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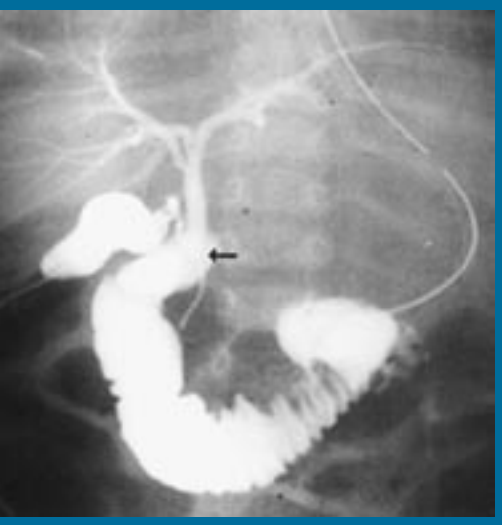

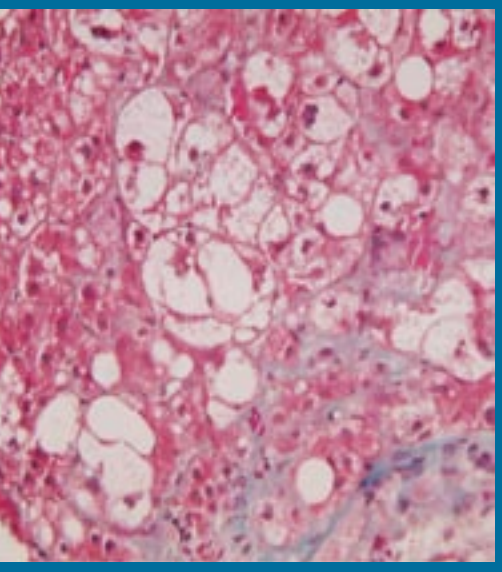

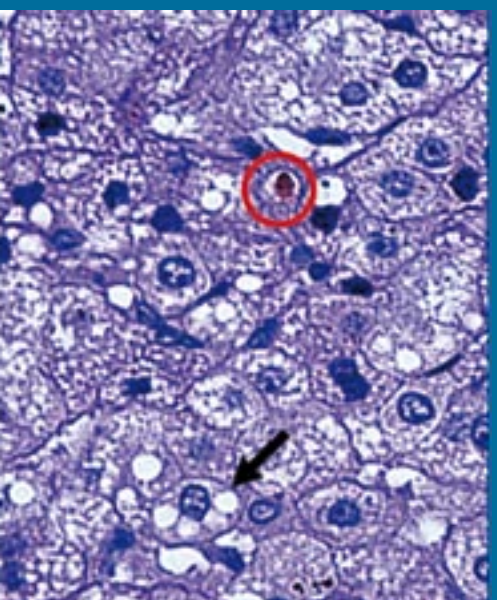

Liver Disease in Children

Third Edition

Edited by FREDERICK J. SUCHY
RONALD J. SOKOL
WILLIAM F. BALISTRERI

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Liver Disease in

Liver Disease in Children, 3rd Edition is a completely revised new edition of the premier reference on pediatric liver disease, it provides authoritative coverage of every aspect of liver disease affecting infants, children, and adolescents. With an integrated approach to the science and clinical practice of pediatric hepatology it charts the substantial progress in understanding and treating these diseases.

Chapters are written by international experts and address the unique pathophysiology, manifestations, and management of these disorders in the pediatric population.

The third edition has been thoroughly updated and features new contributions on liver development, cholestatic and autoimmune disorders, fatty liver disease, and inborn errors of metabolism.

With the continued evolution of pediatric hepatology as a discipline, this text remains an essential reference for all physicians involved in the care of children with liver disease.

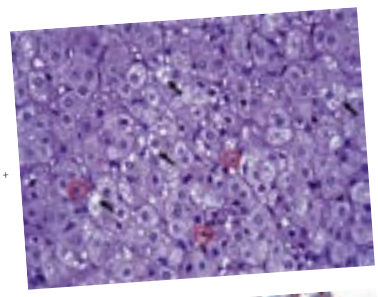


Figure 33.3. Higher power views of liver histology from patient with mtDNA depletion syndrome in Figure 33.2, showing microvesicular steatosis (arrows) and canalicular cholestasis (circles). PAS + diastase, x800.d

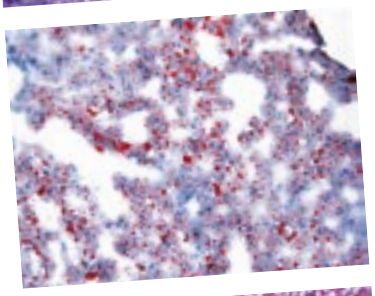


Figure 33.4. Oil-red-O stain of frozen section of liver biopsy in Figure 33.2, showing marked microvesicular steatosis in most hepatocytes, despite benign appearance of the biopsy in Figure 33.2. Oil-red-O x100.

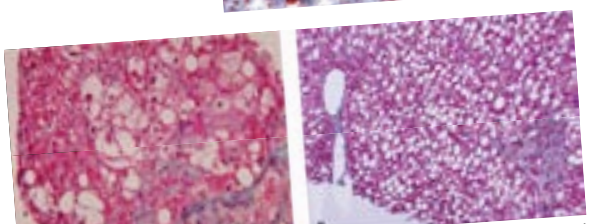


Figure 34.1. Histologic patterns of pediatric NASH. Shown are liver biopsies from two children with NASH. (A) A biopsy typical of type 1 NASH with ballooning degeneration of hepatocytes and perisinuosoidal fibrosis. (B) A biopsy typical of type 2 NASH with a normal central vein, no hepatocytes ballooning but with portal inflammation and fibrosis.

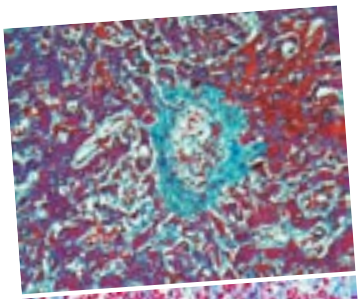
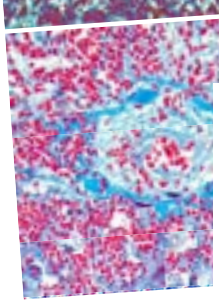
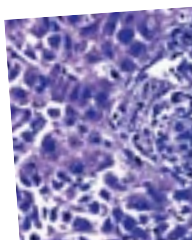


Figure 38.1. Pathology of hepatic veno-occlusive following bone marrow transplantation. (A) Partial occlusion of hepatic venule shows endothelial proliferation overlying cell debris. The vein wall is fibrotic. Perivenular zone is hemorrhagic due to obstruction. (B) Complete obstruction of a hepatic venule with sinusoidal congestion. (hematoxylin and eosin stain, original magnification x350). Courtesy of Drs. Howard Shulman and Laurie Deleve.





10

Medical and Nutritional Management of Cholestasis in Infants and Children

Andrew P. Feranchak, M.D., and Ronald J. Sokol, M.D.

When first encountering an infant or child with cholestatic liver disease, it is essential that diagnostic evaluation be conducted promptly in order to (i) recognize disorders amenable either to specific medical therapy (e.g., galactosemia, tyrosinemia, hypothyroidism, urinary tract infection) or to early surgical intervention (e.g., biliary atresia, choledochal cyst), (ii) institute treatment directed toward enhancing bile flow, and (iii) prevent and treat the varied medical, nutritional, and emotional consequences of chronic liver disease. Because many of the treatable causes require early diagnosis and prompt institution of therapy, the evaluation of the cholestatic infant should never be delayed. Although "physiologic cholestasis" (hypercholemia, or elevated bile acids) may be present in the infant, there is no state of "physiologic conjugated hyperbilirubinemia." For the jaundiced infant, historical and clinical information such as color of the stools, birth weight, and presence of hepatomegaly may provide important clues as to the etiology of cholestasis. Consanguinity or liver disease in siblings suggests the possibility of metabolic, familial, or genetic disease. Review of the prenatal and postnatal course may reveal intrauterine infection, occurrence of hypoglycemia or seizures, and exposure to toxins/drugs (i.e., total parenteral nutrition [TPN]). Careful physical examination may reveal features of typical disorders or syndromes. For the older child and adolescent, a history of exposure to drugs/toxins (e.g., acetaminophen), the presence of vascular insufficiency, and the presence of underlying disease (e.g., inflammatory bowel disease) provide helpful clues. The diagnostic evaluation of the infant with cholestasis is detailed in Chapter 9.

Once the diagnosis is made, a limited number of disorders are amenable to specific treatments. Although less than 10% of infants with neonatal cholestasis are found to have treatable medical disorders, the individual patient will derive important benefits from early diagnosis and treatment. Those infants found to require surgical correction of anatomic causes of cholestasis likewise require early identification and therapy for optimal outcome [1]. A classification scheme relating the availability of specific therapy to the individual causes of prolonged neonatal cholestasis is listed in Table 10.1. In the majority of cases in which there is no "curable" etiology or in which surgical correction of biliary atresia is unsuccessf
agement is largely supportive; directed at in
optimizing growth and nutrition, minimizin
disability, and aiding the child and his fami
the stress, social, and emotional effects of chr
The success of therapeutic intervention, how
the residual functional capacity of the liver a
progression of the underlying liver disease. Be
liver transplantation (OLT) in children has
therapy for end-stage liver disease, it is increa
to optimize the care, growth, and developmen
chronic liver disease in order to enhance thei
cessful liver transplantation.

The ultimate prognosis for an affected chi
severity of the complications resulting from
sis. These complications are attributable direc
diminished bile flow and reflect (i) retention
mally excreted in bile (bile acids, bilirubin, cho
elements) with resultant hepatocyte apoptosis
induction of portal fibrosis progressing to por
cirrhosis, and liver failure; (ii) transfer of co
into the systemic circulation, leading to pruriti
cholesterolemia, and xanthoma formation;
delivery of bile to the small bowel with decre
bile acid concentrations, leading to malabso
fat-soluble vitamins. These departures from n
lead to discomfort, failure to thrive, specific
cies, and psychological/behavioral problems
child. A summary of medical treatment opti
sis, including medications, doses, and toxi
Table 10.2 [2–43].

RETENTION OF BILE CONSTITUE

Hepatocellular Injury

Pathogenesis of Cholestatic Injury

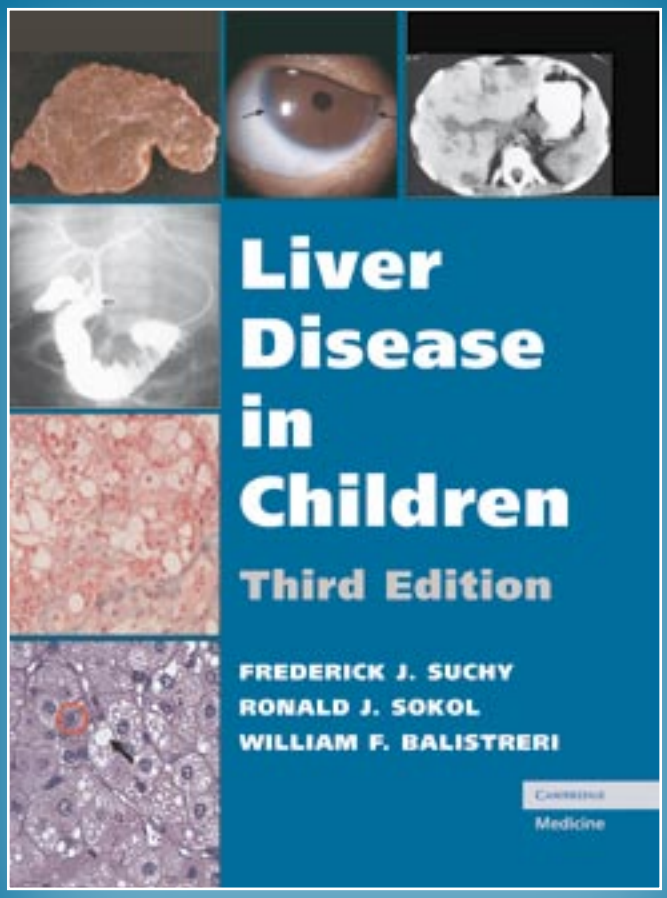
The retention of endogenous bile acids
during cholestasis is believed to be involved
esis of progressive liver injury and may lead

Review from 2nd edition

'With this textbook, the field of pediatric hepatology steps out from behind the shadow of its adult counterparts and should be within arm's length of each medical and surgical practitioner who encounters children with liver disease.'

PRACTICAL GASTROENTEROLOGY

Children



Features

- *Thoroughly updated with new chapters on liver development, cholestatic and autoimmune disorders, fatty liver disease and inborn errors of metabolism*
- *Provides a comprehensive, integrated approach to the science and clinical practice of pediatric hepatology*
- *Includes an eight page colour insert with over ninety colour photos*

Table 10.1: Treatable Causes of Neonatal Cholestasis

Disease	*Liver Involvement*	*Treatment*	*References*
Congenital infectious hepatitis			
Herpes simplex virus	Coagulative necrosis	Intravenous (IV) acyclovir	[2]
Syphilis	Hepatitis, periportal and interlobular fibrosis	IV penicillin G (50,000 units/kg/d for 10–14 d)	[3,4]
Listeria monocytogenes infection	Granulomatous hepatitis	IV ampicillin (neonatal doses)	[5,6]
Tuberculosis	Granulomatous hepatitis	Consult neonatal infectious disease expert	[7]
Toxoplasmosis	Cholestasis	Pyrimethamine (1 mg/kg every 2–4 d) and sulfadiazine (50–100 mg/kg/d) for 21 d	[8,9]
HIV	Cholestasis	Consult neonatal infectious disease expert	
Metabolic diseases			
Galactosemia	Cholestasis, steatosis, fibrosis, cirrhosis	Galactose-free diet	[10,11]
Hereditary tyrosinemia	Steatosis, fibrosis, cirrhosis	Low tyrosine/phenylalanine diet, NTBC	[12–18]
Hereditary fructose intolerance	Steatosis, fibrosis	Fructose/sucrose-free diet	[19,20]
Hypothyroidism/hypopituitarism	Cholestasis	Thyroid, adrenal, growth hormone replacement	[21]
Cystic fibrosis	Biliary mucus plugging, cholestasis, focal biliary cirrhosis, multilobular cirrhosis, cholelithiasis	Oral pancreatic enzyme replacement, pulmonary therapy, fat-soluble vitamin supplements, UDCA	[22,23]
Bile acid synthesis defects:			
Δ^4-3-oxosteroid-5β-reductase def.	Cholestasis, giant-cell hepatitis	UDCA and cholic acid	[24,25]
3β-hydroxysteroid dehydrogenase/isomerase def.	Cholestasis, giant-cell hepatitis	UDCA	[26,27]
Neonatal iron storage disease	Cholestasis, fibrosis, cirrhosis	Antioxidant therapy,* liver transplantation	[28]
Drugs and toxins			
Drugs	Variable	Discontinue drug	[29]
Bacterial endotoxin (sepsis, urinary tract infections, etc.)	Cholestasis, hepatocyte necrosis	Appropriate IV antibiotic therapy	[6,30,31]
TPN-associated	Cholestasis, steatosis, bile duct proliferation, portal fibrosis, cirrhosis	Institute early enteral feedings, avoid excessive (IV) calories and protein, use neonatal amino acid solutions, ursodeoxycholic acid (?)	[32–36]
Anatomic lesions			
Extrahepatic biliary atresia	Cholestasis, bile duct proliferation, fibrosis, cirrhosis	Hepatoportoenterostomy	[1,37–39]
Choledochal cyst	Cholestasis, fibrosis, cirrhosis	Choledochoenterostomy	[40]
Spontaneous perforation of common bile duct	Peritonitis, ascites, cholestasis	Surgical drainage	[41]
Inspissated bile/calculi in common bile duct	Cholestasis, bile duct proliferation, fibrosis, cirrhosis	Biliary tract irrigation	[42,43]

*Vitamin E (TPGS) 25 IU/kg/d oral; desferrioxamine 15 mg/kg/h IV continuous infusion until ferritin <500 μg/L; selenium 2–3 μg/kg/d IV (in TPN); *N*-acetylcysteine 70 mg/kg/dose every 4 hr via nasogastric tube or IV for 20 doses.
NTBC, 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohexanedione; TPGS, tocopherol polyethylene glycol-1000 succinate; TPN, total parenteral nutrition; UDCA, ursodeoxycholic acid.
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Contents

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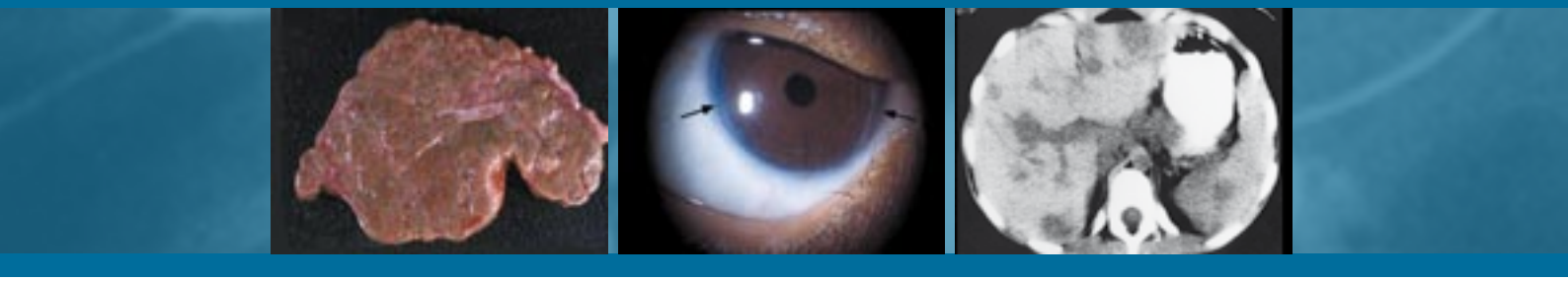

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