CHANGES IN ENZYMIC ADAPTATIONS OF THE GASTRIC GLANDS DURING THE ACTION OF PRODUCTS OF PROTEIN HYDROLYSIS ON THE MUCOUS MEMBRANE OF THE SMALL INTESTINE

(UDC 612.323-06:612.398.19)

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 61, No. 2, pp. 17-21, February, 1966
Original article submitted July 13, 1964

Investigations by workers at the laboratory of physiology and pathology of digestion [7,8,etc.] have shown that the operative exclusion of certain parts of the alimentary tract leads to compensatory reorganization of the secretory, motor-evacuatory, and absorptive functions of the remaining parts. In particular, it has been shown [3,4] that extensive resection of the proximal and distal portions of the small intestine leads not only to quantitative changes in the acid-forming and enzyme-producing secretory functions of the stomach, but also to changes in the spectrum of proteolytic activity of the gastric glands in relation to certain types of proteins of plant and animal origin.

Since the secretory activity of the stomach is largely dependent on changes in the qualitative properties of the chyme and the speed with which it enters the lower segments of the small intestine [1,9,etc.], the object of the present investigation was to determine the role of products of protein hydrolysis acting on the mucous membrane of the jejunum and ileum, in the enzymic adaptations of the gastric gland to meat and gluten proteins.

EXPERIMENTAL METHOD

The investigations took the form of chronic experiments on 5 dogs (4 with a gastric fistula and one with an isolated Heidenhain's gastric pouch). In addition, an intestinal fistula was formed in each dog in the middle part of the jejunum and the terminal part of the ileum (12-50 cm proximal to the ileocecal region). The dogs received the ordinary diet of the animal house, containing mainly vegetable proteins (200 g meat, 200-500 g porridge, 250 g bread, 8 g fish oil, 8 g yeast, and 2.5-3 liters broth). The level of gastric secretion was determined in response to sham feeding with meat for 2 min (the pieces of meat fell out through the open gastric fistula and, at the end of feeding, the stomach was washed out) and in response to hematogen (200 ml of 20% solution). Samples of gastric juice were collected every 15 min throughout the experiment and kept on ice until the time for testing. In each experiment, the total secretion of juice, the volume of HCl,and the volume of pepsin secreted were determined. The pepsin concentration was estimated by the author's modification of Hunt's colorimetric tyrosine method [2]. The enzymic adaptations of the gastric glands were judged from the intensity of enzymic hydrolysis of gluten and muscle proteins and the ratio between them, indicating the relative phytolytic and zoolytic activity of the gastric juice (P/Z index) [6]. The method of the determination was described previously [4,5]. The proteolytic activity of the gastric juice with respect to the different substrates was expressed in pepsin units (P.U.) [2].

After establishment of the normal gastric secretion and enzymic adaptations of the gastric glands to meat and gluten proteins in response to the stimuli used, in the next series of experiments the effect of introduction of products of protein hydrolysis of different degrees of digestion into the intestine on the gastric secretion was studied. These products included a solution of peptone, the chyme obtained from the jejunum of a "donor" dog, and an "artificial" chyme [1], the products of enzymic hydrolysis of proteins in vitro by gastric juice or by gastric and pancreatic juices in succession. For this purpose, immediately after the action of the stimulus of gastric secretion, protein hydrolyzate was introduced slowly into the intestinal fistula over a period of 5 min, unknown to the dog.

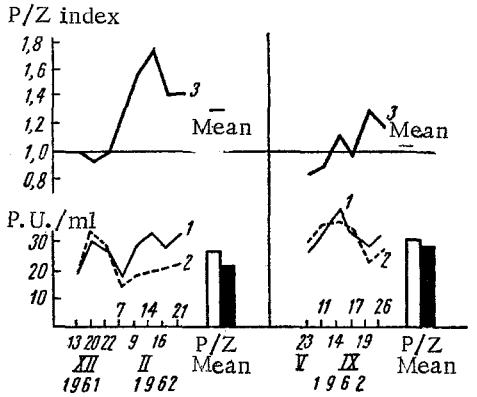

Fig. 1. Activity of digestion of meat and gluten proteins by gastric juice and P/Z index. The dog Lata with a fistula of the stomach and of the terminal portion of the ileum. On the left – secretion to sham feeding with meat; on the right – the same, with subsequent introduction of 10 ml "artificial" chyme, products of hydrolysis of meat proteins by gastric juice, into the intestinal fistula: 1) activity with respect to gluten; 2) activity with respect to muscle proteins; 3) P/Z index. Columns – mean values.

The proteolytic activity of the gastric juice was investigated in samples taken from the whole volume of juice obtained during the experiment. The numerical results were subjected to statistical analysis by the Fisher–Student method.

EXPERIMENTAL RESULTS

The introduction of products of protein hydrolysis of animal origin into the middle part of the jejunum and the terminal part of the ileum led in most cases to changes in the properties of the gastric juice in relation to gluten and meat proteins, although the degree of the changes differed.

Following injection of the products of protein hydrolysis into the fistula in the terminal portion of the ileum, against the background of gastric secretion caused by sham feeding with meat, as a rule, the proteolytic activity of the gastric juice was increased and the spectrum of its activity in relation to gluten and meat protein was modified (Fig. 1). It is clear from Fig. 1 that the introduction of "artificial" chyme, the products of enzymic hydrolysis of meat proteins by gastric juice, into the intestinal fistula caused a clear increase in the activity of hydrolysis of the muscle proteins. The activity of hydrolysis of gluten showed only a slight change, so that the value of the P/Z ratio fell substantially ($P < 0.02$).

Similar changes were obtained following introduction of a hydrolyzate of different types of protein into the intestinal fistula (chyme from the jejunum of a "donor" dog, products of enzymic hydrolysis of meat proteins by gastric and pancreatic juice successively, and peptone solution), although the change in the ratio between the activity of digestion of gluten and of meat proteins in the last two cases was not statistically significant ($P < 0.05$).

The changes in response to introduction of protein hydrolyzates (peptone solution and products of digestion of meat by gastric and pancreatic juice) immediately after a sham feed of meat into the fistula of the middle portion of the jejunum were not statistically significant ($P < 0.05$).

Results different from those described above were obtained during the study of the secretion of an isolated Heidenhain's gastric pouch. The introduction of peptone solution into the terminal portion of the ileum against the background of gastric secretion in response to hematogen led in most experiments to changes bearing the opposite relationship, the proteolytic activity of the gastric juice with respect to gluten was increased and with respect to meat proteins was reduced, and marked fluctuations of the P/Z index were observed from experiment to experiment.

The results of the investigation of the enzymic adaptations of the gastric glands of the dog following extensive resection (50%) of the proximal portion of the small intestine are given in Fig. 2. These results show that, as a result of the operation, considerable variations took place in the ratio between the activity of hydrolysis of gluten and of muscle proteins on different experimental days. The introduction of peptone into the fistula of the terminal portion of the ileum against the background of secretion caused by sham feeding with meat increased the fluctuations of the P/Z index.

Analysis of the results obtained shows that the entry of products of protein hydrolysis into the terminal portion of the ileum and the middle portion of the jejunum in the conditioned-reflex phase of gastric secretion led to changes in the spectrum of proteolytic activity of the gastric juice. These changes were most marked following introduction of products of protein hydrolysis into the terminal portion of the ileum, thus suggesting particularly intimate connections between this part and the ileocecal region of the intestine with the stomach. The changes in the enzymic adaptations of the gastric glands were to some extent dependent on the degree of hydrolysis of the protein substances entering the intestine.

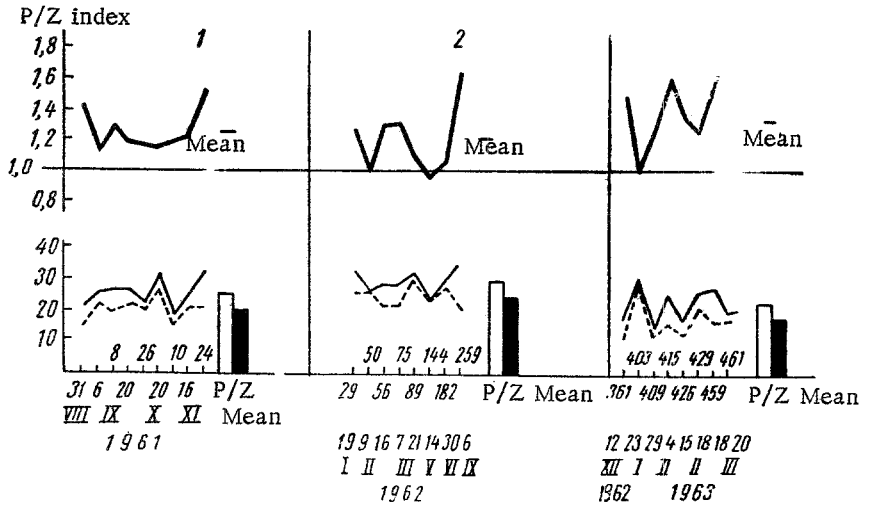

Fig. 2. Activity of digestion of meat and gluten proteins by gastric juice and P/Z index. The dog Pirat with a fistula of the stomach and of the terminal portion of the ileum: 1) secretion to sham feeding with meat before extensive resection of 50% of proximal portion of the small intestine; 2) the same, 29-250 days after resection; 3) secretion in response to sham feeding with meat followed by introduction of 20 ml of 5% peptone solution into the intestinal fistula after resection of the intestine. Legend as in Fig. 1.

For instance, when chyme from the jejunum of a " donor" dog and products of enzymic hydrolysis of meat proteins by gastric juice were introduced into the terminal portion of the ileum, the changes were maximal, whereas after introduction of more strongly hydrolyzed products (protein hydrolyzate incubated with gastric and pancreatic juice, and peptone solution) the changes were less marked.

One of the important mechanisms lying at the basis of the increase in the digestion of muscle proteins and the decrease in the digestion of gluten, suggested by data in the literature and the results of these experiments [6,4], may be the increase in the active acidity of the gastric juice observed experimentally [9] under the influence of products of protein hydrolysis acting on the terminal portion of the ileum. On the other hand, it may be suggested that the increase in the intensity of hydrolysis of meat proteins in the stomach is a specific reaction of its glands to the introduction of muscle proteins into the intestine. Evidently the entry of proteins of a particular type into the intestine may stimulate their digestion in the higher regions of the alimentary tract, and especially in the stomach. However, a final answer to the question of the specificity of this reaction of changes in the spectrum of proteolytic activity of the gastric juice following introduction of various types of protein (of animal or plant origin) can be reached only by further investigation.

The normal mechanism of the enzymic adaptations of the gastric glands may probably be modified in pathological states, for example, during disturbances of the innervation of the secretory apparatus of the stomach (as in the isolated Heidenhain's gastric pouch) or changes in the function of various parts of the gastro-intestinal tracts concerned in gastric secretion (in particular, after extensive resection of the small intestine). In the last case, the qualitative properties of the chyme and the rate of its entry into the lower portions of the small intestine have a considerable influence on the character of the changes in activity of the gastric glands.

It may be concluded from the results of this investigation that the changes in the spectrum of proteolytic activity of the gastric glands observed in most animals for a period of 2-4 months after extensive resection of the small intestine [4] may possibly be associated with the entry of products of incomplete hydrolysis of protein into the intestine, for after removal of a considerable portion of the intestine, the first batches of chyme may reach the lower portions much more rapidly. The spectrum of proteolytic activity of the gastric juice with respect to meat and gluten proteins was subsequently restored, although the normal ratios were not reached. In some animals, in later periods after the operation, sharp fluctuations of the adaptive properties of the gastric juice were observed on different days of the experiments. The fact that these fluctuations intensified further after introduction of products of protein hydrolysis into the small intestine (Fig. 2) is evidence of the important role of the qualitative properties

of the chyme and the rate of its entry into the intestine in determining the changes in the spectrum of proteolytic activity of the gastric juice. The results obtained also suggest that the poor tolerance to gluten, or even its marked toxic action on the animal, may be associated with a disturbance of the normal proteolysis of vegetable proteins in the gastro-intestinal tract as a result of disturbances of the normal mechanisms of the adaptive reactions of the enzyme systems.

The results of these investigations demonstrate the great importance of the study of the spectrum of enzymic activity of the digestive glands in normal conditions, and especially in pathological conditions, for the treatment and prophylaxis of the enzymic adaptations to the food entering the body and thereby for maintaining a more perfect regulation of the compensatory processes in the gastro-intestinal tract.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
