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Effect of Histidine on Gastric Secretion.

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The therapeutic effect claimed for histidine in the treatment of peptic ulcer seems to be based on the allegation that it prevents experimental ulcer in dogs. The exact mode of action has not been well explained. Those originally advocating the treatment claim that it probably supplies the missing product of protein digestion. However, there is no tangible evidence to show that peptic ulcer is a result of amino-acid deficiency. Martin[1] postulates the interesting theory that histidine may stimulate secretion of mucus which exerts a buffer action on the gastric juice and protects the ulcer. Volini and McLaughlin[2] actually observed in a series of 21 ulcer patients treated with this drug a uniform decrease in the amount and acid of the fasting and stimulated gastric juice. Sandweiss[3] failed to obtain similar results and could not correlate the clinical response to any change in gastric acidity. This report deals with a study of the fasting, basal, and histamine-stimulated gastric secretions following a single injection of 0.2 gm. of histidine monohydrochloride (Larostidin) in 2 normal subjects, one case of nutritional edema, 2 cases each of gastric neurosis, chronic appendicitis and chronic dysentery, and 5 cases of peptic ulcer, with various degrees of gastric acidity represented. The control and histidine observations were made on separate days but under exactly identical conditions. Histidine was injected intragluteally 30 minutes before the collection of basal secretion was begun. After 4 ten-minute samples of basal juice were obtained, histamine (Ergamine acid phosphate 0.5 mg.) was given subcutaneously and the specimen collected during the second 10-minute period was chosen as representing the stimulated secretion because the maximum acidity is usually attained in this sample. Aspiration was made continuously with a Luer syringe in order to minimize the loss of secretion through the pylorus. The volume was measured with the accuracy of one cc. For comparison of acidity only total acid was used because the free HCl titer varied considerably with the amount of blood present and with the continuous aspiration technic it was extremely difficult to avoid trauma.

1 Martin, K. A., *J. A. M. A.*, 1936, **106**, 1468.

2 Volini, I. F., and McLaughlin, R. F., *Med. Rec.*, 1935, **141**, 364.

3 Sandweiss, D. J., *J. A. M. A.*, 1936, **106**, 1452.

TABLE I.

Volume and acidity of gastric secretion with and without histidine injection. Basal juice represents the average ten-minute sample and post-histamine juice always the second ten-minute specimen. All samples obtained by continuous aspiration.

Case No.	Control observation: Fasting juice Vol. cc.	Fasting juice Acidity N/10%	Basal juice Vol. cc.	Basal juice Acidity N/10%	Post-histamine juice Vol. cc.	Post-histamine juice Acidity N/10%	After injection of histidine: Fasting juice Volume cc.	Fasting juice Volume % Diff.	Fasting juice Acidity N/10%	Fasting juice Acidity % Diff.	Basal juice Volume cc.	Basal juice Volume % Diff.	Basal juice Acidity N/10%	Basal juice Acidity % Diff.	Post-histamine juice Volume cc.	Post-histamine juice Volume % Diff.	Post-histamine juice Acidity N/10%	Post-histamine juice Acidity % Diff.	Diagnosis
1	80	59	25	103	35	107	65	—18.8	71	+20.3	24	—4.0	90	—12.6	45	+28.6	112	+4.7	Gastric neurosis
2	44	50	9	65	18	108	45	+2.3	65	+30.0	15	+66.7	41	—36.9	26	+44.4	71	—34.2	Chronic dysentery
3	72	73	32	84	40	106	49	—31.9	75	+2.7	16	—50.0	87	+3.6	38	—5.0	94	—11.3	Duodenal ulcer
4	205	70	39	78	46	92	220	+7.3	51	—27.2	40	+2.5	69	—11.5	46	0	74	—19.6	Gastric ulcer
5	21	51	7	77	18	101	13	—38.0	20	—60.8	4	—42.8	74	—3.9	14	—22.2	109	+7.9	Gastric neurosis
6	171	57	47	76	62	90	158	—7.6	62	+8.8	53	+12.8	76	0	48	—22.6	90	0	Gastric ulcer
7	50	39	27	84	33	97	31	—38.0	47	+20.5	18	—33.3	76	—9.5	33	0	93	—4.1	Normal
8	40	18	8	20	34	62	24	—40.0	6	—66.6	6	—25.0	6	—70.0	13	—61.8	64	+3.2	Chronic dysentery
9	105	52	17	56	32	80	95	—9.5	48	—7.7	10	—41.2	49	—12.5	38	+18.8	76	—5.0	Normal
10	120	56	10	52	25	98	85	—29.2	36	—35.7	11	+10.0	53	+1.9	27	+8.0	96	—2.0	Chronic appendicitis
11		72		84		110			43	—40.2			56	—33.4			110	0	Duodenal ulcer
12	43	37	20	48	21	78	57	+32.6	50	+35.1	22	+10.0	74	+54.2	13	+38.1	84	+7.7	Chronic appendicitis
13	27	2	13	25	10	41	27	0	4		11	—15.4	22	—12.0	10	0	34	—17.1	Nutritional edema
14	105	72	20	91	32	100	*86	—18.1	78	+8.3	34	+70.0	78	—14.3	41	+28.1	84	—16.0	Duodenal ulcer
							*174	+65.7	99	+37.5	18	—10.0	92	+1.1	20	—37.5	105	+5.0	

*These examinations were made on the 3rd and 6th days of histidine treatment (0.2 gm. of histidine monohydrochloride intramuscularly, once a day) respectively.

Table I summarizes the results. No consistent change in the volume or acidity of the different phases of the gastric secretion is noted as a result of histidine injection. It might be argued that these observations were made after a single dose of histidine and therefore might not detect the effect of the drug on repeated administration. The patient in Case 14 received this medicine on 6 consecutive days and the study carried out on the 3rd and 6th days, respectively, also yielded negative results. Incidentally, this patient derived no apparent benefit from the therapy, while a standard Sippy regimen which soon followed brought on the usual expected remission.

It may thus be concluded that under the conditions of these observations histidine does not seem to exert any influence on the gastric acidity or the rate of gastric secretion.

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Contraction of Muscle and Denaturation of Myosin.

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It is recognized that the protein myosin takes part directly in the contraction of muscle, and there is even reason to believe that myosin itself is the contractile substance of muscle.[1, 2] If so significant a rôle in contraction is ascribed to myosin, it is important to know how myosin changes during contraction. Experiments concerning the effect of heat on both muscle and myosin show that, under some conditions at least, shortening of muscle may be made possible by the denaturation of myosin. In this note I shall briefly describe these experiments.

A thermal stimulus can cause either a reversible or an irreversible shortening of muscle. If the sartorius muscle of a frog is gradually warmed, its length remains unchanged until a temperature of about 37° is reached, when the muscle suddenly shortens. On cooling, the muscle recovers its original length. If the muscle is heated to higher temperatures a further shortening is observed, beginning at 39° and reaching an end-point at about 45°C. This time the muscle does not relax on cooling. The 2 responses of muscle to heat were first

[1] Weber, H. H., *Ergeb. d. Physiol.*, 1934, **36**, 109.

[2] Muralt, A. J., *Ergeb. d. Physiol.*, 1935, **37**, 406.