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Relationship of K^+ to H^+ in Histamine-Stimulated Canine Gastric Juice.* (28621)

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A constant relationship between potassium ion (K^+) and hydrogen ion (H^+) in histamine-stimulated gastric juice has been noted by some observers(1) but denied by others (2,3). This investigation presents evidence from canine Heidenhain pouch juice which indicates that such a relationship exists.

Methods. Vagally denervated Heidenhain pouches were prepared in 8 mongrel dogs weighing between 10 and 16 kg. A nylon cannula served to connect the pouch to the exterior. Dogs were on regular kennel ration, and were fasted 20 hours before study. Half of the experiments were carried out on conscious dogs lying quietly on the table. In the other half, where intravenous infusions were required, light Nembutal anesthesia was used. Results were the same in the 2 groups.

The experimental procedure was as follows: The pouch was evacuated at timed intervals (10 to 20 minutes) by gentle aspiration with a 2-inch length of thin-walled, collapsible rubber tubing connected to a one-inch narrow bore glass adapter, and a 10 ml syringe. The aspirate was placed in a 15 ml graduated centrifuge tube. Four ml of distilled water were then drawn into the same syringe, instilled into the pouch and immediately withdrawn and added to the centrifuge tube. Two ml of air were next injected into the pouch and withdrawn along with the fluid remaining in the cannula. The opening was closed by flattening and clamping the rubber tubing close to the cannula.

Pouch secretion was stimulated either by subcutaneous injections of 0.5 or 1 mg histamine phosphate, singly, or intermittently every 10 minutes, or by intravenous injection of histamine phosphate in 5% glucose at a rate between 2.6 and 4.9 $\mu\text{g/kg/min}$.

The volume of the juice plus the wash was measured in the graduated tube and the volume of juice determined by deducting the volume of the wash from the total.

Na^+ and K^+ were measured on the Beckman DU flame photometer; Cl^- was measured by the Schales method(4), and acid by titration to pH 7 with 0.01 N NaOH using phenol red indicator.

Results. Fig. 1a summarizes the typical pattern of electrolyte secretion in an experiment in which 2 injections of histamine were given sequentially, the pouch being allowed to return to base line secretion rate before the second injection. After each injection, the Na^+ and K^+ , then the Cl^- , H^+ and volume had peak outputs. Fig. 1b is a plot of the K^+ against H^+ output showing that whereas points fell above the line in periods 1 and 2 after the first injection, and in periods 1, 2 and 3 after the second injection, all subsequent points after both injections fell on the same line.

In 6 experiments the pouch was stimulated continuously (see methods). Fig. 2 and 3 show the relation of the K^+ to the H^+ output in 2 such experiments. The numbers near the points indicate the sequence of the first 6 samples, and show that the first 4 in Fig. 2, and the first 3 in Fig. 3 fell above the straight line formed by all subsequent points. The lines drawn are regression lines calculated

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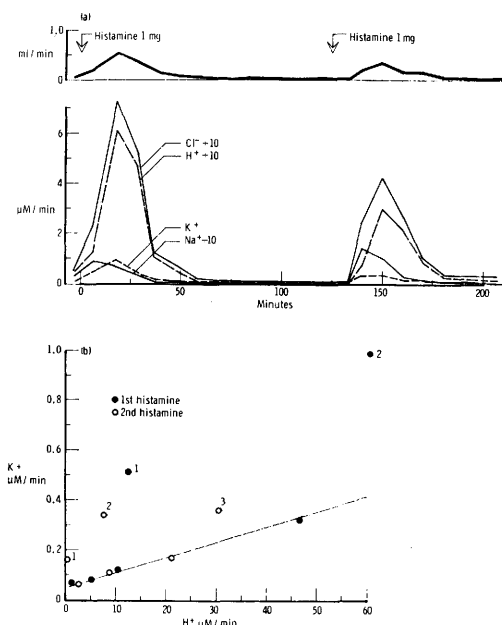


FIG. 1. Heidenhain pouch juice after histamine given 2 times 126 minutes apart. a. Volume and electrolytes in ml and μEq per minute are plotted against minutes after first injection. b. Relation between K^+ and H^+ . Numbers denote sequence of samples whose points fall above the straight line which the later points form. This line was drawn by best fit.

from the points representing all the samples after the first 4 in Fig. 2 and first 3 in Fig. 3.

Table I summarizes the data on the regression coefficient of the K^+ to H^+ line in all 11 experiments, the first group of 5 being sequential studies similar to that in Fig. 1, and the second group those in which stimulation was continuous as shown in Fig. 2 and 3. The regression coefficient was calculated in each experiment from the H^+ and K^+ output per minute of all the gastric juice samples starting with the first one to reach a straight line as determined tentatively by graphing as in Fig. 1b. This occurred after 18 to 38 minutes in the sequential stimulation group and after 52 to 60 minutes in the continuous group. The Table shows that the regression coefficient (b) varied from 0.006 to 0.082, and that within each experiment the standard error and the *t* value indicates a significant relationship between K^+ and H^+ in histamine-stimulated juice(5). It is noteworthy that the K/H relationship became linear sooner after a single injection of histamine

than after repeated or continuous stimulation.

Discussion. These studies indicate that within 30 to 60 minutes after histamine stimulation is begun a significant correlation develops between the output of K^+ and that of H^+ in canine gastric juice from a Heidenhain pouch. The regression of K^+ to H^+ is the same after repeated sets of stimuli in one day. Blair observed such a relationship in juice from the whole stomach of the cat (1). Others have failed to observe it in dog gastric fistula juice and in Heidenhain pouch juice, possibly because in the one case(2) the investigators averaged results from several experiments and in the other(3) the consistently

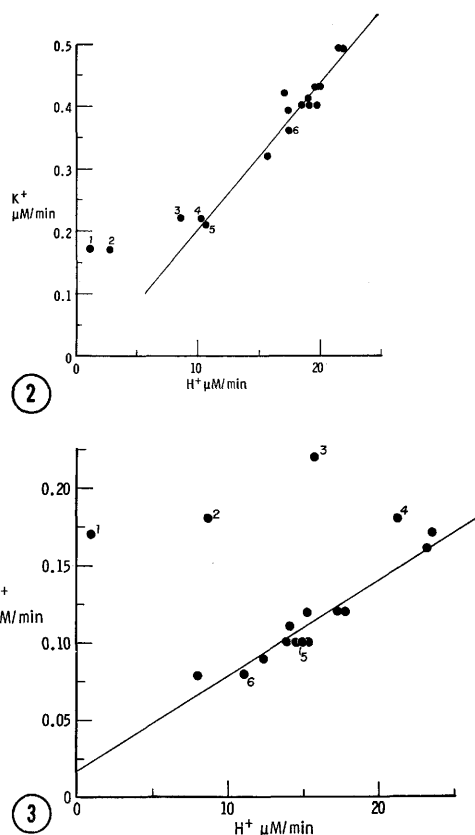


FIG. 2. Exp No. 26.5. Heidenhain pouch juice during continuous intravenous stimulation. Relation between K^+ and H^+ . Numbers denote sequence of first 6 samples. Regression line is calculated from all points after first 3.

FIG. 3. Exp No. 28.3. Heidenhain pouch juice during continuous intravenous stimulation. Relation between K^+ and H^+ . Numbers denote sequence of first 6 samples. Regression line is calculated from all points after first 4.

TABLE I. Regression Coefficient (b) of K+ on H+ Output in Histamine Stimulated Gastric Juice.

Exp No.	1	2	3	4	5	6	7	8
	Histamine PO ₄	Time between histamine inj (min.)	Time before K+/H+ became linear (min.)	No. periods in analysis	Avg length of period (min.)	H+ range (μEq/min.)	b(sb)	t
	Subcut (mg)	i.v. (μg/kg/min.)						
Sequential histamine								
10.5	1/1		126	3/3	10	3-47	.006(.0002)	29.4
14.4	2/3		62*	3/4	10	19-35	.009(.0010)	9.4
17.1	1/1		171	3/3	10	4-49	.014(.0013)	10.0
13.1	1/1		184	2/3	13	4-50	.050(.0034)	14.5
23.1	2/2		134*	3/3	15	4-61	.082(.0058)	14.2
Continuous histamine								
10.6	7/9		45*	3/4	15	18-86	.007(.0011)	6.2
28.3		4.9	58	13	15	8-24	.006(.0003)	20.4
26.4		3.9	56	12	20	8-23	.014(.0015)	9.6
26.5		2.6	52	15	15	11-22	.023(.0015)	15.9
20.16		3.4	45	7	15	38-78	.032(.0028)	11.6
20.14		3.1	60	16	15	42-76	.033(.0021)	15.4

Sequential histamine: Two sets of 1 to 3 one mg subcutaneous injections (see col. 1) were given minutes apart as shown in col. 2.

* Minutes between last injection of first set and the first of the second set. In all sequential experiments pouch juice had reached the base line secretion rate before reinjection.

Continuous histamine: In Exp No. 10.6, 0.5 mg histamine phosphate was injected subcutaneously every 10 minutes in 2 series of 7 and 9 injections, respectively. In the subsequent experiments continuous histamine was given intravenously.

b (sb) (col. 7): Regression coefficient of K+ on H+ (standard error).

high early K+ output was over-emphasized.

The present findings support the idea that primary parietal cell secretion contains K+ and that this ion is an essential factor in the mechanism of acid secretion. Why the range of regression coefficients is so wide is not known, but anatomic variability of the pouches may be at least partially responsible.

Several possible explanations for the early high K+ are being studied. Since repeated or continuous histamine stimulation tended to prolong the time for the K+ to H+ relationship to become linear, it would seem that the drug plays some role in the early high K+. One possibility is that a relatively greater reabsorption of H+, Cl- and H₂O than of K+ may occur after the beginning of histamine stimulation.

Summary. By serial sampling at 10- to 20-minute intervals, electrolytes and water secre-

tion per minute were measured in dog Heidenhain pouch juice after stimulation with histamine. Thirty to 60 minutes after the beginning of stimulation, a highly significant correlation of K+ to H+ was observed. The regression coefficient of K+ on H+ ranged from 0.006 to 0.082 in 11 experiments. The early high K+ output after histamine is still under investigation.

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