

Effect of Celiac Ganglionectomy and Thoracolumbar Sympathectomy or Adrenal Medullectomy on Histamine Ulcer in Dogs. (17796)

F. JOHN LEWIS AND OWEN H. WANGENSTEEN.

From the Department of Surgery, University of Minnesota Medical School, Minneapolis.

In former reports from these laboratories it has been shown that postganglionic sympathectomy of the upper gastrointestinal tract through excision of the celiac or of the celiac and superior mesenteric ganglia accelerates the production histamine provoked peptic ulcer in dogs(1), and that preganglionic sympathectomy by excision of the thoracolumbar sympathetic trunks does not alter the sensitivity of dogs to histamine ulcer significantly from the normal(2). The present studies have been undertaken to elaborate upon these observations and to clarify if possible the mechanism of accelerated ulcer production following celiac ganglionectomy.

Experiments. The healthy, dewormed, adult, mongrel dogs used in these experiments were divided into 4 groups as follows: Group I, dogs in which the celiac ganglia was removed and both thoracolumbar sympathetic chains were excised. Group II, dogs in which the medulla of the left adrenal was removed and an adrenalectomy was done on the right side. Group III, dogs with the celiac ganglia removed in addition to a left adrenal medullectomy and right adrenalectomy. Group IV was a control series of normal dogs. All of the dogs in these 4 groups were given injections of histamine-base-in-beeswax as a stimulus to ulcer production after a recovery period of at least 30 days following surgical procedures. The histamine-in-beeswax was prepared according to the method of Code and Varco(3) and injected intramuscularly daily in the afternoon in 30 mg doses, after which time the food pans were removed until the following morning. Each new lot of histamine was tested for potency on a Heidenhain pouch preparation.

Operative Procedures. Celiac ganglionectomy was done by carefully stripping the celiac axis of all adjacent tissue from the aorta well out onto its 3 branches, removing both semilunar ganglia and their branches in one segment. Thoracolumbar sympathectomy was done bilaterally in 2 stages. The 12th and 13th ribs were resected and the sympathetic trunk was removed transthoracically and retroperitoneally from the 8th thoracic ganglia through the 2nd lumbar ganglia along with the splanchnic nerves as far as the celiac ganglia. Adrenal medullectomy was done by incising the gland lengthwise with a sharp knife and curetting the medulla while a rubber shod clamp occluded the blood supply, according to the technic of Houssay and Lewis(4). The right adrenal gland was subsequently removed completely after recovery from the first operation. Animals with a celiac ganglionectomy in addition to an adrenal medullectomy had both procedures done at the same time.

Results. The results are summarized in Table I. I. *Celiac ganglionectomy with thoracolumbar sympathectomy.* Of 12 dogs with celiac ganglionectomy alone, reported previously(1), all developed gastric or duodenal ulcer with 5 or less daily injections of histamine-in-beeswax, however when bilateral thoracolumbar sympathectomy was added as in the present study not one of 13 dogs developed ulcers with 5 daily histamine injections. One of 2 dogs that received histamine during longer periods developed a duodenal ulcer, suggesting that no protection is offered by this type of denervation but rather that thoracolumbar sympathectomy acts in some manner to abolish the accelerating effect on the production of histamine ulcers exerted by celiac ganglionectomy alone.

II. *Adrenal medullectomy.* Bilateral removal of the adrenal medulla in Group II re-

1. Lillehei, C. W., and Wangenstein, O. H., *Proc. Soc. Exp. Biol. and Med.*, 1948, v68, 369.

2. Lillehei, C. W., and Wangenstein, O. H., unpublished.

3. Code, C. F., and Varco, R. L., *Proc. Soc. Exp. Biol. and Med.*, 1940, v44, 475.

4. Houssay, B. A., and Lewis, J. T., *Am. J. Physiol.*, 1923, v64, 512.

TABLE I.
Ulcer Production in Dogs.
(30 mg histamine-base-in-beeswax injected intramuscularly daily).

Group	Type of procedure	No. dogs	No. inj.	Erosions only*		Ulcers	
				No.	%	No.	%
I	Celiac ganglionectomy + bilateral thoracolumbar sympathectomy						
	a. Short course of histamine	13	5	2	15	0	0
	b. Long " " "	2	10-45	0	0	1	50
II	Adrenal medullectomy	8	5	2	25	3†	37
III	Celiac ganglionectomy + adrenal medullectomy						
	a. Short course of histamine	9	5	3	33	1	11
	b. Long " " "	2	7-44	0	0	2†	100
IV	Normal dogs	16	5	2	12	4	25

* An erosion is a circumscribed destruction of the mucous membrane limited by the muscularis mucosa while ulcers penetrate deeper into the wall.

† 1 perforated ulcer.

sulted in an incidence of ulcer after 5 daily injections of histamine not significantly different from that found in the normal controls. This is similar to the results described previously(2) in a series of dogs with bilateral thoracolumbar sympathectomy.

III. *Celiac ganglionectomy with bilateral adrenal medullectomy.* Bilateral adrenal medullectomy seems to have a similar effect to that of bilateral thoracolumbar sympathectomy in that it also reduces the ulcer abetting influence of a celiac ganglionectomy alone. Two animals given longer courses of histamine both developed ulcers, showing that no protection against histamine ulcers is afforded by this operation.

Discussion. Stomach emptying time which is decreased by celiac ganglionectomy is also decreased by thoracolumbar sympathectomy or by adrenal medullectomy(5). Combining these operations does not alter the stomach emptying time; it remains faster than normal. We have data on total pouch dogs which indicates that neither celiac ganglionectomy nor thoracolumbar sympathectomy changes the gastric secretory response to histamine from that observed before these nerves were cut(5). It therefore seems improbable that changes in the stomach emptying time or gastric acid

secretory response to histamine could be the main effect produced by thoracolumbar sympathectomy or adrenal medullectomy when added to celiac ganglionectomy. However it might be suggested as an hypothesis that adrenalin sensitivity in the stomach and duodenal blood vessels of the animals with a post-ganglionic denervation(6), that is a celiac ganglionectomy, is a factor in the accelerated rate of histamine ulcer production noted. There is a greatly decreased output of adrenalin with either adrenal medullectomy or adrenal denervation by thoracolumbar sympathectomy(7). Anatomical dissection shows that bilateral thoracolumbar sympathectomy effects a denervation of the adrenal glands not obtained by celiac ganglionectomy alone. These operative procedures, which reduce the adrenalin output, when added to a celiac ganglionectomy would then permit less adrenalin stimulation of the sensitized gastric and duodenal vessels. In a similar manner, as noted by Cannon, Lewis, and Britton(8), the denervated cat heart, which is sensitive to adrenalin, responds to excitement with an in-

6. Hampel, C. W., *Am. J. Physiol.*, 1935, v111, 611.

7. Stewart, G. N., and Rogoff, J. M., *Am. J. Physiol.*, 1919, v48, 397.

8. Cannon, W. B., Lewis, J. T., and Britton, S. W., *Am. J. Physiol.*, 1926, v77, 326.

5. Lewis, F. J., and Wangenstein, O. H., unpublished data.

creased rate until the adrenals and liver have been denervated. It has been shown that adrenalin-in-beeswax increases the susceptibility of normal dogs to histamine provoked ulcer(9). The adrenalin output normally stimulated by histamine administration(10) might then, in the animals with postganglionic denervation and consequent increased sensitivity to adrenalin, be a factor in explaining their increased histamine ulcer susceptibility.

9. Baronofsky, I., and Wagensteen, O. H., *Bull. Am. Coll. Surg.*, 1945, v30, 59.

10. Dale, H. H., *Brit. J. Exp. Path.*, 1920, v1, 103.

This increased histamine ulcer sensitivity is abolished by operations which markedly reduce the output of adrenalin.

None of this work suggests that any of the operations described afford protection against histamine provoked ulcers. Animals given histamine for longer periods up to 45 days developed ulcers just as control animals do.

Conclusion. The potentiating effect of postganglionic sympathectomy, by a celiac ganglionectomy, on histamine induced ulcer in dogs is abolished by a bilateral thoracolumbar sympathectomy or adrenal medullectomy.

Received March 2, 1950. P.S.E.B.M., 1950, v74.

Nutrition of Animal Cells in Tissue Culture. II. Use of Tweens in Synthetic Feeding Mixtures.*† (17797)

HELEN J. MORTON, JOSEPH F. MORGAN, AND RAYMOND C. PARKER.

From the Connaught Medical Research Laboratories, University of Toronto.

A previous communication(1) from this laboratory reported the development of a synthetic feeding mixture, No. 199, that maintained chick embryo mesenchyme cells in a living, healthy state for an average period of 4 to 5 weeks, and kept certain cultures alive for over 70 days. During the course of this work, it was considered desirable to supply the cells with a source of water-soluble fatty acid and to devise a means of dissolving certain fat-soluble compounds in a vehicle other than alcohol. Consequently, an extensive investigation was made of the Tween series of surface active agents,† which have been widely used in bacteriological media(2). The

results of this study are contained in the present report.

Materials and method. All cultures were prepared from the leg muscle of 11-day-old chick embryos; and the cells were grown di-

TABLE I.
Main Distinguishing Features of Basal Synthetic Feeding Mixtures Employed.

Mixture No.	Composition
24B	Amino acids and vitamins as in Mixt. 199(1), but stock solutions of Vit. A and D in 95% ethyl alcohol. Total alcohol in mixt., 0.1%.
199	Amino acids, vitamins, purines, pyrimidines, intermediary metabolites, and other growth factors. Stock solutions of Vit. A and D and cholesterol dissolved in Tween 80 with min. alcohol. Final conc.: .002% Tween and .01% ethyl alcohol.
281	Same as 199, but stock solutions of Vit. A and D and cholesterol prepared in 95% ethyl alcohol (without Tween). Total alcohol, 0.3%.
313	Same as 199, but with ethyl alcohol brought to the level (0.3%) used in Mixt. 281.

* This investigation was supported, in part, by grants from the National Cancer Institute of Canada and the Ontario Cancer Treatment and Research Foundation.

† Grateful acknowledgment is made to Mrs. M. G. Pearce, Mrs. C. J. Porter and Miss O. E. Rockett for technical assistance.

1. Morgan, J. F., Morton, H. J., and Parker, R. C., *Proc. Soc. Exp. Biol. and Med.*, 1950, v73, 1.

‡ Produced by the Atlas Powder Company, Wilmington, Del.

2. Dubos, R. J., and Davis, B. D., *J. Exp. Med.*, 1946, v83, 409.