

CHAPTER 130

Liver Disease

CHOLESTASIS

Etiology and Epidemiology

Cholestasis is defined as reduced bile flow and is characterized by elevation of the conjugated, or direct, bilirubin fraction. This condition must be distinguished from physiologic neonatal jaundice, in which the direct bilirubin is never elevated (see [Chapter 62](#)). Neonatal jaundice that is secondary to unconjugated hyperbilirubinemia is the result of immature hepatocellular excretory function or hemolysis, which increases the production of bilirubin. When direct bilirubin is elevated, many potentially serious disorders must be considered ([Fig. 130.1](#), [Table 130.1](#)). Emphasis must be placed on the rapid diagnosis of treatable and potentially lethal

TABLE 130.1 Differential Diagnosis of Conjugated Hyperbilirubinemia in Infants

OBSTRUCTIVE/ANATOMIC DISORDERS	Niemann-Pick disease
Biliary atresia	Beta-oxidation defects
Choledochal cyst	Gaucher disease
Caroli disease (cystic dilatation of intrahepatic ducts)	DISORDERS OF BILE ACID SYNTHESIS AND METABOLISM
Congenital hepatic fibrosis	Primary Enzyme Deficiencies
Neonatal sclerosing cholangitis	3β-hydroxy-Δ5-C27-steroid dehydrogenase/isomerase
Bile duct stenosis	Δ4-3-oxosteroid 5β-reductase
Spontaneous bile duct perforation	Oxysterol 7α-hydroxylase
Anomalous choledocho-pancreatico-ductal junction	Secondary
Cholelithiasis	Zellweger syndrome (cerebrohepatorenal syndrome)
Inspissated bile or mucous	Infantile Refsum disease
Mass or neoplasia	Smith-Lemli-Opitz syndrome
INFECTIONS	Other enzymopathies
Bacterial (gram negative) sepsis	Mitochondrial disorders (respiratory chain)
Urinary tract infection	Intrahepatic Cholestasis
Listeriosis	Alagille syndrome (arteriohepatic dysplasia)
Syphilis	Nonsyndromic paucity of intrahepatic bile ducts
Toxoplasmosis	Progressive familial intrahepatic cholestasis (PFIC)
Tuberculosis	Type 1: Byler disease
Cytomegalovirus	Type 2: Defect in the bile salt export pump
Herpesvirus (herpes simplex, herpes zoster, human herpesvirus 6)	Type 3: Defect in canalicular phospholipid transporter
Rubella virus	Benign recurrent intrahepatic cholestasis
Hepatitis B virus	Greenland familial cholestasis (Nielsen syndrome)
HIV	North American Indian cirrhosis
Coxsackievirus	Hereditary cholestasis with lymphedema (Aagaens syndrome)
Echovirus	Toxin or Drug Related
Parvovirus B19	Cholestasis associated with total parenteral nutrition
Adenovirus	Chloral hydrate
Measles	Home remedies/herbal medicines
METABOLIC DISORDERS	Venoocclusive disease
α ₁ -antitrypsin deficiency	Miscellaneous
Cystic fibrosis	Idiopathic neonatal hepatitis
Citrin deficiency	GALD
ENDOCRINE DISORDERS	Autoimmune hemolytic anemia with giant cell hepatitis
Panhypopituitarism	Shock or hypoperfusion (including cardiac disease)
Hypothyroidism	Intestinal obstruction
DISORDERS OF CARBOHYDRATE METABOLISM	Langerhans cell histiocytosis
Galactosemia	Neonatal lupus erythematosus
Hereditary fructose intolerance (fructosemia)	Dubin-Johnson syndrome
Glycogen storage disease type IV	North American Indian childhood cirrhosis
DISORDERS OF AMINO ACID METABOLISM	Trisomies (18, 21)
Tyrosinemia	Congenital disorders of glycosylation
Hypermethioninemia	Kabuki syndrome
DISORDERS OF LIPID METABOLISM	Donahue syndrome (leprechaunism)
Wolman disease	Arthrogryposis, cholestatic pigmentary disease, renal dysfunction syndrome
Cholesterol ester storage disease	Familial hemophagocytic lymphohistiocytosis
Farber disease	

GALD, Gestational alloimmune liver disease (neonatal hemochromatosis).

Modified from Balistreri WF. Liver disease in infancy and childhood. In: Schiff ER, Sorrell MF, Maddrey WC, eds. Schiff's Diseases of the Liver. 8th ed. Philadelphia: Lippincott-Raven; 1999:1370; Suchy FJ. Approach to the infant with cholestasis. In: Suchy FJ, Sokol RJ, Balistreri WF, eds. Liver Disease in Children. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2001:188.

disorders, especially biliary atresia, sepsis, urinary tract infection, hemophagocytic or histiocytic syndromes, and treatable metabolic disorders, such as galactosemia or tyrosinemia.

Clinical Manifestations

The jaundice of **extrahepatic biliary atresia** (biliary atresia) usually is not evident immediately at birth but develops in the first week or two of life. The reason is that extrahepatic bile ducts are usually present at birth but are then destroyed by an idiopathic inflammatory process. Aside from jaundice, these infants do not initially appear ill. The liver injury progresses rapidly to cirrhosis; symptoms of portal hypertension with splenomegaly, ascites, muscle wasting, and poor weight gain are evident by a few months of age. If surgical drainage is not performed successfully early in the course (ideally by 2 months), progression to liver failure is inevitable.

Idiopathic neonatal hepatitis is defined as inflammation of the liver, occurring in infancy, without an identifiable cause. It is characterized clinically by an ill-appearing infant with an enlarged liver and jaundice. This diagnosis can only be made after thorough testing for identifiable infectious, anatomic, and metabolic/genetic causes of neonatal cholestasis have been performed and are negative (see later). If liver biopsy is performed, the presence of hepatocyte giant cells is characteristic. Hepatobiliary scintigraphy typically shows slow hepatic uptake with eventual excretion of isotope into the intestine. These infants have a good prognosis overall, with spontaneous resolution occurring in most.

α_1 -antitrypsin deficiency presents with clinical findings indistinguishable from neonatal hepatitis. Only about 10–20% of all infants with the genetic defect exhibit neonatal cholestasis. Of these affected infants, about 20–30% develop chronic liver disease, which may result in cirrhosis and liver failure. Life-threatening α_1 -antitrypsin deficiency occurs in only 3–5% of affected pediatric patients. α_1 -antitrypsin deficiency is the leading metabolic disorder requiring liver transplantation.

Alagille syndrome is characterized by chronic cholestasis with the unique liver biopsy finding of *paucity of bile ducts* in the portal triads. Associated abnormalities in some (syndromic) types include peripheral pulmonic stenosis or other cardiac anomalies; hypertelorism; unusual facies with deep-set eyes, prominent forehead, and a pointed chin; butterfly vertebrae; and a defect of the ocular limbus (*posterior embryotoxon*). Cholestasis is variable but is usually lifelong and associated with hypercholesterolemia and severe pruritus. Progression to end-stage liver disease is uncommon early in life. Liver transplantation sometimes is performed electively to relieve severe and uncontrollable pruritus. Alternative surgical treatments to prevent intestinal reabsorption of pruritus-inducing bile acids can also be effective. These include partial or complete drainage to an ostomy and bypass of the terminal ileum, the location of most bile acid reabsorption.

Laboratory and Imaging Studies

The laboratory approach to diagnosis of a neonate with cholestatic jaundice is presented in Table 130.2. Noninvasive studies may aid a rapid diagnosis. Early imaging studies are performed to evaluate for biliary obstruction and other anatomic lesions that may be surgically treatable. When necessary to rule out biliary atresia or to obtain prognostic

TABLE 130.2 Laboratory and Imaging Evaluation of Neonatal Cholestasis

EVALUATION	RATIONALE
INITIAL TESTS	
Total and direct bilirubin	Elevated direct fraction confirms cholestasis
AST, ALT	Hepatocellular injury
GGT	Biliary obstruction/injury
RBC galactose-1-phosphate uridylyltransferase	Galactosemia
α_1 -antitrypsin level and phenotype	α_1 -antitrypsin deficiency
Urinalysis and urine culture	Urinary tract infection can cause cholestasis in neonates
Blood culture	Sepsis can cause cholestasis
Serum amino acids	Aminoacidopathies
Urine organic acids	Organic acidurias
Very-long-chain fatty acids	Zellweger syndrome, peroxisomal disorders
Carnitine profile	Mitochondrial and fatty acid oxidation disorders
Sweat chloride or CF mutation analysis	Cystic fibrosis
Urine culture for cytomegalovirus	Congenital cytomegalovirus infection
GENETIC TESTING	
Rapidly advancing genetic diagnosis capabilities can identify Alagille syndrome, progressive familial cholestasis syndromes, α_1 -AT deficiency, familial HLH, and bile acid synthesis disorders. Some laboratories offer PCR-based testing for most or all of these in a single panel.	
INITIAL IMAGING STUDY	
Abdominal ultrasound	Choledochal cyst, gallstones, mass lesion, Caroli disease
SECONDARY IMAGING STUDY	
Hepatobiliary scintigraphy	Evaluate for biliary atresia
Pathology	Liver; salivary gland (GALD)
Percutaneous liver biopsy	Biliary atresia, idiopathic giant cell hepatitis, α_1 -antitrypsin deficiency

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; CF, cystic fibrosis; GALD, gestational alloimmune liver disease; GGT, γ -glutamyltransferase; HLH, hemophagocytic lymphohistiocytosis; RBC, red blood cell.

information, liver biopsy can be very helpful; surgical exploration is a final option (Fig. 130.2). When cholestasis persists, biliary atresia has been ruled out, and routine testing fails to yield a diagnosis, genetic testing for rare etiologies should be considered.

Treatment

Treatment of extrahepatic biliary atresia is the surgical **Kasai procedure**, in which the fibrotic extrahepatic bile duct remnant is removed and replaced with a Roux-en-Y loop of

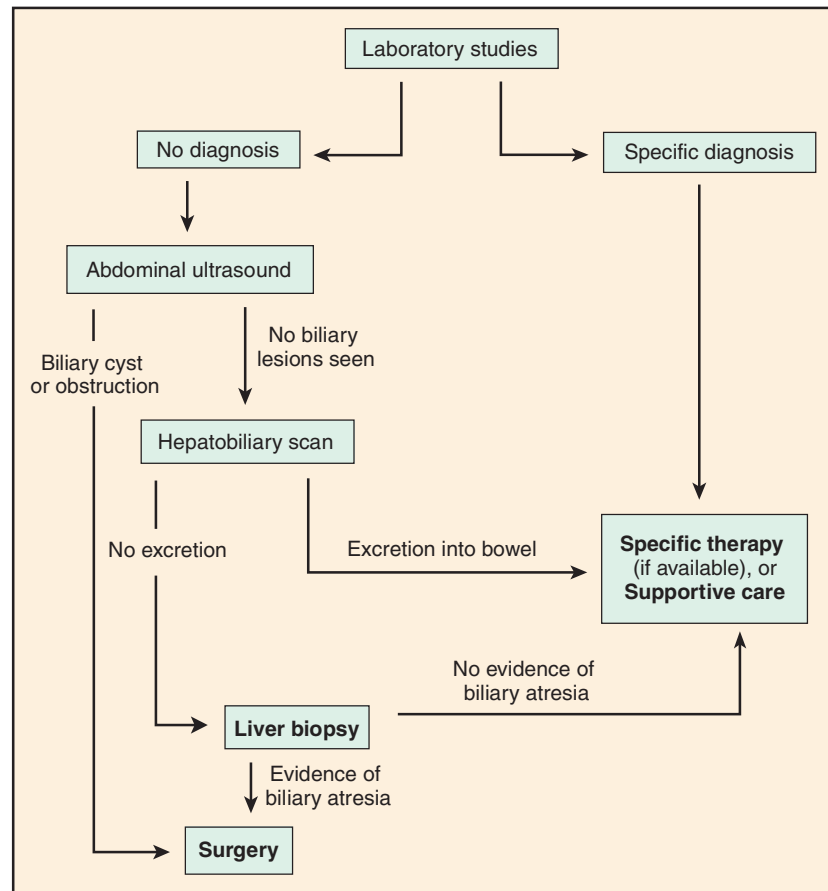


FIGURE 130.2 Flow chart for evaluation of neonatal cholestasis.

jejunum. This operation must be performed before 2 months of age to have the best chance of success. Even so, the success rate is low, and many children require liver transplantation. Some metabolic causes of neonatal cholestasis are treatable by dietary manipulation (galactosemia) or medication (tyrosinemia); all affected patients require supportive care. This includes fat-soluble vitamin supplements (vitamins A, D, E, and K) and formula containing medium-chain triglycerides, which can be absorbed without bile salt-induced micelles. Choleric agents, such as ursodeoxycholic acid, may improve bile flow in some conditions.

VIRAL HEPATITIS

See Chapter 113.

FULMINANT LIVER FAILURE

Etiology and Epidemiology

Fulminant liver failure is defined as severe liver disease with onset of hepatic encephalopathy within 8 weeks after initial symptoms, in the absence of chronic liver disease. Etiology includes viral hepatitis, metabolic disorders, autoimmune hepatitis, ischemia, neoplastic disease, and toxins, but in ~50% no etiology is identified (Table 130.3).

Clinical Manifestations

Liver failure is a multisystem disorder with complex interactions among the liver, kidneys, vascular structures, gut, central nervous system (CNS), and immune function. Hepatic encephalopathy is characterized by varying degrees of impairment (Table 130.4). Respiratory compromise occurs as severity of the failure increases and requires early institution of ventilatory support. Hypoglycemia resulting from impaired glycogenolysis and gluconeogenesis must be prevented. Renal function is impaired, and frank renal failure, or **hepatorenal syndrome**, may occur. This syndrome is characterized by low urine output, azotemia, and low urine sodium content. Ascites develops secondary to hypoalbuminemia and disordered regulation of fluid and electrolyte homeostasis. Increased risk of infection occurs and may cause death. Esophageal varices may cause significant hemorrhage, whereas hypersplenism from portal hypertension may produce thrombocytopenia and other cytopenias.

Laboratory and Imaging Studies

Coagulation tests and serum albumin are used to follow hepatic synthetic function. These tests are confounded by administration of blood products and clotting factors. Vitamin K should be administered to maximize the liver's ability to synthesize factors II, VII, IX, and X. In addition to monitoring

TABLE 130.3 Causes of Fulminant Liver Failure in Childhood

METABOLIC
Gestational alloimmune liver disease (neonatal hemochromatosis)
Electron chain transport and other mitochondrial defects
Disorders of fatty acid oxidation
Galactosemia
Tyrosinemia
Hereditary fructose intolerance
Bile acid synthesis disorders
Wilson disease
CARDIOVASCULAR
Shock, hypotension
Congestive heart failure
Budd-Chiari syndrome
INFECTIOUS
Hepatitis virus A, B
Echovirus
Coxsackievirus
Adenovirus
Parvovirus
Cytomegalovirus
Sepsis
Herpes simplex
NEOPLASTIC
Acute leukemia
Lymphoproliferative disease
TOXIC
Acetaminophen
Valproic acid
Phenytoin
Isoniazid
Halothane
<i>Amanita</i> mushrooms
IMMUNOLOGIC
Autoimmune hepatitis
Familial hemophagocytic lymphohistiocytosis
Unknown

prothrombin time and partial thromboplastin time, many centers measure factor V serially as a sensitive index of hepatic synthetic function. The INR (international normalized ratio) reflects liver synthetic function (~ to prothrombin time) and predicts the severity of hepatic failure. Renal function tests, electrolytes, serum ammonia, blood counts, and urinalysis also should be followed. In the setting of acute liver failure,

TABLE 130.4 Stages of Hepatic Encephalopathy

STAGE I
Alert and awake
Agitated and distractible
Infants and young children—irritable and fussy
Normal reflexes
Tremor, poor handwriting
Obeys age-appropriate commands
STAGE II
Confused and lethargic
Combative or inappropriate euphoria
Hyperactive reflexes
Asterixis present
Purposeful movements, but may not obey commands
STAGE III
Stuporous but arousable
Sleepy
Incoherent speech
Motor response to pain
Hyperreflexic
Hyperventilation
Asterixis present
STAGE IV
Unconscious, not arousable
Unresponsive or responds nonpurposefully to pain
Reflexes hyperactive
Irregular respirations
Pupil response sluggish
STAGE V
Unconscious
Hypoactive reflexes
Flaccid muscle tone
Apneic
Pupils fixed

liver biopsy may be indicated to ascertain the nature and degree of injury and estimate the likelihood of recovery. In the presence of coagulopathy, biopsy must be done using a transjugular or surgical approach.

Treatment

Because of the life-threatening and complex nature of this condition, management must be carried out in an intensive

TABLE 130.5 Treatment of Fulminant Liver Failure

Hepatic encephalopathy	Avoid sedatives Lactulose via nasogastric tube—start with 1–2 mL/kg/day, adjust dose to yield several loose stools per day Rifaximin or neomycin Enemas if constipated Mechanical ventilation if stage III or IV
Coagulopathy	Administer intravenous vitamin K Fresh frozen plasma only if active bleeding, monitor coagulation studies frequently Platelet transfusions as required
Hypoglycemia	Intravenous glucose supplied with $\geq 10\%$ dextrose solution, electrolytes as appropriate
Ascites	Restrict fluid intake to 50–60% maintenance Restrict sodium intake to 0.5–1 mEq/kg/day Monitor central venous pressure to maintain adequate intravascular volume (avoid renal failure)
Renal failure	Maintain adequate intravascular volume, give albumin if low Diuretics Vasoconstrictors Dialysis or hemofiltration Exchange transfusion Liver transplantation

care unit at a liver transplant center. Treatment of acute liver failure is supportive; the definitive lifesaving therapy is liver transplantation. Supportive measures are listed in Table 130.5. Efforts are made to treat metabolic derangements, avoid hypoglycemia, support respiration, minimize hepatic encephalopathy, and support renal function.

CHRONIC LIVER DISEASE

Etiology and Epidemiology

Chronic liver disease in childhood is characterized by the development of cirrhosis and its complications and by progressive hepatic failure. Causative conditions may be congenital or acquired. Major congenital disorders leading to chronic disease include biliary atresia, tyrosinemia, untreated galactosemia, and α_1 -antitrypsin deficiency. In older children, hepatitis B or C virus, autoimmune hepatitis, Wilson disease, primary sclerosing cholangitis, cystic fibrosis, and biliary obstruction secondary to choledochal cyst are leading causes.

Clinical Manifestations

Chronic liver disease is characterized by the consequences of portal hypertension, impaired hepatocellular function, and cholestasis. **Portal hypertension** caused by cirrhosis results in risk of gastrointestinal bleeding, ascites, and reduced hepatic blood flow. Blood entering the portal vein from the splenic and mesenteric veins is diverted to collateral circulation that bypasses the liver, enlarging these previously tiny vessels in the esophagus, stomach, and abdomen. **Esophageal varices** are particularly prone to bleed, but bleeding also can occur from

hemorrhoidal veins, engorged gastric mucosa, and gastric varices. **Ascites** develops as a result of weeping of a high-pressure ultrafiltrate from the surfaces of the viscera and is at risk of becoming infected (spontaneous bacterial peritonitis); ascites can often be massive and interfere with patient comfort and respiration. The spleen enlarges secondary to impaired splenic vein outflow, causing excessive scavenging splenic entrapment of platelets and white blood cells; this increases the patient's susceptibility to bleeding and infection.

Impaired hepatocellular function is associated with coagulopathy unresponsive to vitamin K, low serum albumin, elevated ammonia, and **hepatic encephalopathy**. The diversion of portal blood away from the liver via collateral circulation worsens this process. Malaise develops and contributes to poor nutrition, leading to muscle wasting and other consequences.

Chronic cholestasis causes debilitating pruritus and deepening jaundice. The reduced excretion of bile acids impairs absorption of fat calories and fat-soluble vitamins, which contributes to the poor nutritional state. Deficiency of vitamin K impairs production of clotting factors II, VII, IX, and X and increases the risk of bleeding. Vitamin E deficiency leads to hematologic and neurologic consequences unless corrected.

Laboratory and Imaging Studies

Laboratory studies include specific tests for diagnosis of the underlying illness and testing to monitor the status of the patient. Children presenting for the first time with evidence of chronic liver disease should have a standard investigation (Table 130.6). Monitoring should include coagulation tests, electrolytes and renal function testing, complete blood count with platelet count, transaminases, alkaline phosphatase, and γ -glutamyltransferase at appropriate intervals. Frequency of testing should be tailored to the pace of the patient's illness. Ascites fluid can be tested for infection by culture and cell count and generally is found to have an albumin concentration lower than that of serum.

Treatment

Treatment of chronic liver disease is complex. Supportive care for each of the many problems encountered in these patients is outlined in Table 130.7. Ultimately, survival depends on the availability of a donor liver and the patient's candidacy for transplantation. When transplantation is not possible or is delayed, palliative procedures, such as portosystemic shunts to treat portal hypertension, can be considered. The transjugular intrahepatic portosystemic shunt is an expandable stent placed between the hepatic vein and a branch of the portal vein within the hepatic parenchyma. This procedure is performed using catheters inserted via the jugular vein and is entirely nonsurgical. All portosystemic shunts carry increased risk of hepatic encephalopathy.

SELECTED CHRONIC HEPATIC DISORDERS

Wilson Disease

Wilson disease is characterized by abnormal storage of copper in the liver, leading to hepatocellular injury, CNS dysfunction, and hemolytic anemia. It is an autosomal recessive trait caused by mutations in the *ATP7B* gene. The encoded protein

TABLE 130.6 Laboratory and Imaging Investigation of Chronic Liver Disease

METABOLIC TESTING		
Serum α_1 -antitrypsin level	AST, ALT, GGT, alkaline phosphatase	
α_1 -antitrypsin phenotype if low serum level	Total and direct bilirubin	
Serum ceruloplasmin	Serum cholylglycine or bile acids	
Sweat chloride, CF gene tests if CF suspected	Serum cholesterol	
Testing for other specific conditions as indicated by clinical/ laboratory findings	Ultrasound examination of liver and bile ducts	
VIRAL HEPATITIS		
HBsAg	Doppler ultrasound of hepatic vessels*	
Hepatitis B viral DNA, HBeAg if HBsAg positive	Magnetic resonance cholangiography*	
Hepatitis C antibody	Magnetic resonance angiography of hepatic vessels*	
Hepatitis C antibody confirmatory test if positive	Percutaneous or endoscopic cholangiography*	
Hepatitis C viral RNA, genotype if antibody confirmed	Liver biopsy*	
AUTOIMMUNE HEPATITIS		
Antinuclear antibody	ANATOMIC EVALUATION	
Liver-kidney microsomal antibody	Ultrasound of liver, pancreas, and biliary tree	Consider magnetic resonance cholangiography or ERCP if evidence of biliary process
Anti-smooth muscle antibody	Liver biopsy—as required for diagnosis or prognosis	
Antineutrophil cytoplasmic antibody	TESTS TO EVALUATE NUTRITIONAL STATUS	
Total serum IgG (usually elevated)	Height, weight, skinfold thickness	25-hydroxyvitamin D level
TESTS TO EVALUATE LIVER FUNCTION AND INJURY		
Prothrombin time and partial thromboplastin time	Vitamin A level	Vitamin E level
Serum ammonia	Prothrombin time and partial thromboplastin time before and after vitamin K administration	
CBC with platelet count	Serum albumin and prealbumin	Serum albumin and prealbumin
Serum albumin		

*Perform when indicated to obtain specific anatomical information.

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; CBC, complete blood count; CF, cystic fibrosis; ERCP, endoscopic retrograde cholangiopancreatography; GGT, γ -glutamyltransferase; HBeAg, hepatitis B early antigen; HBsAg, hepatitis B surface antigen; Ig, immunoglobulin.

TABLE 130.7 Management of Chronic Liver Disease

PROBLEM	CLINICAL MANIFESTATIONS	DIAGNOSTIC TESTING	TREATMENT
Gastrointestinal variceal bleeding*	Hematemesis, rectal bleeding, melena, anemia	CBC, coagulation tests, Doppler ultrasound, magnetic resonance angiography, endoscopy	Somatostatin (octreotide) infusion, variceal band ligation or sclerotherapy, propranolol to reduce portal pressure, acid-blocker therapy, TIPSS or surgical portosystemic shunt if transplant not possible
Ascites	Abdominal distention, shifting dullness and fluid wave, respiratory compromise, spontaneous bacterial peritonitis	Abdominal ultrasound, diagnostic paracentesis; measure ascites fluid albumin (and serum albumin), cell count, WBC differential, culture fluid in blood culture bottles	Restrict sodium intake to 0.5–1 mEq/kg/day, restrict fluids, monitor renal function, treat peritonitis and portal hypertension. Central portosystemic shunt may be required.
Nutritional compromise	Muscle wasting, fat-soluble vitamin deficiencies, poor or absent weight gain, fatigue	Coagulation studies, serum albumin, 25-hydroxyvitamin D level, vitamin E level, vitamin A level	Fat-soluble vitamin supplements: vitamins A, D, E, and K; use water-soluble form of vitamins. Supplemental feedings—nasogastric or parenteral if necessary.
Hepatic encephalopathy	Irritability, confusion, lethargy, somnolence, coma	Serum ammonia	Lactulose orally or via nasogastric tube, avoid narcotics and sedatives, liver transplantation

*May also have peptic ulcerations.

CBC, Complete blood count; TIPSS, transjugular intrahepatic portosystemic shunt; WBC, white blood cell.

of this gene functions as an adenosine triphosphate (ATP)-driven copper pump. The **diagnosis** is made by identifying low serum levels of ceruloplasmin, elevated 24-hour urine copper excretion, the presence of Kayser-Fleischer rings in the iris, evidence of hemolysis, and elevated hepatic copper content. In any single patient, one or more of these measures may be normal. **Clinical presentation** varies but seldom occurs before age 3 years. Neurologic abnormalities may predominate, including tremor, decline in school performance, worsening handwriting, and psychiatric disturbances. Hemolytic anemia may be the first noted symptom. Hepatic presentations include appearance of jaundice, spider hemangiomas, portal hypertension and its consequences, and fulminant hepatic failure. **Treatment** consists of administration of copper-chelating drugs (penicillamine or trientine), with monitoring of urine copper excretion at intervals. Zinc salts often replace chelating agents after chelation therapy has successfully reduced excessive body copper stores. Adequate therapy must be continued for life to prevent liver and CNS deterioration. Patients whose initial presentation is with severe liver disease may require immediate transplantation.

Autoimmune Hepatitis

Immune-mediated liver injury may be primary or occur in association with other autoimmune disorders, such as inflammatory bowel disease or systemic lupus erythematosus. **Diagnosis** is made on the basis of elevated serum total IgG and the presence of an autoantibody, most commonly antinuclear, anti-smooth muscle, or anti-liver-kidney microsomal antibody (see Table 130.6). Liver biopsy specimens show the presence of a plasma cell-rich portal infiltrate with piecemeal necrosis. **Treatment** consists of corticosteroids initially, usually with the addition of an immunosuppressive drug after remission is achieved. Steroids are tapered gradually as tolerated to minimize glucocorticoid side effects. Many patients require lifelong immunosuppressive therapy, but some may be able to stop medications after several years under careful monitoring for recurrence.

Nonalcoholic Fatty Liver Disease

Nonalcoholic fatty liver disease (NAFLD) is characterized by the presence of macrovesicular fatty change in hepatocytes on biopsy. When accompanied by evidence of hepatic inflammation, the diagnosis is termed NASH (non-alcoholic steatohepatitis). Varying degrees of inflammation and portal fibrosis may be present. This disorder chiefly occurs in obese children, sometimes in association with insulin-resistant (type 2) diabetes and hyperlipidemia. Children with marked obesity, with or without type 2 diabetes, who have elevated liver enzymes and no other identifiable liver disease are likely to have this condition. NASH can progress to cirrhosis. Treatment is weight loss and exercise. Efforts should be made to control blood glucose and hyperlipidemia and promote weight loss. In general, the rate of progression to end-stage liver disease is slow.

PEARLS FOR PRACTITIONERS

See *The Digestive System: Pearls for Practitioners* at the end of this section.