METHODS OF REPRODUCING EXPERIMENTAL CHRONIC LIVER DISEASE

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A 33% solution of sodium salicylate was injected into the portal venous system of dogs. In acute experiments the flow of bile and lymph was increased and the pressure in the portal vein was unchanged. Disturbances of function were reflected in morphological changes in the organ. In chronic experiments the development of sclerosis was observed, with thickening of Glisson's capsule, proliferation of connective-tissue bands, coarsening of the network of argyrophilic fibers, fatty infiltration of the parenchymatous cells, and a decrease in their glycogen content, diapedetic hemorrhages, and infiltration by leukocytes. The portal venous pressure was raised.

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Disturbances connected with the development of liver pathology are difficult to investigate without the availability of a long-term model of a liver disease. Most agents used for this purpose require prolonged and repeated administration [5-7, 9, 14, 15]. According to data in the literature, sodium salicylate, which influences metabolic processes, promotes sclerosis and stimulates the flow of bile and digestive juices [1, 3, 4, 8, 10-13, 16].

In the present investigation the function and morphology of the liver were studied during the development of acute and chronic changes in the liver produced by injection of sodium salicylate. The experiments were based on the method suggested by Litvak [2] with modifications added by the writers (a series of acute experiments, long periods of observations, and more thorough histological investigation).

EXPERIMENTAL METHOD AND RESULTS

In the experiments of series I (7 dogs) a 33% solution of sodium salicylate was injected into the portal vein in fractional doses (up to 10-12 ml each time). During these experiments the pressure in the portal vein, the flow of bile, and the lymph flow in the horacic duct was measured.

In a series of chronic experiments (25 dogs) a solution of sodium salicylate was injected into the portal vein (0.6 ml/kg body weight) in 1, 2, or 3 doses at intervals of 1-6 months. Observations were continued for 2-2.5 years after the last injection. Morphological and biochemical investigations were carried out.

In the acute experiments the sodium salicylate increased the flow of bile by 4-6 times. The content of bilirubin and cholesterol in the bile was reduced, and erythrocytes were found. The later flow of lymph was increased by 2-3 times, and the lymph was stained with blood. The portal pressure varied within normal limits. Sections of the liver showed erythrocytes in the lumen of the bile ducts, and the lymphatic capillaries were dilated (especially in the region of the collecting veins). Branches of the portal system were only slightly dilated, but frequently spasm of some of the collecting veins was present, with perivascular hemorrhages. In the subcapsular region there were numerous hemorrhages with atrophy and necrosis of the cells. These observations indicate an intimate connection between the blood, lymphatics, and biliary systems, changes in the function of which could be the cause of the necrobiotic changes in the liver.

In the chronic experiments, 1 month or more after injection the portal pressure was increased, the surface of the liver and spleen had become whitish, the ventral border thickened, and the consistency was firm.

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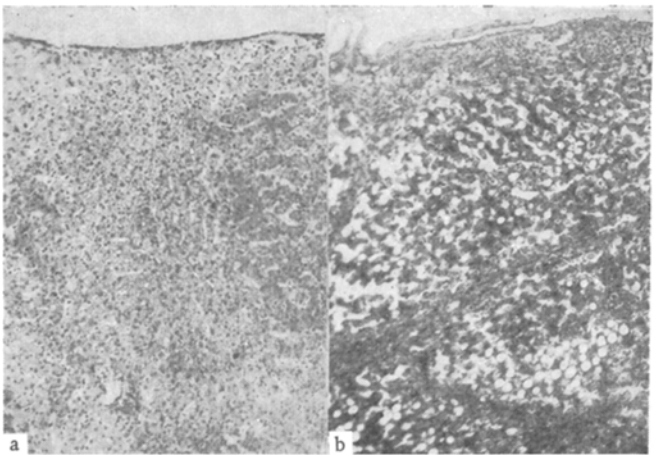

Fig. 1. State of fibrous connective tissue in dog's liver (biopsy): a) before experiment; b) 1 year after 3rd injection of salicylate. Duration of experiment 1.5 years. Van Gieson, 60×.

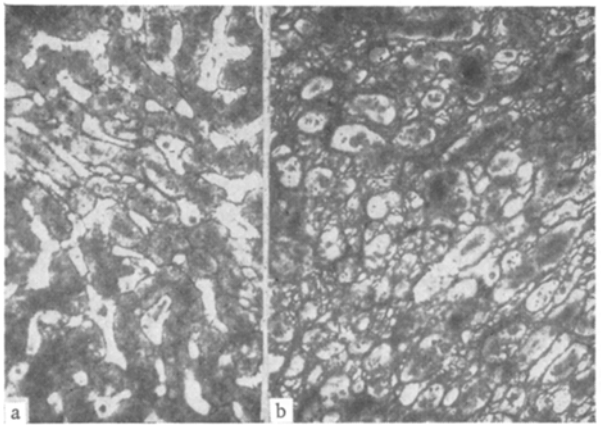

Fig. 2

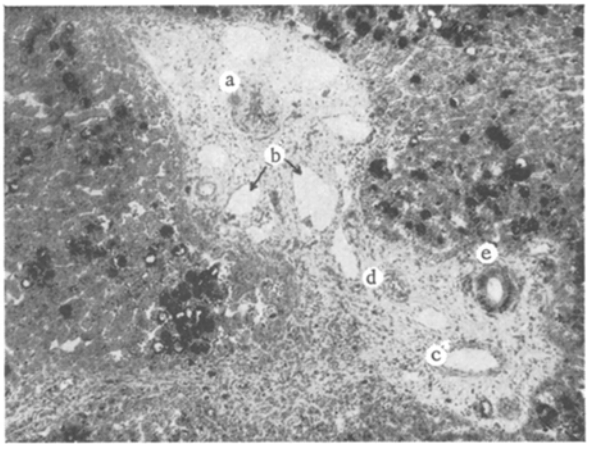

Fig. 3

Fig. 2. State of argyrophilic fibers in dog's liver (biopsy): a) before experiment; b) 2 months after 2nd injection of salicylate. Duration of experiment 6 months. Impregnation with silver by Tibor – Pape's method, 200×.

Fig. 3. Liver of dog (biopsy) 1 year after the 3rd injection of salicylate. Fatty degeneration of liver parenchyma with fine and coarse droplets. Collecting vein in spasm (a) surrounded by dilated lymphatics (b), branch of portal vein (c), collapsed branch of renal artery (d), bile duct with fatty infiltration of epithelium (e) present in a common band of connective tissue. Duration of experiment 1.5 years. Sudan III, 60×.

As a result of repeated injections of sodium salicylate, sclerotic changes increased in intensity (thickening of Glisson's capsule and of the interlobular septa, presence of atypical connective-tissue bands) (Fig. 1). Thin bands of collagen fibers divided the parenchyma into isolated areas. In the subcapsular zone, and also in the region of veins of the efferent system, hyperplasia and coarsening of the network of argyrophilic fibers was observed (Fig. 2), together with widening of the spaces of Desse and Mall, and also of the lymphatic vessels (especially around the veins of the efferent system) (Fig. 3), diapedetic hemorrhages, and foci of leukocytic infiltration near the collecting veins and in the subcapsular zone. Repeated injections caused fatty degeneration of the parenchymatous cells (Fig. 3), a decrease in the glycogen content, an increase in the content of mucopolysaccharides, breakdown of the complex structure of the parenchyma with disappearance of the argyrophilic fibers near the periportal zones, and the appearance of foci of necrosis.

Biochemical tests showed an increase in the aldolase and transaminase activity of the blood, an increase in the blood protein content, and a decrease in the protein index with a relative increase in the content of globulin fractions. Regression of the sclerotic changes began to take place 2-2.5 years after the last injection. Consequently, under the influence of sodium salicylate, pathological changes develop in the liver and persist for a long time without further injection of the irritant, These changes consist of the development of sclerosis, degenerative change, reorganization of the parenchyma, splenomegaly, and changes in some biochemical indices of the blood. Despite the prolonged (1-2 years without reinforcement) physiological and morphological changes, the liver did not lose its power of compensatory regeneration.

This experimental model thus provides a means for various investigations against the background of prolonged liver pathology.

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