

# THE EXTERNAL SECRETORY FUNCTION OF THE PANCREAS IN EXPERIMENTAL DYSENTERY TOXICOSIS AND THE MECHANISM OF ITS DISTURBANCE

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It has now been established that the external secretory function of the pancreas is disturbed in patients with dysentery. Some authors [5, 13] account for the hypofunction of the pancreas under these conditions by the influence of depression of the secretory power of the gastric glands, others [3, 10] — by the influence of the diseased intestine, and a third group [2, 9, 11] — by the general effect of the dysentery toxicosis on the body. The weakened and perverted secretory reaction of the pancreas (to hydrochloric acid) is explained [4] by disturbance of the regulation of its activity by the central nervous system.

In view of the importance of the specific toxicosis in the pathogenesis of dysentery, we investigated in animals the influence of dysentery toxicosis on the external secretory function of the pancreas, and the mechanism of this influence.

## EXPERIMENTAL METHOD

Experiments were carried out on dogs with a pancreatic fistula, created by A. N. Bakuradze's method [1].

It was possible, in these animals, to study the pancreatic secretion during eating (bread, meat, milk) and during injection of hydrochloric acid (30 ml of a 0.5% solution) into the duodenum. When not taking part in the experiments the animals did not lose their pancreatic juice. There were two variants of the experiments in which hydrochloric acid was injected. When one injection of acid was given, the pancreatic secretion was observed for one hour; when a sequence of several injections was given (every 30 minutes), observations were made for 4 hours.

In the course of the investigation estimations were made of the volume of pancreatic juice in ml during each hour and during the whole experiment, and also of its carbonate alkalinity (by a gasometric method in a Van Slyke apparatus), its amylase content (by our modification of the Goldstein-Michaelis method), the trypsin (by the Fuld — Gross — Michaelis method), lipase (by the method adopted at the Institute of Nutrition of the AMN SSSR) and the contents of organic and inorganic matter.

Dysentery toxicosis was induced in the dogs by the intravenous injection of toxin (0.15 mg of whole antigen of toxin from Hiss — Flexner dysentery bacteria per kg body weight). From 2 to 3 hours after receiving the injection of toxin, the animals developed the typical picture of dysentery toxicosis. In all, 128 experiments were performed on the two dogs Starik and Ledi over a long period of time.

TABLE 1

Changes in the Pancreatic Secretion during Eating before and after Induction of Experimental Dysentery Toxicosis

Indices of secretion	Initial background					2-4 days after injec. of toxin				
	Hours of secretion					Hours of secretion				
	1st	2nd	3rd	4th	5th	1st	2nd	3rd	4th	5th
The Dog Starik										
Secretion in response to 300 ml milk										
Indices of secretion	24,5	13,0	19,5	10,5	9,0	65,5	39,0	15,5	12,6	14,1
Alkalinity (in volumes per cent)....	105	67	90	105	50	250	240	200	135	140
Amylase content (in seconds).....	330	375	210	195	210	720	600	480	330	285
Trypsin content (in conventional units)	1280	640	1280	1280	2560	320	320	320	640	640
Lipase content(in%)	14,5	14,5	17,4	37,8	37,8	8,7	14,5	17,4	20,3	20,3
Organic matter(in%)	1,85	1,91	1,86	3,86	1,69	1,17	1,09	1,51	1,85	1,35
Inorganic matter (in %).....	0,77	0,83	0,76	0,70	0,94	0,86	0,93	1,02	0,86	0,84
Secretion in response to 125 g white bread										
Indices of secretion	51	37	26	19	12	84	61	40	34	26
Alkalinity (in volumes per cent)....	150	110	55	60	55	215	252	210	162	130
Amylase content (in seconds).....	345	280	255	180	105	765	840	675	510	495
Trypsin content (in conventional units)	2560	2560	2560	2560	2560	640	640	640	640	640
Lipase content(in%)	11,6	11,6	11,6	17,4	23,2	5,8	0	5,8	17,4	20,3
Organic matter(in%)	2,09	1,97	1,76	1,14	1,72	0,98	0,89	1,87	1,47	1,88
Inorganic matter(in%)	0,85	1,00	0,45	0,99	0,45	1,00	0,95	0,93	0,80	0,77
The Dog Ledi										
Secretion in response to 50 g pounded meat										
Indices of secretion..	10,5	23,0	20,0	17,0	6,0	29,0	26,5	26,0	22,5	22,0
Alkalinity (in volumes per cent)....	60	105	105	95	50	155	140	130	120	120
Amylase content (in seconds).....	270	210	180	135	90	915	945	910	750	645
Trypsin content (in conventional units)	1280	1280	1280	1280	1280	320	160	160	320	320
Lipase content(in%)	26,1	20,3	23,2	26,1	26,1	14,5	11,6	17,4	14,5	14,5
Organic matter (in%)	2,47	1,98	1,27	1,78	1,48	1,56	0,90	1,10	0,98	0,39
Inorganic matter(in%)	0,76	0,46	0,91	1,03	0,83	1,26	0,88	0,84	0,78	0,87

TABLE 2

Changes in the Pancreatic Secretion in Response to a Single Injection of Hydrochloric Acid

Time of investigation	Vol. of juice (in ml)	Carbonate alkalinity (in vol. per cent)	Amylase content (in seconds)	Trypsin content (in conventional units)	Lipase content (% de-composition of tributyrin)	Organic matter (in %)
The Dog Starik						
Initial background values	34,0	185	390	640	8,72	1,68
2nd day after injec. of toxin	42,4	200	502	640	5,81	1,13
The Dog Ledi						
Initial background values	24	157	645	640	8,72	—
2nd day after injec. of toxin	35	225	900	320	8,72	—

TABLE 3

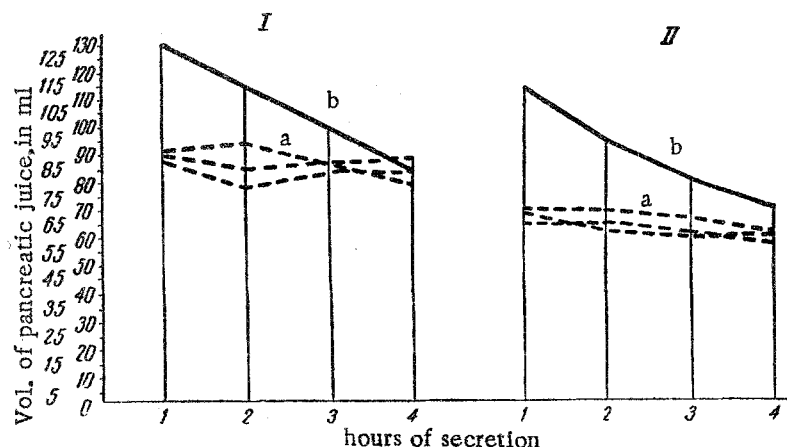
The Course of Recovery of the Pancreatic Secretion during Experimental Dysentery Toxicosis (secretion in response to 50 g meat)

	Initial background values	Days after Injection of toxin						
		2nd	6th	11th	18th	36th	48th	64th
The Dog Starik								
Volume of juice (in ml)	66,5—89,0	122,1	117,5	106,5	105,8	98	96	91
Alkalinity (in vol. per cent)	81	140,5	134	113	109,1	112	107	107
	76—101							
Amylase content (in seconds)	88	402	333	306	264	240	216	210
	180—248							
Trypsin content(in conventional units)	219	898	1 024	1 352	1 664	1 536	1 780	2048
	1280—2048							
Lipase content(in%)	1536	13,9	13,4	15,8	21,8	18,6	20,4	23,8
	17,4—29,4							
Organic matter(in%)	23,4	1,46	2,09	2,19	1,60		2,00	
	2,12—2,66							
Inorganic matter (in %)	2,19	0,6	0,79	0,84	0,98		0,70	
	0,44—0,97							
	0,74							

**Note:** In the column headed "Initial background values", the numerator gives the variations in the indices in 6 experiments and the denominator the mean value. The volume of juice is given as the total for the experiment; the other indices are the mean values for the hourly samples during the same 5 hours of the experiment.

#### EXPERIMENTAL RESULTS

It will be seen from the results in Table 1 that during experimental dysentery toxicosis, a sharp alteration took place in the typical course of pancreatic secretion in response to each of the food stimuli. The volume of



Changes in the volume of pancreatic juice during each hour of an experiment in which hydrochloric acid was introduced repeatedly (before and after injection of dysentery toxin).

1) In the dog Starik; II) in the dog Ledl. a) Determination of the background values (several experiments); b) on the 2nd day after injection of dysentery toxin.

pancreatic juice during each hour of working of the gland and throughout the whole experiment was increased. The alkalinity of the juice and the content of inorganic matter rose. The enzyme content (amylase, trypsin, lipase) and the organic matter decreased in amount. The pancreatic secretion evoked by injection of hydrochloric acid into the duodenum changed in the same direction (Table 2).

The changes were more pronounced in the first days after injection of the toxin. Gradually (in the course of about two months) recovery of the external secretory function of the pancreas took place (Table 3).

When the initial background values were studied in the experiment, it was found that the concentrations of enzymes and organic matter in the pancreatic juice secreted during eating were higher than those in response to injection of hydrochloric acid.

In the course of experimental dysentery toxicosis the changes in the quantitative and qualitative aspects of the secretory process were dissimilar. During eating, for instance, whereas the volume of the secretion was increased  $1\frac{1}{2}$ –2 times, the enzyme concentration was lowered 3–11 times\*. In response to injection of hydrochloric acid the increase in the volume of secretion was roughly the same, but the enzyme concentrations were lowered to a lesser degree or were quite unchanged. In the process of recovery of the secretory function of the pancreas, the volume of juice secreted recovered first and more completely.

These facts demonstrate that during experimental dysentery toxicosis, the enzyme-producing function of the pancreas was disturbed to a greater degree than the secretory function. In this connection it may be suggested that the nervous reflex mechanism was interfered with more than the humoral mechanism of regulation of the external secretory function of the pancreas.

As we know [8, 12], the role of the humoral mechanism in the regulation of the pancreatic secretion is considerable. If the pancreatic secretion during dysentery toxicosis was increased during eating or administration of hydrochloric acid into the duodenum, then the cause of this phenomenon had to be sought in the mechanism of the secretory process caused by the introduction of hydrochloric acid into the duodenum. The hydrochloric acid of the gastric juice is known to play an important part in the combined working of the two organs.

Our investigations into the secretory function of the stomach in dogs with the same experimental dysentery toxicosis showed that the secretion of gastric juice and its acidity were lowered. The paradoxical increase in the pancreatic secretion may be connected with a change in the evacuatory power of the stomach (with accelerated

\* According to the Borisov–Schütz rule, the concentrations of the enzymes are proportional to the squares of the values expressed.

entry of the acid gastric contents into the duodenum), or with a change in the functional capacity of the pancreas (with increased sensitivity of its neuroglandular apparatus to stimulation with hydrochloric acid).

These hypotheses were tested experimentally. For this purpose a series of experiments was carried out on two dogs with a Basov gastric fistula. It was found that the evacuatory power of the stomach in animals with experimental dysentery toxicosis was slowed. This slowing was shown especially in the first days after injection of the toxin, when the rate of the pancreatic secretion was increased maximally. For instance, whereas before injection of toxin, evacuation of 250 ml of a sour milk — starch mixture from the stomach was completed in 2 hours 45 minutes, after injection of dysentery toxin evacuation was completed in 4 hours 15 minutes, and after a further injection of toxin, in 5 hours 15 minutes.

The increased pancreatic secretion in dysentery toxicosis could not, therefore, be accounted for by changes in the secretory and evacuatory functions of the stomach.

In order to ascertain the functional state of the pancreas in experimental dysentery toxicosis, we carried out experiments in which pancreatic secretion was induced successively by repeated injections of hydrochloric acid into the duodenum for a long period of time. The results of some of the experiments in this series (see figure) show that whereas before injection of toxin the secretion after 4 hours of intensive working of the pancreas fell by 2.5-14.3% by comparison with that after one hour, on the second day after injection of the dysentery toxin it fell by 35.4-36.4%. With the course of time the functional capacity of the pancreas was restored.

The disturbance of the functional state of the pancreas in experimental dysentery toxicosis was thus demonstrated as a paradoxical secretory reaction to hydrochloric acid and food products, and also as a more intensive exhaustion of the gland after prolonged activity. In turn, the disturbance of the functional capacity of the pancreas was evidently connected with changes in the adaptive and trophic influences of the nervous system.

There are indications in the literature of functional and organic changes in the different divisions of the nervous system in dysentery toxicosis [6, 7].

#### SUMMARY

Considering the significance of specific intoxication in dysentery pathogenesis, the author undertook the study of the external secretory function of the pancreas in conditions of experimental dysentery intoxication. Experiments were conducted on 2 dogs for a period of 2 months.

A considerable disturbance of the pancreatic response to food stimuli and hydrochloric acid was noted, manifesting itself by an increased rate of juice secretion and reduced concentration of the enzymes. Dysentery intoxication disturbs the mechanism of the nervous and humoral control of the gland external secretion and also deranges its functional condition. The glandular function is restored very slowly after administration of the toxin.

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