FUNCTIONAL AND MORPHOLOGICAL CHANGES IN THE STOMACH OF DOGS WITH EXPERIMENTAL HEPATITIS

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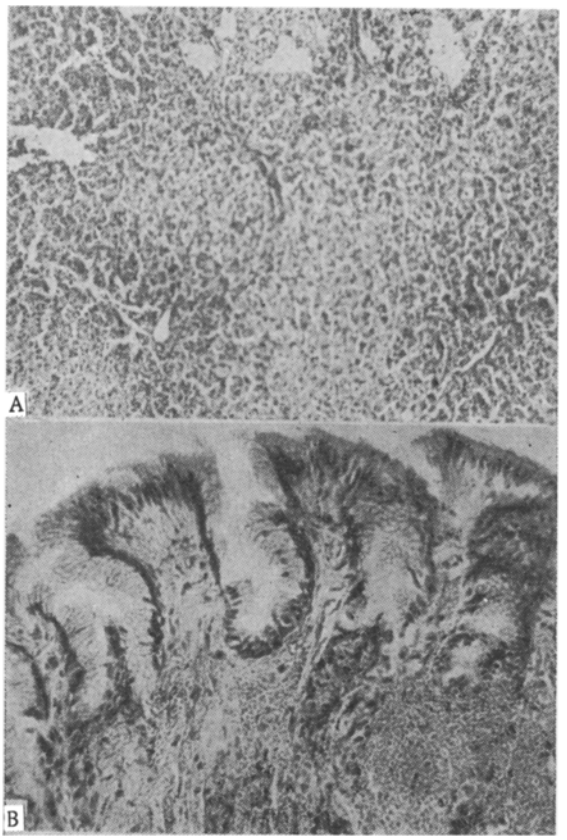
An important feature of the clinical picture of epidemic hepatitis is pain in the stomach, and in the history of patients with chronic diseases of the stomach there is frequently mention of a previous attack of Botkin's disease [4]. The results of studies of gastric function in patients with epidemic hepatitis [1, 3, 6, 9, 13] have revealed disturbances of the secretory, excretory, and motor functions of the stomach. However, information concerning the character of these disturbances is conflicting. So far as the morphological state of the gastric mucous membrane in patients with epidemic hepatitis is concerned, the information in the literature is limited to accounts of isolated gastroscopic investigations and postmortem observations [12, 14-18].

It is now generally accepted that carbon tetrachloride is a hepatotropic poison which causes profound liver damage and disturbances of metabolism which are similar both experimentally and clinically to the change observed in epidemic hepatitis [2, 7, 8, 10].



Changes in the liver (A) and gastric mucous membrane (B) in the dog Laika with toxic hepatitis. Photomicrograph. Hematoxylin-eosin. Magnification: A) 8 x 10; B) 40 x 10. Explanation in text.

For this reason carbon tetrachloride was used to create a model of hepatitis in three dogs with a Pavlov's gastric pouch and the function and morphological changes in the stomach of these animals were studied in a chronic experiment.

EXPERIMENTAL METHOD

To study the initial state of the stomach, the volume of gastric juice in hourly portions, the acidity, the peptic activity, and the leukopedesis were determined in the animals on three days in the week, for a period of 5 h on each occasion. Standard test meals were used: meat, milk, and bread. After 10 days an aspiration biopsy of the gastric mucous membrane was performed through the fistula. The material was fixed in 10% formalin and the material was embedded in paraffin wax.

Histological sections were stained with hematoxylin and eosin.

The initial state of the liver was assessed from the serum protein formula and the blood levels of aldolase, glutamate-pyruvate and glutamate-oxaloacetate transaminases, bilirubin, cholesterol, C-reactive protein, nonprotein nitrogen, and indican and by the thymol test. These investigations were carried out on every 7 days.

After the background investigations had been completed the dogs were given a subcutaneous injection of a 50% solution of carbon tetrachloride in peach oil in a dose of 0.2 ml/kg body weight. The poison was given at intervals of 5-7 days. Subsequently, the same indices of the

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Secretion (in ml) and Acidity of Gastric Juice (in titration units) per Hour in Response to Test Meals of Meat, Milk, and Bread, M

Dog's name	Hour of expt.	Meat				Milk				Bread			
		background		experiment		background		experiment		background		experiment	
		secretion	acidity	secretion	acidity	secretion	acidity	secretion	acidity	secretion	acidity	secretion	acidity
Laika	1 st	5,8	79/94	5,8	116/134	2,5	32/56	2,6	112/114	0,9	40/60	1,0	140/165
	2 nd	3,9	84/104	4,6	126/138	3,9	70/89	3,7	114/128	0,9	10/40	0,5	130//30
	3 rd	2,2	65/92	2,7	113/119	1,3	58/78	2,3	111/122	1,4	10/30	0,8	105/105
	4 th	2,5	50/73	2,0	106/117	1,7	17/47	2,0	93/105	1,4	10/30	1,0	55/55
	5 th	1,8	30/57	1,7	70/80	1,1	0/17	1,3	82/95	1,2	0/30	1,1	50/60
Tsygan	1st	11,5	79/107	12,8	92/119	7,8	76/112	7,7	36/84	3,4	0/54	5,7	22/68
	2 nd	7,3	57/94	11,8	114/132	10,9	113/144	6,6	93/124	1,7	0/47	3,8	24/81
	3 rd	5,8	23/72	12,9	114/134	5,7	47/101	4,0	80/120	1,7	0/48	3,2	33/81
	4 th	6,3	17/80	8,6	84/122	2,2	0/45	2,4	40/85	1,9	0/32	3,2	29/81
	5 th	6,1	21/77	6,8	77/114	2,2	0/45	2,2	33/83	3,7	0/42	2,8	14/66
Pal'ma	1 st	10,9	74/102	13,1	86/122	7,4	59/94	8,0	81/104	4,7	43/73	6,2	78/96
	2 nd	9,0	85/109	10,8	93/131	9,8	94/112	10,1	103/136	3,6	0/29	5,8	56/73
	3 rd	8,6	91/119	10,6	102/136	4,7	62/88	5,0	84/113	3,0	0/25	4,9	63/84
	4 th	5,2	70/106	7,4	81/118	2,3	20/54	2,6	47/72	2,8	0/30	3,2	55/92
	5th	4,1	50/87	5,1	64/92	3,7	14/44	3,5	30/58	3,3	0/32	2,7	48/73

Note. The free acidity of the gastric juice is shown in the numerator and the total acidity in the denominator.

functional state and morphology of the gastric mucous membrane and liver were studied as when the background was determined, and these investigations were described as experimental. The experiment lasted for 6 months.

EXPERIMENTAL RESULTS

Toxic signs appeared within a few hours after injection of the poison. The dogs became lethargic and refused to eat. By the end of the first day their body temperature was elevated. The clinical picture of poisoning was severest during the first 24 h. At the end of the 2nd day the dogs began to eat and became more active. The clinical manifestations of poisoning had completely disappeared by the 4th-5th day. One month after the beginning of administration of carbon tetrachloride the body weight of the animals had fallen. Punch biopsy of the liver showed marked fatty degeneration and infiltration by small cells, and areas of necrosis were found in individual groups of liver cells and blood vessels, with the development of hemorrhages.

After repeated injections of carbon tetrachloride proliferation of the connective tissue was observed (see figure, A). The changes in the serum proteins were demonstrative and indicated the development of hepatitis. A marked decrease in the albumin content with a corresponding increase in the globulin content developed, so that the albumin-globulin ratio fell from 1.05 to 0.61.

The latent period of gastric secretion in the animals with toxic hepatitis varied from experiment to experiment, although if the pathological process in the liver was of long duration, it was regularly shortened.

The volume of gastric juice in response to a test meal of meat was increased in all the animals, in response to a meal of bread it was increased in two and decreased in one, while in the dogs receiving milk, it showed no significant change.

The results for the acidity of the gastric juice were very demonstrative and convincing. They demonstrated an increase in the functional activity of the gastric glands. In all the animals the acidity of the gastric juice rose considerably, in some experiments to 13 times the background level. No free hydrochloric acid was secreted by two dogs in the initial state in response to a test meal of bread, but after the development of hepatitis, free hydrochloric acid was regularly secreted (see the table).

The peptic activity of the gastric juice determined by Mett's method showed no significant change.

The gastric leukopedesis decreased parallel to the increase in acidity, evidently on account of the destructive action of hydrochloric acid on the leukocytes.

The work of I. P. Razenkov [11] shows that the gland cell is not something constant, but with an extremely dynamic and labile reactive ability. The response reaction of the gastric glands is a product of two values: the strength and the character of the stimulus and the reactive ability of the gland cell. In the present experiments the first value was constant. It is logical to assume that the reactivity, the degree of excitability of the gland cells was considerably increased. This is confirmed by the shortening of the latent period of secretion which, as K. S. Zamychkina [5] has shown, is fully dependent on the degree of excitability of the gastric glands: the more excitable the gland cell, the shorter the latent period.

The study of the histological preparations of the gastric mucous membrane revealed inflammatory and degenerative changes, an excessive quantity of mucous in the surface epithelium and the glandular epithelium, desquamation of the surface epithelium with the formation of areas of erosion, pycnosis of the nuclei, eccentrically situated nuclei, distention of the vessels of the mucous membrane with blood, stasis, hemorrhages in the tunica propria, and foci of leukocyte infiltration (see figure, B).

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