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Research Article

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STIMULATION OF GASTRIC PEPSIN BY HISTAMINE

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In studying gastric secretion, as many data as possible should be obtained. Although the determination of the enzyme secretory power of the stomach is not as important as the determination of the acid secretory power, it has been pointed out by Polland and Bloomfield (1) that in certain cases the measurement of pepsin output may be a more delicate index of gastric damage than the measurement of acid values. Since the histamine test meal has come into use, it has been generally assumed that the enzyme secretion of the gastric juice is stimulated by histamine. However, recent observations by Gilman and Cowgill (2), and independently by Babkin (3) on pepsin secretion after histamine stimulation indicate that histamine does not stimulate pepsin secretion. Using dogs with Pavlov or Heidenhain pouches, it was found that with the increased volume of secretion in response to histamine there was a relative decrease in pepsin concentration, with the result that the total output of pepsin remained constant. They also noted that after the first stimulation by histamine, the increase in volume of juice was proportionately greater than the decrease in concentration of pepsin, with the result that the total amount of pepsin secreted per unit of time was substantially increased. This effect was interpreted as due to a mechanical washing out of pepsin from the lumina of the glands by the sudden secretion of gastric juice.

Polland and Bloomfield (1) described the curves of pepsin concentration and of total pepsin output before and after stimulation by histamine in normal human subjects, and in people with various gastric lesions. It was observed that after histamine stimulation the concentration of pepsin falls markedly, but the total output was usually increased. It was during the course of these studies that an occasional observation was made on pepsin secretion after repeated histamine stimulation. The results indicated that after each histamine stimulation the pepsin secretion was increased. It was thought that more careful observations were warranted, and the following studies were made.

MATERIAL AND METHODS

Four male patients were studied. Three presented no evidence of organic disease of the stomach; one was a case of duodenal ulcer. Table 1

shows their age, clinical diagnosis and highest acid and volume response to histamine. Case 1 had high acids and high volumes, case 2 had high acids and normal volumes, case 3 had normal acids and high volumes, and case 4 had low acids and low volumes. This gives a wide range of types of gastric secretion as seen in human subjects.

TABLE 1

Data concerning cases studied

Name	Age	Diagnosis	Maximum 10-minute volume of secretion	Maximum free HCl	Maximum total acid
	years		*cc.*	*cc. N/10 per 100 cc.*	*cc. N/10 per 100 cc.*
Oh...	68	Duodenal ulcer	36	140	144
Cl....	41	Psychoneurosis	26	136	142
Zi....	46	Indigestion	39	102	112
To...	49	Irritable colon	8.5	45	68

All subjects were in bed in the hospital and had fasted for twenty-four hours. A mercury-weighted tube was inserted into the stomach and the fasting contents withdrawn. The total secretion over ten-minute periods after an injection of histamine (0.1 mgm. per 10 kilos body weight) was then collected exactly as previously outlined (4). After the volumes had returned to the fasting level, a second and later a third injection of the same dose of histamine was given. Volume, titratable acidity and pepsin were measured in all. Titratable acidity was determined with dimethyl and phenolphthalein and pepsin by the method of Polland and Bloomfield (5). Pepsin is expressed in milligrams of edestin digested by one cubic centimeter of gastric juice in 30 minutes at 37.6 degrees centigrade.

Although the gastric juice was obtained by stomach tube, quantitative technique under these conditions can be simply obtained if certain precautions are followed. First, a cooperative patient, preferably of a phlegmatic temperament must be selected; second, the patient is urged not to swallow saliva and this point is emphasized throughout the test; and third, continuous aspiration must be maintained. Under these conditions a watery clear fluid containing a minimum of mucus is obtained. Duodenal regurgitation rarely occurs, and if bile appears the test is always discarded. This procedure has the distinct advantage that the secretion from the whole stomach is obtained, as contrasted to the partial secretion obtained by pouch methods in dogs. Furthermore, the volume of secretion is large and slight errors in technique are not appreciable.

Table 2 is a complete protocol of Case 2 to illustrate the procedure.

TABLE 2

Complete protocol of a typical experiment (Case 2)

Number of specimen	Time	Amount	Character	Acid titratable		Pepsin	
				Free	Total	Edestin digested by 1 cc. of juice	Total edestin digested per 10 minute period
	p.m.	*cc.*		*cc. N/10 per 100 cc.*	*cc. N/10 per 100 cc.*	*mgm.*	*mgm.*
1....	1:00	11.5	Fasting contents. Water clear, small amount mucus	28	48	2505	28,808
			Histamine 0.6 mgm.				
2....	1:10	19.5	Water clear	56	74	2505	48,848
3....	1:20	24.5	Water clear	120	126	2250	55,125
4....	1:30	24.5	Water clear	126	143	1509	36,971
5....	1:40	23.5	Water clear	130	136	1640	38,540
6....	1:50	19.0	Water clear	136	142	1411	26,809
7....	2:00	13.0	Water clear	118	126	1411	18,343
			Histamine 0.6				
8....	2:10	17.0	Water clear	122	128	1480	25,160
9....	2:20	27.0	Water clear	130	136	1334	36,018
10....	2:30	25.0	Water clear	130	136	1200	30,000
11....	2:40	25.0	Water clear	126	132	1480	37,000
12....	2:50	17.0	Water clear	130	136	1334	22,678
13....	3:00	9.0	Water clear	128	134	1270	11,430
			Histamine 0.6				
14....	3:10	16.0	Water clear	122	130	1553	24,848
15....	3:20	25.0	Water clear	132	138	1480	37,000
16....	3:30	26.0	Water clear	126	132	1334	34,684
17....	3:40	16.0	Water clear	112	118	1270	20,320
18....	3:50	12.5	Water clear	130	136	1005	12,563
19....	4:00	6.5	Water clear	124	132	899	5,844

RESULTS

Volume and acidity. As has been reported from all previous histamine studies, the volume and acidity rapidly increase, reaching the maximum in 20–30 minutes after injection. The volumes then diminish, while acidity, on the other hand, reaches a level which is maintained throughout the test. The most striking feature of the acid and volume responses was the constancy of their response to repeated doses of the same amount of histamine in a given individual. This is well illustrated in Table 2, the maximum volumes being 24.5 cc., 27 cc., and 26 cc.; the maximum total acidities being 142, 136 and 138. This is strong evidence as to the reliability of the technique.

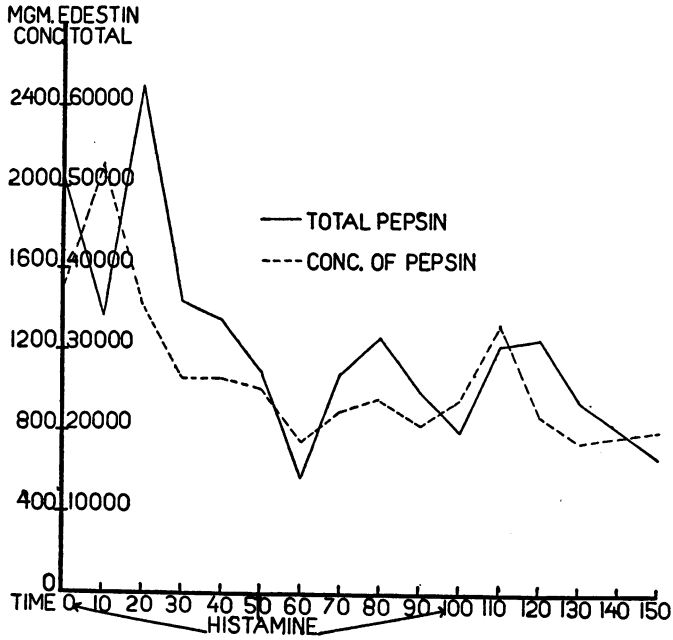

CHART 1. CURVES OF CONCENTRATION, AND TOTAL OUTPUT OF PEPSIN FROM CASE 1 AT TEN-MINUTE INTERVALS AFTER REPEATED DOSES OF HISTAMINE.

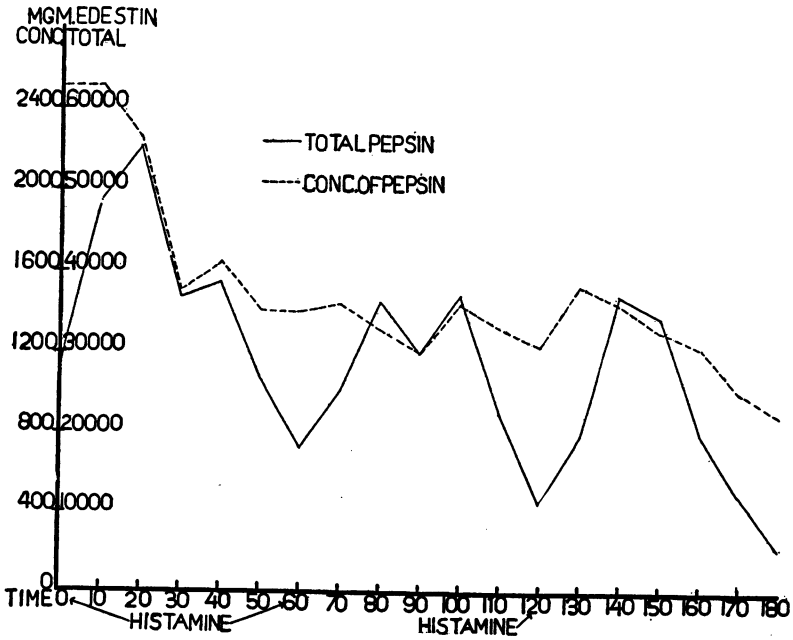

CHART 2. CURVES OF CONCENTRATION, AND TOTAL OUTPUT OF PEPSIN FROM CASE 2 AT TEN-MINUTE INTERVALS AFTER REPEATED DOSES OF HISTAMINE.

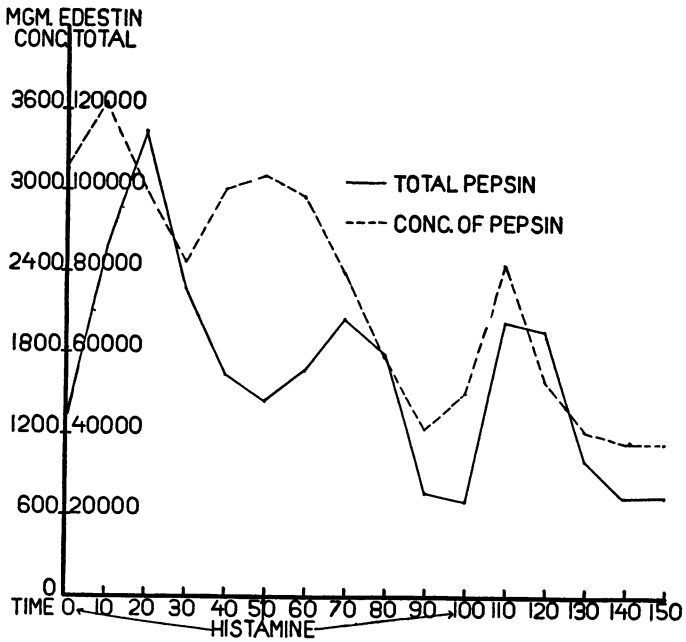

CHART 3. CURVES OF CONCENTRATION, AND TOTAL OUTPUT OF PEPSIN FROM CASE 3 AT TEN-MINUTE INTERVALS AFTER REPEATED DOSES OF HISTAMINE.

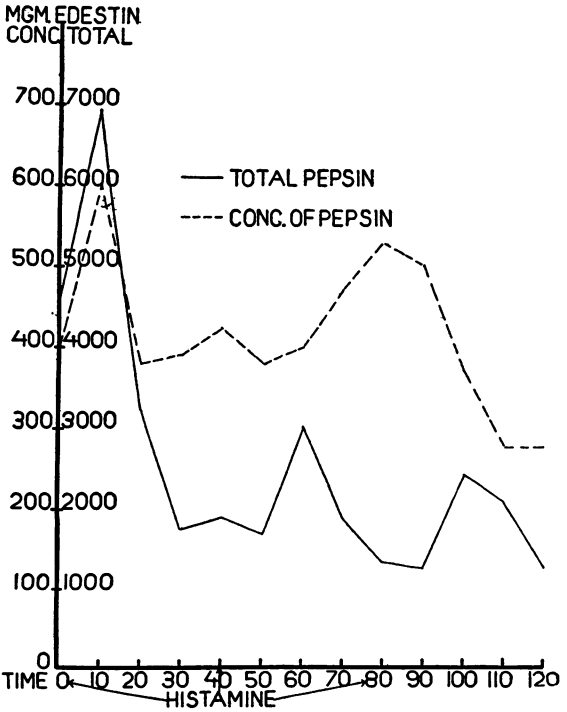

CHART 4. CURVES OF CONCENTRATION, AND TOTAL OUTPUT OF PEPSIN FROM CASE 4 AT TEN-MINUTE INTERVALS AFTER REPEATED DOSES OF HISTAMINE.

Pepsin. Charts 1, 2, 3 and 4 show the curves of pepsin concentration and of total output of pepsin per ten-minute period after repeated stimulation in the four cases studied. The total output after the initial dose is striking, and is much higher than the subsequent responses. However, after each stimulus *there is a definite rise in the total output amounting to approximately 100 per cent*, and the magnitude of this rise is practically identical after the second and third injections of histamine. The concentration of pepsin is very variable, and is apparently independent of volume or acid secretion. However, in all cases there is a constant fall in the concentration of pepsin during the height of secretion after the first stimulus.

DISCUSSION

Contrary to the experience of Gilman and Cowgill, and of Babkin, the results indicate that histamine has a definite stimulating effect upon pepsin. The character of the curve and the similarity of the response after the second and third injection of histamine can only be interpreted satisfactorily by assuming that histamine stimulates the peptic cells. The effect after the first stimulus is probably best explained by a mechanical lavaging of pepsin which has accumulated in the furrows and tubules of the gastric mucosa, as has been pointed out by Gilman and Cowgill, and by Babkin, plus an actual stimulating effect by the histamine. Therefore, it appears that in studying gastric secretion in human subjects, histamine is suitable for determining the capabilities of the pepsin-secreting glands, as well as the acid-secreting glands. Although the two processes are independent, they are influenced by the same stimulus.

SUMMARY

Evidence is presented to show that in human subjects, histamine stimulates secretion of gastric pepsin.

BIBLIOGRAPHY

1. Polland, W. S., and Bloomfield, A. L., J. Clin. Invest., 1930, ix, 107. The Diagnostic Value of Determinations of Pepsin in Gastric Juice.
2. Gilman, A., and Cowgill, G. R., Am. J. Physiol., 1931, xcvii, 124. The Effect of Histamine Upon the Secretion of Gastric Pepsin.
3. Babkin, B. P., Can. Med. Assoc. J., 1930, xxiii, 268. The Value of Histamine as a Test of Gastric Secretion from a Physiological Point of View.
4. Bloomfield, A. L., and Polland, W. S., J. Am. Med. Assoc., 1929, xcii, 1508. The Diagnostic Value of Studies of Gastric Secretion.
5. Polland, W. S., and Bloomfield, A. L., J. Clin. Invest., 1929, vii, 45. A Quantitative Method for the Estimation of Pepsin.