Intravenous Histamine and Gastric Pepsin in the Unanesthetized Dog. (25806)

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The effect of histamine on gastric pepsin secretion remains uncertain. Thus, some investigators have concluded that following histamine there is only a "washing-out" of preformed pepsin(1). Others have described a true stimulation similar to that caused by pilocarpine although less potent(2). Still others have mentioned an inhibition of pepsin secretion(3,4). These observations have been made on a variety of animal preparations, including dogs with gastric fistulae or pouches (1), or dogs with vagotomized pouches of the entire stomach(2), or on anesthetized, intubated dogs having intact stomachs(5). To gain more precise information on this subject, we have employed maximal histamine stimulation to the intact canine stomach for a 3-hour period. A quantitative method was used for measuring pepsin.

Methods. Five mongrel dogs (wt. 13-19 kg) were fitted with gastric and duodenal cannulae(6). Gastric content was collected from a rubber tube inserted through the gastric fistula and from a mushroom-type catheter which was pulled against the gastric side of the pylorus and emerged from the duodenal fistula. Histamine diphosphate was infused intravenously at the rate of 1.8 μg of histamine base per kg body weight per minute(7) for 3 hours. Gastric juice was collected every 15 minutes. In the pre-infusion columns of Tables I and II, only those 15 minute samples in which free acid was present were included in "number of samples." Free and total acidity were measured by microtitration(8). Peptic activity was determined by a hemoglobin substrate method(9) and by a turbidimetric method(10). Because the low concentrations of pepsin caused the color value to be present in the unreliable portion of Anson's curve(9), we digested the hemoglobin substrate† (11,12) with known quantities of crystalline pepsin,‡ and compared the color value of the unknown gastric juice samples with these. The apparent linear relation between small amounts of a particular sample of crystalline pepsin and color value of the digested filtrate may be seen in Fig. 1. After completion of the animal experiments 2 more samples of crystalline pepsin were obtained from the same company. They gave the same linear relation, but the slopes of the lines were $\hat{Y} = 11X$ and $\hat{Y} = 15X$ rather than $\hat{Y} = 16X$.

Results. Peptic activity as determined by the Riggs and Stadie method (Table II) decreased from the level of the first half-hour of infusion to less than one-third of this activity in the third hour. There were significant differences between velocity constants in the first half-hour and the second half-hour ($p<.01$)

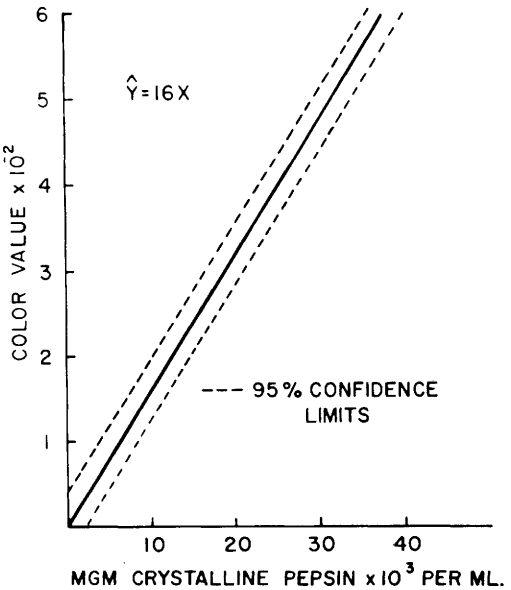

FIG. 1. Relation between pepsin and optical density of digested hemoglobin filtrate.

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† Worthington Biochem. Corp.

‡ Nutritional Biochemicals Corp.

TABLE I. Volume and Acid Response of Gastric Juice in Dogs to Maximal Histamine Stimulation.

	Pre-infusion	First half hr	Second half hr	Second hr	Third hr	Post-infusion
Volume, ml/15 min.	8 ± 5.5* (42)†	31 ±17.3 (21)	46 ±12.6 (22)	48 ±11.4 (44)	40 ±11.6 (44)	14 ± 8.2 (9)
Free acid conc., meq/l	29 ±29.4 (31)	85 ±34.4 (26)	121 ±20.5 (28)	130 ±13.2 (56)	131 ±11.9 (54)	113 ±17.5 (7)
Total acid conc., meq/l	53 ±33.5 (25)	109 ±54.5 (20)	135 ±30.4 (20)	146 ±23.2 (40)	141 ±13.3 (40)	127 ±12.5 (6)
Free acid output, meq/15 min.	.41 ± .32 (22)	2.62 ± 2.02 (22)	5.76 ± 2.05 (24)	6.19 ± 1.60 (45)	5.16 ± 1.38 (44)	1.77 ± .59 (7)
Total acid output, meq/15 min.	.49 ± .31 (23)	3.42 ± 2.47 (22)	6.77 ± 2.59 (23)	6.95 ± 1.64 (45)	5.59 ± 1.51 (44)	2.01 ± .82 (7)

* Stand. dev. † No. of samples.

TABLE II. Gastric Pepsin Response in Dogs to Maximal Histamine Stimulation.

	Pre-infusion	First half hr	Second half hr	Second hr	Third hr	Post-infusion
Velocity constant ("K" $\times 10^2$)		8.2 ± 3.41 (10)	4.0 ± 1.52 (12)	2.9 ± .93 (24)	2.4 ± .97 (22)	2.0 ± .45 (3)
Pepsin conc. (mg crystalline pepsin $\times 10^{-2}$/ml)	57 ± 50 (9)	21 ± 22 (10)	5 ± 3 (10)	3 ± 4 (20)	3 ±4 (20)	5 ±8 (3)
Pepsin output (mg crystalline pepsin $\times 10^{-2}$/15 min.)	131 ± 84 (9)	227 ±175 (10)	103 ±51 (10)	53 ±23 (20)	35 ±9 (20)	14 ±8 (3)

and also between those of the second half-hour and the second hour of infusion ($p<.01$). Pepsin concentration, as determined by the quantitative method of Anson, also showed a progressive decrease from pre-infusion levels throughout experiment. Concentration in the first half-hour was noticeably less than pre-infusion concentration ($p<.02$), output of pepsin in the second hour was less than pre-infusion output ($p<.01$), and output in the third hour was less than that in the second hour ($p<.01$).

Summary. Output of hydrochloric acid rose to 5.2-6.2 meq/15 minutes after second hour of a 3 hour intravenous infusion of histamine. Pepsin output, on the other hand, fell from output equivalent to 227 x 10^{-2} mg crystalline pepsin/15 minutes in the first 30 minutes to 35 x 10^{-2} mg crystalline pepsin/15 minutes in the third hour. The high output during the first half-hour supports the "washout" hypothesis of Babkin(1), while the continued presence of pepsin after 3 hours could be the result of a "basal" rate of pepsin discharge or a true histamine-stimulated secretion.

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