

histamine was doubled or trebled, indicating that there must have been a release of histamine from cells to plasma. There is no reason to doubt that a similar release of histamine from cells to plasma occurs when trypsin is injected into the intact animal. In the latter instance the plasma histamine undoubtedly diffuses rapidly into the various tissues so that the reduction in total blood histamine which results when trypsin is injected into rabbits is partially due to the removal of leukocytes from the circulating blood and partially to the diffusion of histamine from blood cells to plasma to tissues.

Summary. The intravenous injection of trypsin into rabbits results in a prompt reduction in the total blood histamine with an associated leukopenia. The addition of trypsin to heparinized rabbit's blood *in vitro* results in a shift of histamine from cells to plasma. In both respects the effects of trypsin are similar to those produced by antigen in sensitized animals.

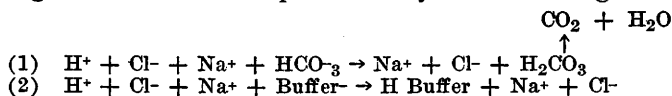
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Relationship Between Osmotic Activity and Sodium Content of Gastric Juice.*

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Several investigators¹ have advanced evidence for the view that gastric juice consists of a mixture of component secretions. Hollander has postulated at least two such components, one a solution of hydrochloric acid isosmotic with blood and the other an alkaline fluid with an electrolyte distribution more or less similar to that of plasma.² It was his conclusion that the mixture of these two component secretions would have a total ionic concentration less than either of the "pure" components. Under such circumstances buffering would occur as represented by the following reactions:



*We are indebted to Mr. Charles Carr for carrying out the sodium determinations for this study.

¹ Gamble, James L., and McIver, Monroe A., *J. Exp. Med.*, 1928, **48**, 837; Hollander, Franklin, *J. Biol. Chem.*, 1932, **97**, 585; Dienst, C., *Ges. Exp. Med.*, **88**, 718; Liu, A. C., Yuan, I. C., and Lim, R. K. S., *Chinese J. Physiol.*, 1934, **8**, 1.

² Hollander, Franklin, *Am. J. Dig. Dis. and Nut.*, 1936, **3**, 651.

where Na^+ represents a typical cation and "Buffer-" represents any buffer anion other than bicarbonate. The resulting diminution of the concentration of osmotically active constituents should reflect itself in a decrease in osmotic activity of the mixture. In the present study, therefore, the osmotic activity of gastric juice samples has been plotted as a function of the sodium content, the latter being assumed tentatively to be a measure of the relative amounts of alkaline component in the mixed juice.

Methods. Medium size, healthy, mongrel dogs, possessing a functioning Heidenhain and/or pyloric pouch which had been constructed a minimum of 3 months prior to these experiments, were employed. All dogs were trained to remain standing for the duration of a particular experiment. Gastric secretion was stimulated by a subcutaneous injection of 1.5 mg of histamine diphosphate, or 12 mg of pilocarpine, in aqueous solution. Secretions were collected in clean test tubes, capped by a rubber diaphragm, to reduce evaporation and external contamination, with a single perforation allowing free flow from the pouch via a mushroom catheter. Plasma was obtained from femoral arterial blood samples drawn at the conclusion of each gastric juice collection period. All blood was secured and centrifuged under oil. Heparin was employed as the anticoagulant. Osmotic activities were determined with the Hill-Baldes³ thermoelectric osmometer at 37.5°C (except for 3 initial samples determined at 25°C) and in a gas phase of 5% CO_2 in oxygen. Results are expressed in terms of milli-equivalents of NaCl per kilo of water. Samples were analyzed for sodium by the micro zinc uranyl acetate method of Dean.⁴

Results. Fig. 1 presents in graphic form the results of the determinations. The feature to which we wish mainly to call attention is emphasized by the curve drawn as an approximate fit to the data. Regardless of the condition of stimulation or of the type of pouch from which samples were obtained, the osmotic activity of the juice appeared, under the circumstances of this investigation, to be a function of the sodium content. Specifically, (1) the samples with low sodium content (less than 20 m.E./L.) *i. e.*, those presumably representing acid juices with relatively little admixture of alkaline component, showed osmotic activities of the same order as, or higher than, that of the corresponding plasma; (2) the samples with the highest sodium contents (120-135 m.E./L.) *i. e.*, presumably those representing the alkaline component with relatively little admixture

³ Baldes, E. J., *J. Sc. Instrum.*, 1934, **11**, 223.

⁴ Dean, R. B., unpublished.

of acid juice, likewise tended to exhibit an osmotic activity of the same order as, or higher than, that of plasma; (3) samples with intermediate values were, with a few exceptions, hypotonic. It is precisely in these samples that a lowering of osmotic activity due to buffering would, by prediction, be most extensive. Therefore the general distribution of experimental values appears consistent with the two-component theory and the implied buffering mechanism.

Certain other features of these results with reference to the conditions of stimulation may also be briefly noted: (a) Histamine stimulated juices were all 2-6 m.E./K. hypertonic (relative to the corresponding plasma); (b) pilocarpine stimulated juices were either

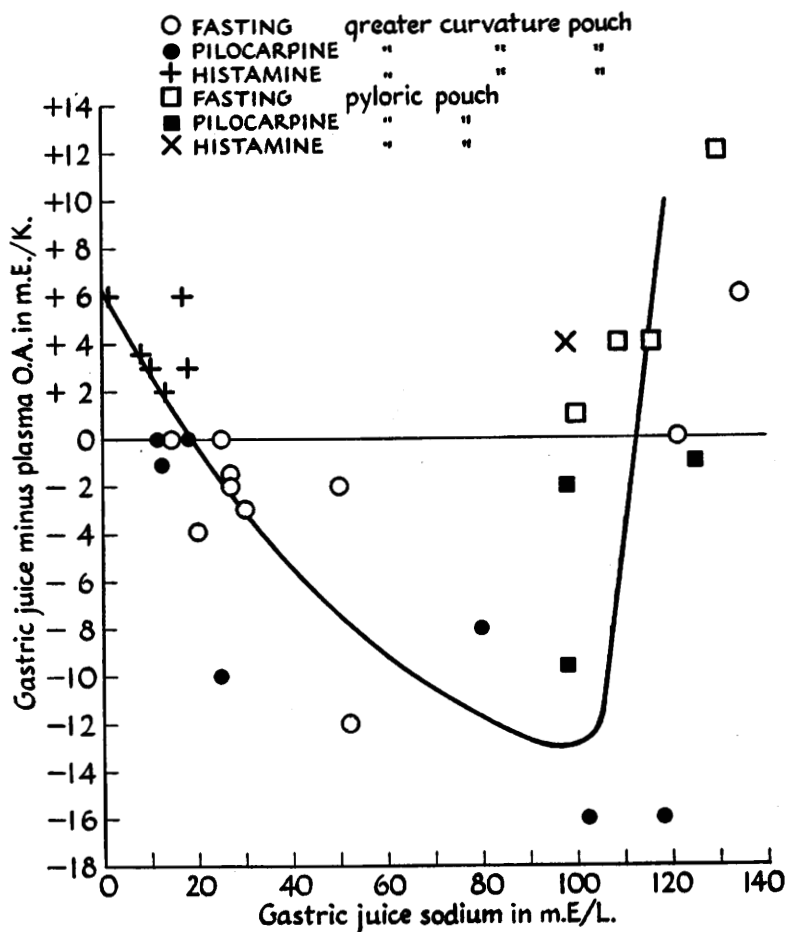


FIG. 1.

Relationship between relative osmotic activity of gastric juice and its sodium content.

isotonic of hypotonic, but not hypertonic; (c) fasting juices were hypertonic, isotonic, or hypotonic.

The mean osmotic activity of 30 plasma samples was 159.8 m.E./K. with a standard deviation of the distribution of ± 2.8 m.E./K.

Summary. The osmotic activity of pouch gastric juice samples relative to that of the plasma is presented as a function of the sodium content of the gastric juice.

The general features of the resulting distribution are in qualitative agreement with the predictions based on the two-component theory of Hollander and the buffering process which it implies.

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The First Appearance of Functional Activity in the Pars Intermedia in the Frog, *Xenopus*.

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The development of functional activity in the pars intermedia of the pituitary has evoked considerable interest since the first workers on the amphibian gland found evidence of early activity in the gland. From the original observations of Smith and Allen (see Smith¹) on hypophysectomy in the frog embryo it was apparent that the operated animals could be distinguished from the controls in pigmentation by the time the animal assumed its definitive tadpole form. In my own experience with *Rana sylvatica* and *pipiens* this is at about 13 mm and about 7-8 days after the tail bud stage at 26°C. Blount² in his multiple pituitary transplants in *Amblystoma* noted some differences in general tone of pigmentation between hypophysectomized, normal and multiple pituitary animals at earlier stages than reported in the frog. He interpreted his observations to indicate hypophyseal function at about stage 41 of Harrison, apparently the stage at which the limb buds

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¹ Smith, P. E., *Amer. Anat. Mem.*, No. 11, 1920.

² Blount, R. F., *J. Exp. Zool.*, 1932, **63**, 113.