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Gastrin.

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The existence of the pyloric chemical phase of gastric secretion has been sufficiently proved experimentally, but its hormonal mechanism, postulated by Edkins,¹ has been doubted. The many attempts made to establish the chemical identity of the hypothetical "gastrin" did not produce conclusive results (for literature, see Babkin² and Ivy³). Recently Sacks, Ivy, Burgess and Vandolah⁴ isolated histamine from the pyloric mucosa, and concluded that "histamine is the gastric hormone, or if not, there is no gastric hormone, or the gastric hormone has never been extracted from pyloric mucosa." This view was reiterated recently by Schnedorf and Ivy.⁵

The experiments reported below demonstrate clearly that a protein-like substance, having a specific secretagogue effect on the fundic glands can be extracted in a histamine-free form from the pyloric mucosa, and in lesser quantity from the duodenum. Twenty-one experiments were carried out on cats under chloralose-urethane anesthesia, in which the gastric and pancreatic secretion, the bile flow, and occasionally also the blood pressure, following intravenous administration of various extracts prepared from different parts of the dog's stomach and intestines, were studied. The chemical procedure that was adopted for the preparation of crude extracts is as follows: The mucous membrane from different parts of the stomach of freshly killed, fasting dogs is removed with the aid of a knife and minced; intestinal mucosa is removed by scraping and ground with sand. The tissues are boiled with 10 volumes of n/10 HCl, partially neutralized with n/1 NaOH to the point where it remains only slightly acid to Congo. After cooling, the extract is centrifuged. The supernatant fluid is filtered through cotton and precipitated with 10% crystalline trichloroacetic acid. The precipitate is centrifuged and washed 3 times with 40 to 50 volumes of

¹ Edkins, J. S., *J. Physiol.*, 1906, **34**, 133.

² Babkin, B. P., *Die äussere Sekretion der Verdauungsdrüsen*, 2nd ed., 1928, J. Springer, Berlin, p. 347 ff.

³ Ivy, A. C., *Kosmos* (J. of Polish Kopernik Soc. of Naturalists), 1931, **56**, 304.

⁴ Sacks, J., Ivy, A. C., Burgess, J. P., and Vandolah, J. E., *Am. J. Physiol.*, 1932, **101**, 331.

⁵ Schnedorf, J. G., and Ivy, A. C., *Proc. Soc. Exp. Biol. and Med.*, 1937, **36**, 192.

10% solution of trichloroacetic acid in saline, twice with 50 volumes of acetone, once with benzene, and twice with ether, and dried *in vacuo*. For injection such preparations were extracted at 40°C with saline, rendered slightly acid with HCl or slightly alkaline with Na₂CO₃. These extracts were assumed to contain no histamine, choline or other extractives; some of them were tested biologically by the methods of Best and McHenry⁶ and Barsoum and Gaddum,⁷ and proved to be actually histamine-free. The secretagogue properties of the extracts are illustrated in Fig. 1.

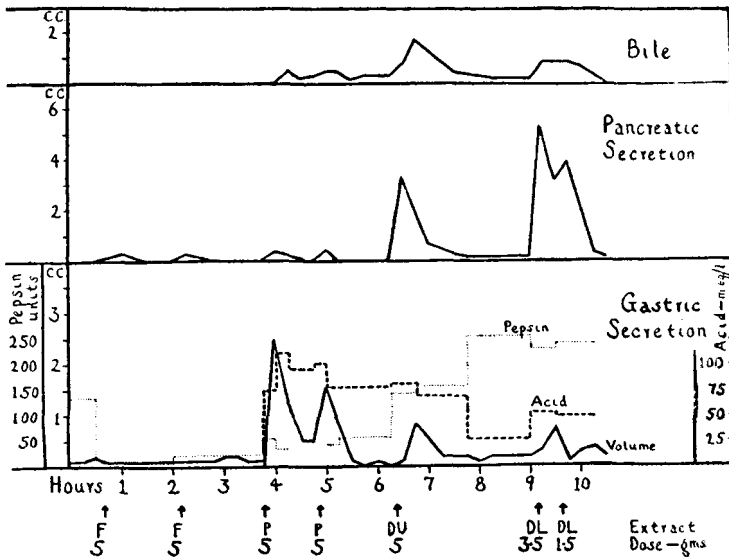


FIG. 1.

The arrows indicate the intravenous injection of extracts prepared from the mucous membrane of the fundus (F) and pyloric region (P) of the stomach, and from the upper duodenum (DU) and lower duodenum (DL). The figure below each symbol denotes the weight of mucosa equivalent to the dose of extract administered. Previous to the injection of the pyloric extract, there was only a slight secretion of alkaline mucus from the stomach.

In all cases without exception the pyloric preparations, injected in quantities equivalent to 5 gm. of mucosa, elicited a copious secretion of gastric juice, which was characterized by high acidity and low peptic power and which was not affected by atropine even in large doses. In some experiments a small pancreatic secretion and a slight acceleration in the bile flow were also observed. Fundic preparations elicited a slight secretion from the pancreas but none whatever from the gastric glands. Preparations obtained from

⁶ Best, C. H., and McHenry, E. W., *J. Physiol.*, 1930, **70**, 349.

⁷ Barsoum, G. S., and Gaddum, J. N., *J. Physiol.*, 1935, **85**, 1.

duodenal mucosa produced a copious pancreatic secretion and a considerable increase in the bile flow; they also evoked some gastric secretion but were much less potent in this respect than the pyloric extracts. Extracts from jejunal mucosa produced a secretion from the pancreas, but none from the gastric glands.

The active principle of the pyloric extracts was found to be soluble in 80% methyl and 80% ethyl alcohol and in dilute acetone, and to be precipitable from aqueous solutions by 10 to 30% NaCl, depending on the pH. By utilizing these properties, further purification of the pyloric principle was carried out, with resulting higher potency and complete elimination of secretin effect on the pancreas.

The above observations appear to support the "gastrin" theory of gastric secretion. They also suggest that "gastrin" may play some part in the intestinal phase of gastric secretion.

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Effect of Adrenal Cortical Hormone on Carbohydrate Stores of Fasted Hypophysectomized Rats.*

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Russell¹ and others have shown that the 24-hour fasted hypophysectomized rat is unable to maintain its carbohydrate stores within normal limits. Furthermore, Russell² has found that the injection of anterior pituitary extracts, while bringing about a preservation of the muscle glycogen, does not prevent the depletion of liver glycogen and hypoglycemia.

While the effect of anterior pituitary extract in maintaining the muscle glycogen appears to be independent of the adrenals,³ Bennett⁴ has recently found that the treatment of hypophysectomized rats for some days before and during fasting with an adrenotropic

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¹ Russell, J. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 279.

² *Ibid.*, *Endocrinology*, 1938, **22**, 80.

³ Bennett, L. L., *Endocrinology*, 1938, **22**, 193.

⁴ *Ibid.*, *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 50.