RESORPTION OF CASEIN LABELED WITH I^{131} AND METHIONIN LABELED WITH S^{35} FROM THE DIGESTIVE TRACT AT VARIOUS INTERVALS AFTER RESECTION OF TWO-THIRDS OF THE STOMACH

K. S. Zamychikina and L. V. Kryukova

Laboratory of Physiology and Pathology of Digestion, (Director: Professor S. I. Filippovich), Institute of Normal and Pathological Physiology (Director: Academician V. N. Chernigovskii), Academy of Medical Sciences, U.S.S.R., Moscow

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The influence of stomach resection upon the resorptive capacity of the digestive tract has been inadequately studied. The assimilation of nutrient substances after stomach resection has attracted somewhat more attention [1, 2, 3].

Recently a number of authors used radioactive isotopes to study the process of resorption after stomach resection. It was a defect of these studies that they were carried out within short times after the operation not exceeding three-four weeks [5, 6].

Disorders in the resorption of fat labelled with I^{131} were observed in human subjects after Billroth II resection of the stomach. A group of Japanese authors [4] emphasized that in patients and in experimental animals the resorption of fat labelled with I^{131} and of protein labelled with P^{32} slowed down within a short time after total stomach resection. We set ourselves the task of following up experimentally the changes in the resorption of orally ingested protein or amino-acids from the intestine after extensive resection of the stomach.

In our opinion the results of such investigation would enhance our understanding concerning the causes of the alimentary disorders observed in patients after gastric operations.

METHODS

The experiments were carried out on dogs and consisted of the resection of the stomach according to the scheme of the Billroth II operation in the modification of Finsterer.* Healthy animals served as control. Casein labelled with I^{131} and methionin labelled with S^{35} were used to study the resorption. The casein was iodized in the following manner: two mixtures were prepared: 1) 200 mg casein dissolved in 5 ml phosphate buffer (pH 8.6) and 2) 0.4% potassium iodide solution (4 ml) and a 0.4% solution of potassium iodate (2 ml). To this mixture we added a solution of I^{131} with an activity of 500-1000/μC. Before the protein was iodized one-two drops of 0.5 N hydrochloric acid were added into the second solution after which the latter solution was immediately added in small portions to the first solution under continuous mixing. The mixture was stored for two-three hours in the refrigerator and then the iodized protein was dialyzed against normal saline or against tap water. The dialyzate was checked with regard to the presence of excess I^{131}. One of the control methods used consisted of the paper chromatography of the preparation obtained using NaI^{131} as indicator.

*The gastric operations were carried out by the research worker N. Sh. Amirov, for which we express our gratitude.

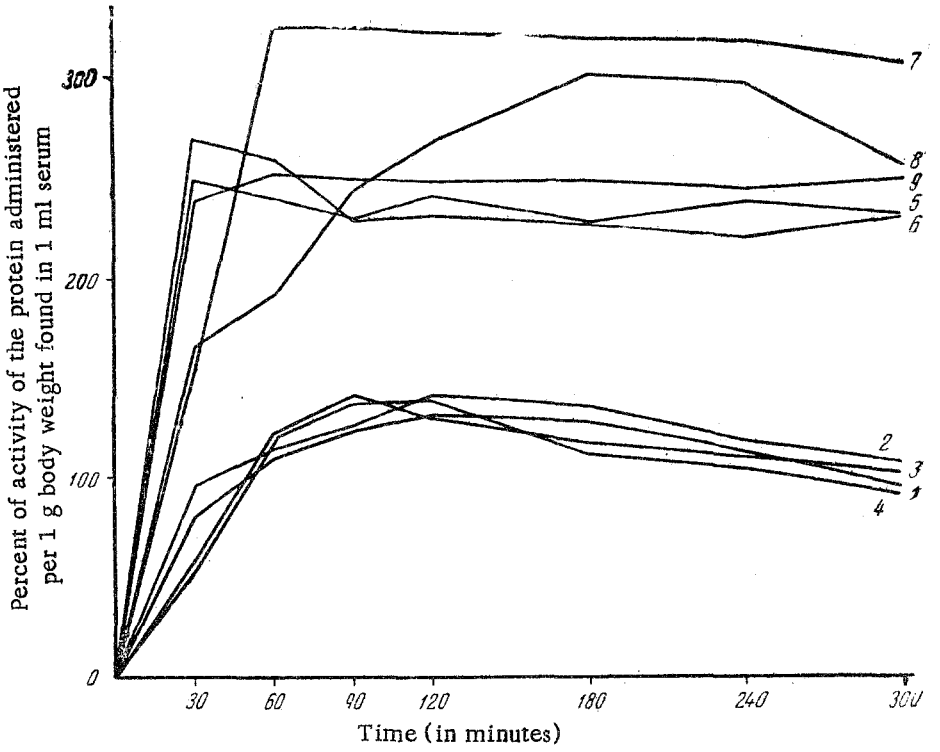

Fig. 1. Rate of resorption of breakdown products of casein labelled with I^{131} in the digestive tract. 1,2,3,4 – control experiments (curves 1 and 2: the dog Veta, the curves 3 and 4: the dog Gaga); 5,6,7,8,9 – experiments on the dog Veta after resection of the stomach (curve 5: 36 days after the resection; curve 6: three months and 26 days; curve 7: seven months and 13 days; curve 8: seven months and 20 days; curve 9: ten months and five days after the resection) (in this experiment a large volume of the mixture – 250 ml instead of 150 ml – was given).

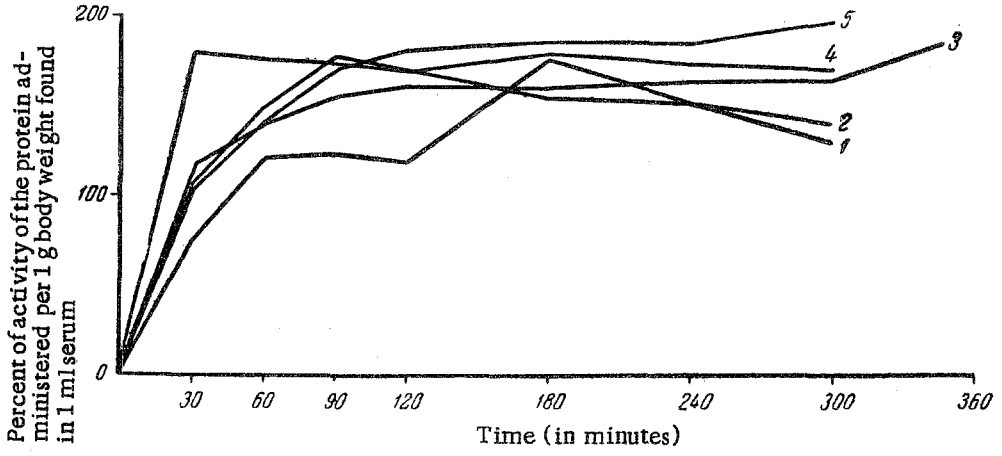

Fig. 2. Rate of resorption of breakdown products of casein labelled with I^{131} in the digestive tract. Experiments on the dog Nag. 1,2 – control experiments; 3,4,5 – after stomach resection (curve 3: 37 days, curve 4: four months, curve 5: seven months (15 days) after the resection).

Per Cent of Activity of the Protein Administered per 1 g Body Weight Found in 1 ml Serum after Administration of Casein Labelled with I^{131} in Various Ways (control dog Chernushka)

Method of administration	No. of exp.	Time (in minutes)					
		30	60	90	120	180	240
Oral ingestion	1	117	153	162	167	166	154
	2	82	144	156	161	157	153
Ingestion through a fistule in the ileum	3	216.	267	253	257	243	230
	4	240	250	245	240	236	225

To evaluate the quality of the labelled protein obtained and to establish whether it was suitable for physiological experiments, in vitro experiments were performed, in which the protein preparations obtained were decomposed with digestive enzymes: pancreatic and intestinal enzymes, incubating the proteins for different periods. The results of paper chromatography of this mixture performed after various periods of incubation showed that casein labelled by the method described above is decomposed to amino acids by a mixture of pancreatic and intestinal juice; no inorganic I^{131} could be found.

To prevent the accumulation of I^{131} in the thyroid gland the experimental animals were given a few drops of Lugol's solution three-four days before the experiment. Casein labelled with I^{131} in a dose of 100-200 counts per 1 g of weight was given to the dogs in a mixture with milk and water. The total volume of the liquid amounted to 150 ml out of which 50 ml were milk. In other experiments the volume of the liquid given to the dogs was increased to 250 ml out of which 150 ml consisted of milk. The dogs were given this drink 20 hours after the preceding consumption of food. At different times after the administration of protein labelled with I^{131} (after 15, 30, 60, 90, 120, 180, 240, 300 and 360 mins and in some experiments even later: after 12, 14 and 24 hrs) blood samples were taken from the dogs, (from the v. saphena parva with the animal standing, under light ether anesthesia of the skin) the serum was separated and its ratioactivity was measure by the β-radiation on a Geiger counter. The result in per cent of radioactivity administered per 1 g weight found in 1 ml serum. The experiments were repeated on one and the same animal at various times between 1-16 months after the subtotal stomach resection. Investigations were carried out on the same dogs after oral ingestion of methionin labelled with S^{35}. Throughout the period of observation the animals were kept on a standard diet and were given shredded food two or three times a day. The animals were regularly weighed and their stools were observed. The experiments were carried out on ten dogs in six of which the stomach was resected.

RESULTS

In the control experiments the maximum increase in the activity of their blood could be observed between 60 and 90 minutes after the administration of labelled protein in a range between 130 and 160 per cent of the radioactivity of the protein administered per g weight; later the activity gradually decreased. After one day the activity of the serum had decreased to 30-50 per cent.

After the resection of the stomach the radioactivity of the serum reached the maximum in the dogs earlier: within 30-60 mins after the administration of labelled protein. The peak of the radioactivity found in the blood was much higher than in the control experiments and reached 210-280 per cent. This high level usually persisted throughout the duration of the whole experiment (Fig. 1). After one day the radioactivity decreased just as in the control experiments to 30-50 per cent.

The increased rate of resorption of protein breakdown products from the digestive tract into the blood in dogs after partial resection of the stomach is mainly due to disorders in the evacuatory function of the stomach. The food enters the intestine more rapidly than under normal conditions.* If the evacuation of the food was de-

* The X-ray investigations were carried out by the research worker A. N. Pomel'tsov.

layed (which could be observed in one of the six dogs in which the stomach had been resected, named Naf) the breakdown products of protein enetered the blood at a slower rate and accumulated gradually in the blood (Fig. 2).

Chernushka either orally or through an intestinal fistule into the ileum bypassing the stomach. In this case the values for the radioactivity of the blood and the character of the radioactivity curves at different periods of time was quite different from the findings obtained in experiments with oral ingestion of protein: the breakdown products of protein were rapidly resorbed from the intestine and the curves were similar to those obtained in experiments on dogs after stomach resection (see table).

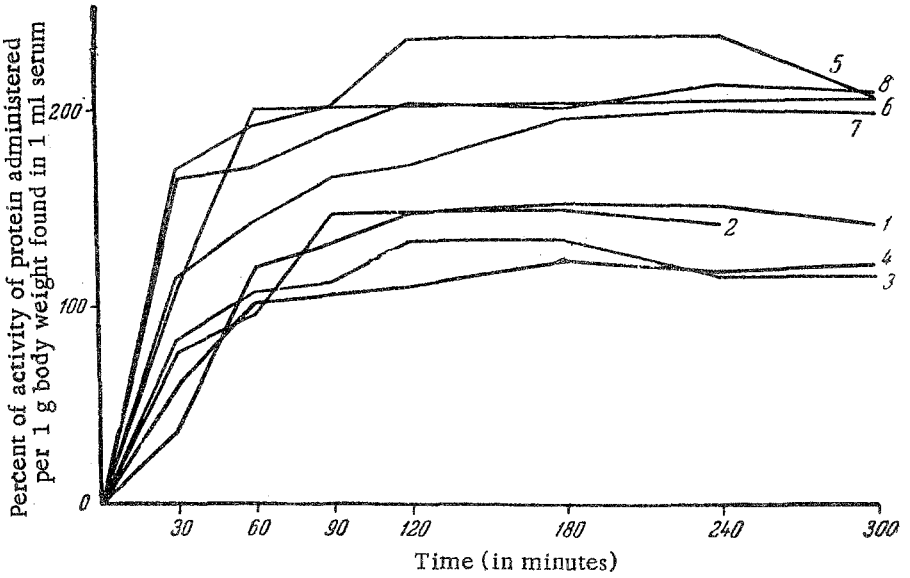

Fig. 3. Rate of resorption of methionin labelled with S^{35} in the digestive tract. 1, 2,3,4 – control experiments (curves 1 and 2: the dog Dick; curves 3 and 4: the dog Murzik); 5,6,7,8 – experiments on the dog Veta after stomach resection (curve 5: 11 months; curve 6: 12 months; curve 7: 13 months; curve 8: 15 months after the resection).

To establish whether the casein is deiodized in the intestine and also to establish in what form the breakdown products of casein labelled with I^{131} circulate in the blood we carried out the following experiments:

1) The thyroid gland of the dogs was not blocked with Lugol's solution before the oral ingestion of radioactive protein. Had inorganic I^{131} entered the blood from the intestine it would in this case accumulate in the thyroid gland. Measurements of the α-radiation in the region of the thyroid gland and the pause led to identical results. Consequently no accumulation of iodine took place in the thyroid gland.

2) Paper chromatography (ascending, in a mixture of butyl alcohol and water) of the radioactive serum revealed that the Rf of the radioactive spot was equal to 0.22 and the Rf of NaI^{131} was equal to 0.45. Hence it follows that no I^{131} was liberated from the protein in the shape of iodide.

3) Precipitation of the proteins from the radioactive serum with trichloracetic acid or alcohol revealed that the whole radioactivity was present in the trichloracetic or alcoholic extract. No radioactivity could be found in the protein. Consequently it must be assumed that the breakdown of casein labelled with I^{131} in the intestine proceeded down to amino acids which were then resorbed into the blood.

Changes in the normal entrance of food from the stomach into the intestine were of the greatest importance in the increased rate of resorption of protein breakdown products from the intestine after stomach resection. This follows from the experiments with methionin labelled with S^{35}. The labelled amino acids were ingested orally with milk into dogs possessing their whole stomach and dogs after partial resection of the stomach (100-200 counts per g body weight). Fig. 3 shows some of the results obtained in these experiments. Here again the considerable difference between the increase in the radioactivity of the blood serum between non-operated and operated dogs

became clearly manifest. In the latter the rate of resorption and the peak was higher.

In the control experiments the maximum activity found was 120-150 per cent of the protein administered per 1 g body weight in 1 ml serum whereas in operated animals it varied between 190-235 per cent. Here too the experiments on the dog Naf constituted an exception. After administration of both, labelled protein and methionine labelled with S^{35} the rate at which the labelled products entered the blood was not different from the normal conditions; in this dog, however, as we mentioned above, the evacuatory function of the stomach was slowed down after the operation.

Repeated investigations, carried out on one and the same dogs after the resection showed that the changes observed by us: rapid resorption and a high concentration of the labelled products in the serum soon after the administration of casein labelled with I^{131} and methionine labelled with S^{35} do not subside after a certain time but persist throughout the period of observation up to 16 months after the operation (See Fig. 1, 2 and 3).

Observation of the animals' weight showed that it decreased in the course of the 1st month following the operation by 2-4 kg. Later the dogs usually gained weight. No relation between the changes in the animals' weight and the resorptive function of the digestive tract could be established.

The results of our experiments broaden our conception concerning the role of the stomach in the regulation of the metabolism after food consumption.

It can be assumed that the poor subjective condition so frequently observed after meals in patients who underwent stomach resection can be explained with the inundation of the blood by protein breakdown products.

SUMMARY

The speed of absorption of the splitting products of labelled I^{131} and S^{35} methionine was studied in dogs at various intervals (ranging from 1 to 16 months) after partial resection of the stomach by the Billroth II method (Finsterer's modification). Experiments were staged on 10 dogs, 6 of which underwent stomach resection.

After gastic resection there was an accelerated absorption of the I^{131} casein-splitting products from the digestive tract and a reduced rate of their disappearance from the blood. The changed absorption rate of the protein-splitting products into the blood depends on the accelerated (in these conditions) gastric evacuatory function (x-ray investigations). Data obtained with I^{131} casein were confirmed by experiments with S^{35} methionine administration per os to control and operated animals. Some changes in the process of intestinal absorption are retained by the animal for the subsequent period of the animal's life. The longest follow-up period after the operation was 16 months.

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