5A. Normal Anatomy, Development, Physiology and Microanatomy

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I. Development of Biliary Tree/Gallbladder
   A. Primitive anlagen appears at end of 2nd month of gestation
      1. Hepatic diverticulum gives rise to hepatic parenchyma, intrahepatic biliary tree and common bile duct
      2. Cystic diverticulum gives rise to cystic duct and the gallbladder
   B. Gall bladder is initially solid, then becomes cystic during development
      1. Congenital absence of gall bladder caused by failed development of cystic diverticulum
         a. Usually of little clinical significance
         b. May be associated with congenital heart disease, situs inversus, polysplenia, asplenia, biliary atresia (splenic malformation syndrome)
      2. Fetal cystic duct fuses with common bile duct. Abnormalities at this stage may produce choledochal cyst anomalies
   C. Bipotential hepatoblasts give rise to cholangiocytes and hepatocytes
      1. Hepatoblasts in mesenchyme nearest the portal vein form a bilayered structure (ductal plate)
      2. Ductal plate cells remodel to form bile ducts in the intrahepatic portal tracts
      3. Abnormal development of intrahepatic bile ducts due to ductal plate malformations are likely the underlying cause of:
         a. Congenital hepatic fibrosis with cystic kidney disease
         b. Ciliopathies—Joubert syndrome, Meckel-Gruber and Ivemark syndrome
      4. The smallest intrahepatic bile ducts (canaliculi) are formed from junction between hepatocytes
      5. Intrahepatic bile duct development starts at the hilum and progresses to the periphery of the liver
         a. At birth, the most peripheral intrahepatic bile ducts are immature with persistence of ductal plate
         b. Maturity of intrahepatic biliary tree achieved by 4 weeks of life

II. Anatomy and Physiology
   A. Biliary ducts
      1. Hepatocytes secrete bile into canaliculi
      2. Bile passes from canaliculi to canals of Hering (lined by combination of hepatocyte and cholangiocytes)
      3. Canals of Hering empty into interlobular bile ducts
      4. Interlobular biliary ducts join larger portal tract bile ducts
      5. Portal tract bile ducts join to form right and left hepatic ducts, which form the common hepatic duct at the porta hepatis
      6. Cystic duct joins the common hepatic duct, forming common bile duct
      7. Common bile duct and main pancreatic duct join at the ampulla of Vater at the 2nd portion of the duodenum
   B. Vascular supply
      1. Vascular supply for the intrahepatic biliary ducts is the hepatic artery
      2. In fetuses, the umbilical vein joins the portal vein to form the ductus venosus
      3. The oxygenated blood from the placenta is largely shunted to IVC via the ductus venosus
4. At birth, functional closure of ductus venosus occurs within minutes, while the structural closure occurs slowly, over the 1st week of life, and may take longer in premature infants.

5. After closure, the ductus venosus becomes the ligamentum venosum.

C. Gall bladder vasculature
1. Gall bladder supplied by cystic artery branch of the right hepatic artery.
2. The cysto-hepatic triangle (Calot triangle) is composed of the cystic duct, cystic artery and the common hepatic duct.

D. Hepatic innervation
1. Hepatic plexus contains sympathetic fibers (celiac plexus) and parasympathetic fibers (vagus nerve).
2. Hepatic nerve supply mediates hepatic vasoconstriction. Other functions are unclear.

III. Histology

A. Biliary histology
2. Loss of intrahepatic bile ducts occurs in:
   a. Chronic biliary tract obstruction.
   b. Primary sclerosing cholangitis.
   c. Primary biliary cirrhosis.
   d. Ischemia.
   e. Chronic graft vs host disease.
   f. Chronic graft rejection.
3. Paucity of intrahepatic bile ducts is a feature of premature neonates and is more severe in Alagille syndrome.

B. Gall bladder histology and pathology
1. Three tissue layers: mucosa, muscularis propria and serosa. There is no muscularis mucosa or submucosa.
2. Surface epithelium composed of single layer columnar cell.
3. Lamina propria contains:
   a. Loose connective tissue.
   b. Blood vessels, lymphatics.
   c. Occasional chronic inflammatory cells.
4. Heterotopic tissue may occur in gall bladder wall:
   a. Gastric and hepatic most common.
   b. Also reported: adrenal, thyroid, pancreas.
5. Cystic duct has mucosal folds with smooth muscle near gallbladder neck, functioning as spiral valve of Heister.
6. Aberrant bile ducts (Luschka ducts):
   a. 10% of cholecystectomy specimens.
   b. Often buried in gallbladder wall.
   c. May communicate with intrahepatic bile ducts.

Recommended Reading


Most gallstones are not chemically pure, but are mixtures of calcium, bilirubin, cholesterol and other substances. For the purposes of this study guide, gallstones will be classified into three types: cholesterol stones, black pigment stones and brown pigment stones.

I. Cholesterol Stones
   A. Formation requires the following conditions:
      1. Increased secretion of cholesterol into bile causing supersaturation of bile has several common causes:
         a. ↑ cholesterol delivery to the liver via LDL and chylomicrons (increased dietary cholesterol intake, estrogen, oral contraceptive use)
         b. ↑ endogenous cholesterol production (obesity and hypertriglyceridemia)
         c. ↓ conversion of cholesterol to bile acids (older age)
         d. ↑ conversion of cholesterol to cholesterol esters (progesterone, clofibrate)
      2. Nucleation of soluble cholesterol into solid crystals
      3. Gallbladder stasis, allowing aggregation of cholesterol crystals into stones
      4. ↑ mucin secretion by gallbladder provides a nidus for crystal formation
   B. Clinical conditions associated with higher risk of cholesterol gallstones
      1. Pregnancy
         a. Estrogen induces cholesterol hypersecretion
         b. Progesterone reduces bile acid production → decreased ability to solubilize cholesterol
         c. Progesterone decreases gallbladder motility → stone formation
      2. Obesity
         a. ↑ exogenous cholesterol intake
         b. ↑ endogenous cholesterol synthesis (increased HMG-CoA reductase activity)
      3. Hypertriglyceridemia
   4. Oral contraceptive pills
      a. Due to estrogen effects (cholesterol hypersecretion)
      b. Risk appears to be 1.5–1.8:1 compared to controls
   5. Female gender: female:male ratio during childbearing years approaches 3:1 and the ratio decreases with advancing age
   C. Other facts about cholesterol stones
      1. Yellow/white in color
      2. Cholesterol content is >50%
      3. Not radio opaque on plain x-ray, due to minimal calcium salt content

II. Black Pigment Stones
   A. Formation occurs when there is increased conjugated bilirubin secreted into bile
      1. Endogenous glucuronidase activity in gall bladder releases free bilirubin anions into bile with resulting supersaturation
      2. Unconjugated bilirubin monohydrate precipitates with calcium in bile
   B. Clinical conditions associated with black pigment stones:
      1. Hemolytic disease (excess bilirubin load)
      2. Dysfunctional erythropoiesis with increased bilirubin load
      3. Ileal resection and/or ileal inflammation (↑ enterohepatic circulation of bilirubin and ↓ bile acid reabsorption causing ↓ bile acid pool)
      4. Cystic fibrosis with pancreatic insufficiency (increased enterohepatic circulation of bilirubin and ↓ bile acid resorption)
      5. Parenteral nutrition (↓ bile acid reabsorption and ↓ bile acid pool)
      6. Cirrhosis (bile salt malabsorption)
   C. Other characteristics of black pigment stones:
      1. Black or brown color
2. 50%–75% of black pigment stones are radio opaque (high calcium content)
3. Often occur in multiples
4. Calcium carbonate, calcium phosphate, mucin and cholesterol account for <20% by weight
5. No gender predominance

III. Brown Pigment Stones
A. Occur in the presence of the following risk factors:
   1. Infection of bile (bacterial infection, parasitic infection)
   2. Bile stasis (bile duct abnormalities)
   3. Bile infection and stasis result in increased mucin production. Mucin is the nidus for brown pigment stone formation
B. Clinical conditions associated with brown pigment stones:
   1. Bacterial infections (often *E. coli* but other enteric pathogens implicated) → bacteria can be found/cultured from the stone core
   2. Parasitic infections (e.g., *Ascaris*)
   3. Bile duct anomalies causing stasis, e.g. stricture
C. Other characteristics of brown pigment stones
   1. Brown to orange in color (due to high calcium bilirubinate content)
   2. Not radiopaque on plain film (calcium carbonate and phosphate content is too low)
   3. Typically form in the common bile duct and intrahepatic bile ducts

IV. Risk Factors
Gallstones are rare in childhood but are increasing in frequency due mostly to ↑ prevalence of obesity. Risk factors for gallstones in children include:
A. Obesity:
   1. Excessive hepatic cholesterol secretion due to increased cholesterol synthesis
   2. Prevalence of 2.0% in asymptomatic obese children (8–19 years old)
B. Female gender (only after puberty)
   1. After puberty, prevalence ratio F:M is at least 4:1
C. Hemolytic disease
   1. Sickle cell disease (prevalence 14%–36% in children 6–20 years old, prevalence increases with age)
   2. Hereditary spherocytosis
   3. Thalassemias
   4. Wilson disease
D. Reduced bile salt pool, etc
   1. History of ileal resection (only after puberty when cholesterol secretion increases and bile salt secretion declines)
   2. Small bowel Crohn disease
   3. Cystic fibrosis with pancreatic insufficiency (prevalence of 13.2% in children and increases with age). Pancreatic enzyme supplements decrease the risk
E. Total parenteral nutrition (biliary stasis → gallbladder sludge → pigment stones)
   1. Prevalence in children as high as 13% after 4 weeks of TPN
F. Medications:
   1. Ceftriaxone (displaces bilirubin from albumin binding sites)
   2. Furosemide (in patients with other risk factors like prematurity and sepsis)
   3. Octreotide (induces gallbladder stasis)
   4. Cyclosporine (especially in bone marrow and solid organ transplant patients; mechanism is unknown)
G. Down syndrome (4.7% prevalence in 21 children in one study; etiology unknown)
H. Hypertriglyceridemia
I. Pregnancy
J. Some Native American tribes have very high risk of gall stones - Pima, Hopi, Araucan
V. Complications of Gallstone Disease
   A. Cholecystitis
   B. Choledocholithiasis
   C. Pancreatitis secondary to cholecystitis or choledocholithiasis
   D. Cholangitis
   E. Gallbladder perforation

VI. Management of Symptomatic and Asymptomatic Gallstones
   A. Asymptomatic gallstones in infancy:
      1. Generally resolve spontaneously and do not require surgery
      2. Gallstones identified on intra-uterine ultrasound are a common, normal finding not requiring therapy
   B. Asymptomatic gallstones in older children:
      1. Spontaneous resolution is rare, but there is no consensus on whether they should be removed
      2. Parenteral nutrition–associated pigment gallstones that appear after short-term PN may resolve spontaneously and should be monitored, unless they become symptomatic
      3. Adult studies support watchful waiting in asymptomatic patients with incidental gallstones, but this has not been studied in children
   C. Symptomatic gallstones in older children:
      1. Remove via cholecystectomy
      2. Cholecystostomy tube for drainage is an option if patient is critically ill
      3. ERCP before surgery is indicated in some situations
         a. Suspicion of common bile duct stones
         b. Dilation of intra- or extrahepatic bile ducts on ultrasound
         c. Associated pancreatitis
   D. Nonsurgical techniques for gallstone removal not well studied in children
      1. Ursodeoxycholic acid and/or chenodeoxycholic acid inhibit HMG-Coa reductase, reducing cholesterol synthesis. They also increase bile acid concentration in bile, promoting dissolution of cholesterol stones

Recommended Reading


I. **Acute Calculous Cholecystitis**
   A. Essential features: fever, right upper quadrant abdominal pain, leukocytosis associated with gallbladder inflammation
   B. Etiology/pathogenesis: gallbladder stasis is common to all
      1. Cholelithiasis: responsible for vast majority of childhood cases
      2. External compression of biliary tree with stasis (mass, lymph nodes)
      3. Trauma
      4. Structural duct abnormalities (choledochal cyst)
   C. Risk factors for cholelithiasis and cholecystitis in childhood (see section on Gallstones)
   D. Clinical features
      1. Symptoms
         a. RUQ/epigastric abdominal pain ± radiation to the right shoulder
         b. Nausea and nonbilious emesis, anorexia
         c. Fever
         d. Murphy sign: inspiratory pause on deep palpation of the RUQ
      2. Laboratory findings
         a. Leukocytosis with left shift
         b. Serum transaminases normal to slightly elevated
         c. Serum amylase elevated in ~8% of cases, even in the absence of obstructive pancreatitis
         d. Direct and total serum bilirubin elevated in children
         e. Marked elevations of $\gamma$ glutamyl transferase, alkaline phosphatase and direct bilirubin suggest choledocholithiasis
   E. Diagnosis
      1. Sonography findings
         a. Gallstones
         b. Gallbladder wall thickening >4–5 mm in adults and >3.0–3.5 in some pediatric reports
         c. Pericholecystic fluid
         d. Sonographic Murphy sign – tenderness over the gallbladder from pressure of the U/S transducer
         e. Common bile duct dilation raises suspicion for choledocholithiasis
      2. Cholescintigraphy (HIDA)
         a. Technetium-99m labeled iminodiacetic acid (IDA) given via IV is taken up by the liver and secreted into the bile. Concentrated in the gallbladder
         b. Normal hepatic uptake of IDA with reduced concentration in gallbladder bile after 60 minutes is consistent with cholecystitis
         c. Morphine administration decreases false positives by increasing sphincter of Oddi pressure, causing back pressure in the common bile duct and forcing more radionuclide into the gallbladder
         d. False-positive results on HIDA scan caused by:
            1) Obstruction of the cystic duct by stone, inflammation or tumor
            2) Hyperbilirubinemia (total bili >4.4 mg/dL)
            3) Severe parenchymal liver disease decreases hepatic uptake of IDA
            4) Prior biliary sphincterotomy decreases resistance to bile flow and bypasses the gallbladder
            5) Prolonged fasting or TPN (gallbladder already full resists further filling)
         e. Results of HIDA are 94% sensitive and 65%–85% specific for acute cholecystitis in adults
F. Management

1. Morbidity and mortality
   a. Complications occur in up to 30% of patients
      1) Gallbladder perforation
      2) Abscess
      3) Empyema
   b. Surgery to remove stones prevents subsequent attacks

2. NPO

3. Intravenous fluid – more aggressive therapy needed in sickle cell hemoglobinopathies

4. Analgesics
   a. Ketorolac
   b. Morphine and derivatives were formerly avoided because of concern about increase in sphincter of Oddi pressure
   c. Morphine is now routinely used for analgesia with no adverse effects on outcome

5. Antibiotics are universally used but clear evidence for benefit is lacking
   a. Common regimens designed to combat enteric flora – cefoxitin or piperacillin/tazobactam

6. Percutaneous cholecystostomy tube
   a. Relieves biliary obstruction and allows for gallbladder irrigation and, sometimes, removal of sludge and small stones
   b. Reserved for critically ill patients

7. Cholecystectomy
   a. Procedure of choice for calculous cholecystitis
   b. Laparoscopic surgery preferred over open
   c. Laparoscopy associated with shorter hospital stay, smaller incision and less postoperative pain, but more common bile duct injury
   d. Timing of surgery controversial
      1) Patients too sick for surgery should have percutaneous cholecystostomy
      2) Patients deteriorating after 24 hours of medical therapy should have cholecystectomy
      3) Patients with uncomplicated course and recovering on medical therapy generally have cholecystectomy within 1–5 days
      4) Patients with sickle cell disease benefit from transfusion of RBCs and aggressive fluid resuscitation prior to cholecystectomy
   e. Complications
      1) Gangrene of the gallbladder
      2) Perforation of gallbladder is rare in children
      3) Pancreatitis – especially with cholelithiasis
   f. Management of choledocholithiasis
      1) Confirm presence of stones by imaging
      2) ERCP with stone removal often performed prior to cholecystectomy
         a) Endoscopic stone removal lowers the risk of retained common bile duct stones
      3) MRCP can be helpful in some cases to identify common duct stones

G. Acute Acalculous Cholecystitis (AAC)

1. Associated underlying conditions usually present
   a. Sepsis
   b. Gastroenteritis
   c. Abdominal trauma or surgery
   d. Extensive burns
   e. Shock, cardiac resuscitation
   f. IV nutrition and prolonged fasting
   g. Systemic inflammatory diseases – SLE, Kawasaki disease, polyarteritis nodosa
   h. Malignancy
   i. Congestive heart failure

2. Pathophysiology – the root cause appears to be gallbladder stasis and/or ischemia
3. Clinical features
   a. Fever
   b. Abdominal pain typically RUQ
   c. Vomiting
   d. Leukocytosis in 70%–80% of children
   e. Bilirubin and transaminase elevation in 60% of children
   f. RUQ mass found in 25% of children in one pediatric study

4. Radiographic features
   a. Ultrasound shows:
      1) Gallbladder distension
      2) Gallbladder wall thickening
      3) Sludge but not stones
      4) Pericholecystic fluid
      5) Sonographic Murphy sign
      6) Intramural gas sometimes occurs
      7) Abscess and perforation rare
   b. Cholescintigraphy (HIDA scan)
      1) Normal hepatic uptake with failure to opacify the gall bladder
      2) Increased pericholecystic radiotracer accumulation in the gallbladder fossa (Rim Sign) is associated with gangrene
      3) Leakage of tracer into fossa indicates perforation

5. Management
   a. Antibiotics and serial ultrasounds to follow for progression and complications
   b. Nonoperative management successful in 30%–75% of children
   c. Percutaneous cholecystostomy with drainage in critically ill patients
   d. Cholecystectomy

H. Chronic Acalculous Cholecystitis/Biliary Dyskinesia
   1. Definition – abnormal gallbladder contractility as measured by decreased gallbladder ejection fraction on HIDA scan
   2. Clinical features
      a. Chronic RUQ pain in absence of other findings with normal imaging of the gallbladder
      b. Fatty food causes abdominal pain
      c. Normal liver function blood tests
   3. 50%–93% of surgically resected gallbladders show chronic inflammatory changes
   4. Diagnosis
      a. HIDA scan before and after CCK or fatty meal stimulation is used to calculate the gallbladder ejection fraction
      b. Gallbladder ejection fraction is defined as the difference between the amount of tracer in the gallbladder before and after the fatty meal or CCK, divided by the amount of tracer in the gallbladder before CCK or fatty meal stimulation
      c. Ejection fraction in adults <35% is considered abnormal. Norms not established for children
      d. Protocols for timing of the post-stimulation measurement are not established

5. Management
   a. Cholecystectomy
   b. Pediatric studies after cholecystectomy show short-term improvement in 85% of patients
   c. Long-term improvement is only 48%–70%
   d. Preoperative ejection fraction does not predict postoperative outcome
Recommended Reading


Biliary atresia, a process of bile duct obliteration, is on the differential diagnosis for neonatal cholestasis. Early identification is vital to improve survival and delay liver transplantation. While there are several theories, the etiology has not yet been identified.

I. Background
   A. Inflammation of the bile ducts with progressive obliteration of the extrahepatic biliary tract in newborn infants results in obstruction to bile flow
   B. Types
      1. BA without associated malformations (perinatal form)
         a. Type I: obliteration of common bile duct
         b. Type II: atresia of the hepatic duct
         c. Type III (most common): atresia of the right and left hepatic ducts to the level of the porta hepatis
      2. BASM (embryonal form): BA with splenic malformation is associated with situs inversus, asplenia, polysplenia, intestinal malrotation, annular pancreas and cardiac anomalies
   C. Etiology is not completely defined
      1. Animal model studies have focused on pre- or immediate postnatal infection of liver and biliary tract in association with immune dysregulation. Most commonly cited organisms possibly associated are CMV and rotavirus
      2. The following genetic mutations have been identified in small numbers of patients with biliary atresia, but none can be defined as the sole cause of biliary atresia: JAG 1, CFC1, ICAM1, CD14 endotoxin receptor, hepcidin antimicrobial peptide gene

II. Presentation
   A. Apparently healthy newborn with gradual onset of jaundice, hepatosplenomegaly, acholic stools and dark urine between 6 and 12 weeks of age. Poor weight gain, frequent stools, bleeding diathesis (vitamin K deficiency) are also reported
   B. The embryonal form presents with cholestasis at birth
   C. Laboratory findings: conjugated hyperbilirubinemia, mild to moderate elevation of transaminases, more significant elevation of GGT and alkaline phosphatase

III. Diagnosis
   A. Abdominal US may show absent or small, thick-walled gallbladder
      1. Test is neither sensitive nor specific enough to make a diagnosis
      2. Normal gallbladder is often hard to identify in newborns because of small size and high frequency of postprandial contractions
      3. False-positive diagnosis is common
      4. Triangular cord sign (hyperechoic triangular area in the porta hepatis that corresponds with the fibrous remnant of the hepatic duct) is 80% sensitive and 98% specific for BA
   B. Hepatobiliary scintigraphy
      1. Technetium-99 diisopropyl iminodiacetic acid is given intravenously
      2. Scanning repeatedly over 24 hours shows good, prompt hepatic parenchymal uptake but absent or reduced excretion into the intestine within 24 hours
   C. Liver biopsy
      1. To differentiate BA from other causes of intrahepatic cholestasis
         a. Histologic changes are nonspecific, but in unoperated infants usually include expanded portal tracts with edema and inflammation, bile duct proliferation, and canalicular and bile duct bile plugs
IV. Complications
A. Ascending cholangitis after Kasai procedure (hepatic portoenterostomy)—incidence of 40%–90%; increased risk due to abnormal anatomy and bacterial stasis; recurrent cholangitis can lead to progressive cirrhosis
B. Portal hypertension due to biliary cirrhosis

V. Treatment
A. Kasai procedure is mainstay of management
   1. Goal is to help restore bile flow from intrahepatic bile ducts to small bowel
   2. 10-year survival rate of patients diagnosed and treated prior to 60 days of age is 73% vs 11% in those diagnosed and treated after 90 days of age
   3. >50% of patients who undergo Kasai will require liver transplantation by 2 years of age
   4. At 3 months postoperatively, a total serum bilirubin <2 mg/dL is associated with low likelihood of requiring hepatic transplant within 2 years, whereas a total serum bilirubin ≥6 mg/dL is associated with failure of adequate bile flow and higher likelihood of need for hepatic transplantation
B. Supportive care after Kasai procedure
   1. Nutrition management of cholestatic liver disease; diet supplemented with medium-chain fatty acids and fat-soluble vitamins (ADEK)
   2. Prophylaxis against cholangitis with trimethoprim/sulfamethoxazole is recommended for the first year after Kasai procedure
   3. Prevention of fibrosis: ursodiol may be beneficial to prolong native liver survival and delay liver transplantation in patients after Kasai
   4. Treatment of portal hypertension
      a. Variceal bleeding controlled with sclerotherapy or banding
      b. If ascites develops, use diuretics, β-blockers, salt and/or water restriction
C. Liver transplant for patients who develop biliary cirrhosis

Recommended Reading


I. Differential Diagnosis of Bile Duct Disorders

A. Caroli disease
1. Congenital dilation of large intrahepatic ducts
2. Affects 1:100,000
3. Mode of inheritance is controversial
4. Caroli disease: bile ductular ectasia without hepatic abnormalities
5. Caroli syndrome (more common): bile duct dilatation associated with congenital hepatic fibrosis (CHF)
   a. Associated with autosomal recessive polycystic kidney disease (ARPKD)
   b. Develop cholangitis and portal hypertension
   c. Increased risk of biliary carcinoma

B. Sclerosing cholangitis
1. Primary sclerosing cholangitis: progressive chronic inflammation and fibrosis of intra- and/or extrahepatic bile ducts of unknown etiology with eventual obliteration of peripheral bile ducts, development of bile duct strictures and resultant dilation
   a. Associated with inflammatory bowel disease, mostly ulcerative colitis
2. Secondary causes include histiocytosis X, immunodeficiencies (HIV), bacterial cholangitis, cancers, recurrent pancreatitis, choledocholithiasis and trauma
3. Diagnosis
   a. Elevated serum alkaline phosphatase, GGTP, AST/ALT
   b. 50% with modest increase in bilirubin
   c. ERCP/MRCP shows beading (strictures and dilatation) of bile ducts
   d. Classic liver biopsy finding is periductal, concentric, onion-skin fibrosis. Often, histology is nonspecific and not useful to confirm diagnosis
4. Treatment
   a. Ursodiol is used to promote bile flow. Adult studies have not confirmed efficacy of this therapy
   b. Vitamin ADEK for fat-soluble vitamin deficiency
   c. Liver transplant indicated for recurrent bacterial cholangitis, jaundice refractory to medical and/or endoscopic treatment, decompensated cirrhosis or complications of portal hypertension
5. Complications
   a. Ascending cholangitis, portal hypertension, dominant stricture
   b. Lifetime risk of cholangiocarcinoma is 10%–15%
   c. Cancer screening includes yearly abdominal ultrasonogram and serum carbohydrate antigen 19-9 (CA19-9), but neither test is adequately sensitive or specific

C. Congenital hepatic fibrosis
1. Characterized by hepatic fibrosis, portal hypertension, and autosomal-recessive (ARPKD) or autosomal-dominant (ADPKD) polycystic kidney disease
2. Etiology
   a. Pathogenesis: abnormalities of the ductal plate during hepatic organogenesis
   b. Genetics: ARPKD is caused by mutations in the polycystic kidney and hepatic disease 1 (PKHD1) gene
3. Symptoms:
   a. Most patients present with symptoms of portal hypertension, often a sudden bleed from unsuspected esophageal varices
   b. Large, hard liver on physical exam
4. Treatment
   a. Treat symptomatic esophageal varices with banding/sclerotherapy/ligation/beta-blockers
   b. Transjugular intrahepatic portosystemic shunt (TIPS) if endoscopic and medical management fails
   c. Liver transplant for recurrent cholangitis or progressive hepatic dysfunction despite medical/surgical care

D. Bile duct paucity
   1. Alagille Syndrome (see section on Alagille Syndrome)

E. Choledochal cysts
   1. Frequency 1:15,000 births in West and 1:1,000 in Japan
   2. Female: male ratio 3–4:1
   3. Five types classified by location:
      a. Type I—cystic dilatation of the common bile duct (most common, 80%–90% of cases)
      b. Type II—diverticulum of the extrahepatic bile duct proximal to the duodenum
      c. Type III—cystic dilatation limited to the intraduodenal portion of the common bile duct
      d. Type IVa—multiple intrahepatic and extrahepatic biliary cysts
      e. Type IVb—multiple dilation of only extrahepatic bile ducts
      f. Type V—multiple intrahepatic biliary cysts (Caroli disease)

4. Symptoms
   a. Infants: jaundice and acholic stools, often diagnosed during evaluation for suspected biliary atresia
   b. Children: intermittent biliary obstruction or recurrent bouts of pancreatitis
   c. Mass in the right upper quadrant sometimes seen
   d. Classic triad of jaundice, mass and abdominal pain is more common in adults and only comprises 10%–20% of cases in infants and children

5. Diagnosis
   a. Variable elevations of AST and ALT, direct bilirubin, alkaline phosphatase and/or GGTP
   b. Ultrasound: imaging of choice but effectiveness is operator dependent
   c. MRCP is more sensitive and will give more anatomical detail of neighboring structures

6. Treatment: surgical excision of cyst

7. Complications
   a. Increased risk of cholangiocarcinoma (9%–28%) in any part of the biliary tree
   b. Screening for cholangiocarcinoma is recommended yearly. Ultrasound and serum CA-19-9 are used but there are no evidence-based guidelines in pediatrics

F. Choledocholithiasis (see section on Gallstones)

G. Bile duct stricture
   1. Can be benign (trauma, iatrogenic, PSC) or malignant (cholangiocarcinoma or adjacent compressing tumor of liver, gallbladder, pancreas); can be single or multiple
   2. Symptoms
      a. Varied presentation: asymptomatic; jaundice, fever and RUQ tenderness if complicated by ascending cholangitis; symptoms of portal hypertension if complicated by cirrhosis
   3. Diagnosis
      a. Direct bilirubin, alkaline phosphatase and GGT are usually elevated
      b. Ultrasound: imaging of choice, but MRCP is more sensitive
   4. Treatment: ERCP with dilatation and stenting
   5. Complications
      a. Ascending cholangitis
      b. Liver abscess
      c. Secondary biliary cirrhosis
H. Bile duct perforation
   1. Etiology: usually a result of trauma or iatrogenic (e.g., ERCP/surgery), although can occur spontaneously
   2. Symptoms: range from vague abdominal pain to peritonitis
   3. Diagnosis: imaging (x-ray/ultrasound/CT/MRCP/HIDA) will show free air in retroperitoneum
   4. Treatment: surgical repair

Recommended Reading


