mammary gland, 3 weeks of hormonal stimulation leads to MTV activity in mammary ducts of 6-week-old BALB/cfC3H female mice. In addition, both BALB/c normal lobules and BALB/c hyperplastic nodule outgrowths possess MTV activity after 6 weeks in a MTV-positive host, following 3 or more weeks of hormonal stimulation.

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Congenital Lipoprotein Lipase Deficiency and Hyperlipemia in the Young Puppy* (33834)

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In man, exogenous hyperlipemia is characterized by large amounts of chylomicrons in plasma in the presence of a normal fat-containing diet, and their disappearance when dietary fat is withdrawn. The disorder results from a defect in the removal of chylomicrons and of triglyceride-rich lipoprotein associated with a deficiency of lipoprotein lipase, the enzyme located predominately in adipose tissue capillaries and presumed to be important in the regulation of particulate triglyceride removal from the circulation. A congenital deficiency of this enzyme appears to be the basis for the familial form of exogenous lipemia (1). A low plasma lipolytic activity after heparin injection (2) closely reflects reduced tissue lipoprotein lipase activity (3). In the present study hyperlipemia was found in a young dog in association with deficient lipoprotein lipase activity, as manifested by reduced postheparin plasma lipolytic activity. Although "essential hyperlipemia" has been described in a 2-year-old dog (4), we know of no canine case of hyperlipemia in whom a deficiency of lipoprotein lipase or postheparin lipolytic activity has been demonstrated.

Methods, Materials, and Results. The subject of this report is a male puppy who was the product of an uncomplicated gestation to a seemingly normal mongrel bitch. Nothing is known of its father. This puppy was the smallest of the litter of three, and grew more slowly than the others. At 28 days of age, the unweaned animal was taken from his mother to be used in an experiment, and was found to weigh 950 g (1210 ± 280 g; mean ± SD in 19 N mongrel puppies, 27–29 days of age). He was irritable and weak. The liver was palpably enlarged. A blood sample obtained from a femoral artery cannula looked like "cream-of-tomato soup." After cold centrifugation of a blood sample collected in a heparinized tube, a lactescent zone was visible in the upper half of the plasma layer. The triglyceride concentration (5) of this plasma was 830 mg/100 ml, the cholesterol concentration (6) was 312 mg/100 ml, and the glucose concentration (7) was 126 mg/100 ml (122 ± 23 mg/100 ml; mean ± SD in 19 normal mongrel puppies). Unfortunately, the plasma was frozen and therefore unsuit-

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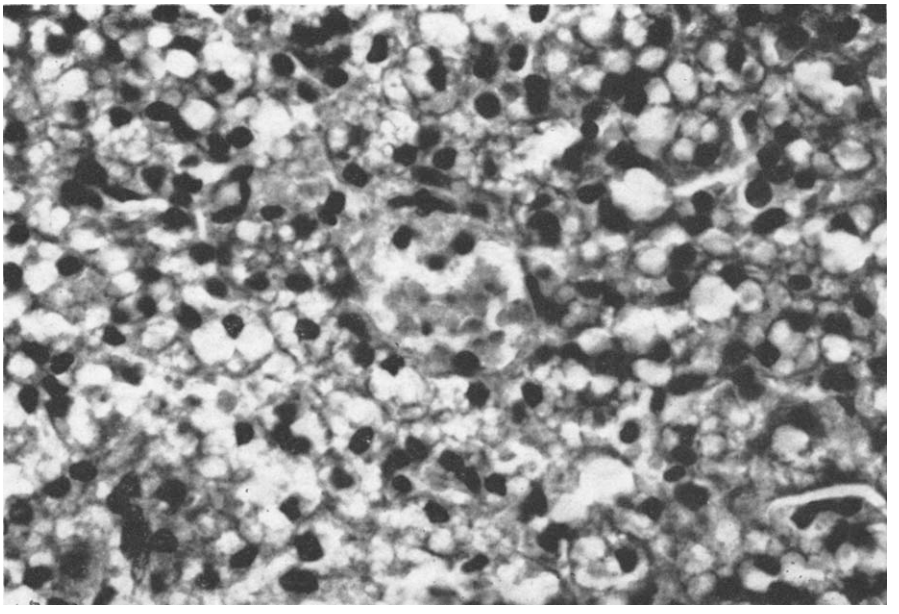

FIG. 1. Severe fatty change in hepatocytes surrounding central vein; Hematoxylin and eosin, 528×.

able for lipoprotein separation. Three thousand units of heparin sulfate were given intravenously after obtaining a base-line blood sample for lipolytic activity. No demonstrable lipolytic activity (8) was found in the preheparin and the 5-min postheparin plasma, and only minimal activity (0.012 μeq of FFA/ml of plasma/min) was present 15 min after heparin administration. Visible clearing of the puppy's cooled plasma did not take place at 15, 30, 45, and 60 min following heparin. Upon completion of the study, the puppy was given an infusion of 10% glucose and water, and returned to a cage separate from his mother, because of the presumptive diagnosis of exogenous hyperlipemia. During the next 4 days, oral intake progressively diminished and it became necessary to administer infusions of glucose and saline. Despite these measures, the puppy died at 33 days of age.

Pathologic findings. At autopsy the puppy weighed 850 g. There was a thin layer of subcutaneous fat. The lungs together weighed 19 g. The pleura were pink and glistening, except over foci of hemorrhage in the adjacent parenchyma. After sectioning, the cut surfaces exuded pink fluid. Firm areas of consolidation were present. Microscopically, the alveoli were filled with protein-rich fluid. In the consolidated areas, alveoli and bronchioles were packed with inflammatory exudate. Numerous bacterial colonies were observed. The heart (9.5 g), spleen (2.5 g), kidneys (12.2 g together) and other viscera including the pancreas were unremarkable. The most striking alteration was found in the liver. This was enlarged (53.8 g) and uniformly yellow. The cut surface was greasy. Microscopically, lobular architecture was maintained. The hepatocytes, however, were diffusely swollen by lipid (Fig. 1). The entire parenchyma was affected, although the cells of the periportal plates contained less fat than those nearer the central veins. Lipid droplets stained intensely with Sudan IV.

Controls. The two litter mates were used as research subjects and destroyed prior to finding the hyperlipemic puppy. However, plasma taken from the male (wt 1070 g) at 21 days of age, and the female (wt 1100 g) at 22 days revealed respective triglyceride concentration of 42 and 46 mg/100 ml, cholesterol concentrations of 102 and 119 mg/100 ml, and glucose concentrations of 110 and 116 mg/100 ml.

Since information concerning postheparin lipoprotein lipase activity in the litter mates was unavailable, two other mongrel puppies of similar age and sex were each given 3000 units of heparin for comparison. In these latter animals, plasma postheparin lipolytic activity 15 min after administration of heparin was 0.329 and 0.222 μeq of FFA/ml of plasma/min. Plasma triglyceride concentrations in these animals were 57 and 60 mg/100 ml.

Discussion. The studied puppy appears to have had a disease similar to lipoprotein lipase deficiency associated with hyperchylomicronemia found in man (1). "Cream-of-tomato soup" blood, a large creamy upper layer in cooled plasma, marked hypertriglyceridemia with associated hypercholesterolemia in proportions consistent with the presence of large, triglyceride-rich fat particles, and negligible postheparin lipoprotein lipase activity in the young dog support this conclusion. The fatty liver found at autopsy is also consistent with the abnormality. The early onset of symptoms, the magnitude of hyperlipemia, and the degree of hepatic steatosis, indicate that the animal had a severe form of this congenital metabolic abnormality. Nevertheless, the cause of death in this animal was judged from autopsy findings to be pneumonia. There was no evidence of diabetes mellitus which, when severe, may be associated with hyperlipemia and low post heparin lipase activity in man (9).

The purpose of this report is to alert investigators to the possible presence of lipoprotein lipase deficiency associated with hyperchylomicronemia in mammals other than man. It is hoped that another animal with this enzyme deficiency can be found, kept alive, and bred to develop a strain that would provide an animal model for study of this disease.

Summary. A young puppy with hyperlipemia presumably associated with lipoprotein lipase deficiency is reported. It appears that this rare abnormality of lipid metabolism may occur in mammals other than man.

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