Failure of Histamine-Beeswax Mixture to Produce Gastrointestinal Lesions in Dogs after Total Gastrectomy.* (18494)

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It has been demonstrated by numerous investigators that ulcers of the stomach, duodenum, and, to a much lesser extent, the remaining portions of the gastro-intestinal tract, occur consistently after the daily or frequent injections of a histamine-beeswax mixture in dogs and other laboratory animals(1). This method has been utilized for the evaluation of various pharmacologic preparations and for the study of surgical alterations of the stomach and duodenum in relation to the etiology and pathogenesis of peptic ulcer. Thus, it has been shown that a three-quarter gastrectomy with a short duodenal loop will prevent the occurrence of histamine-induced ulcers(2). Ulcer formation after histamine-beeswax injections was delayed or prevented by administering sodium lauryl sulfate, a pepsin inhibiting substance, twice daily(3), or by a Sippy dietary regimen(4). That a disturbed motility is not concerned in this type of experimental ulcer production is indicated by reports that neither atropine(5) nor bilateral vagotomy(6) prevent histamine-beeswax ulceration. 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 of these histamine provoked lesions(7), and that preganglionic sympathectomy does not alter the sensitivity of dogs to histamine ulcerations(8). Venous stasis induced by ligation of the splenic and portal veins increases this type of ulcer formation(9), as does chronic arterial spasm induced by epinephrine injections(10), hemoconcentration after severe burns(11), and experimental fatty embolism of the gastro-duodenal arterial system(12).

Most observers believe that peptic ulcer formation is due to excessive peptic acid activity, although the factors of local tissue susceptibility cannot be ignored(13). Recently we have observed(14) varying degrees of ulceration in the intestinal tract of dogs (jejunum, ileum, and colon) following the daily injection of a histamine-beeswax mixture. Perhaps these ulcers should be considered the result of an increase in volume of gastric secretion caused by histamine stimulation with insufficient neutralization (buffering)(15) and subsequent stasis in the small intestine and colon, thus allowing its proteolytic action to continue unchecked. Pos-

* Supported by U.S.P.H. Grant RG-321.

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TABLE I. Necropsy Results After Daily Intramuscular Injections of Histamine-Beeswax in Dogs Following Total Gastrectomy.

Dog No.	Date of oper.	Wt, kg	Date inj. begun	Wt, kg	No. of inj.	Wt at necropsy	Pathological changes				
							Esoph.	Duo.	Jej.	Ileum	Colon
37	12/6	9.8	12/29	7.9	34	7.4	0	0	0	+	0
42	10/31	7.8	12/16	5.9	21	4.5	0	0	+	+	0
46	12/6	7.1	12/29	5.7	34	5.1	0	0	0	0	0
53	1/6	10.7	1/20	9.4	31	5.5	0	0	0	0	0
54	4/19	11.1	5/20	8.3	40	—	0	0	0	0	0
64	1/9	10.2	1/23	8.8	40	9.2	0	+	0	0	0
84	5/25	13.7	6/8	9.9	13	9.7	0	0	0	0	0
110	8/19	11.4	9/18	9.5	40	7.4	0	0	0	0	0

Pathological changes: 0, no change noted; +, slight hyperemia only.

sibly significant are the effects of histamine-beeswax on pancreatic and small intestinal secretions, and its angiotoxic action(16).

Our attempt to clarify the role of gastric juice in the pathogenesis of histamine-beeswax induced gastrointestinal ulcers concerns observations made on 8 healthy mongrel dogs subjected to transthoracic total gastrectomy. Several weeks after operation, depending upon their recovery and their ability to eat and retain food, the dogs were given daily intramuscular injections of histamine-beeswax (2.5 mg of the histamine base per kilogram of animal weight), prepared according to the original description of Code and Varco(17). Injections were administered daily for periods varying from 21 to 40 days. The histamine-beeswax mixture was first tested for its efficacy on total gastric pouch dogs. The animals were maintained on a semi-soft diet of milk, protein supplements, eggnog, and ground meat. They were fed several times during the day. The histamine mixture was injected late in the day and following the injection all food was removed from the animals' cages. The animals were sacrificed at varying intervals after receiving the histamine-beeswax mixture. Complete necropsy was performed with particular scrutiny of the gastro-intestinal tract. The gross observations were supplemented by microscopic examinations. The results are summarized in Table I.

In no instance was any evidence of erosion or ulceration of the esophagus, small intestine, or large intestine present. This supports the contention that ulcerating lesions observed in the small intestine and large intestine of intact dogs after repeated injections of histamine-beeswax are dependent upon the action of gastric juice, and that other possible modes of histamine action are not prominent, if present at all.

Conclusions. 1. Eight dogs were subjected to total transthoracic gastrectomy and following this were given daily intramuscular injections of a histamine-beeswax mixture for periods varying from 21 to 40 days. 2. In no instance did any ulcers of the esophagus, small intestine or large intestine develop. 3. This supports the hypothesis that histamine-induced ulcers of the gastro-intestinal tract of the intact dog are due to the excessive production of gastric juice.

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Received January 17, 1951. P.S.E.B.M., 1951, v76.