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Chemical Differentiation of Nervous and Hormonal Pancreatic Secretion.

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We have previously presented data to show that the secretion of pancreatic juice is continuous[1] and can be clearly demonstrated in dogs if the use of ether anesthesia is avoided. We suggested then that a continuous phase of secretion is produced by means other than secretin. We are now presenting observations concerning the mechanism of secretion and the composition of pancreatic juice produced by various means. Our data confirm the observations of J. Mellanby,[2] who came to conclusions very similar to ours. As new observations we offer those on spontaneous secretion, on the uncomplicated action of pilocarpin, together with more extensive analytical data including comparison with blood.

To obtain juice under conditions of complete exclusion of secretin action, the entire small intestine was removed under amytal or avertin anesthesia after tying off the pylorus. This was accompanied by loss of blood (in the intestine) and considerable shock. In some cases no flow was found, while in others a slow steady secretion was shown. Infusion of glucose solution just before the removal of the intestine materially lessened the shock and tended to restore blood volume. In spite of unfavorable conditions juice could be collected at a rate of 0.01 cc. per minute. This juice was a real pancreatic secretion, *i. e.*, a product specifically of pancreatic cell activity. Its amylase content, the other enzymes running parallel, was as high as 150,000 units per cc., while that for 24 hour samples of mixed juice is maximally 10,000 units and for pure secretin juice maximally 4,000 units. The amylase content was determined by a modified[3] Wohlgemuth method. Because atropin stops the flow of this juice, we were inclined to consider its mechanism as nervous (parasympathetic). To further substantiate such a nervous mechanism we did a series of experiments with pilocarpin.

[1] Zucker, T. F., Newburger, P. G., and Berg, B. N., *Am. J. Physiol.*, 1932, **102**, 193.

[2] Mellanby, J., *J. Physiol.*, 1925, **60**, 85.

[3] Zucker, T. F., Newburger, P. G., and Berg, B. N., *Am. J. Physiol.*, 1932, **102**, 209.

Here we obtained pancreatic secretion in every way similar to that obtained spontaneously under conditions where secretin action was excluded.

In comparing the composition of the various secretions we find: secretin juice: low in enzymes (1,000 to 4,000 amylase units). Low in solids 1-2%. Low in chloride (38 to 77 m. eq.). High in bicarbonate (112 to 140 m. eq.). The total base was uniformly higher than the corresponding blood by 6 to 20 m. eq. ranging from 175 to 192 m. eq. Spontaneous and pilocarpin juice: high in enzymes (70,000 to 150,000 amylase units). High in solids (8-14%). Low in bicarbonate (69 to 77 m. eq.). High in chloride (92 to 101 m. eq.). The total base was approximately that of the blood plasma or lower by about 10 m. eq. (All figures expressed in m. eq. are calculated per kilogram of water. Bicarbonate as an approximation is calculated as difference between total base and chloride.)

These findings have a considerable bearing on pancreatic function. In a certain sense the spontaneous or nervous secretion seems to be functionally of more importance than the secretin juice. It is perfectly evident that pancreatic external secretory activity is not dependent entirely on the gastric activity as was definitely claimed by Bayliss and Starling.[4] Thereby the issues between Pawlow and the British School are acutely revived with strong evidence against the sweeping claims for exclusive hormonal control. A very significant, if not the major part of the enzyme output certainly is due to nervous rather than hormonal action. The experimental animal in marked shock, with its entire small intestine removed, cannot be expected to show more than a fraction of normal nervous secretory activity. It seems remarkable that secretory activity survived at all.

Interpretation of other phases of gastro-intestinal activity is also affected. In achlorhydria, with an absence of the assumed necessary stimulus for pancreatic secretion, a surprisingly normal intestinal digestion has been noted and the high probability of non-hormonal pancreatic secretion suggested.[5] In the absence of gastric HCl the nervous mechanism evidently is sufficient to provide digestive enzymes. The absence of secretin juice affects intestinal digestion principally by a lessened volume of secretion, the loss of bicarbonate in pancreatic secretion being somewhat balanced by the absence of gastric HCl. This latter phase of acid-base balance in the intestine and the amount of water secreted merits further study. We may well look for compensatory phenomena.

[4] Bayliss and Starling, *Erg. d. Physiol.*, 1905, **5**, 665.

[5] Dodds and Bennett, *J. Physiol.*, 1921, **55**, 382.