulcer formation beforehand were sacrificed for autopsy by the administration of nembutal 18 hours after their fifth histamine injection. Obviously moribund animals were sacrificed earlier in order to obtain fresh autopsy specimens.

All dogs were fed the same stock diet consisting of 300 g of dry dog biscuit,[†] 250 cc of pasteurized milk, and 200 g of fresh horse meat daily at 9:30 A.M. The daily histamine injections were given at 4:00 P.M. and at that time the feed pans were removed from the cages and the dog's food intake for the day recorded. The histamine-in-beeswax is prepared fresh once each week, and each batch is tested before use for potency by its effect on the gastric secretion of a pouch dog. By observance of these conditions and the use of dogs of the same relative age,⁵ ulcer production by this method will be found to be consistent, so that in a group of healthy normal

dogs of medium size and age, typical peptic ulcers will develop in an average period of 23 days⁴ and likewise most normal animals will not show gastroduodenal ulceration after just 5 consecutive histamine injections.

Results. A. Celiac Ganglionectomy. There is a certain immediate mortality related to the operative procedure essentially from hemorrhage. However, dogs surviving the operation recover quickly and without special care. These dogs are able to eat the regular stock diet beginning the first postoperative day and do not manifest any gastrointestinal disturbances such as vomiting or diarrhea. The stools are normal in character and contain no gross blood.

Table I indicates the incidence of gastroduodenal ulceration occurring in this group of dogs with their celiac ganglia removed when histamine-in-wax injections are instituted. Table I is to be compared with the incidence of ulceration in normal dogs (Table III) given a like amount of histamine. The symptoms of a developing ulcer were usually easily recognized and did not differ in the two groups. Such animals, when developing an ulcer, became listless, refused to eat, and often bloody stools or vomitus were observed.

B. Celiac and Superior Mesenteric Ganglionectomy. Following the removal of these ganglia, the dogs invariably exhibit a severe bloody diarrhea only slightly less severe than previously reported¹ for animals with celiac, superior and inferior mesenteric ganglionectomy.

Six animals had celiacectomy with superior mesenteric ganglionectomy. Three of these animals died in the postoperative period as a result of the severe diarrhea, inanition, and pathological changes in the gastrointestinal tract before histamine-in-beeswax injections

⁴ Hay, L. J., Vareo, R. L., Code, C. F., and Wangenstein, O. H., *Surg., Gyn. and Obst.*, 1942, **75**, 170.

[†] Standard Brands, Inc., N.Y.—Vitamin D₂ fortified.

⁵ Lillehei, C. W., and Wangenstein, O. H., *Proc. Soc. Exp. Biol. and Med.*, 1948, **68**, 129.

TABLE IV.
Summary of Pathologic Findings in Dogs Dying After Celiac and Superior Mesenteric Ganglionectomy. (No histamine injections.)

Dog No.	Postoperative Day of death	Wt (lb)		Autopsy findings
		Initial	Final	
16	56	27	11¾	Entire G. I. T. filled with blood from multiple bleeding gastric ulcers and erosions
17	16	31	19	Multiple bleeding erosions in stomach, duodenum, sm. intestine, severe hyperemia of intervening mucosa
18	11	34	24	Hemorrhagic gastritis, duodenitis, and enteritis, pneumonia

were begun. The survival period and autopsy findings for these animals are summarized in Table IV. Likewise, the severe weight losses experienced by these animals are to be noted. The other three animals, subjected to celiac and superior mesenteric ganglionectomy, following recovery from the effects of the operation were given histamine-in-beeswax injections as indicated in Table II. The extreme ulcer susceptibility of this group is evident.

Discussion. The essential physiologic changes occurring within the gastrointestinal tract after postganglionic sympathectomy have been commented on by several investigators. These changes are hypersecretion (Thomsen),⁶ hyperemia (Laignel-Lavastine),⁷ and hypermotility (Koennecke and Meyer;⁸

Lium).⁹ The occurrence of any of these changes would be expected to predispose to ulcer formation. Furthermore, our own studies tend to confirm the physiologic changes noted by other observers after postganglionic sympathectomy of the gastrointestinal tract. The above results would likewise suggest that the postganglionic sympathetic fibers of the gastrointestinal have a mitigating effect upon vagus action under normal conditions.

Moreover, it would not seem premature on the basis of our own studies to suggest that there appears to be a real difference in the physiologic effects of pre- and postganglionic sympathectomy on the gastrointestinal tract.

Conclusion. 1. Postganglionic sympathectomy of the gastrointestinal tract potentiates the susceptibility to the histamine-induced ulcer in dogs. 2. This increased susceptibility to ulcer formation has continued over the longest interval during which a dog was observed, in one instance for 499 days following celiac ganglionectomy.

⁶ Thomsen, E., *Acta Medica Scand.*, 1924-25, **61**, 377.

⁷ Laignel-Lavastine, M., *Recherches Sur Plexus Solaire*, Paris, 1903, Georges Steinheil.

⁸ Koennecke, W., and Meyer, H., *Mitteilungen, Aus den Grenzgebieten der Medizin und Chirurgie*, 1922, **35**, 297.

⁹ Lium, R., *Surgery*, 1941, **9**, 538.