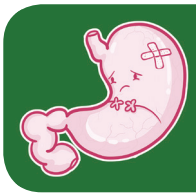

NOTES
BILIARY TRACT DISEASES

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Diverse spectrum of diseases affecting biliary system (gallbladder, bile ducts, liver)
- Bile stored in gallbladder → stasis/chemical constituents change → precipitate to solid stone → travel down biliary tract → obstruction → decreased bile drainage → symptoms

SIGNS & SYMPTOMS

- Symptoms vary, based on location
  - Pain, jaundice, infection, inflammatory response, sepsis
- Right upper quadrant (RUQ) epigastric pain
- Jaundice
- Nausea, vomiting
- Fever, chills → sepsis

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/ultrasound

- Locations of stones, gallbladder wall thickening/inflammation

X-ray

- Pigmented gallbladder stones (radiopaque)

Magnetic resonance cholangiopancreatography (MRCP)

- MRI for detailed images of hepatobiliary, pancreatic systems

Endoscopic retrograde cholangiopancreatography (ERCP)

- Down esophagus, stomach, duodenum, ducts → contrast medium injected into ducts → X-ray shows narrow areas/blockages
  - *Complications:* pancreatitis (most common); intraluminal/intraductal bleeding, hematomas; perforation; infection (cholangitis, cholecystitis); cardiopulmonary complications (cardiac arrhythmia, hypoxemia, aspiration)

LAB RESULTS

- See table

TREATMENT

MEDICATIONS

- Antibiotics

SURGERY

- Cholecystectomy

OTHER INTERVENTIONS

- Sepsis management, biliary drainage, ERCP

LAB RESULTS OF BILIARY TRACT DISEASES

	BILIARY COLIC	CHOLECYSTITIS	CHOLEDOCHOLITHIASIS	CHOLANGITIS
TOTAL BILIRUBIN	Normal	Normal	↑	↑
DIRECT BILIRUBIN	Normal	Normal	↑	↑
WBC	Normal	↑	↑	↑
AST	Normal	Normal	↑	↑
ALT	Normal	Normal	↑	↑
ALP	Normal	Normal	↑	↑
GGT	Normal	Normal	↑	↑
LIPASE, AMYLASE	Normal	Normal	Normal	↑

ASCENDING CHOLANGITIS

osms.it/ascending-cholangitis

PATHOLOGY & CAUSES

- Acute infection of bile duct caused by intestinal bacteria ascending from duodenum
- Bacterial infection of bile duct superimposed on obstruction of biliary tree; due to choledocholithiasis
- Gallstones form in gallbladder → slip out → travel through cystic bile duct, lodge in common bile duct → obstruction of normal bile flow → bacteria ascend from duodenum to bile duct → infect stagnant bile, surrounding tissue
- Common bacteria: *E. coli*, *Klebsiella*, *Enterobacter*, *Enterococcus*
- Medical emergency

RISK FACTORS

- Gallstones (most common)
- Stenosis of bile duct due to neoplasm/injury from laparoscopic procedure

COMPLICATIONS

- Sepsis, septic shock
  - High pressure on bile duct → obstruction → cells lining ducts widen → bacteria, bile enter bloodstream
- Multiorgan failure

SIGNS & SYMPTOMS

- Charcot's triad
  - RUQ pain, jaundice, fever/chills
- Reynold's pentad
  - Charcot's triad + hypotension/shock, altered consciousness
  - Associated with significant morbidity, mortality

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound, ERCP

- Biliary dilation
- Bile duct wall thickening
- Evidence of etiology (stricture/stone/stent)

LAB RESULTS

- Assess infection, jaundice
  - Increased WBC
  - Increased serum C-reactive protein (CRP)
  - *Elevated LFTs:* ALP, GGT, ALT, AST

TREATMENT

MEDICATIONS

- Antibiotics + IV fluids

SURGERY

- Cholecystectomy
  - Avoid future complications

OTHER INTERVENTIONS

- ERCP
  - Removes gallstones
- Shockwave lithotripsy
  - High frequency sound waves break down stone
- Stent
  - Widen bile ducts in areas of stricture

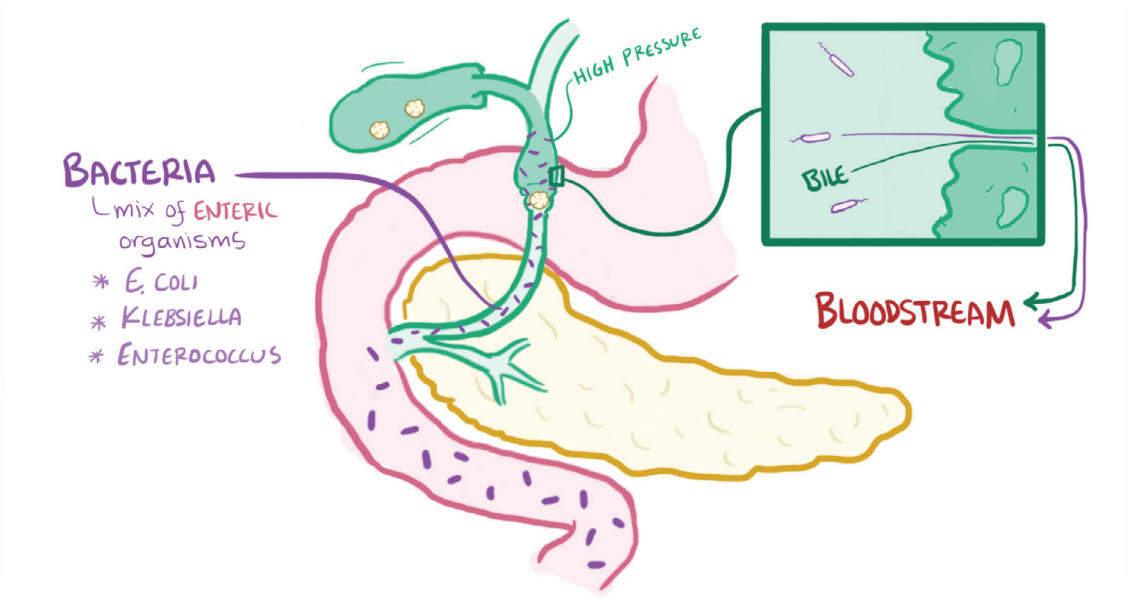

Figure 28.1 The pathophysiology of ascending cholangitis.

BILIARY COLIC

osms.it/biliary-colic

PATHOLOGY & CAUSES

- AKA "gallbladder attack"
- Gallstones lodged in bile ducts → temporary severe abdominal pain
- After meal, gallbladder contracts → gallstone ejected into cystic duct, lodged → gallbladder contracts against lodged stone → severe abdominal pain
- Pain subsides when gallstone dislodged

CAUSES

- Gallstones
- Narrow bile duct
- Pancreatitis
- Duodenitis
- Esophageal spasms

RISK FACTORS

- More common in individuals who are biologically female
- Obesity
- Pregnancy
- Age ≥ 40

COMPLICATIONS

- Acute cholecystitis
  - Inflammation of gallbladder wall
  - Gallstone doesn't dislodge from cystic duct

SIGNS & SYMPTOMS

- Pain
  - Severe right upper quandrant pain; radiates to right shoulder/shoulder blades
  - Intensity increases for 15 minutes, plateaus for few hours (< six), subsides
  - Starts hours after meal/at night/laying flat
- Nausea, vomiting, anorexia

DIAGNOSIS

- Recurrent symptoms

DIAGNOSTIC IMAGING

Ultrasound

- Confirmation of obstruction

X-ray, CT scan, MRI

TREATMENT

SURGERY

- Cholecystectomy
  - Gallbladder removal
  - Definitive

OTHER INTERVENTIONS

- Pain, symptom management

CHOLECYSTITIS (ACUTE)

osms.it/acute-cholecystitis

PATHOLOGY & CAUSES

- Stone lodged in cystic duct/common bile duct → acute inflammation → pain
  - 90% of acute cholecystitis resolves within month as stone dislodges
- Fatty meal → small intestine cholecystokinin (CCK) signals gallbladder to secrete bile → gallbladder contracts → stone lodged in cystic duct → blocks bile flow → irritates mucosa → mucosa secretes mucus, inflammatory enzymes → inflammation, distention, pressure
- Cholesterol stones
  - More potent ability to stimulate inflammation compared to pigment gallstones
- Possible progressions
  - Stone ejected out of cystic duct → cholecystitis subsides, symptoms subside
  - Stone remains in place → pressure builds → pushes down on blood vessels supplying gallbladder → ischemia → gangrenous cell death → gallbladder walls weaken → perforation/rupture → bacteria seeds to bloodstream → sepsis → medical emergency
  - Stone lodged in common bile duct → blocks flow of bile out of liver
- Bacterial growth (cholangitis)
  - Cholelithiasis → stone descends to cystic duct → cholecystitis → stone descends from cystic duct, lodges in common bile duct → choledolithiasis → secondary infection due to obstruction → cholangitis
  - Most commonly *E. coli*, *Enterococci*, *Bacterioides fragilis*, *Clostridium*

Acalculous cholecystitis

- Acute inflammation of gallbladder without gallstones/cystic duct obstruction; high morbidity, mortality rate
- 5–10% of acute cholecystitis cases
- Rare, difficult to diagnose
- Multifactorial etiology
- Often occurs in critically ill individuals/ following major surgery
- Pathogenesis
  - Gallbladder ischemia, reperfusion injury
  - Bacterial invasion of ischemic tissue

COMPLICATIONS

- Biliary peritonitis (from rupture)
- Gallbladder ischemia → rupture → sepsis
- Acalculous cholecystitis

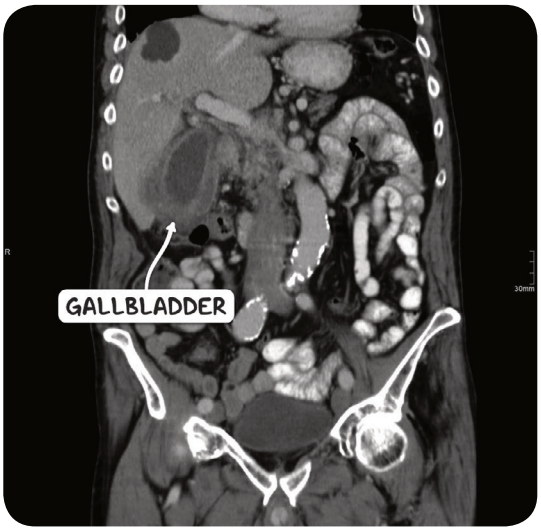

Figure 28.2 A CT scan in the coronal plane demonstrating a thickened, oedematous gallbladder, indicative of acute cholecystitis.

SIGNS & SYMPTOMS

- Midepigastric pain → dull right upper quadrant pain radiates to right scapula/shoulders (esp. after a meal in chronic cholecystitis)
- Hypoactive bowel sounds; nausea, vomiting, anorexia; jaundice; low grade fever
- Blumberg's sign/rebound tenderness
  - RUQ pain when pressure rapidly released from abdomen; peritonitis (secondary to gallbladder perforation/rupture)
- Positive Murphy's sign
  - Sudden cessation of inhalation due to pain when inflamed gallbladder reaches examiner's fingers
  - Examiner asks individual to exhale → places hand below right costal margin in midclavicular line → individual instructed to breathe in → cessation due to pain
  - Differentiates cholecystitis from other causes of right upper quadrant pain

DIAGNOSIS

DIAGNOSTIC IMAGING

Cholescintigraphy/hepatic iminodiacetic acid (HIDA) scan

- Radioactive tracer injected into individual → marked HIDA taken up by hepatocytes, excreted in bile → drains down hepatic ducts
- Location of blockage

Diffusion-weighted MRI

- Differentiate between acute, chronic cholecystitis

Ultrasound

- Gallstones/sludge
  - Gallbladder wall thickening, distention
  - Air in gallbladder wall (gangrenous cholecystitis)
  - Pericholecystic fluid from perforation/exudate

LAB RESULTS

- Elevated ALP
  - Concentrated in liver, bile ducts
  - Bile backs up, pressure in ducts increase → cells damaged, die → ALP released
- Elevated leukocyte count

TREATMENT

MEDICATIONS

- Antimicrobials

SURGERY

- Cholecystectomy

CHOLECYSTITIS (CHRONIC)

osms.it/chronic-cholecystitis

PATHOLOGY & CAUSES

- Obstruction of cystic duct (not infection) → inflammation of gallbladder wall
- Constant state of inflammation due to gallstones repeatedly blocking ducts
  - Changes gallbladder mucosa → deep grooves (Rokatansky–Aschoff sinus)
  - Pain esp. after meal; gallbladder attempts to secrete bile to small intestine for digestion
- Fatty meal → small intestine cholecystokinin (CCK) signals gallbladder to secrete bile → gallbladder contracts → stone lodged in cystic duct → blocks bile flow → irritates mucosa → mucosa secretes mucus, inflammatory enzymes → inflammation, distention, pressure
- Cholesterol stones
  - More potent ability to stimulate inflammation compared to pigment gallstones
- Possible progressions
  - Stone ejected out of cystic duct → cholecystitis subsides, symptoms subside
  - Stone remains in place → pressure builds → pushes down on blood vessels supplying gallbladder → ischemia → gangrenous cell death → gallbladder walls weaken → perforation/rupture → bacteria seeds to bloodstream → sepsis → medical emergency
  - Stone lodged in common bile duct → blocks flow of bile out of liver
- Bacterial growth (cholangitis)
  - Cholelithiasis → stone descends to cystic duct → cholecystitis → stone descends from cystic duct, lodges in common bile duct → choledolithiasis → secondary infection due to obstruction → cholangitis
  - Most commonly *E. coli*, *Enterococci*, *Bacterioides fragilis*, *Clostridium*

COMPLICATIONS

- Biliary peritonitis (from rupture)
- Gallbladder ischemia → rupture → sepsis
- Porcelain gallbladder (chronic cholecystitis)
  - Chronic state of inflammation → epithelial fibrosis, calcification
  - Bluish discoloration of gallbladder; becomes hard, brittle
  - Bile stasis → calcium carbonate bile salts to precipitate out → deposit into walls
  - Increased risk of gallbladder cancer
- Acalculous cholecystitis

SIGNS & SYMPTOMS

- Midepigastric pain → dull right upper quadrant pain radiates to right scapula/shoulders (esp. after a meal in chronic cholecystitis)
- Hypoactive bowel sounds; nausea, vomiting, anorexia; jaundice; low grade fever
- Blumberg's sign/rebound tenderness
  - Right upper quadrant pain when pressure rapidly released from abdomen; peritonitis (secondary to gallbladder perforation/rupture)
- Positive Murphy's sign
  - Sudden cessation of inhalation due to pain when inflamed gallbladder reaches examiner's fingers
  - Examiner asks individual to exhale → places hand below right costal margin in midclavicular line → individual instructed to breathe in → cessation due to pain
  - Differentiates cholecystitis from other causes of right upper quadrant pain

DIAGNOSIS

DIAGNOSTIC IMAGING

Cholescintigraphy/hepatic iminodiacetic acid (HIDA) scan

- Radioactive tracer injected into individual → marked HIDA taken up by hepatocytes, excreted in bile → drains down hepatic ducts
- Location of blockage

Diffusion-weighted MRI

- Differentiate between acute, chronic cholecystitis

Ultrasound

- Gallstones/sludge
  - Gallbladder wall thickening, distention
  - Air in gallbladder wall (gangrenous cholecystitis)
  - Pericholecystic fluid from perforation/exudate

LAB RESULTS

- Elevated ALP: concentrated in liver, bile ducts
  - Bile backs up, pressure in ducts increase → cells damaged, die → ALP released
- Elevated leukocyte count

TREATMENT

MEDICATIONS

- Antimicrobials

SURGERY

- Cholecystectomy

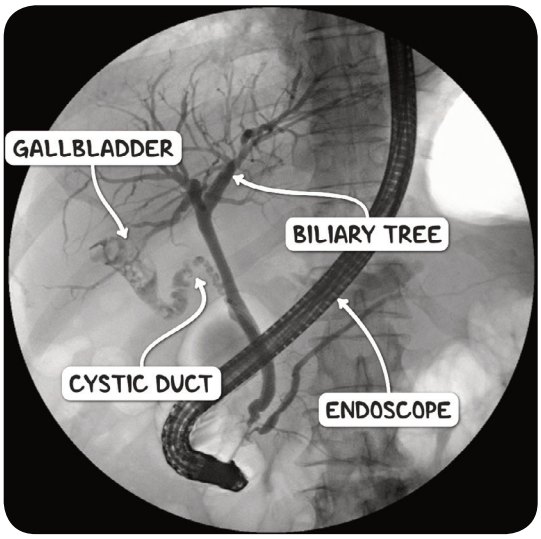

Figure 28.3 Endoscopic retrograde cholangiopancreatography demonstrating gallstones in the cystic duct.

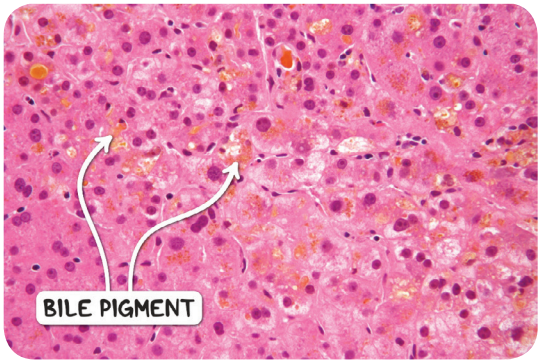

Figure 28.4 Histological appearance of cholestasis in the liver. There is build up of bile pigment in the hepatic parenchyma.

SUMMARY OF BILIARY TRACT DISEASES

	CHOLECYSTITIS	CHOLELITHIASIS	CHOLEDOCHO-LITHIASIS	CHOLANGITIS
LOCATION	Cystic duct	Gallbladder	Common bile duct	Biliary tree
SYMPTOMS	Nausea, vomiting, fever, RUQ pain, pain lasting > 6 hrs, midepigastric pain, hypoactive bowel sounds, Blumberg's sign, positive Murphy's sign	Asymptomatic, sudden intense abdominal pain, normal liver enzymes, nausea/vomiting, jaundice	Abnormalities in liver enzymes, pain, no fever	Elevations in liver enzymes, WBC, pancreatic enzymes, bilirubin, Charcot's triad, Reynold's pentad
COMPLICATIONS	Acalculous cholecystitis, blockage of bile outflow, cholangitis, biliary peritonitis, porcelain gallbladder	Choledocholithiasis, cholecystitis, ascending cholangitis, blockage of common bile/pancreatic duct, increased risk of gallbladder cancer	Cholangitis, acute pancreatitis	Septic shock, multiorgan failure
DIAGNOSIS	Elevated ALP, HIDA scan, ultrasound, cholescintigraphy, diffusion-weighted MRI	Ultrasound, CT, X-ray, ERCP	Ultrasound, CT, X-ray, ERCP	Labs (WBC count, CRP, LFTs), ERCP
TREATMENT	Cholecystectomy	Treatment only if symptomatic, pain reduction, cholecystectomy, ursodiol, shock wave therapy, ERCP	Treatment only if symptomatic, pain reduction, cholecystectomy, ursodiol, shock wave therapy, ERCP	Antibiotics, IV fluids, cholecystectomy, ERCP, shockwave lithotripsy, stent

GALLSTONE

osms.it/gallstone

PATHOLOGY & CAUSES

- Solid stones inside gallbladder composed of bile components
- Form based on imbalance of chemical constituents → precipitate out to form solid stone

TYPES

- Categorized by location (choledocholithiasis, cholelithiasis) or major composition (cholesterol, bilirubin stones)

Choledocholithiasis

- Gallstones in common bile duct → obstruction of outflow tract
  - Stasis, infection (primary cause)
  - Affects liver function; may cause liver damage

Cholelithiasis

- Gallstones in gallbladder
  - *Primary cause:* imbalance of bile components
  - Bile flow out of liver not obstructed; liver function not affected

Cholesterol stones

- Most common, 80%
- Composed primarily of cholesterol
- *Cholesterol precipitation out of bile:* supersaturation; inadequate salts/acids/phospholipids; gallbladder stasis
- Radiolucent (not visible on X-ray)

Bilirubin stones (pigmented stones)

- Composed primarily of unconjugated bilirubin
  - Formed from nonbacterial, nonenzymatic hydrolysis of conjugated bilirubin
- Occurs when too much bilirubin in bile
- Combines with calcium → solid calcium bilirubinate

Figure 28.5 Cholesterol gallstones.

- Radiopaque (visible on X-ray)
- Can be caused by excessive extravascular hemolysis
  - Extravascular hemolysis → macrophages consume RBCs → increased unconjugated bilirubin production → too much unconjugated bilirubin for liver to conjugate → unconjugated bilirubin binds to calcium instead of bile salts → precipitate out to form black pigmented stones
- *Brown pigmented gallstone:* gallbladder/biliary tract infection
  - Stones enter common bile duct
  - *Brown pigment due to unconjugated/hydrolyzed bilirubin, phospholipids:* infectious organism brings hydrolytic enzymes → hydrolysis of conjugated bilirubin, phospholipids → combine with calcium ions → precipitate out to form stones
  - *Common infections: E. coli, Ascaris lumbricoides, Clonorchis sinensis* (trematode endemic to China, Korea, Vietnam)
  - Commonly seen in Asian populations

RISK FACTORS

- More common in individuals who are biologically female, who use oral contraceptive
  - ↑ estrogen → ↑ cholesterol in bile + bile hypomotility → ↑ risk of gallstones
- Obesity
- Rapid weight loss
  - Imbalance in bile composition → ↑ risk of calcium-bilirubin precipitation
- Total parenteral nutrition (prolonged)

COMPLICATIONS

- Cholecystitis (inflammation of gallbladder)
- Ascending cholangitis
- Blockage of common, pancreatic bile ducts
- *Gallbladder cancer:* history of gallstones → ↑ risk of gallbladder cancer

SIGNS & SYMPTOMS

- May be asymptomatic
- Sudden, intense abdominal epigastric/substernal pain; radiates to right shoulder/shoulder blades
- Nausea/vomiting; jaundice; abdominal tenderness, distension; fever, chills; flatulence, belching
- See mnemonic for summary

MNEMONIC: 6 Fs

Typical clinical presentation of an individual with gallstones

Fat
Female
Fertile
Forty
Fatty food intolerance
Flatulence

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound, CT scan, X-ray, ERCP

- Visualize stones

LAB RESULTS

- Elevated bilirubin levels
- Liver function tests (LFTs)
  - Elevated gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate transaminase (AST)

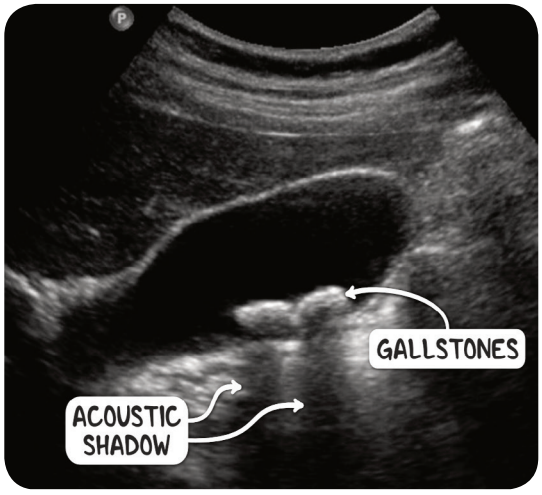

Figure 28.6 Abdominal ultrasound demonstrating cholelithiasis. The gallstones cast an acoustic shadow.

TREATMENT

- Necessary only if symptomatic

MEDICATIONS

- Bile salts
  - Dissolve cholesterol stones

Figure 28.7 Numerous gallstones, of mixed-type, in a cholecystectomy specimen. The wall of the gallbladder is thickened and fibrotic, consistent with long-standing disease.

SURGERY

- Cholecystectomy

OTHER INTERVENTIONS

- Pain management
- Shock wave therapy (lithotripsy)
  - High-frequency sound waves fragment stones

PRIMARY SCLEROSING CHOLANGITIS (PSC)

osms.it/primary-sclerosing-cholangitis

PATHOLOGY & CAUSES

- Autoimmune disorder in which T-cells attack, destroy bile duct epithelial cells in genetically predisposed individuals exposed to environmental stimuli
  - HLA-B8, HLA-DR3, HLA-DRw52a
- Associated with ulcerative colitis, Crohn's disease
- Sclerosis, inflammation of intra-, extrahepatic ducts
- Cells around bile ducts inflamed, die → fibrose
- Death of epithelial cells lining bile ducts → bile leaks into interstitial space, bloodstream
- "Beaded" appearance of bile ducts
  - Stenosis of affected ducts, dilation of unaffected ducts
- Severity depends on bilirubin levels, encephalopathy, presence/absence of ascites, serum albumin level, prothrombin time

COMPLICATIONS

- Portal hypertension
  - Fibrosis builds around bile ducts → constricts portal veins → ↑ pressure
- Hepatosplenomegaly
  - Portal hypertension → backup of fluid, enlargement of spleen, liver
- Cirrhosis
  - Recurrent cycle of inflammation, healing → tissue scarring → fibrosis
- ↑ risk of cholangiocarcinoma, gallbladder cancer, hepatocellular carcinoma

SIGNS & SYMPTOMS

- May remit, recur spontaneously
- Jaundice, RUQ pain, weight loss, pruritus (deposition of bile salts, acids in skin), hepatosplenomegaly
- Liver failure
  - Ascites, muscle atrophy, spider angiomas, increased clotting time, dark urine, pale stool

DIAGNOSIS

DIAGNOSTIC IMAGING

MRCP

- Intrahepatic and/or extrahepatic bile duct dilation; multifocal or diffuse strictures

ERCP

- Intrahepatic and/or extrahepatic bile duct dilation; multifocal or diffuse strictures

LAB RESULTS

- Liver function tests (LFTs)
  - Elevated conjugated bilirubin, ALP, GGT
- Elevated serum IgM antibody, p-ANCA (targets antigens in cytoplasm/nucleus of neutrophils; 80% of individuals with PSC)
- Bilirubinuria
- Liver biopsy
  - Stage disease, predict prognosis

OTHER DIAGNOSTICS

- Histology
  - "*Onion-skin fibrosis*": concentric rings of fibrosis around bile duct, resembles onion skin

TREATMENT

- No effective treatment

MEDICATIONS

- Treat symptoms, manage complications, not curative (e.g. antibiotics)
- Immunosuppressants, chelators, steroids

SURGERY

- Liver transplant
  - Advanced liver disease

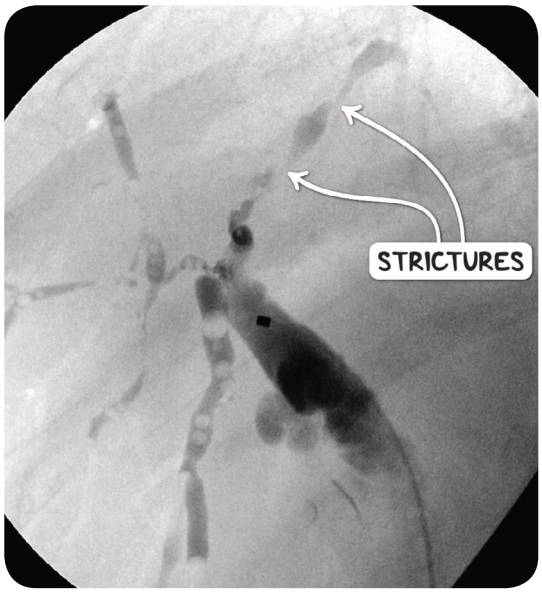

Figure 28.8 Cholangiogram demonstrating multiple biliary strictures in a case of primary sclerosing cholangitis.

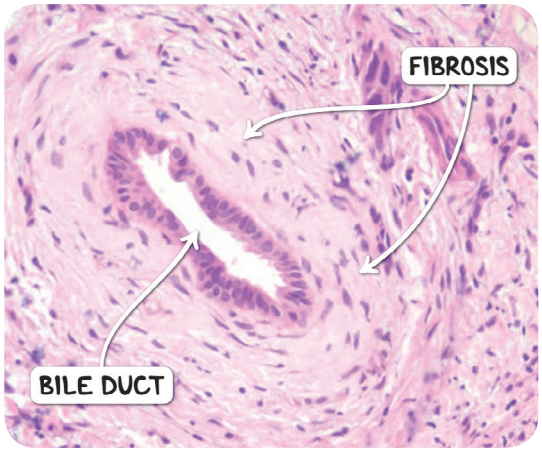

Figure 28.9 Histological appearance of primary sclerosing cholangitis. There is onion-skin fibrosis of the biliary ducts.