# CHANGES IN THE SPECTRUM OF ENZYMIC ACTIVITY OF THE GASTRIC GLANDS AFTER EXTENSIVE RESECTION OF THE SMALL INTESTINE IN DOGS

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Investigations conducted in our laboratory have shown that after resection of various parts of the gastro-intestinal tract, compensatory processes develop in the residual portions, providing more complete digestion of food substances. In particular, the volume of digestive juices secreted is increased and their enzymic activity is intensified [1, 2, 9]. In a previous paper [6] we showed that extensive resection of the small intestine in dogs causes significant changes in the secretory, acid-forming, and enzyme-secreting functions of the stomach.

It has been found that during adaptation of the gastric glands to the entry of food into the body not only quantitative, but also qualitative changes take place in the secreted enzymes—changes in their activity to split vegetable and animal proteins [7, 8]. In this connection it may be postulated that the changes in pepsin secretion after extensive resection of the intestine may affect not only the amount of enzyme secreted, but also its qualitative properties —the spectrum of its proteolytic activity in relation to proteins of plant and animal origin.

The adaptation of the gastric glands to the quality of the food may be judged from the phytolytic and zoolytic activity of the gastric juice. The ratio between the phytolytic and zoolytic activity (the P/Z index) characterizes the adaptive properties of the gastric juice. The object of the present investigation was to study the phyto- and zoolytic activity of the gastric juice in dogs before and after extensive resection of the proximal and distal segments of the small intestine.

## EXPERIMENTAL METHOD

The investigation was carried out on six dogs: three with a Pavlov or Heidenhain gastric pouch and three with a Basov gastric fistula. The following were used as stimuli of gastric secretion: meat (200 g), hematogen (12.5 and 20% solutions), subcutaneous injection of histamine (0.5-1.0 mg), and injection of alcohol (100 ml of a 10% solution) into the rectum. Samples of gastric juice were collected every 10-15 min and kept on ice until required for analysis. The pepsin concentration was determined by the method described previously [5], using blood serum as substrate, and the activity of splitting vegetable and animal proteins (phyto- and zoolytic activity of the gastric juice) was determined by Ugolev's method [7], with slight modifications: to standard weighed samples of casein, gluten, and muscle proteins (50 mg) 1 ml of natural gastric juice was added, and after careful and rapid mixing with a glass rod the mixture was incubated for 30 min at 38° in a Warburg's apparatus, on a special stand with provision for mixing the samples. The activity of enzymic hydrolysis was determined by the increase in the free tyrosine, using a phenol reagent [10]. After control experiments had been carried out, an extensive resection of 50-70% of the small intestine was performed on the dogs. The experimental results were analyzed by statistical methods [3].

TABLE 1. Gastric Secretion in Response to Meat (200 g) Before and After Extensive Resection of 70% of the Proximal Segment of the Small Intestine in the Dog Seryi with an Isolated Pavlov Gastric Pouch (Mean Results of 2 Series of Experiments)

| Index of gastric secretion | Before operation (7 experiments) | After operation (8 experiments) | Increase in secretion (in %) | P |
|---|---|---|---|---|
| | M ± m | | | |
| Volume of gastric juice (in ml/experiment) | 28.9±2.21 | 69.9±7.93 | +142 | <0.001 |
| Concentration of free HCl (in %) | 0.3999±0.0163 | 0.4927±0.027 | + 23 | <0.01 |
| Total acidity (in %) | 0.4552±0.0006 | 0.5343±0.008 | + 17 | <0.001 |
| Content of free HCl (in mg) in: | | | | |
| 1 ml gastric juice | 3.99±0.16 | 4.93±0.27 | + 23 | <0.01 |
| juice obtained during experiment | 117.3±12.3 | 348.0±47.6 | +197 | <0.001 |
| Content of pepsin (in pepsin units) in: | | | | |
| 1 ml gastric juice | 25.0±0.67 | 25.2±1.89 | +0.8 | > 0.5 |
| juice obtained during experiment | 726±80 | 1691±113 | +113 | <0.001 |
| Proteolytic activity of gastric juice (in pepsin units): | | | | |
| in relation to casein, in: | | | | |
| 1 ml gastric juice | 22.8±0.84 | 27.4±1.7 | + 20 | > 0.05 |
| juice obtained during experiment | 659±53 | 1850±132 | +180 | <0.001 |
| in relation to gluten, in: | | | | |
| 1 ml gastric juice | 19.5±0.84 | 19.9±0.58 | + 2 | > 0.5 |
| juice obtained during experiment | 567±54.7 | 1369±121.5 | +141 | <0.001 |
| in relation to muscle proteins, in | | | | |
| 1 ml gastric juice | 21.0±0.85 | 29.0±1.57 | + 38 | <0.002 |
| juice obtained during experiment | 609±20 | 1964±99 | +222 | <0.001 |
| P/Z ratio | 0.94 | 0.69 | -27% | |

## EXPERIMENTAL RESULTS

Extensive resection of the proximal segment of the small intestine was performed on three dogs: two animals with a Pavlov (Seryi) or Heidenhain (Prima) gastric pouch and one dog with a gastric fistula (Pirat). Removal of 50-70% of the proximal segment of the small intestine caused a considerable increase in the volume of juice secreted, in its acidity, and in its pepsin concentration. The specific activity of digestion of casein and muscle proteins by the gastric juice was increased, while that of gluten was unchanged or increased. For instance, the gluten digesting activity in response to meat (Seryi) and histamine (Pirat) remained within the preoperative limits; in response to the remaining stimuli it rose slightly, although to a much smaller degree than the activity of digestion of muscle proteins. The increase in the intensity of hydrolysis of the muscle proteins in all the dogs was greater than the increase in the intensity of digestion of gluten. This inequality of the change in the proteolytic activity of the gastric juice in relation to gluten and to muscle proteins after extensive resection of the intestine led to a relative lowering of the phytolytic activity of the gastric juice. In connection with the increase in the secretion of gastric juice the digestive power of all the juice obtained during the experiment rose in relation to all the protein substrates. The greatest increase was observed in the zoolytic activity of the gastric juice, and by comparison the change in the phytolytic activity was less marked. The amount of free HCl secreted in the course of the experiment rose considerably in Seryi (Table 1).

Changes similar to those described above took place in the same dog and in Prima in response to hematogen (200 ml of a 12.5% solution) and in Pirat during sham feeding with meat and after administration of histamine.

Extensive resection of the distal segment of the small intestine was carried out on three dogs: on two with a gastric fistula (Egoza and Tsygan) and on one with a Heidenhain gastric pouch (Ryzhii). The results of this investigation showed that the specific activity of pepsin in relation to casein, gluten, and muscle proteins was not substantially altered after removal of the distal portion of the small intestine, although the digestion of gluten in these

TABLE 2. Gastric Secretion in Response to Hematogen (200 ml of a 20% Solution) before and after Extensive Resection of 70% of Distal Portion of Small Intestine in the Dog Ryzhii, with a Heidenhain Gastric Pouch (Mean Results of 2 Series of Experiments)

| Index of gastric secretion | Before operation (12 experiments) | After operation (19 experiments) | Increase in secretion (in %) | P |
|---|---|---|---|---|
| | M±m | | | |
| Volume of gastric juice (in ml/experiment) | 8.1±0.59 | 8.7±0.58 | + 7.4 | > 0.5 |
| Concentration of free HCl (in %) | 0.385±0.0106 | 0.395±0.0112 | + 2.8 | > 0.5 |
| Total acidity (in %) | 0.4468±0.0101 | 0.4693±0.0970 | + 5 | > 0.5 |
| Content of free HCl (in mg) in: | | | | |
| 1 ml gastric juice | 3.85±0.106 | 3.95±0.111 | + 2.8 | > 0.5 |
| juice obtained during experiment | 31.4±1.67 | 34.3±2.62 | + 9.3 | > 0.25 |
| Content of pepsin (in pepsin units) in: | | | | |
| 1 ml gastric juice | 36.5±1.35 | 37.0±1.33 | + 1.4 | > 0.5 |
| juice obtained during experiment | 297±13.4 | 314±26.8 | + 5.8 | > 0.5 |
| Proteolytic activity of gastric juice (in pepsin units): | | | | |
| in relation to casein, in: | | | | |
| 1 ml gastric juice | 35.8±0.97 | 37.0±3.57 | + 3.4 | > 0.5 |
| juice obtained during experiment | 300±15.5 | 332±32 | +10.8 | > 0.25 |
| in relation to gluten, in: | | | | |
| 1 ml gastric juice | 21.2±1.15 | 19.9±1;29 | - 6.1 | > 0.25 |
| juice obtained during experiment | 173±13 | 180±14 | + 1.1 | > 0.5 |
| in relation to muscle proteins, in | | | | |
| 1 ml gastric juice | 30.2±1.2 | 32.4±2.4 | + 7.3 | > 0.25 |
| juice obtained during experiment | 253±5 | 294±8 | +16.0 | < 0.01 |
| P/Z ratio | 0.70±0.02 | 0.62±0.09 | -11.0 | |

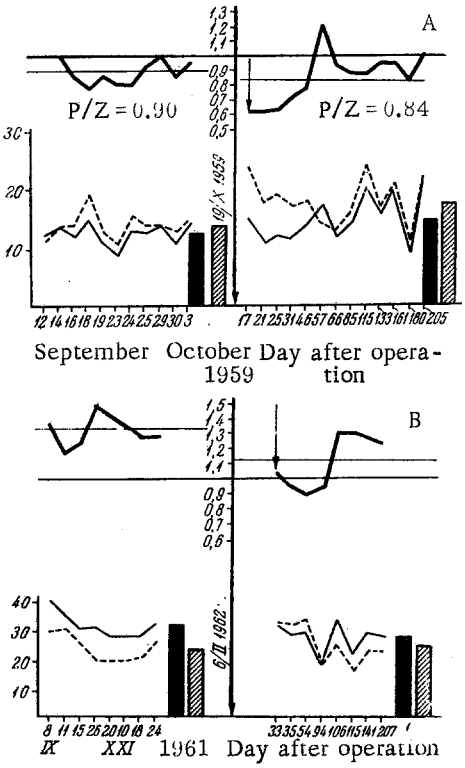
dogs also was less active than the digestion of muscle proteins. Furthermore, the observed decrease in the secretion of juice in response to certain stimuli (to sham feeding with meat, in Egoza and Tsygan) led to a substantial fall in the total proteolytic activity of the gastric juice in relation to gluten. The digestion of muscle proteins in response to various stimuli remained within normal limits or increased in intensity, and the acidity of the gastric juice was not significantly altered (Table 2).

The results of the investigation of the relationship between the photolytic and zoolytic activity of the gastric juice were as follows. During the preoperative period the ratio between the activity of hydrolysis of gluten and muscle proteins (the P/Z ratio) by the gastric juice obtained in response to various stimuli became stabilized at a particular level for each stimulus applied. For example, when meat was used the zoolytic activity was higher than the proteolytic, when hematogen was used the P/Z ratio was close to unity, and in response to the other stimuli its value was greater than unity because of preponderance of the phytolytic activity.

Extensive resection of the small intestine in all dogs caused obvious changes in the spectrum of enzymic activity of the gastric juice, expressed by a lowering of its phytolytic activity for a period of 2-4 months after the operation (see figure).

In our experiments the relative decrease in the phytolytic activity of the gastric juice could have been caused by a decrease in the gluten hydrolyzing activity or by an increase in the intensity of hydrolysis of the muscle proteins. In several experiments a combination of both these factors was observed.

Vegetable and animal proteins possess their own optimum pH of digestion, as Pavlov originally pointed out [4]. The relationship between the optimum pH and the nature of the substrate was demonstrated in the experiments of Fruton, Bergmann, and Anslow [11]. A. M. Ugolev established from extensive experimental material that a higher acidity favors the zoolytic activity of the gastric juice, and a lower acidity favors the phytolytic activity [7, 8].




Phytolytic and zoolytic activity of the gastric juice of dogs and ratio between them (P/Z ratio) before and after extensive resection of the small intestine. A—dog Prima with Heidenhain gastric pouch (gastric secretion in response to hematogen—200 ml of 20% solution); B—dog Tsygan with gastric fistula (gastric secretion in response to sham feeding with meat). Continuous line—phytolytic activity, broken line—zoolytic activity of gastric juice in pepsin units/ml. Top—P/Z ratio. Arrow—time of operation. Left—control experiments, right—after resection.

Hence, the decrease in the activity of digestion of the vegetable proteins and the increase in the activity of hydrolysis of the animal proteins in the dogs after extensive resection of the small intestine may be associated with an increase in the active acidity of the gastric juice secreted.

However, the increase in the acidity of the gastric contents only partially explains the changes in the enzymic adaptation of the gastric glands after resection of the intestine. The fact that resection of the intestine in the majority of cases caused a sharp decrease in the P/Z ratio, even in the animals whose gastric juice acidity underwent no substantial change after the operation, indicates that the decrease in the phytolytic activity was caused by the extensive resection of the intestine itself. This is also confirmed by the fact that the P/Z ratio was gradually restored and regained its initial level 2-4 months after the operation, whereas the acidity of the gastric juice was substantially unchanged during this period. Likewise, the changes in the phyto- and zoolytic activity of the gastric juice during the period of a few months after the operation could not have been caused by a change in the composition of the diet, for the dogs resumed their normal diet on the 4th-5th day after resection of the intestine.

## SUMMARY

Chronic experiments were staged on 6 dogs with Pavlov and Heidenhain's pouches and gastric fistulae. A study was made of some proteins of animal and plant origin (casein, gluten and muscle proteins) by means of gastric juice obtained in response to various stimuli before and after extensive resection of the proximal and distal portions of the small intestine.

It was concluded from these investigations that the proteolytic activity of the gastric juice of dogs in relation to vegetable proteins undergoes a relative decrease during the period of 2-4 months after extensive resection of the small intestine. The changes in the enzymic adaptation of the gastric glands and the relative decrease in the phytolytic activity of the gastric juice may play an important role in the mechanism of the compensatory modifications of the gastric glands after extensive resection of the small intestine.

## LITERATURE CITED

1. I. V. Malkiman and A. P. Mukhina, Byull. éksper. biol., 4, 57 (1962).
2. M. S. Martsevich, Byull. éksper. biol., 5, 41 (1962).
3. I. A. Oivin, Pat. fiziol., 4, 76 (1960).
4. I. P. Pavlov, Lectures on the Work of the Principal Digestive Glands [in Russian] Leningrad (1949).
5. B. I. Sabsai, Byull. éksper. biol. 9, 117 (1961).
6. B. I. Sabsai, Byull. éksper. biol. 4, 32 (1963).
7. A. M. Ugolev, Adaptation of the digestive glands to the quality of the food. Doctorate dissertation, Moscow (1958).
8. A. M. Ugolev, Digestion and its Adaptive Evolution [in Russian], Moscow (1961).
9. S. I. Filippovich, Adaptive Processes in Connection with Disturbances of the Activity of the Digestive System [in Russian], Moscow (1962).
10. O. Folin and V. Ciocalteu, J. biol. Chem. (1927), v. 73, p. 627.
11. J. S. Fruton, M. Bergmann, and W. P. Anslow, Jr., Ibid. (1939), v. 127, p. 627.