

eliminated the idea that this reaction might be a reversal of the one which causes conversion of fibrinogen into fibrin. A further study on the soluble products resulting from this treatment revealed the fact that they are largely proteose in character and that the larger percentage of the compounds falls between the limits of 50 to 100 saturation with ammonium sulphate. We have then, here, a definite demonstration of extremely rapid proteolysis at room temperature.

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Some Effects of Histamine on the Acid-Base Balance.

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The "alkaline tide" in the urine during the digestive period is commonly regarded as a compensatory process, eliminating the excess of base left in the blood after the formation of HCl in the stomach. Some of the observed variations in urine reaction, however, may be indirectly dependent on the absorption of food. So far as we are aware the alkaline tide has not been shown to accompany gastric secretion in the fasting subject. Ackman¹ studied the urine reaction in man, giving a test meal followed immediately by the administration of histamine. The food factor was therefore not eliminated. It seems that the use of histamine alone might give more valuable information as to the cause of the tide.

Female dogs, weighing from 9.0 to 12.5 kg., and having fasted for 16 to 20 hours, were used in our experiments. Measurements of pH were made on urine by the potentiometer, and on blood plasma by the method of Hastings and Sendroy.² In the studies on urine, each animal was as a rule used for a single experiment of 4 to 6 hours, in order to avoid the effects of a possible cystitis from the use of the catheter. Histamine dichloride was injected subcutaneously, the usual dose corresponding to 0.7 mg. of histamine base.

Such a dose of histamine invariably produces a rise in urinary pH, lasting for about 2 hours, after which the reaction returns to near the original level. The duration of this effect suggests that it is related to the gastric secretory activity. The following table is a typical record from a Pavlov pouch dog, showing the gastric and urinary effects.

TABLE I.
Dog M38. Female, Pavlov pouch, weight 11.0 kilos.

Time	Urine cc.	pH	Gastric Juice cc.	Free acid (clinical units)	Remarks
9:05	115	5.95			Residual urine
10:05	5	5.96	4.8	23	Control period
					(At 10:05, gave 1 mg. of histamine dichloride subcutaneously and 100 cc. water by stomach tube)
11:05	4	6.95	37.0	115	
12:05	3	7.16	3.5	68	
1:05	4	5.99	5.2	0	
					(At 1:05, gave 1 mg. histamine dichloride)
2:05	5	7.82	39.0	115	
3:05	7	8.02	7.0	102	
4:05	3	5.90	3.5	0	

We believe that our experiments furnish additional evidence that the alkaline tide is due to the formation of HCl in the stomach. While we have found it always present in normal dogs, it seems less pronounced than in the pouch animals, perhaps because of the loss of acid from the fistulae in the latter.

Hiller³ has reported that histamine lowers plasma pH while raising that of the urine. These observations would seem to indicate that the change in urinary pH after histamine is not brought about by any excess of base, and is perhaps unrelated to gastric secretion. We have confirmed her findings on blood pH following large doses of histamine (1 mg. per kilo or more) but not with such doses as were used in our urine studies (0.06 to 0.08 mg. per kilo). There is following the small doses a rise in blood pH, of 0.02 to 0.06, lasting for 1 to 2 hours.

¹ Ackman, F. D., *Canad. Med. Assn. J.*, 1925, xv, 1099.

² Hastings, A. B., and Sendroy, J., *J. Biol. Chem.*, 1924, lxi, 696.

³ Hiller, Alma, *J. Biol. Chem.*, 1926, lxxviii, 833.

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The Regeneration of Acid-Fastness by Animal Passage.

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By following up the regeneration of tubercle bacilli reported in a study of the granules of this organism,¹ several strains of non-acid-fast or partially acid-fast organisms have been studied. One or-