NOTES
LIVER & GALLBLADDER CONGENITAL CONDITIONS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Inherited metabolic/congenital structural anomalies, affect hepatobiliary system → hyperbilirubinemia

COMPLICATIONS

- Kernicterus
- Recurrent cholangitis, cirrhosis
- Portal hypertension
- Metabolic problems, impaired growth

SIGNS & SYMPTOMS

- Jaundice, dark urine, light stools
- Impaired liver function
- Neurologic alterations

DIAGNOSIS

DIAGNOSTIC IMAGING

- Ultrasound
- Oral cholecystogram

LAB RESULTS

- Conjugated vs. unconjugated bilirubin, liver function tests
- Biopsy

TREATMENT

- See individual disorders

BILIARY ATRESIA

osms.it/biliary-atresia

PATHOLOGY & CAUSES

- Congenital anomaly of extrahepatic duct fibrosis, obstruction of bile flow
- Infections, environmental toxins, immune dysregulation, genetic mutations → perinatal injury to biliary system
- Bile prevented from entering duodenum → impaired fat digestion, absorption + cholestasis, distension of gallbladder, ducts

TYPES

- Biliary atresia only; not accompanied by other anomalies (most common)
- Biliary atresia + laterality malformations (left-right axis patterning/malpositioning of organs)
  - Dextrocardia, situs inversus, asplenia/polysplenia, interrupted inferior vena cava
  - Related *CFC1* gene mutation
- Biliary atresia + intestinal atresia, imperforate anus, kidney anomalies

COMPLICATIONS

- Liver cirrhosis, portal hypertension, hepatic encephalopathy
- Recurrent cholangitis, cirrhosis
- Metabolic problems, impaired growth (associated with malabsorption)

SIGNS & SYMPTOMS

- Neonates asymptomatic at birth; stools gradually become acholic, clay-colored
- Persistent jaundice
  - Skin gradually turns yellow, greenish-bronze
- Dark urine
  - Increased bilirubin concentration
- Portal hypertension
  - Splenomegaly, ascites, enlarged abdominal veins
- Impaired liver function → decreased coagulation factors, bleeding tendencies
  - Impaired coagulation also related to decreased vitamin K absorption

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound

- Abnormal gallbladder size, shape, contractility; absent common bile duct; "triangular cord" sign (triangle-shaped echogenic density above porta hepatis)

Hepatobiliary scintigraphy

- Decreased/absent patency of extrahepatic biliary tree

LAB RESULTS

- Increased conjugated serum bilirubin, aminotransferases

Liver biopsy

- Identifies obstruction-related histological changes

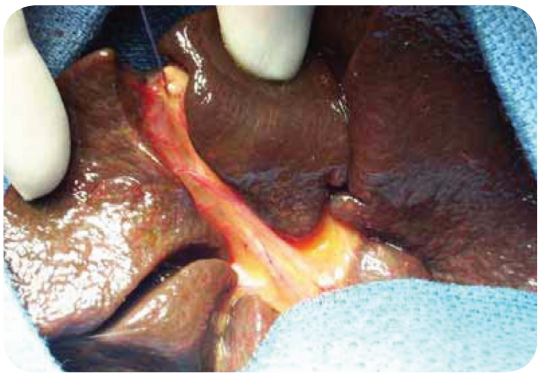


Figure 35.1 Intraoperative photography of extra-hepatic biliary atresia. The underside of the liver displays only connective tissue in the gallbladder fossa.

TREATMENT

MEDICATIONS

- Ursodeoxycholic acid (hydrophilic bile acid)

SURGERY

- Type indicated by blood chemistry, imaging, biopsy

Intraoperative cholangiogram

- Gold standard for confirming obstruction, diagnosis

Hepatoportoenterostomy (Kasai HPE)

- Restores bile flow from liver; may need subsequent revision

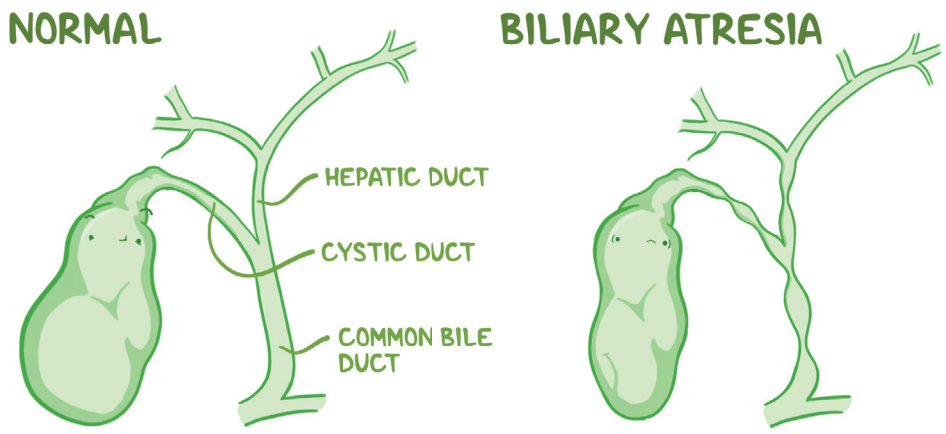
Liver transplant

- If Kasai procedure unsuccessful

OTHER INTERVENTIONS

Diet

- Fat-soluble vitamin supplements; high protein diet, medium-chain triglyceride supplements



CRIGLER–NAJJAR SYNDROME

osms.it/crigler-najjar-syndrome

PATHOLOGY & CAUSES

- Rare inherited metabolic disorder; nonhemolytic hyperbilirubinemia
- Autosomal recessive inheritance pattern
- AKA congenital nonhemolytic jaundice with glucuronosyltransferase deficiency

TYPES

Type I

- Severe jaundice, bilirubin encephalopathy, possible kernicterus-associated neurologic impairment

Type II

- Lower serum bilirubin concentration; no neurologic impairment

CAUSES

- Mutation in coding area of *UGT* gene, encodes for bilirubin-conjugating enzyme UGT1A1 (bilirubin-uridine diphosphate glucuronosyltransferase) → structurally abnormal enzyme → decreased/absent conjugation of bilirubin

RISK FACTORS

- Consanguinity

COMPLICATIONS

- Kernicterus (Type I), if not promptly addressed

SIGNS & SYMPTOMS

- Persistent jaundice in first few days of life
- Neurological symptoms as kernicterus develops

DIAGNOSIS

LAB RESULTS

Unconjugated hyperbilirubinemia

- *Type I*: 20–50 mg/dL
- *Type II*: < 20 mg/dL

Stool color

- *Type I*: pale yellow, low fecal urobilinogen (significantly decreased bilirubin conjugation)
- *Type II*: normal

Normal liver histology, liver function tests

TREATMENT

MEDICATIONS

Phenobarbital

- Useful in Type II, induces residual UGT activity

SURGERY

Liver transplant

- Definitive treatment for Crigler-Najjar syndrome Type I

OTHER INTERVENTIONS

Phototherapy

- In first years of life; effectiveness decreases over time

Exchange transfusion

Plasmapheresis + albumin infusions

- Removes bilirubin tightly bound to serum albumin

DUBIN–JOHNSON SYNDROME

osms.it/dubin-johnson-syndrome

PATHOLOGY & CAUSES

- Inherited metabolic disorder; mild, fluctuating elevations in conjugated (predominantly), unconjugated bilirubin, no evidence of hemolysis
- Autosomal inheritance pattern
- *MRP2* (*ABCC*) gene mutation → impaired hepatic excretion of non-bile-salt organic anions, bilirubin into bile via canalicular membrane → cholestasis → hyperbilirubinemia

SIGNS & SYMPTOMS

- Mild jaundice; evident during physiological stress (e.g. illness)/hormonal fluctuations (e.g. pregnancy, oral contraceptives)
- Constitutional
  - Vague abdominal pains, weakness
- Occasional hepatosplenomegaly

DIAGNOSIS

DIAGNOSTIC IMAGING

Oral cholecystogram

- Gallbladder may not be visualized

LAB RESULTS

- Hyperbilirubinemia, normal liver function tests
- Total urinary coproporphyrin normal; majority, coproporphyrin I

Liver biopsy, histological exam

- Brown, black discoloration
  - Pigment accumulates in lysosomes

TREATMENT

- None required

GILBERT'S SYNDROME

osms.it/gilberts-syndrome

PATHOLOGY & CAUSES

- Benign, inherited metabolic disorder; recurring unconjugated hyperbilirubinemia, jaundice
- Autosomal recessive inheritance pattern
- AKA Meulengracht disease, familial nonhemolytic jaundice
- Serum bilirubin increases during physiologic stress (e.g. illness, dehydration, fasting, overexertion, menses)
- Differs from other forms of non-hemolytic hyperbilirubinemia
  - Genetic mutation in promoter region of UGT gene → structurally normal enzyme → impaired genetic expression of hepatic UGT with decreased activity → decreased conjugation of bilirubin

SIGNS & SYMPTOMS

- Asymptomatic between episodes, jaundice evident during physiological stress
- Clinical manifestations
  - During adolescence, with effects of sex steroids on bilirubin metabolism

DIAGNOSIS

- Exclude other causes of unconjugated hyperbilirubinemia

TREATMENT

- None required

ROTOR SYNDROME

osms.it/rotor-syndrome

PATHOLOGY & CAUSES

- Rare benign inherited disorder; chronic conjugated, unconjugated hyperbilirubinemia; no hemolysis
- *SLCO1B1*, *SLCO1B3* gene mutations (code for transporter proteins 1B1, 1B3 responsible for bilirubin re-uptake by hepatocytes) → alters bilirubin re-uptake → increases bilirubin in plasma

COMPLICATIONS

- Impaired 1B1 activity → significant drug toxicities (e.g. statin-associated myopathy)

SIGNS & SYMPTOMS

- Mild jaundice; during physiological hormonal fluctuations (e.g. pregnancy, oral contraceptive use)

DIAGNOSIS

DIAGNOSTIC IMAGING

Oral cholecystogram

- Normal gallbladder opacification

LAB RESULTS

- Hyperbilirubinemia, normal liver function tests

- Total urinary coproporphyrin markedly increased; majority coproporphyrin I

Liver biopsy, histological exam

- Normal

TREATMENT

- None required