

# DISTURBANCES OF GASTRIC SECRETION IN EXPERIMENTAL LIVER PATHOLOGY

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Gastric secretion in dogs with a gastric fistula was studied before and after liver damage induced by injecting a 33% solution of sodium salicylate (0.6 ml/kg body weight) into the portal vein. The stimuli were histamine and meat (sham feeding). Observations continued for 2 weeks to 3 years. In liver pathology there is an increase in the volume of gastric juice secreted and in its acidity and proteolytic activity, chiefly in the nervous reflex phase of gastric secretion.

There are many reports in the clinical literature on changes in the functional and morphological state of the gastrointestinal tract in liver disease [2-5, 8, 11, 12, 15, 22, 23, 26, 27]. The experimental data obtained after liver damage by hepatotoxic substances (chloroform, carbon tetrachloride, salicylates, alcohol) are contradictory. Most workers observed an increase in the secretory and acid-forming functions of the stomach under these conditions [1, 13, 17-21, 25], whereas others [14, 24] observed inhibition of the gastric secretion.

The object of this investigation was to clarify the character of the gastric lesion and to determine the mechanisms of the changes in gastric functions in experimental liver pathology.

## EXPERIMENTAL METHOD

Pathological changes in the liver were produced by injecting sodium salicylate into the portal vein by Litvak's method [9] in the writer's modification. By this method a long-term sclerotic process accompanied by degenerative changes and by structural changes in the parenchyma of the organ could be obtained in the liver [7]. Experiments were carried out on 5 mongrel dogs weighing 12-20 kg with Basow-Paylov gastric fistulas. The spontaneous level of gastric secretion was first established in response to subcutaneous injection of histamine (0.1% solution) and to sham feeding with meat (100 g). The stimuli were alternated (at intervals of a few days to 1 week). Under morphine-amobarbital anesthesia a midline laparotomy was performed 1.5-2 months later, a branch of the splenic vein was mobilized, and a polyethylene catheter was introduced through it into the portal vein. A 33% solution of sodium salicylate was then slowly injected through the catheter in a dose of 0.6 ml/kg body weight. After the injection the branch of the splenic vein was ligated and the abdominal wall was sutured in layers without drainage. Two dogs received a second injection of the same dose of salicylate 4-5 months later.

The main investigations were carried out after 10-12 days. The tests were carried out on an empty stomach after the animals had been starved for 18 h.

The volume of gastric juice, the free and total acidity, and the proteolytic activity of the juice were determined.

In 2 dogs, because of the short period of observation, only qualitative data on the disturbances of gastric function could be obtained. The results obtained with 3 dogs, under observation for about 3 years,

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TABLE 1. Gastric Secretion before and after Injection of Sodium Salicylate into the Portal Vein ( $M \pm m$ )

Dog	Index studied	Histamine		Meat (sham feeding)		P
		before injection	after injection	before injection	after injection	
Poprygun'ya	Volume of gastric juice	113 $\pm$ 3.6	105 $\pm$ 8.2	100 $\pm$ 8.5	120 $\pm$ 1.5	<0.05
	Free HCl	222 $\pm$ 13	362 $\pm$ 14	212 $\pm$ 12	322 $\pm$ 26	<0.01
	Total HCl	496 $\pm$ 16	557 $\pm$ 18	339 $\pm$ 53	606 $\pm$ 44	<0.01
	Pepsin	15 $\pm$ 2	32 $\pm$ 4	30 $\pm$ 13	69 $\pm$ 3.7	<0.02
	Free HCl	25 288 $\pm$ 3195	36 406 $\pm$ 9678	21 605 $\pm$ 5534	39 213 $\pm$ 5838	<0.02
	Total HCl	54 951 $\pm$ 3038	56 566 $\pm$ 5243	34 568 $\pm$ 2059	68 470 $\pm$ 1077	<0.001
	Pepsin	1 708 $\pm$ 221	2 650 $\pm$ 334	5 002 $\pm$ 900	12 634 $\pm$ 618	<0.01
	x Volume of juice					
Plaksa	Volume of gastric juice	64 $\pm$ 4	102 $\pm$ 2	117 $\pm$ 6	168 $\pm$ 53	<0.01
	Free HCl	256 $\pm$ 21	311 $\pm$ 12	292 $\pm$ 28	380 $\pm$ 10	<0.01
	Total HCl	444 $\pm$ 17	589 $\pm$ 20	517 $\pm$ 15	625 $\pm$ 23	<0.01
	Pepsin	16 $\pm$ 5	24 $\pm$ 4.2	38 $\pm$ 10	63 $\pm$ 3	<0.05
	Free HCl	15 842 $\pm$ 898	43 046 $\pm$ 362	15 842 $\pm$ 895	64 967 $\pm$ 5222	<0.001
	Total HCl	27 148 $\pm$ 770	62 775 $\pm$ 1604	50 515 $\pm$ 1851	107 069 $\pm$ 1250	<0.001
	Pepsin	603 $\pm$ 101	2 388 $\pm$ 417	4 428 $\pm$ 1499	9 947 $\pm$ 348	<0.001
	x Volume of juice					
Karlik	Volume of gastric juice	30 $\pm$ 2.7	41 $\pm$ 3	39 $\pm$ 2.8	50 $\pm$ 1.6	<0.001
	Free HCl	269 $\pm$ 15	272 $\pm$ 12	280 $\pm$ 16	275 $\pm$ 21	>0.9
	Total HCl	494 $\pm$ 12	527 $\pm$ 19.7	590 $\pm$ 20	528 $\pm$ 6.5	>0.8
	Pepsin	13 $\pm$ 1	16 $\pm$ 1.8	27 $\pm$ 1	35 $\pm$ 3	<0.01
	Free HCl	6 905 $\pm$ 456	10 719 $\pm$ 947	11 216 $\pm$ 132	17 725 $\pm$ 645	<0.001
	Total HCl	14 648 $\pm$ 1110	22 746 $\pm$ 2154	23 559 $\pm$ 2085	32 488 $\pm$ 2583	<0.02
	Pepsin	410 $\pm$ 135	735 $\pm$ 415	1 057 $\pm$ 97	2 646 $\pm$ 427	<0.01
	x Volume of juice					

were subjected to statistical analysis [10]. Besides determining the acidity and proteolytic activity of the juice, the indices of acidity and pepsin were calculated relative to the total volume of gastric juice.

## EXPERIMENTAL RESULTS AND DISCUSSION

In two dogs 10 days after the injection of sodium salicylate the reaction of the fasting gastric juice became acid (in seven of nine tests) instead of neutral; in six of nine tests spontaneous gastric secretion took place (from 10 to 56 ml). In four of six tests on one of these dogs the secretion of gastric juice was greater in response to histamine and sham feeding with meat than before the injection of salicylate. These dogs died 16 and 50 days after the operation.

The dogs Poprygun'ya, Plaksa, and Karlik were under observation for 2 years 6 months, 2 years 5 months, and 3 years, respectively. Karlik and Poprygun'ya received two injections of sodium salicylate. Altogether 134 tests were carried out on these dogs. Spontaneous secretion of acid gastric juice was observed in some of them.

The results obtained with these dogs after injection of histamine and sham feeding with meat are given in Table 1. Injection of histamine into the dog Poprygun'ya led to an increase in the HCl and pepsin concentration. The total volume of gastric juice was unchanged. There was a very small increase in the total quantity of HCl secreted. Sham feeding the same dog with meat led to an increase in all the indices of gastric secretion.

All the indices of gastric secretion except proteolytic activity were increased in the dog Plaksa after injection of histamine. All the indices increased after sham feeding with meat.

In the dog Karlik injection of histamine led to an increase in the volume of gastric juice and in the total HCl production. During sham feeding with meat pepsin secretion also increased.

These results show that in most tests the secretory, acid-forming, and proteolytic functions of the stomach were enhanced in liver pathology caused by sodium salicylate. The more distinct changes in response to sham feeding with meat than to injection of histamine indicate that the greatest changes in gastric function under these circumstances took place during the first (nervous reflex) phase of gastric secretion. The second (humoral-chemical) phase was less affected.

The indices of gastric secretion in all the animals were changed during the first month after the operation. Later they continued to remain high and there was a further sharp increase after a second injection of salicylate. This was observed particularly clearly after sham feeding of the dogs with meat.

No tendency for the gastric secretion to return to normal was observed during the entire period of observation (up to 3 years). This corresponds to the duration of the morphological changes in the liver [7]. The disturbances of gastric activity observed could not be associated with any direct effect of sodium salicylate on the stomach: intravenously injected sodium salicylate is not excreted by the gastric mucosa [6] and, in addition, when administered in this way, it does not alter the acidity of the gastric juice [16] or may even inhibit its secretion [28].

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