

Production of Cirrhosis of the Liver of the Normal Dog by High Fat Diets.*

I. L. CHAIKOFF AND C. L. CONNOR.

From the Divisions of Physiology and Pathology, University of California Medical School, Berkeley and San Francisco

During the course of a study on the maintenance of the completely depancreatized dog, it was observed that cirrhosis of the liver developed in 8 of the 16 animals that had been kept alive with insulin for periods between 2.6 and 5.5 years.¹ Infection and obstruction of the extrahepatic bile passages were ruled out as factors that might have induced the scarring of the liver. The animals received a diet containing lean meat, sucrose, bone ash and vitamin supplements and despite its completeness with respect to calories, proteins, vitamins and salts it has been demonstrated repeatedly that this diet induces fatty livers in depancreatized dogs. Although it was recognized that the absence *per se* of the pancreas might be involved, it was nevertheless suggested that an important causative factor in the production of the hepatic fibrosis was the excessive deposition of fat which appeared in the liver during the first few months after pancreatectomy and remained there for long periods.

In view of the importance of the above findings, it seemed highly desirable to determine whether cirrhosis could be induced in the fatty liver of the normal dog. The observations recorded below establish for the first time that the continued presence of excessively high amounts of fat in the liver for several months stimulates hepatic fibrosis even in normal dogs to the extent that it may be called a true cirrhosis, and cause the death of the animals.

Experimental. Well nourished dogs were selected for use in this experiment. Throughout the periods of observation they were maintained on a high fat diet that contained 10 g of lard and 7 g of lean meat per kilo per day. They were fed twice daily by stomach tube when they would not eat, at 7:00 a.m. and at 2.30 p.m. Each animal also received once daily 1 g of Cowgill's salt mixture,² 1-5 g of bone ash and vitamin supplements in the form of cod liver oil and a rice bran concentrate.

Four dogs died after being maintained on this diet for 138, 246,

* Aided by a grant from the Christine Breon Fund for Medical Research.

¹ Chaikoff, I. L., Connor, C. L., and Biskind, G. R., *Am. J. Path.*, 1938, **14**, 101.

² Cowgill, G. R., *J. Biol. Chem.*, 1923, **56**, 725.

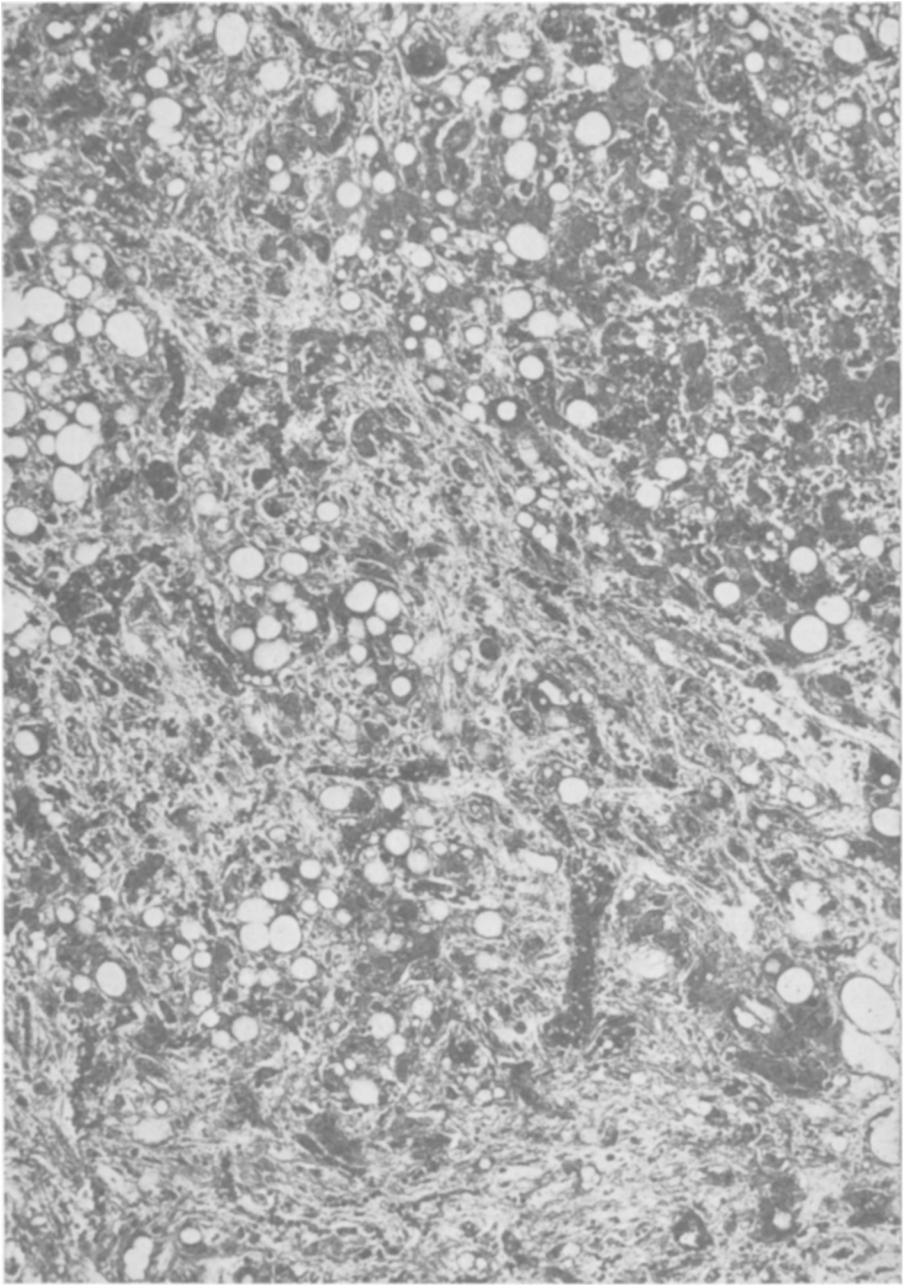


FIG. 1.

Microphotograph of sections stained with Mallory's aniline blue collagen stain. At a magnification at about 170X the uniform distribution of fibrous tissue, fat, and degenerating liver cells can be seen. Many large sinuses are engorged with blood.

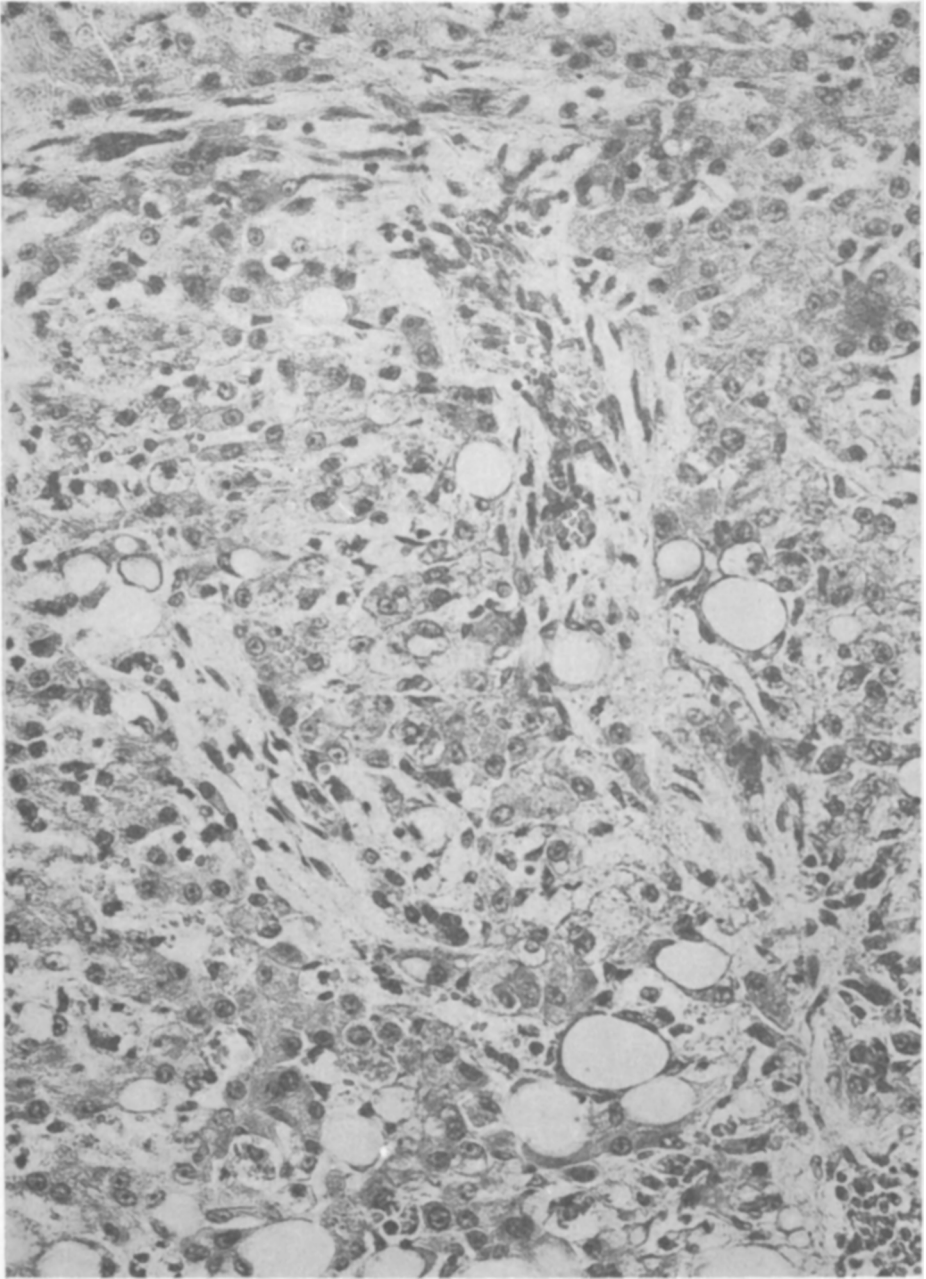


FIG. 2.

Microphotograph of sections stained with Mallory's aniline blue collagen stain. At about 350X, more details of the proliferating fibrous tissue can be seen. In Figs. 1 and 2 the lack of portal or perilobular distribution of the process is evident.

298, and 386 days. The livers of 3 of these animals showed a severe diffuse fibrosis and in all of them a severe fatty infiltration was observed. A typical protocol follows:

Dog F41 was placed on the high fat diet on November 29, 1938, and died December 20, 1939. Its weight at the start was 11.2 kg and at death 12.8 kg. It attained a maximum weight of 16.5 kg during the course of the experiment. The liver weighed 695 g. It was uniformly green in color, firm and rubbery in consistency. It cut with resistance and was lobulated on the surface.

Microscopically (Figs. 1 and 2) the liver showed marked fibrosis and a fatty infiltration. The liver cords were broken up into fragments and in no place had the original pattern of the liver been retained. Fragments of cells were found between proliferating strands of connective tissue that were growing in all directions but had no particular distribution with respect to portal areas or central veins. Blood sinuses were engorged and appeared like fibrous walled blood vessels rather than sinusoids. Some bile duct proliferation had taken place but their duct cells were difficult to recognize because they, too, were enmeshed in connective tissue. Many plugs of inspissated bile were present in large and small masses.

It is of interest to note that the diffuse character of the fibrosis reported here distinguishes this type of cirrhosis from that previously described for dogs receiving alcohol,³ although the outstanding anatomical change preceding the fibrosis in both instances, as well as in the depancreatized dogs, was severe fatty infiltration of the liver.

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Immediate Generalized Skin Reactions in Hypersensitive Guinea Pigs.*

J. L. JACOBS. (Introduced by V. Menkin.)

From the Department of Pathology and Bacteriology, Tufts College Medical School, Boston, Mass.

Immediate generalized skin-reactions following contact with or ingestion of allergens have been observed in humans but not hitherto in animals, although Dienes and Simon¹ reported a generalized

³ Connor, C. L., and Chaikoff, I. L., *PROC. SOC. EXP. BIOL AND MED.*, 1938, **39**, 356.

* This investigation was aided by a grant from the Charlton Research Fund of the Tufts College Medical School.

¹ Dienes, L. and Simon, F. A., *J. Immunol.*, 1935, **28**, 321.