monkey kidney cell system in disposable microplates; virus is detected by the hemadsorption technic and results are read with a standard light microscope. The microneutralization technic was shown to be a highly reliable method for demonstrating significant neutralizing antibody titer rises with sera from patients from whom parainfluenza viruses were isolated and also for detecting antibody to the animal strains in the sera of laboratory animals. The test may also be used for identification of viral isolates, but this application is limited by the fact that certain isolates do not possess sufficiently high titers to produce clear-cut hemadsorption in the micro system.

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Effect of Superior Vena Cava Constriction and Obstruction of Thoracic Duct Lymph Flow on the Liver of the Dog.* (31328)

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"Cardiac cirrhosis" of the liver follows long-standing venous congestion(1,2); part of this extensive hepatic fibrosis may be due to an associated lymph stasis. There is evidence that lymph stasis is present when there is hepatic venous stasis. Dumont *et al*(3) have shown that "venting" the thoracic duct in patients with intractable congestive heart failure results in striking clinical improvement. Ascites, produced by constriction of the superior vena cava, is similarly relieved in dogs when the thoracic duct is shunted to the esophagus(4). These studies have clearly demonstrated that hepatic venous congestion is associated with lymph stasis due to inability of the thoracic duct to handle the added lymph flow. It is known that chronic impairment of lymph flow predisposes to fibrosis in the affected organ(5,6). Thoracic duct lymph pressure is elevated in experimental constrictive pericarditis(7), and it is in this entity, which is undoubtedly associated with marked hepatic lymph stasis as well as venous blood stasis, that "cardiac cirrhosis" is the most severe.

The present studies were initiated to determine whether chronic constriction of the superior vena cava combined with resection of a segment of the thoracic duct can lead to discernible alteration in liver histology in the dog. There is good evidence that elevation of central venous pressure interferes with drainage of thoracic duct lymph(8).

Material and methods. Mongrel dogs were anesthetized with intravenous sodium pentobarbital (25 mg/kg). Using sterile precautions, the chest was opened through a left lateral incision in the third or fourth interspace. Artificial respiration was maintained *via* tracheal intubation with a mixture of 95% oxygen and 5% carbon dioxide. Prior to opening the chest, a wedge liver biopsy

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was obtained through a small abdominal incision, and the specimen was immediately placed in formalin solution. The abdominal wound was left open until the chest surgery was completed, and was closed after checking the liver biopsy site to make sure that there was no bleeding.

Approximately 2.5 cm of the upper thoracic duct was resected between cotton ligatures immediately after the chest was opened. Then the superior vena cava was double-ligated over a glass rod so as to constrict it approximately 50%. These ligatures were placed cephalad to the entrance of the azygos vein into the superior vena cava. In 3 animals only the superior vena cava constriction was performed, and in 2 dogs only a mock opertion was done.

Operated animals were routinely given 600,000 units of procaine penicillin intramuscularly daily for 5 days after surgery. Those dogs which did not die spontaneously were killed with intravenous sodium pentobarbital up to a maximum of 95 days postoperatively. After initial autopsy observation the lungs and heart were removed in a single block, and then, along with the liver, were examined grossly. Subsequently, the histological specimens (treated with hematoxylin-eosin, orcein-Van Gieson, and Mallory stains) were studied by each of the two pathologists participating in this study.

Venous pressures were obtained with a simple water manometer connected to a polythene tube threaded into a foreleg vein.

Results. Table I summarizes the findings in the various groups.§ A total of 35 dogs were operated upon. Seven of these animals were excluded from the study because worms (*Dirofilaria immitis*) were found in the right ventricle and pulmonary artery at autopsy. The 2 mock-operated dogs, in which neither the superior vena cava was constricted nor the thoracic duct was resected, showed no serous membrane or hepatic alterations grossly or histologically.

In 4 of the 8 dogs in which a segment of thoracic duct was resected without constriction of the superior vena cava, there were histologic changes in the liver compared to the biopsy controls, the predominant changes consisting of central venous congestion and dilatation of sinusoids. Two of the dogs also had perivascular fibrosis, and one showed necrosis of centrolobular liver cells. In 3 animals the superior vena cava was constricted without obstructing the thoracic duct. Two of these dogs had pleural effusions, and all 3 showed significant liver changes in comparison to control biopsies.

In 15 dogs the superior vena cava constriction was combined with resection of a segment of thoracic duct. Six of these animals had pleural and/or pericardial effusions at autopsy. In 12 of them changes were noted in the liver when compared to the biopsy controls. Seven of these animals showed perivascular fibrosis (Fig. 1), and 11 had dilatation of the sinusoids (Fig. 2). Central venous congestion (Fig. 3) was observed in 9 animals in this group. In a few of them lymphatic dilatation (Fig. 4) was also seen.

Pleural effusion, considered evidence of continued elevation of pressure in the superior vena cava, occurred in a total of 7 dogs with superior vena cava constriction (with or without thoracic duct obstruction). In all these animals there were changes in liver histology as compared to liver biopsy controls. In general, the pathologic changes seen in the liver were not marked, and in no instance did they approximate quantitatively the degrees of abnormality characteristically seen in cardiac fibrosis of the liver.

Discussion. Resection of a segment of thoracic duct combined with constriction of the superior vena cava undoubtedly results in impaired lymph flow for a substantial period of time. Gryaznova(9) showed that it takes 3 to 4 weeks after section of the thoracic duct between ligatures in the chest for collaterals to become visible, and in her studies no segment of thoracic duct was removed. Even after collateral formation occurs, an elevated pressure in the superior caval system would continue to interfere with lymph drainage. On the other hand, we have no knowledge concerning the adequacy of lymph drainage from the liver into the in-

§ Table I will be provided to readers on request.

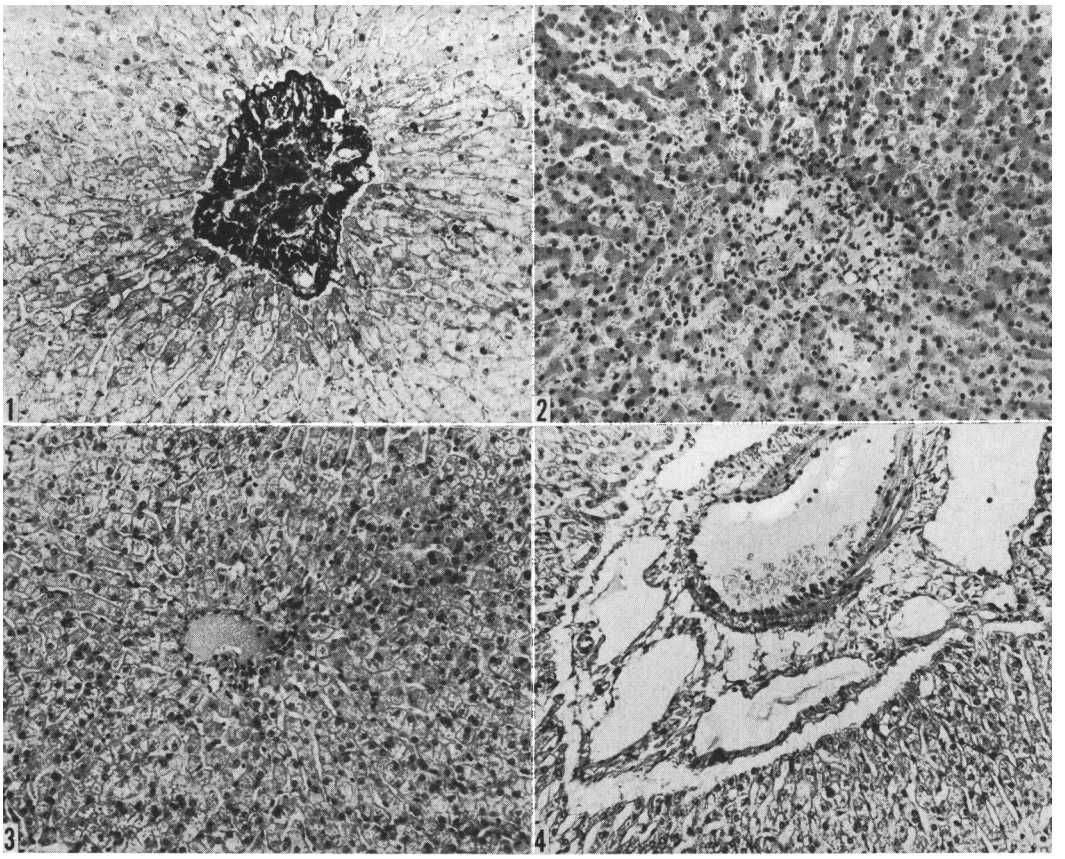

FIG. 1. Section of liver, stained with Mallory's trichrome. Magnification × 150. Note dense perivascular fibrosis (black in photograph).

FIG. 2. Section of liver, stained with hematoxylin and eosin. Magnification × 150. Note dilatation of sinusoids with passive hyperemia.

FIG. 3. Section of liver, stained with hematoxylin and eosin. Magnification × 150. Note dilated and congested central vein.

FIG. 4. Section of liver, stained with hematoxylin and eosin. Magnification × 150. Note dilated lymphatics in a periportal area.

ferior vena cava system *via* lymphatico-venous shunts(10).

Our findings demonstrate that histologic changes occur in the liver after constriction of the superior vena cava, with and without additional resection of a segment of the thoracic duct. The changes which were produced, though certainly not marked, are qualitatively similar to some of the early changes seen with cardiac fibrosis of the liver.

In patients with chronically elevated central venous pressure there is undoubtedly impairment of lymph drainage from various organs(8). As noted above, severe hepatic venous congestion is associated with lymph stasis due to lymph overload on the thoracic duct(3,4). We have previously demonstrated that chronic impairment of cardiac lymph drainage leads to ventricular endocardial fibroelastosis(5,11).

The importance of impairment of lymph flow in those diseases of the heart and great vessels which increase central venous pressure merits emphasis. Protein-losing enteropathy in constrictive pericarditis(12) may represent such an entity. It is likely that the function of many congested organs could be significantly improved if their lymph flow could be shunted into a low pressure area which would allow for adequate drainage and an alleviation of elevated tissue pressures

without the chronic loss from the body of the vital substances carried by the lymph. Perhaps certain forms of permanent organ damage, including fibrosis, might thus be prevented.

Summary. Chronic impairment of hepatic lymph drainage in the dog resulting from resection of a segment of thoracic duct and/or constriction of the superior vena cava leads to discernible changes in liver histology. These changes, though not quantitatively marked, are comparable to those seen in early cardiac fibrosis of the liver (so-called "cardiac cirrhosis"), and support the hypothesis that some of the changes in the liver associated with venous congestion are due to impairment of lymph drainage.

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Effect of Nicotinic Acid on Pool Size and Turnover of Taurocholic Acid in Normal and Hypothyroid Dogs.* (31329)

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The mechanism of the hypocholesterolemic action of large doses of nicotinic acid has not been established. Since the conversion of cholesterol to bile acids is an important step in cholesterol catabolism, we investigated some parameters of bile acid metabolism in normal and hypothyroid dogs before and during the administration of nicotinic acid. Biologic half-life, pool size, and turnover of taurocholic acid (TC), the only primary bile acid present in significant amounts in dog bile (1,2), were determined by labeling the cholic acid pool with cholic-^{14}C acid and following the rate of disappearance of the radioactive label from the bile.

Methods. Female mongrel dogs, weighing 11 to 15 kg, were used. They were fed a commercial meat-type diet to maintain a steady weight. Total plasma cholesterol concentrations were measured by a modification of the Zak method(3).

Multiple small samples of bile were obtained in two different ways. In 2 animals the common bile duct was cannulated proximally and distally with polyethylene tubes which were brought out subcutaneously to the back of the animals and connected *via* a short loop to keep the enterohepatic circulation intact. Bile samples were obtained by interrupting the circuit. (Long-term maintenance of these bile fistulas proved to be difficult.) In 3 dogs a Thomas cannula(4) was placed into the duodenum opposite to the papilla of Vater, and bile was sampled from the duodenum after stimulation of bile flow with cholecystokinin (generously supplied by E. R. Squibb & Sons, New York).

The bile acid pool was labeled by adminis-

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