

Gallbladder disorders

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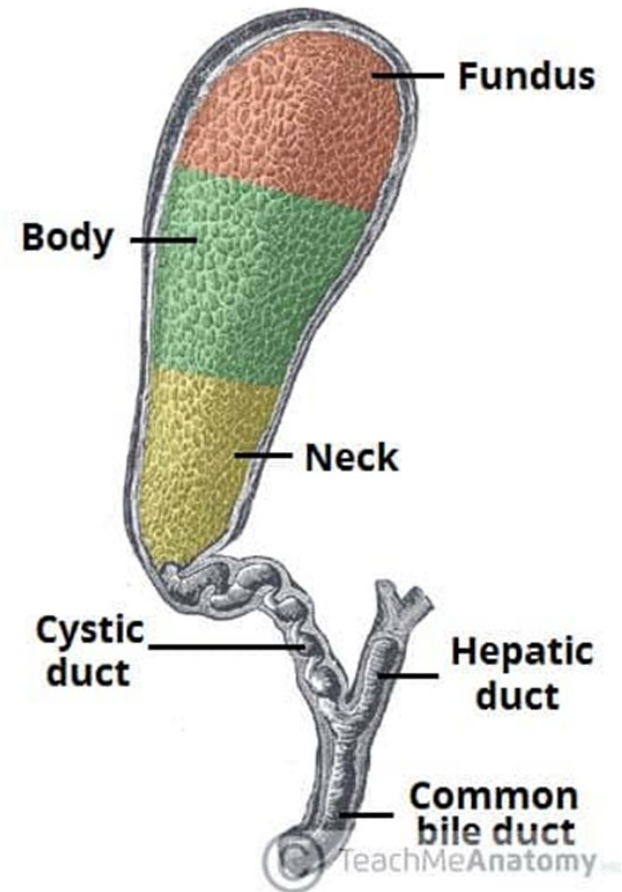
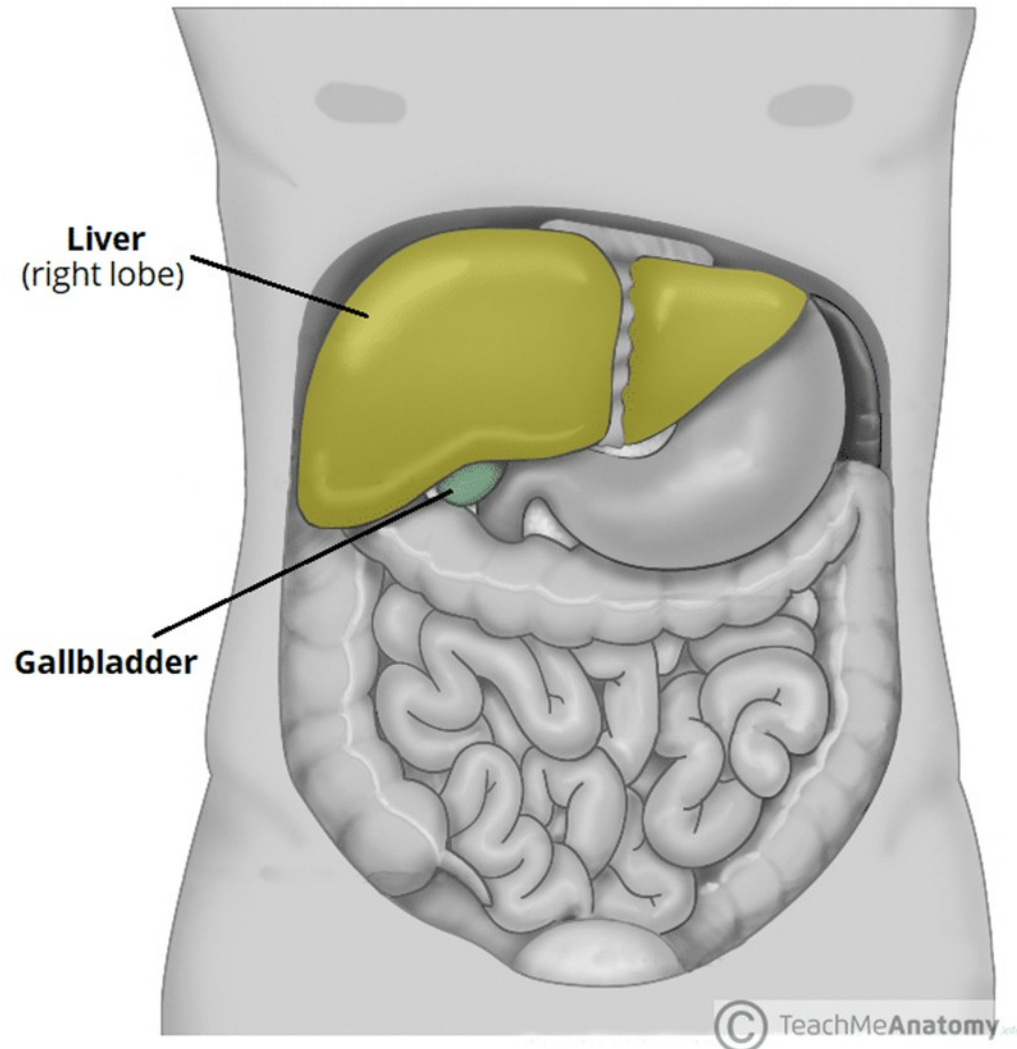


SURGICAL ANATOMY

- The gallbladder is a reservoir for bile located on the undersurface of the liver at the confluence of the right and left halves of the liver.
- lying anterior to the first part of the duodenum. It is typically divided into three parts :
- **Fundus** – the rounded, distal portion of the gallbladder. It projects into the inferior surface of the liver in the mid-clavicular line.
- **Body** – the largest part of the gallbladder. It lies adjacent to the postero-inferior aspect of the liver, transverse colon and superior part of the duodenum.
- **Neck** – the gallbladder tapers to become continuous with the cystic duct, leading into the biliary tree.
 - The neck contains a mucosal fold, known as Hartmann's Pouch. This is a common location for gallstones to become lodged, causing cholestasis.

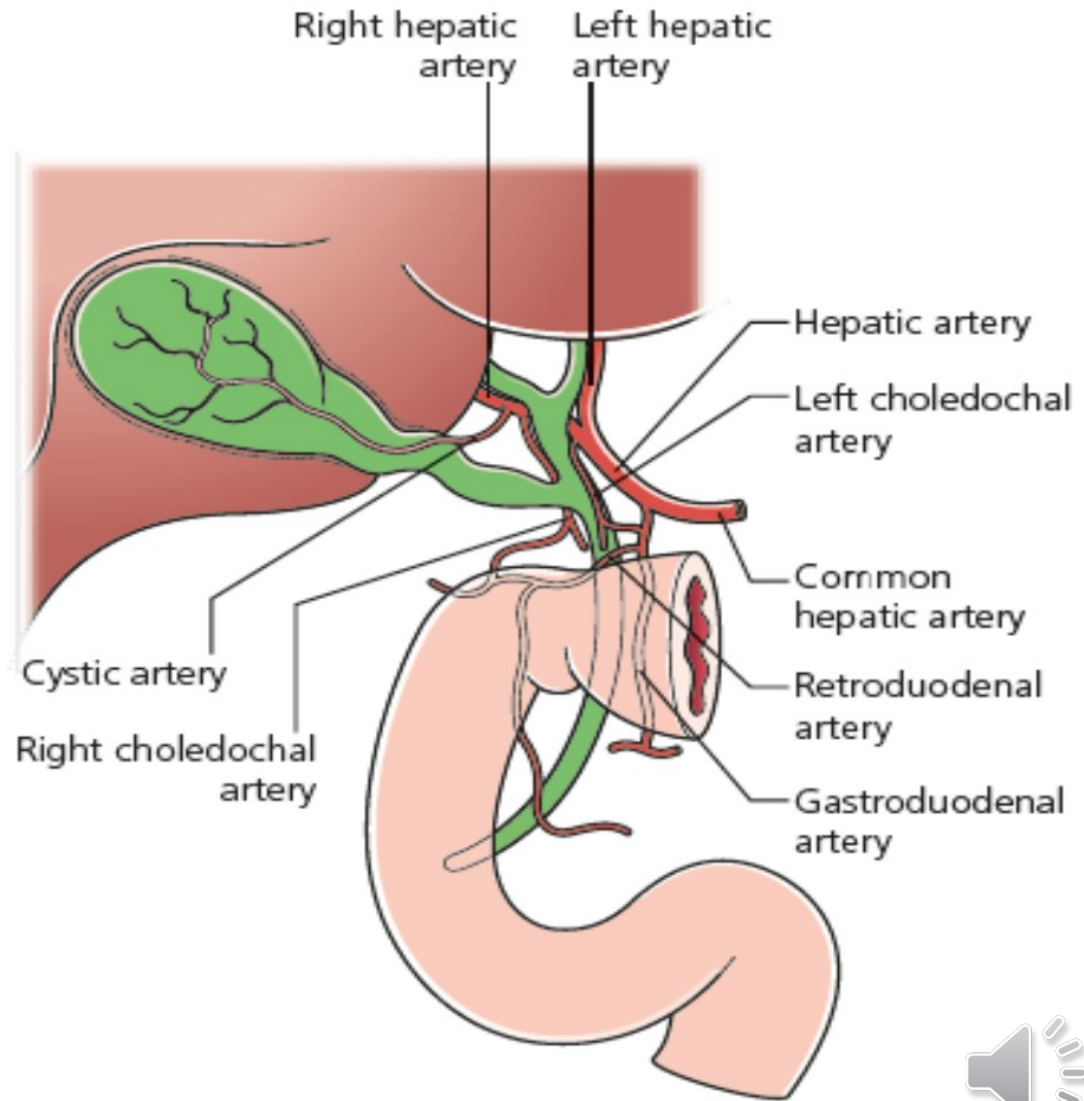


SURGICAL ANATOMY



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- The arterial supply to the gallbladder is via the **cystic artery** – a branch of the right hepatic artery (derived from the common hepatic artery, one of the three major branches of the [coeliac trunk](#)).
- Venous drainage of the neck of the gallbladder is via the **cystic veins**, which drain directly into the [portal vein](#). Venous drainage of the fundus and body of the gallbladder flows into the hepatic sinusoids.



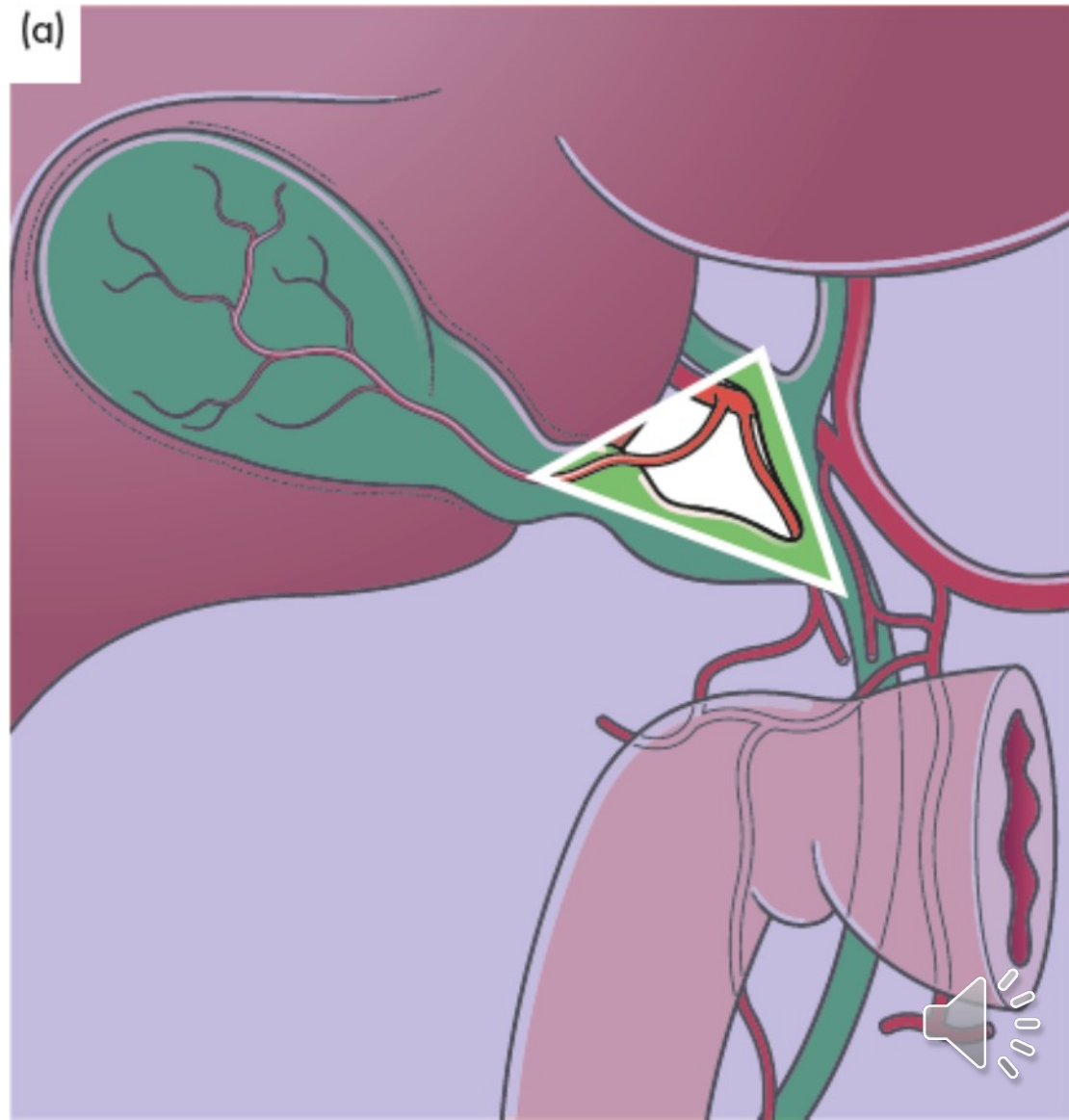
SURGICAL ANATOMY

- The gallbladder receives parasympathetic, sympathetic and sensory innervation.
- The **coeliac plexus** carries sympathetic and sensory fibres, while the [vagus nerve](#) delivers parasympathetic innervation.
- The lymphatic vessels of the gall bladder (subserosal and submucosal) drain into the cystic lymph node of Lund (the sentinel lymph node), which lies in the fork created by the junction of the cystic and common hepatic ducts.
- Efferent vessels from this lymph node go to the hilum of the liver, and to the coeliac lymph nodes.



SURGICAL ANATOMY

- Calots triangle is bounded by the common hepatic duct on left, the cystic duct inferiorly, and the cystic artery superiorly (originates from the right hepatic artery).
- The venous drainage is directly into the liver parenchyma or into the common bile duct plexus.

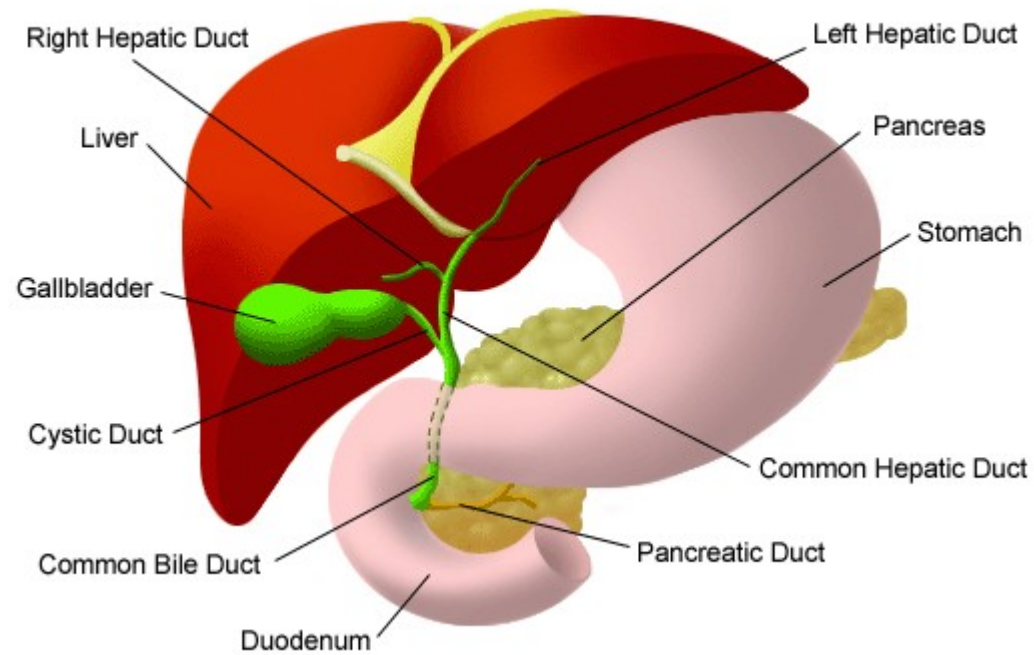


SURGICAL ANATOMY

- Bile is initially secreted from hepatocytes and drains from both lobes of the liver via canaliculi, intralobular ducts and collecting ducts into the **left and right hepatic ducts**. These ducts amalgamate to form the **common hepatic duct** .
- As the common hepatic duct descends, it is joined by the cystic duct – which allows bile to flow in and out of the gallbladder for storage and release . At this point, the common hepatic duct and cystic duct combine to form the **common bile duct**.
- The common bile duct descends and join by the main pancreatic duct, forming the **hepatopancreatic ampulla** (commonly known as the **ampulla of Vater**) – which then empties into the duodenum via the major duodenal papilla. This papilla is regulated by a muscular valve, the sphincter of Oddi.



Biliary System



SURGICAL PHYSIOLOGY

- The primary function of the gallbladder is to concentrate and store bile which is produced by the liver.
- The gallbladder has a storage capacity of 30-50ml
- Bile is composed of 95% water, bile salts (cholic and chenodeoxycholic acids, deoxycholic and lithocholic acids), phospholipids, cholesterol & bilirubin.
- The liver excretes bile at a rate 40 mL/hour.
- 95% of bile salts are reabsorbed in the terminal ileum (enterohepatic circulation).
- As part of the gustatory response, the stored bile is released from the gallbladder in response to cholecystokinin after fatty meal ingestion .



Table 1. Diseases of the Gallbladder

Disease	Description
Cholelithiasis	Microscopic crystals or large stones in the gallbladder
Cholecystitis	Inflammation of the gallbladder
Choledocholithiasis	Common bile-duct stones
Biliary dyskinesia	Motility disorder of the gallbladder caused by scarring or spasm of the sphincter of Oddi
Gallbladder perforation	A hole or opening in the wall of the gallbladder. <i>Acute</i> : generalized biliary peritonitis; <i>subacute</i> : acute plus pericholecystic abscess; <i>chronic</i> : cholecystoenteric fistula
Gallstone pancreatitis	Inflammation of the pancreas caused by obstruction of the pancreatic duct by a gallstone
Gallbladder polyps	Overgrowths or lesions in the gallbladder wall

Source: References 5-8.



Cholelithiasis (Gallstones)



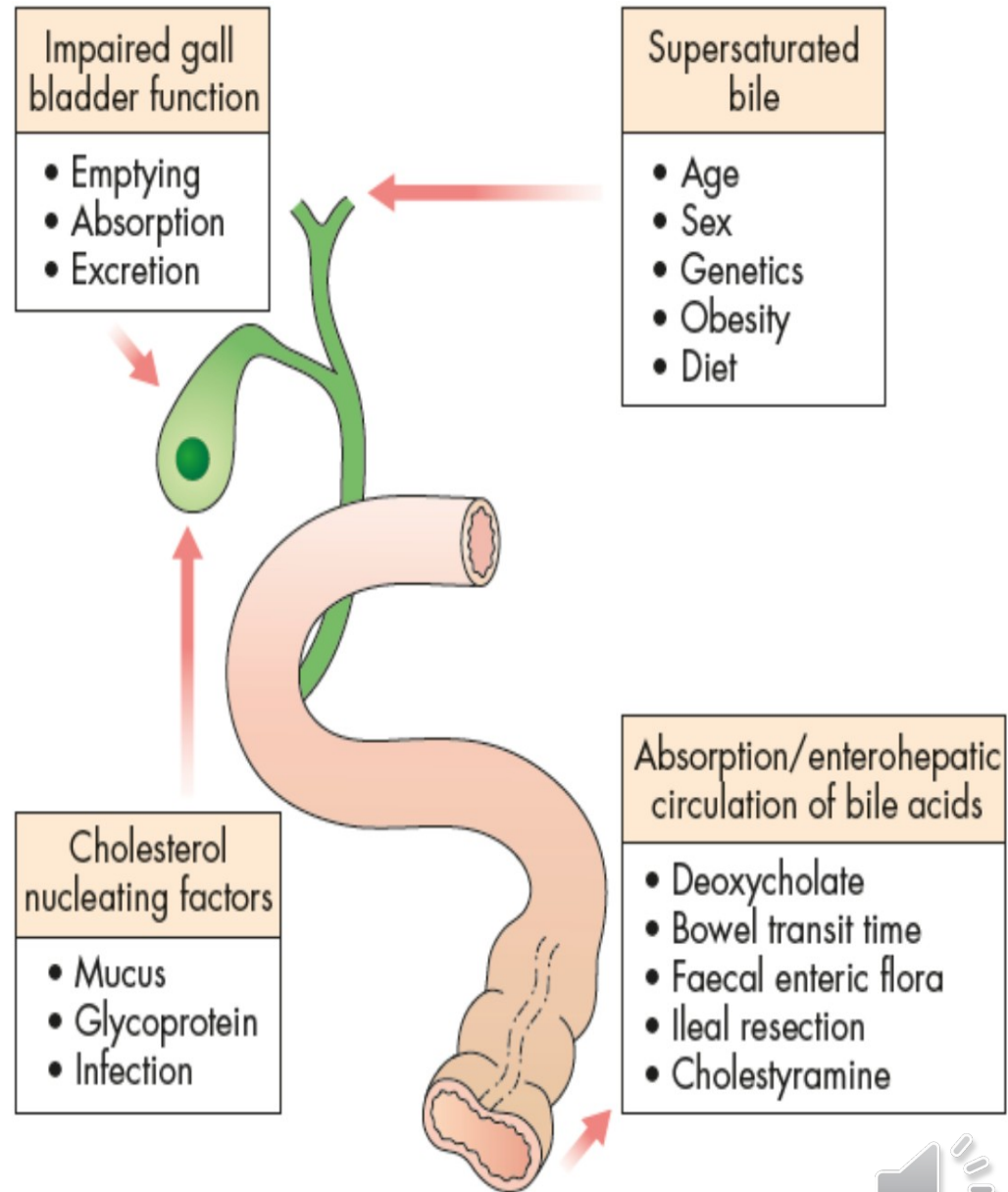
Cholelithiasis (Gallstones)

- Gallstone disease, or cholelithiasis, is one of the most common surgical problems worldwide.
- Gallstones are abnormal, inorganic masses formed in the gallbladder and, less commonly, in the common bile or hepatic ducts
- Although gallstones can form anywhere in the biliary tree, the most common point of origin is within the gallbladder.
- Three types of gallstones exist:
 - pure cholesterol(70 – 80%)
 - pure pigment (black or brown 20-30%)
 - mixed



- Three compounds comprise 80-95% of the total solids dissolved in bile;
 - conjugated bile salts
 - lecithin
 - Cholesterol
- Under normal conditions, a delicate balance occurs among the levels of bile acids, phospholipids and cholesterol .
- A disparity in this balance, especially with the supersaturation of cholesterol, predisposes patients to the formation of lithogenic bile and the subsequent development of cholesterol-type gallstones.
- Pathogenesis of cholesterol gallstones is clearly multifactorial ,but involves four factors : cholesterol supersaturation , crystal nucleation , gallbladder dysmotility , gallbladder absorption.





- Pigmented gallstones are composed of calcium bilirubinate and appear in 2 major forms: black and brown.
- Hemolysis and liver disease are associated with the black stones;
- the brown, earthy stones more frequently are formed outside the gallbladder and often are associated with bacterial infections of the biliary tract.
- Prolonged fasting (5-10 days) can result in the formation of biliary sludge (microlithiasis) which resolves by itself when feeding is reestablished - but it can lead to biliary symptoms or gallstone formation



- Women are more likely to develop gallstones than men, with a ratio of 2:1.
- Classically, gallstones occur in obese, middle-aged women, which leads to the popular mnemonic, fat fertile forties.

Risk factor

Increasing age

Female sex:

Pregnancies

Exogenous estrogens: oral contraceptives, menopausal hormone therapy

Genetics

Social factors:

Low social classes in Western countries

High social classes in Asian countries

Lifestyle factors

Obesity (BMI, waist circumference)

Abstinence of alcohol

Low physical activity

Diet: high caloric, high carbohydrate, low fiber (inconclusive results for smoking and coffee drinking)

Biomarkers

High insulin

High triglycerides (inconclusive results for total cholesterol and HDL cholesterol)

BMI, body mass index; HDL, high-density lipoprotein.



Mortality / Morbidity

- Related directly to the complications of the disease and its surgical treatment
- Approximately 10% patients with gallstones have common bile duct stones
- Gallstones can cause obstruction of the common bile duct, causing jaundice
- Cholangitis, a potentially life-threatening infection, can follow biliary obstruction
- Obstruction of the neck of the gallbladder causes bile stasis, which can lead to inflammation and edema of the gallbladder wall.
- Sequelae of this condition include acute cholecystitis secondary to compromised lymphatic, venous, and, ultimately, arterial supply to the gallbladder.
- The latter can lead to gangrene or abscess formation.



Clinical presentation of gallstones :

- Silent gall stones : accidentally detected by ultrasound and x ray sometimes .
- Recurrent attacks of biliary colic :
 - *Severe colicky upper abdominal pain mostly in the epigastric area and right upper quadrant which may referred to the back of the right chest or to the right shoulder
 - *Usually precipitated by the intake of a fatty meal
 - *On examination the patient usually has tenderness at the right hypochondrium .
- Complications of gallstones



Complications of cholelithiasis

Acute cholecystitis : fever , WCC
Chronic cholecystitis
Mucocoele: obstruction only
Empyema of the gall bladder: abscess
Perforation: peritonitis (localized / diffuse)
Biliary obstruction: CBD stone(s)
Acute cholangitis : CBD stone(s) +jaundice
Acute pancreatitis
Intestinal obstruction(gallstone ileus): fistula

TABLE 2

Gallstone complications

Acute cholecystitis
Chronic cholecystitis
Choledocholithiasis
Acute cholangitis
Acute pancreatitis
Empyema in gallbladder
Obstructive jaundice
Choledochoduodenal fistula
Gallbladder perforation



Complications of cholelithiasis

- The physical examination might indicate complications of cholelithiasis.
 - Passage of gallstones from the gallbladder into the common bile duct can result in a complete or partial obstruction of the common bile duct.
 - Frequently, this manifests as jaundice.
 - In all races, jaundice is detected most reliably by examination of the sclera in natural for yellow discoloration.



Complications of cholelithiasis

- Pancreatitis, another complication of gallstone disease, presents with more diffuse abdominal pain, including pain in the epigastrium and left upper quadrant of the abdomen.
- Severe hemorrhagic pancreatitis occurs in 15% patients and carries a high mortality rate because of multisystem organ failure.
- In a few patients, the hemorrhagic pancreatic process and retroperitoneal bleeding induce discoloration around the umbilicus (Cullen sign) or the flank (Grey-Turner sign).



Complications of cholelithiasis

- Acute cholangitis :
- Charcot triad
 - (right upper quadrant pain, fever, and jaundice)
 - associated with common bile duct obstruction and cholangitis
- Additional symptoms:
 - alterations in mental status and hypotension, indicate Reynaud pentad, a harbinger of worsening, ascending cholangitis.



Lab Studies

- For patients with uncomplicated cholelithiasis, blood work results usually are normal.
- However, labs can detect complications of gallstone disease; complications might alter the course of treatment.

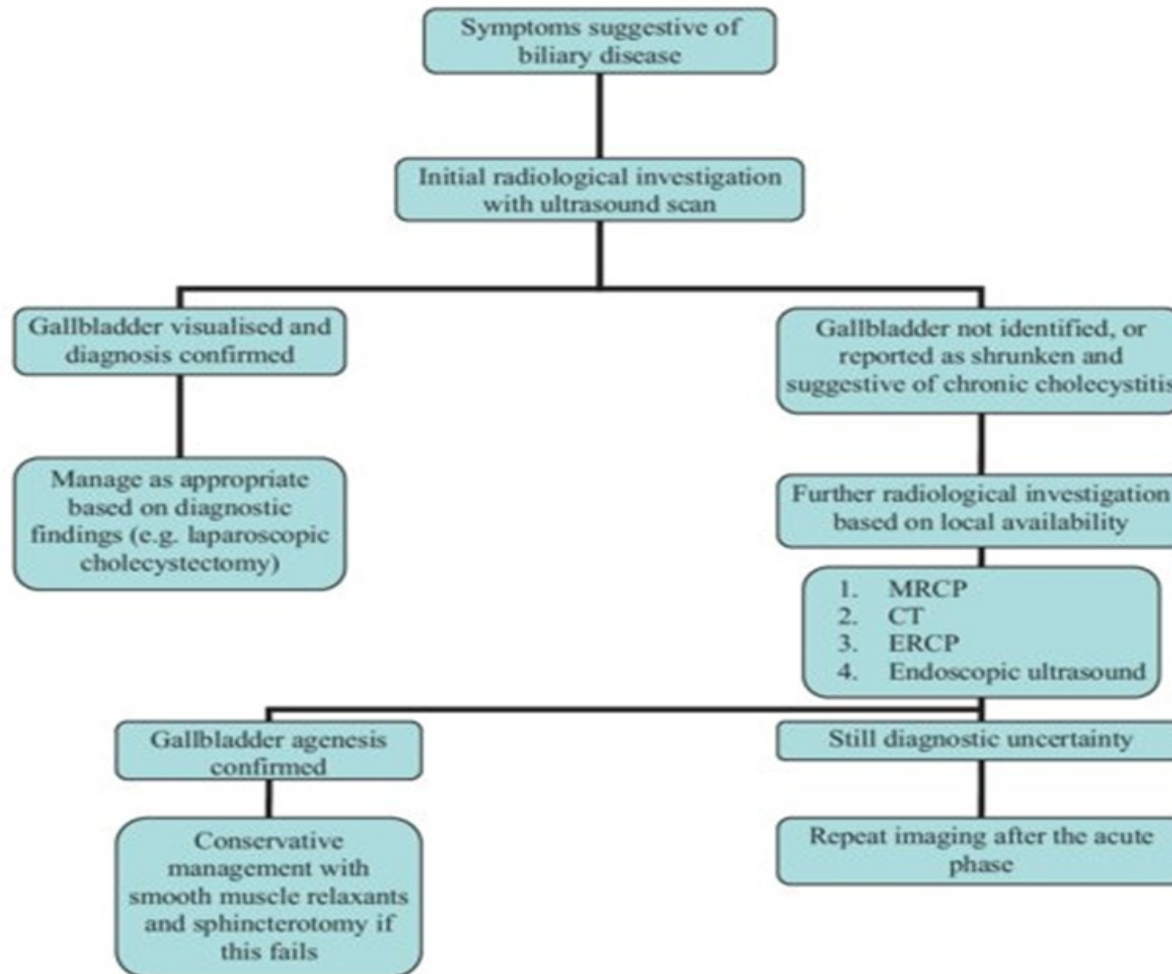


Lab Studies

- CBC
- chemistry panel, including electrolytes, liver enzymes, and bilirubin.
 - Choledocholithiasis can manifest with only elevation of serum alkaline phosphatase or bilirubin.
 - Nearly 50% of patients with symptomatic gallstone disease will have abnormal transaminases
- Serum lipase and amylase levels are helpful in cases of diagnostic uncertainty or suspected concurrent pancreatitis



Radiological investigation of gallbladder



MRCP= magnetic resonance cholangiopancreatography
ERCP= endoscopic retrograde cholangiopancreatography



Imaging Studies

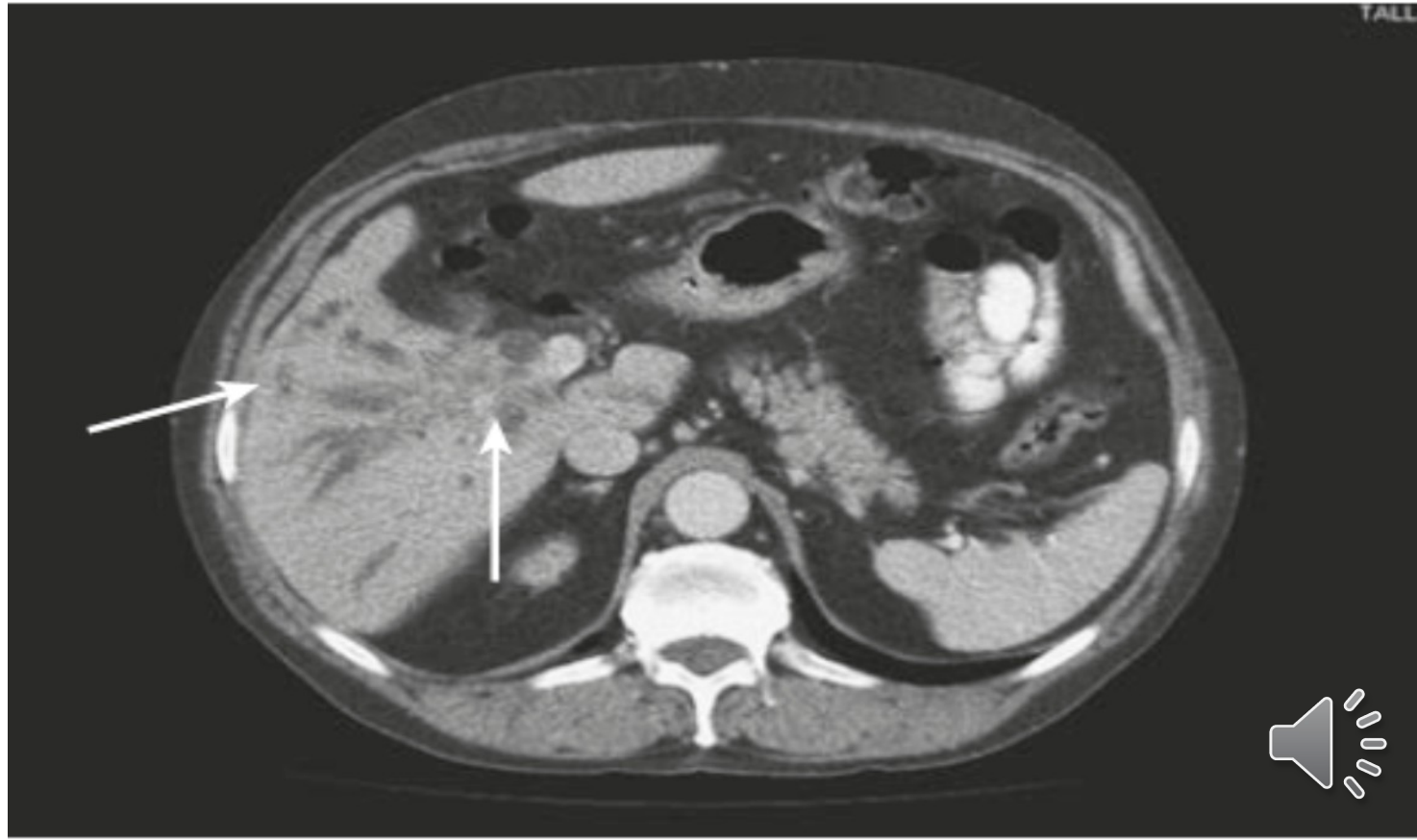
- X-rays
 - Approximately 15% of gallstones are radiopaque and can be visualized on plain x-ray.
 - A porcelain gallbladder (heavily calcified) should be removed surgically because of increased risk of gallbladder cancer.
 - Other causes of abdominal pain diagnosed with the assistance of x-rays include perforated viscus, bowel obstruction, calcific pancreatitis, and renal stones.
- Ultrasound (US) is the most sensitive and specific test for the detection of gallstones.
- US provides information about the size of the common bile duct and hepatic duct and the status of liver parenchyma and the pancreas.
- Thickening of the gallbladder wall and the presence of pericholecystic fluid are radiographic signs of acute cholecystitis





Imaging Studies

- CT scanning often is used in workup of abdominal pain without specific localizing signs or symptoms.
- CT scanning is not a first-line study for detection of gallstones because of greater cost and the invasive nature of the test.
- When present, gallstones usually are observed on CT scan.

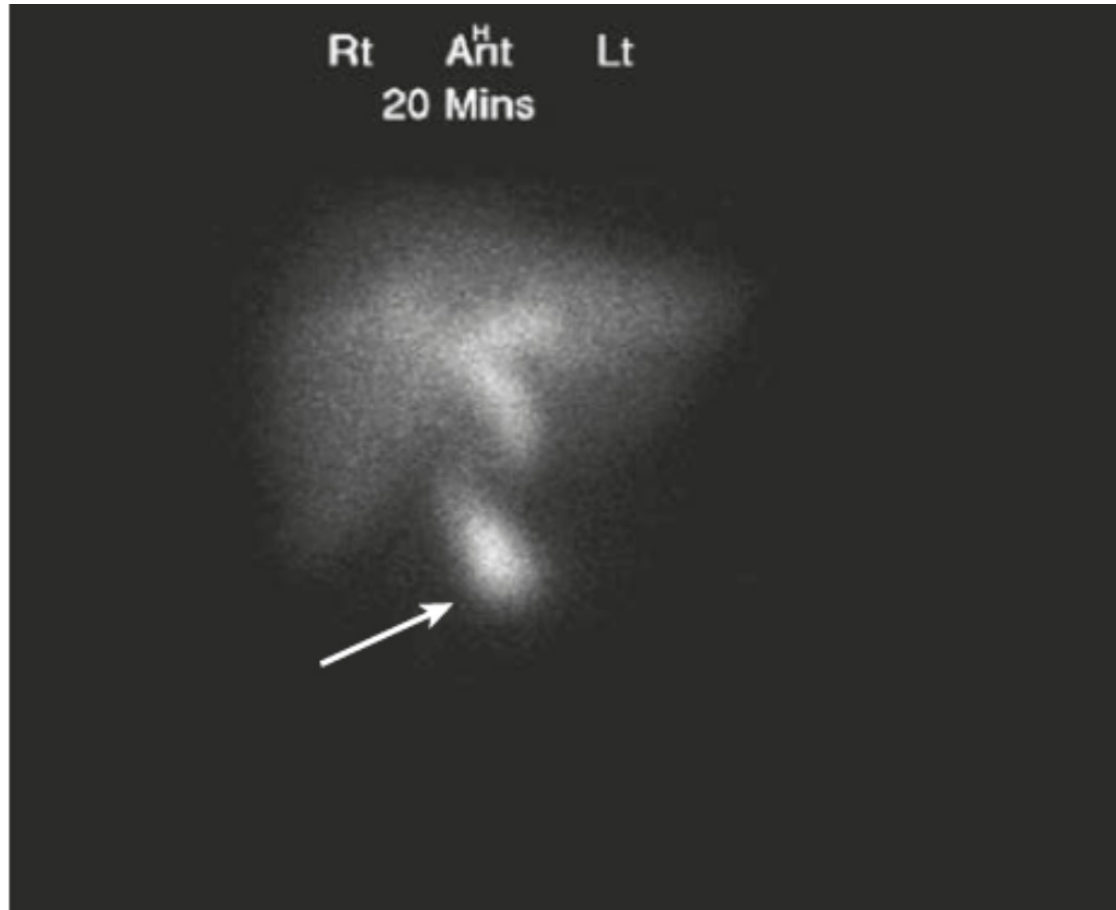


Imaging Studies

- HIDA scan does not detect gallstones
- HIDA scan identifies an obstructed gallbladder (eg, gallstone impacted in the neck of the gallbladder).
 - HIDA scan is the most sensitive and specific test for acute cholecystitis.
 - A poorly contracting gallbladder (biliary dyskinesia) might cause the patient's symptoms, and HIDA scan makes the diagnosis.
 - Acute acalculous cholecystitis is diagnosed most accurately with HIDA scan.



Dimethyl iminodiacetic acid (HIDA) scan: Function of Gallbladder



Treatment

- Removal of the gallbladder laparoscopic cholecystectomy is the treatment of choice for symptomatic gallbladder disease
- Only gallstones that cause symptoms or complications require treatment
- There is generally no reason for prophylactic cholecystectomy in an asymptomatic person unless
 - the gallbladder is calcified
 - gallstones are $> 3\text{cm}$ in diameter



Indications for “Prophylactic” Cholecystectomy

Group	Comments
Children with gallstones	Because of long-term exposure to gallstones
Morbidly obese patients prior to bariatric surgery. Controversial for gallstone-free patients & asymptomatic gallstone patients	High risk of forming cholesterol gallstones and developing symptoms during rapid weight loss
Patients with large gallstones (i.e., > 3cm)	Increased risk for gallbladder cancer
A “porcelain” gallbladder or gallbladder polyps rapidly growing or > 1 cm	Increased risk for gallbladder cancer
Asymptomatic gallstones (even small) <u>and</u> gallbladder polyps (even <1cm)	High risk of gallbladder cancer
Native Americans with gallstones	Increased risk for gallbladder cancer
Gallstone patients with sickle cell anemia	Formation of pigment gallstones due to chronic hemolysis. Patients may become symptomatic with recurrent episodes of abdominal pain
Coexistence of gallstones and gallbladder dysmotility	Increased risk of pancreatitis
Gallbladder polyp >6 mm <u>and</u> other risk factor for malignancy (Age >50, PSC, Indian ethnicity, sessile polyp)	Increased risk for gallbladder cancer



Acute Cholecystitis



Acute Cholecystitis

- Cholecystitis is associated with gallstones in > 90% of cases
 - Inflammation develops behind a stone impacted in the cystic duct
- May be caused by infectious agents (cytomegalovirus, cryptosporidiosis, or microsporidiosis common in AIDS patients) .
- Acalculous cholecystitis 5-10% of cases
 - should be considered in patient with FUO, RUQ pain occurring 2-4 weeks after major surgery



History

- Acute attack often follows a large fatty meal
- sudden, steady pain in epigastrium or right hypochondrium – pain is steady and severe and is typically prolonged greater than 6 hours
- Nausea and vomiting - 75% Of cases
- RUQ tenderness associated with muscle guarding and rebound pain
- Palpable gallbladder 15% of cases
- Jaundice 25% of cases
 - also suggestive of choledocholithiasis
- Fever
- The localization of pain and tenderness in the right hypochondrium with radiation to the infrascapular area or right shoulder strongly favors the diagnosis of acute cholecystitis



physical :

- Ill appearing patient
- Febrile with tachycardia
- RUQ tenderness associated with muscle guarding and rebound pain
- Positive Murphy sign
 - pain on palpation of the right upper quadrant when the patient inhales might indicate acute cholecystitis
- Palpable gallbladder 15% of cases



Labs

- WBC - elevated (12-15,000 usually)
- Total serum bilirubin 1-4mg/dL
- Often elevated levels of:
 - serum aminotransferase
 - alkaline phosphatase
 - serum amylase



Imaging Studies

- X-ray
 - may show radiopaque gallstones 15% of cases
- HIDA Scan
 - useful for obstructed cystic duct
 - reliable if bilirubin < 5mg/dL
- Ultrasound
 - useful for gallstone visualization
 - Signs of acute cholecystitis on ultrasound include :
 - Presence of stones , gallbladder wall thickening (more than 4 to 5 mm) , pericholecystic fluid , edema (double wall sign) , sonographic murphy sign





Differential diagnosis :

- Some disorders that may be confused with acute cholecystitis:
 - perforated peptic ulcer
 - acute pancreatitis
 - appendicitis (high lying appendix)
 - liver abscess
 - hepatitis
 - pneumonia w/pleurisy on right side
 - myocardial ischemia



Treatment

- Due to high rate of recurrence - cholecystectomy advised
- cholecystectomy must be performed when evidence of gangrene or perforation is present (emergency cholecystectomy)
- Early cholecystectomy within 3 days of onset of the attack
- Conservative tx regimen of
 - analgesics (Meperidine preferred drug- less spasm of sphincter of Oddi)
 - Antibiotics
 - TPN
 - Followed by cholecystectomy after 6 weeks



Choledocholithiasis & Cholangitis



Choledocholithiasis

- Choledocholithiasis - common bile duct stones
- Occur in 15% of patients with gallstones
- Increases with age - in elderly w/gallstones occurrence as high as 50%
- Usually condition goes unknown until obstruction occurs



History

- History suggestive of attacks of biliary colic and gallbladder stones with frequent/recurrent attacks of severe RUQ pain- duration of several hours
- History suggestive of jaundice
- Charcot's Triad- classic picture of cholangitis
 - Pain
 - Fever /Chills
 - Jaundice
 - + altered mental status with hypotension (Raynaud pentad)

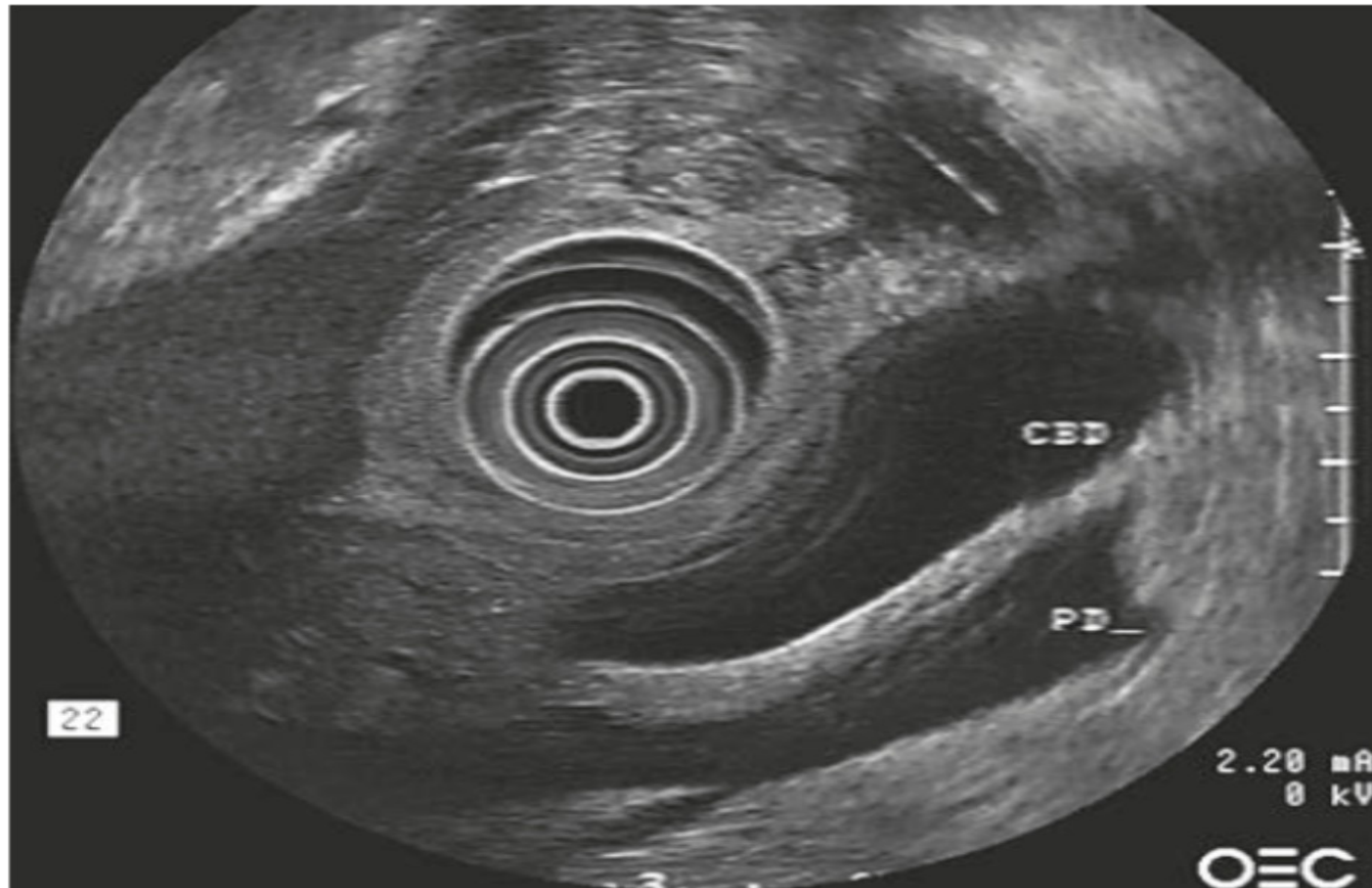


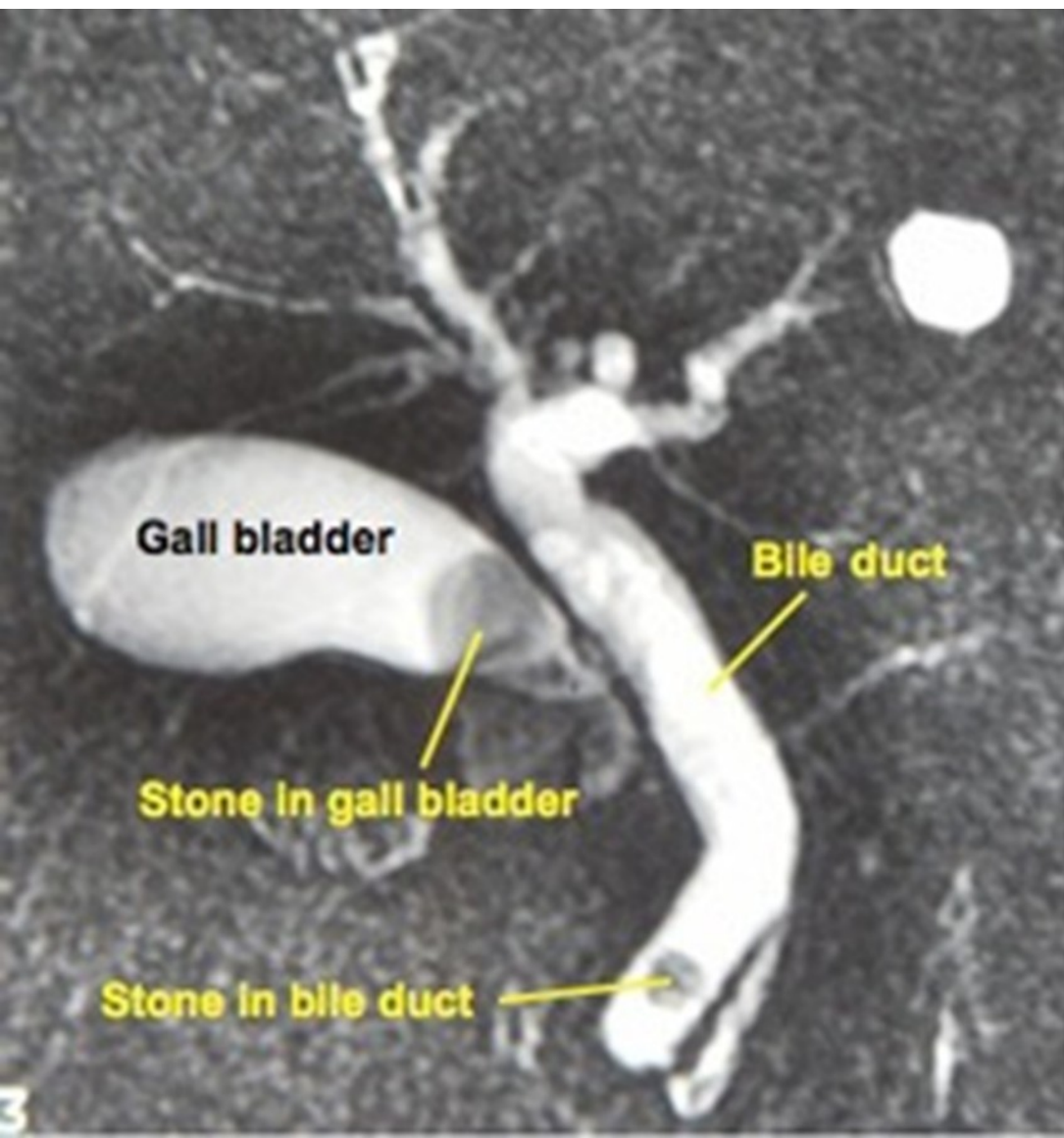
Imaging

- The most direct and accurate way to determine the cause, location, and extent of obstruction:
 - MRI (MRCP) is the gold standard for Gallstones & CBD stones.
 - ERCP : is preserved as a therapeutic rather than diagnostic tool
 - percutaneous transhepatic cholangiography
 - Endoscopic ultrasonography



Endoscopic ultrasonography

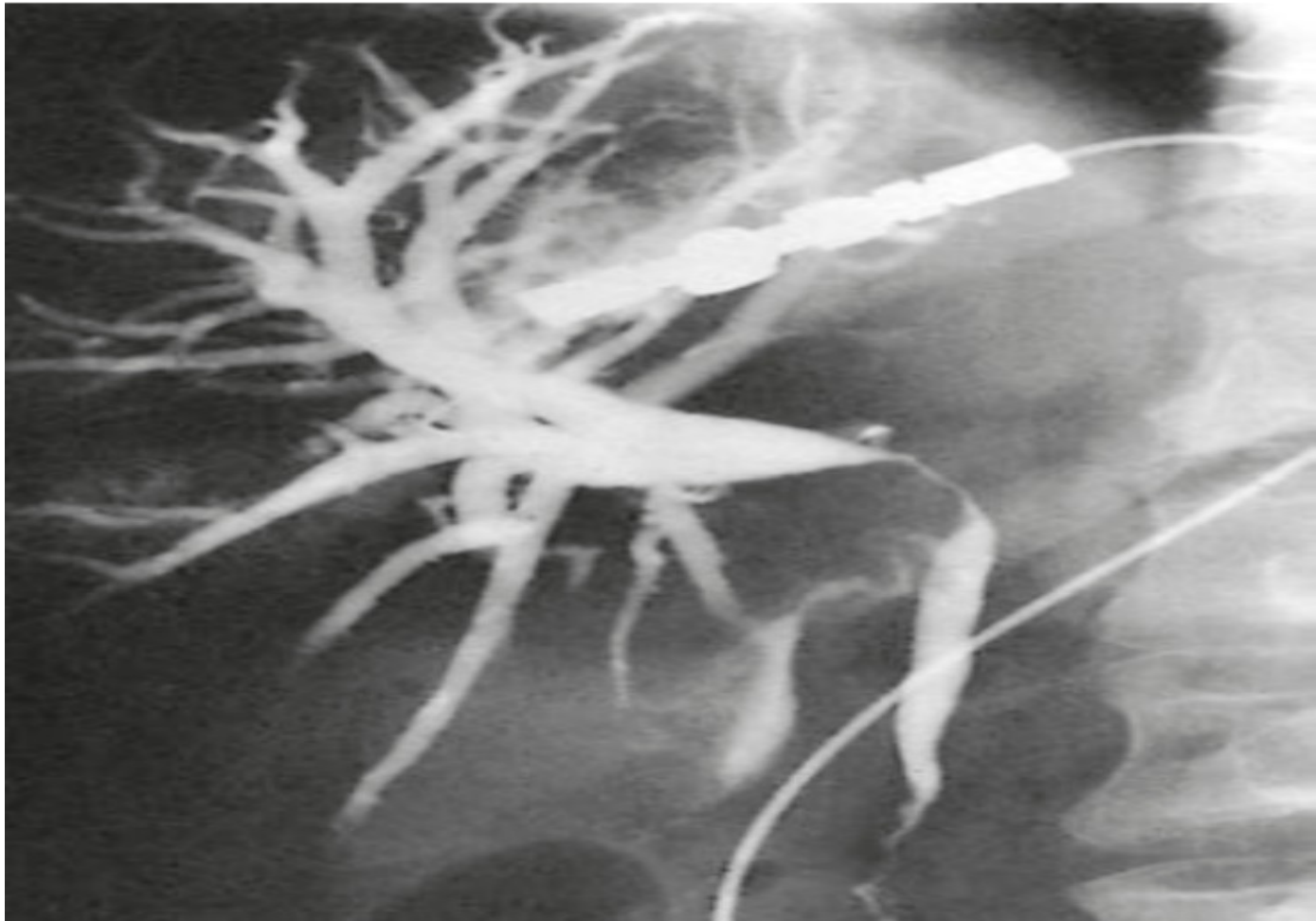




PTC:

When ERCP fails.

Malignant stricture – for stent insertion.



Treatment

- Common duct stone in patient with cholelithiasis and cholecystitis is usually treated with endoscopic papillotomy and stone extraction - followed by laparoscopic cholecystectomy
- Ciprofloxacin, 250mg IV q 12 hours effective tx for cholangitis
- alternative tx - mezlocillin, 3g IV q 4 hours with either metronidazole or gentamicin or both
- Aminoglycosides should not be used for more than several days due to increased risk of aminoglycoside nephrotoxicity in cholestasis



Primary Sclerosing Cholangitis

- Rare disorder
- Characterized by diffuse inflammation of the biliary tract leading to fibrosis and strictures of the biliary system (medium and large ducts in the intrahepatic and/or extrahepatic biliary tree)
- Most common - men aged 20-40
- Associated with histocompatible antigens HLA-B8 and -DR3 or -DR4 - suggestive of genetic etiologic role
- Sclerosing cholangitis may occur in AIDs patients from infections caused by CMV, cryptosporidium, or microsporium



Primary Sclerosing Cholangitis

- PSC may be asymptomatic and diagnosed as part of the evaluation of abnormal laboratory tests, or they may have symptoms such as fatigue and pruritus.
- Symptoms -
 - progressive obstructive jaundice frequently associated with:
 - malaise, pruritus , anorexia and indigestion
 - Early detection in presymptomatic phase may occur due to elevated alkaline phosphatase level



Primary Sclerosing Cholangitis

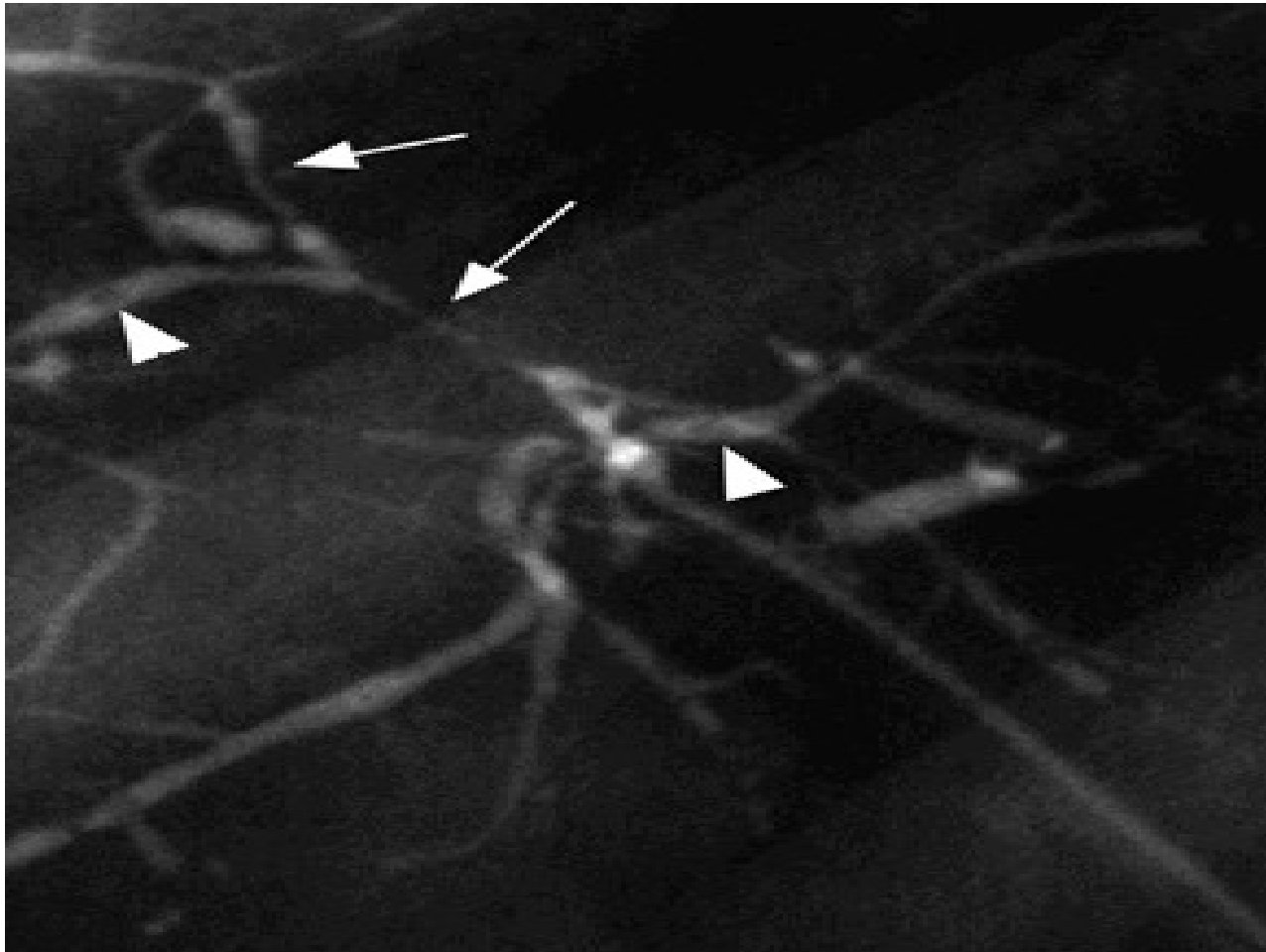
- In patients with ulcerative colitis, primary sclerosing cholangitis is an independent risk factor for development of colorectal dysplasia and cancer- routine colonoscopic surveillance is advised
- Complications of chronic cholestasis such as osteoporosis and malabsorption of fat-soluble vitamins may occur



Primary Sclerosing Cholangitis

- Diagnosis generally made by:
 - Magnetic resonance cholangiography
 - ERCP
- The diagnosis of PSC is typically established by the demonstration of characteristic multifocal stricturing and dilation of intrahepatic and/or extrahepatic bile ducts on cholangiography . A cholangiogram may be obtained using magnetic resonance cholangiopancreatography (MRCP) , endoscopic retrograde cholangiopancreatography (ERCP) , or percutaneous transhepatic cholangiography (PTC). Because it is noninvasive with comparable diagnostic accuracy to ERCP, MRCP is typically the first test of choice . PTC is the most invasive approach and is reserved for patients who are unable to undergo ERCP.





Primary Sclerosing Cholangitis

- Tx w/corticosteroids and broad spectrum antimicrobial agents yields inconsistent and unpredictable results
- Episodes of acute bacterial cholangitis may be treated with ciprofloxacin
- high dose ursodeoxycholic acid (20mg/kg/d) may reduce cholangiographic progression and liver fibrosis
- For patients with cirrhosis and clinical decompensation, liver transplantation is the procedure of choice



Primary Sclerosing Cholangitis

- Survival of patients with primary sclerosing cholangitis averages 10 years once symptoms appear
- Adverse prognostic factors:
 - increased age
 - increased serum bilirubin
 - increased aspartate aminotransferase levels
 - low albumin levels
 - history of variceal bleeding



Carcinoma of Biliary Tract

- Occurs in 2% of people surgically treated for biliary disease
- Insidious onset - usually discovered during surgery
- Similar presentation to benign biliary disease, i.e. gallstones
- Cholelithiasis usually present
- Most patients present with advanced disease
- Surgical resection in less than 10 per cent – remainder receive palliative treatment
- Prognosis is poor – median survival approximately six months
- Other risk factors:
 - Chronic gallbladder infection with salmonella typhi
 - gallbladder polyps over 1cm
 - mucosal calcification of the gallbladder (porcelain gallbladder)
 - anomalous pancreaticobiliary ductal junction



Carcinoma of Biliary Tract

- Carcinoma of the bile ducts (cholangiocarcinoma) accounts for 3% of all US cancer deaths
- Effects both sexes equally
- More prevalent 50-70 age group
- 2/3 Klatskin tumors - arise at the confluence of hepatic ducts
- 1/4 in the distal extrahepatic bile duct
- remainder are intrahepatic
- Majority of patients receive palliative care only
- Complete surgical excision possible in less than 10 per cent
- Prognosis poor – 90 per cent dead in one year from liver failure or biliary sepsis
- Adjuvant chemoradiation therapy has limited role



Carcinoma of Biliary Tract

- Signs/symptoms:
 - Progressive jaundice
 - pain RUQ w/ pain radiating to back present in gallbladder CA but occurs later in course of bile duct carcinoma
 - anorexia, weight loss
 - fever, chills (due to cholangitis)



Carcinoma of Biliary Tract

- A palpable gallbladder w/obstructive jaundice usually is said to signify malignant disease (Courvoisier's Law): however this has only proved to be accurate 50% of the time
- Hepatomegaly, liver tenderness
- Pruritus



Labs

- Conjugated hyperbilirubinemia
- elevated alkaline phosphatase
- elevated serum cholesterol
- AST may be slightly elevated
- CA19-9 (elevated level can help distinguish cholangiocarcinoma from benign biliary stricture)



Imaging Studies

- Ultrasound
- CT
- MRI
- MRCP



Treatment

- Laparoscopic cholecystectomy
 - 5 year survival for localized carcinoma of the gallbladder is as high as 80%
 - survival rates drop dramatically with more extensive disease
 - Carcinoma of the bile ducts is curable by surgery in < 10% of cases

