Chronic active liver disease occurring in adolescents who use drugs: A study of possible etiologies. IRIS F. LITT, MICHAEL I. COHEN, S. KENNETH SCHONBERG, and ILYA SPIGLAND. *Albert Einstein Coll. of Med., Montefiore Hosp. and Med. Ctr., N. Y., N. Y.*

Of 16,800 presumably well teenagers, 3181 were found to be drug abusers. Routine liver function tests in these latter patients revealed abnormalities in 1306, with SGPT elevation the most frequently noted. Forty patients, abnormal for 3 months, had a percutaneous liver biopsy. All specimens exhibited infiltration of the portal area and 75% showed hepatocyte necrosis. One half of the biopsies showed portal fibrosis. This degree of chronicity suggests that the usual course of viral hepatitis may be altered by the abuse of drugs. Alternatively, the drugs themselves may be directly responsible.

Guinea pig liver explants were grown in culture medium and shown to be metabolically active for 96 hours. Transaminase activity was assayed in the culture medium before addition of the explant and serially thereafter. Changes in enzyme activity were followed after the addition of substances commonly abused by teenagers, as well as CCl_4.

The pattern of transaminase elevation at 24 hours by CCl_4 provided the model for acute toxicity. Other drugs tested showed no evidence of acute toxicity, nor did the addition of heroin to this system result in the transaminase elevation associated with acute toxicity.

This study suggests that heroin is not acutely hepatotoxic. The abnormalities of the liver noted in the heroin-using adolescents may be the result of a modifying effect on the usual course of viral hepatitis.

Electron microscopic changes in the liver in Reye's syndrome. JOHN C. PARTIN and WILLIAM K. SCHUBERT. *Children's Hosp. Res. Found., Cincinnati, Ohio.*

Reye's syndrome is acute encephalopathy in children associated with fatty liver. Liver cells are filled with fat droplets throughout the lobule; there is no inflammation. We have examined the electron microscopic (EM) changes in 16 children with Reye's syndrome. Diagnostic Menghini needle biopsies were obtained 6 hours to 4 days after onset of central nervous system signs; follow-up biopsies were obtained 2 months later from 7 of 9 survivors. Distinctive mitochondrial changes were present in all initial biopsy specimens: The matrix was distended (greatly in severe cases) and matrix protein was disorganized. Cristae were disrupted. The swollen mitochondria assumed bizarre contours. In two cases with severely altered mitochondria in the initial biopsy who were treated by exchange transfusion, most but not all mitochondria were normal by 2 months. One of these biopsied on the 3rd day, after onset of CNS signs and 6 exchange transfusions, showed great improvement in mitochondrial morphology. In early biopsy specimens the smooth endoplasmic reticulum (ER) was hypertrophied; in well glycogenated cells extensive "glycogen body" formation was seen. In fatal cases, glycogen depletion was severe. Peroxysomes were increased in all biopsy specimens. In less severe cases there was active peroxysome proliferation from smooth ER. Peroxysome proliferation may represent a compensatory response to deficient mitochondrial respiration. In recovery, rough ER was increased and its cisternae were distended. The Golgi system was hypertrophied with lipid filled saccules. The EM changes show that potentially reversible mitochondrial injury is a main feature of the liver lesion in Reye's syndrome. The etiologic agent may be a mitochondrial toxin.

Effects of phenobarbital on bile salts in cholestasis. ADOLF STIEHL, M. MICHAEL THALER, and WILLIAM H. ADMIRAND. *Univ. of Calif., San Francisco, Calif.* (Intr. by M. M. Grumbach).

Phenobarbital (PB) reduces pruritis in children with cholestasis. Individual bile salts were determined before and during PB treatment in 3 children with intrahepatic cholestasis (2 with benign recurrent cholestasis, 1 with paucity of intrahepatic bile ducts) and in 3 with extrahepatic biliary atresia. In *intrahepatic cholestasis* the cholate/chenodeoxycholate ratio in serum, bile and urine was 2.5–10. Total serum bile salt concentration was 100–400 μg/ml. After 4 days on PB (10 mg/kg/day) total serum bile salts decreased dramatically to 1–10 μg/ml with concomitant disappearance of pruritus. Daily urinary bile salt excretion declined concomitantly from 15–40 mg to 1–2 mg. In contrast, in *extrahepatic cholestasis,* the cholate/chenodeoxycholate ratios were 0.1–0.4 in blood, bile and urine. Total serum bile salt concentration was 60–130 μg/ml. Treatment with PB did not lower serum or urinary bile salt concentrations. Thus, the ratio of cholate/chenodeoxycholate is different in intrahepatic and extrahepatic cholestasis. PB greatly enhances the removal of bile salts from blood in two types of intrahepatic cholestasis, but is ineffective in extrahepatic cholestasis. The simultaneous decrease in serum and urinary bile salt concentrations suggests that PB stimulates the biliary excretion of bile salts.

METABOLISM

Lysosomal bone disease. I. A. SCHAFER, D. W. POWELL, and J. C. SULLIVAN. *Case Western Reserve Univ. Sch. Med. at Cleveland Metro. Gen. Hosp., Cleveland, Ohio.*

For normal bone growth, matrix must be laid down and resorbed. The process of remodeling could be altered if the activity of a single lysosomal hydrolase was deficient since compounds catabolized by the enzyme might then accumulate within bone cells and matrix with resultant abnormalities in bone architecture and growth retardation. We have studied a 9 year old dwarfed white male with normal intelligence whose disease appears limited to bone. He shows no corneal infiltration, visceromegaly or mucopolysaccharidiuria. His radiological diagnosis is spondyloepiphysealmetaphyseal dysplasia. Chemical studies of cultured skin fibroblasts from the patient showed decreased enzyme activity of α-L-fucosidase (controls 2.67 $\pm$ .75 vs patient 0.25 $\pm$ .05 n-moles/min/mg protein) with accumulation of fucose in his cells (controls 5.42 $\pm$ 1.52 vs patient 27 γ/mg protein). Fibroblast enzyme activities for α-L-mannosidase, acid phosphatase, β-D-galactosidase and n-acetyl glucosaminidase were comparable to normal controls. A bone specimen from the patient was compared to 7 control specimens for hydrolase activity. Fucosidase activity was decreased in the patient (controls 3.2 $\pm$ .38 vs patient 0.36 n-moles/hr/mg wet wt.) as were several other acid hydrolyses. Compositional analyses of bone are in progress to define the character of the stored material. Thus far, the data in this patient is consistent with the hypothesis that his bone disease is due to a deficiency of lysosomal hydrolase, α-L-fucosidase. Since lysosomes in