


**Overview of Gallbladder Diseases:
Diagnostic and Therapeutic Trends**



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- No financial disclosure



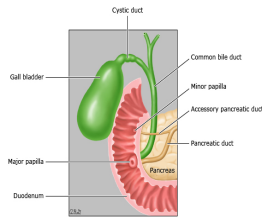
Learning Objectives

- 1) Discuss clinical presentation and evaluation of complicated and uncomplicated gallstone diseases
- 2) Discuss best practices concerning surveillance and management of gallbladder polyps and cancer
- 3) Describe epidemiology and diagnostic criteria for functional gallbladder disorder in adults



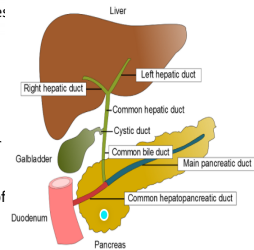
Location and Function of Gallbladder

- The gallbladder is a pear-shaped organ located below the liver, on the right side of the abdomen.
- Its primary function is to store and concentrate bile
- Bile consists mainly of bile salts, phospholipids, cholesterol, conjugated bilirubin, electrolytes, and water.



Physiology of Bile Secretion

- Bile travels through the liver in a series of ducts, eventually exiting through the common hepatic duct into the gallbladder, where it is concentrated and stored.
- When stimulated by the hormone cholecystokinin (CCK), the gallbladder contracts, pushing bile through the cystic duct and into the common bile duct. Simultaneously, the sphincter of Oddi relaxes, permitting bile to enter the duodenal lumen.




Gallstone Disease

- Affects more than 20 million people in the United States.
- Prevalence rates of cholelithiasis increase with age and are higher in females. In the United States, approximately 6 percent of men and 9 percent of women have gallstones.
- Prevalence of gallstone disease also differs based on ethnicity. It is highest in individuals of Northern European, Hispanic, and American Indian descent, and lowest in Asian and African-American populations.



Pathophysiology of Gallstone Formation


- Gallstone formation occurs when levels of substances that compose bile exceed their solubility point.
- **Types of Gallstones:**
 1. **Cholesterol stones** are composed of more than 70% cholesterol
 2. **Pigment gallstones** make up approximately 10% of gallstones and are composed of < 30% cholesterol.
 - **Black pigment gallstones** are composed of calcium bilirubinate. Commonly seen in hemolytic anemia, cirrhosis, cystic fibrosis, and ileal disease.
 - **Brown pigment stones** associated with bacterial and helminthic infections.
 3. **Mixed stones** are composed of 30–70% cholesterol. A combination of calcium carbonate, calcium bilirubinate, cholesterol and bile.



Risk Factors for Gallstone Formation


Risk factors for gallstone formation.

Nonmodifiable risk factors	Modifiable risk factors
Increasing age	Pregnancy
Female sex	Diabetes mellitus
Ethnicity	Dyslipidemia
Genetic susceptibility	Obesity
Family history	Rapid weight loss
	Metabolic syndrome
	Medications: fibrates, estrogens, somatostatin analogues oral contraceptives
	Gallbladder stasis
	Terminal ileal disease/resection
	Cirrhosis
	Hyperbilirubinemia



Gallstone Disease

- ❖ **Asymptomatic**
- ❖ **Uncomplicated gallstone disease** — The term uncomplicated gallstone disease refers to biliary colic in the absence of gallstone-related complications.
- ❖ **Complicated gallstone disease** — The term complicated gallstone disease refers to gallstone-related complications:
 - Acute cholecystitis
 - Cholangitis
 - Gallstone pancreatitis
 - Gallstone ileus, and
 - Mirizzi syndrome.



Asymptomatic Cholelithiasis

- Asymptomatic gallstones are commonly found as incidental findings on abdominal imaging
- Expectant management is the treatment of choice for patients with asymptomatic cholelithiasis.
- Routine cholecystectomy is not indicated for management of asymptomatic patients.
- Patients should be educated about the natural history of gallstone disease and management options if they become symptomatic.



Symptomatic Gallstones

Biliary Colic

- Intense, dull discomfort located in the right upper quadrant, epigastrium, or substernal area that may radiate to the back (particularly the right shoulder blade)
- Diaphoresis, nausea, and vomiting.
- Eating a fatty meal is a common trigger for gallbladder contraction, and many patients report postprandial pain. The pain can be nocturnal.
- The pain typically lasts at least 30 minutes, plateauing within an hour.



Symptomatic Gallstones

- 305 patients with gallstones, 70 percent of those with a history of biliary colic developed recurrent symptoms within two years.



- Laboratory tests (complete blood count, aminotransferases, bilirubin, alkaline phosphatase, amylase, and lipase) are normal.

Management

- Treatment of an acute episode of biliary colic is pain control. NSAIDs are the first-line therapy.
- Definitive treatment of recurrent biliary colic is elective cholecystectomy for patients who are surgical candidates



Acute Calculous Cholecystitis

- Acute cholecystitis refers to a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation that is usually related to gallstone disease.

Epidemiology

- In one systematic review, acute cholecystitis developed in 6 to 11 percent of patients with symptomatic gallstones over a median follow-up of 7 to 11 years.
- Three times more common in women compared to men.

Pathophysiology

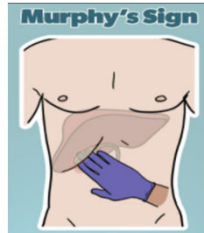
- Occurs in the setting of cystic duct obstruction.
- Continued mucin production from epithelium distends the gallbladder wall and compromises blood flow and lymphatic drainage. The consequence is mucosal ischemia, edema, and inflammation.



Acute Calculous Cholecystitis

Clinical Presentation

- Most commonly presents with right upper quadrant or epigastric pain and fever. Pain can radiate to the right shoulder or back if the inflamed gallbladder makes contact with the diaphragm.



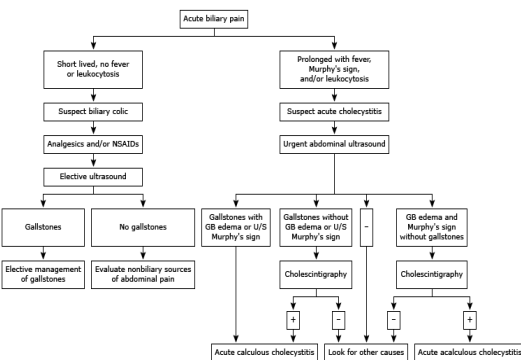
A positive Murphy's Sign indicates potential cholecystitis or inflammation of the gallbladder.

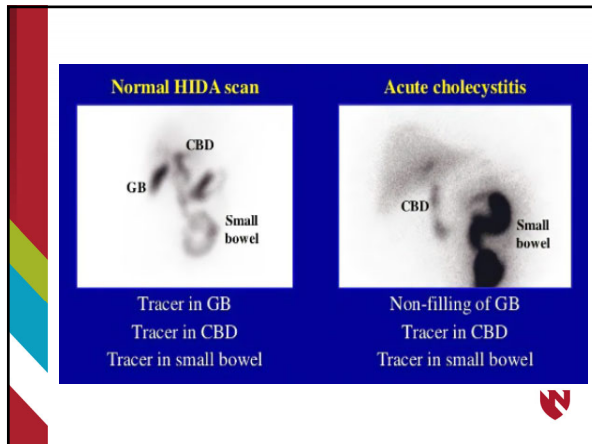
To test, firmly palpate the RUQ subcostal region, pushing under the ribs. Ask the patient to take a deep breath.

A positive sign is when significant pain is elicited by this maneuver, usually stopping them mid-breath.

- Nausea and vomiting.
- Murphy's sign.

Algorithm for the diagnosis of acute cholecystitis





Acute Calculous Cholecystitis

Management

A. Supportive Care

- Intravenous hydration.
- Correction of any electrolyte abnormalities.
- Pain control.
- Intravenous antibiotics.
- Consider placement of a nasogastric tube.

B. Cholecystectomy

- Definitive treatment for acute cholecystitis.
- Laparoscopic approach is preferred in the first instance and converted to open if needed to complete the operation safely.
- "Early" cholecystectomy defined in the literature as gallbladder surgery performed within 3, 7, or 10 days of symptom onset and "delayed" cholecystectomy as that performed 7 or 45 days, or six weeks, after initial diagnosis.

Acute Calculous Cholecystitis

Management


C. Gallbladder drainage

Some form of gallbladder drainage is required as the initial treatment, in conjunction with antibiotics, for patients who are at high surgical risk such as being septic or critically ill.

- > Percutaneous Drainage
- > Endoscopic Drainage

Choledocholithiasis

Choledocholithiasis is a complication of cholelithiasis and indicates that a gallstone has migrated into the common bile duct.




Epidemiology

- Among the million people in the United States who have symptomatic cholelithiasis, 10–20% will have choledocholithiasis.
- Incidence increases with age: 30–50% of patients > 50 years with cholelithiasis have concurrent common bile duct stones.

Clinical Manifestations

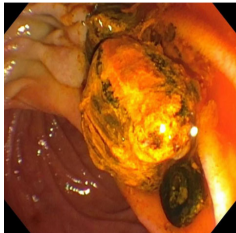
- Present with biliary-type pain and laboratory testing reveals a cholestatic pattern of liver test abnormalities.



Choledocholithiasis

Diagnosis

- Ultrasound is often the initial test.
- Magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS).
- Endoscopic retrograde cholangiopancreatography (ERCP) can be used as a diagnostic and therapeutic tool.




Management

- ERCP


Complications

- Acute pancreatitis
- Acute cholangitis.



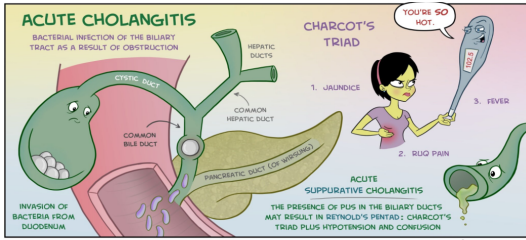
Acute Cholangitis

- Cholangitis is a GI emergency requiring prompt recognition and treatment.
- **Epidemiology:** Biliary calculi (28 to 70 %), benign biliary stricture (5 to 28 %), and malignancy (10 to 57 %). Benign biliary strictures may be congenital, post-infectious (eg, AIDS cholangiopathy) or inflammatory (e.g, primary sclerosing cholangitis).
- **Pathogenesis:** Caused primarily by bacterial infection in a patient with biliary obstruction. The organisms typically ascend from the duodenum; hematogenous spread from the portal vein is a rare source of infection.



Acute Cholangitis

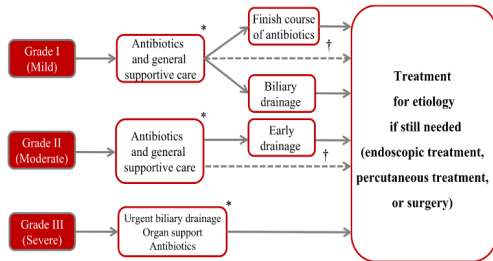
- The classic presentation of acute cholangitis is fever, abdominal pain, and jaundice (**Charcot's triad**).
- The additional presence of hypotension and altered mental status make up **Reynold's Pentad**.
- **Diagnosis:** Abdominal ultrasound, Endoscopic Ultrasound, MRCP, and ERCP



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GUIDELINE

Tokyo Guidelines 2018: initial management of acute biliary infection and flowchart for acute cholangitis





GUIDELINE



ASGE guideline on the management of cholangitis

Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

Recommendation 1: For patients with cholangitis, we suggest ERCP over PTBD.

Recommendation 2: For patients with cholangitis, we suggest the performance of ERCP in ≤48 hours compared with >48 hours.

Recommendation 3: For patients with cholangitis, we suggest that biliary drainage be combined with other maneuvers such as sphincterotomy and stone removal versus stent placement without attempted stone removal.



Gallstone Pancreatitis

- Present with epigastric abdominal pain, fever, nausea, vomiting, and leukocytosis.

How gallstones may cause pancreatitis

Liver

Gallstones form inside the gallbladder

Gallstones may come out of the gallbladder and go down the tube

Gallstones may block the flow of digestive enzymes from the pancreas. Pressure inside the pancreas goes up, eventually leading to pancreas damage and pancreatitis

Gallstone Pancreatitis

Diagnosis

- Elevated serum amylase and lipase. Serum ALT >150 IU/L suggests biliary etiology.
- CT scan: sensitivity of 92 to 95% and a specificity of 98–100%.
- **Revised Atlanta Classification:** requires 2 of 3 criteria to be met
 - 1) amylase or lipase level 3x the upper limit of normal
 - 2) epigastric abdominal pain
 - 3) abdominal imaging consistent with acute pancreatitis.

Management

- Aggressive fluid resuscitation and early cholecystectomy.
- Prophylactic antibiotics are not indicated.
- ERCP
- Cholecystectomy

Gallbladder Polyps

- Gallbladder polyps are outgrowths of the gallbladder mucosal wall.
- Gallbladder polyps are seen in 3–7% of healthy individuals. There is an equal prevalence in males and females.

Type	Frequency
Cholesterol Polyps	60%
Adenomyomas	25%
Inflammatory Polyps	10%
Adenomas	4%

Gallbladder Polyps

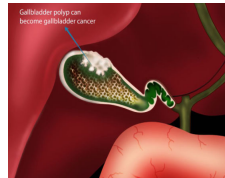
Clinical Features

- Asymptomatic and incidentally found on ultrasound
- Right upper quadrant pain, nausea, vomiting, dyspepsia, and even jaundice.

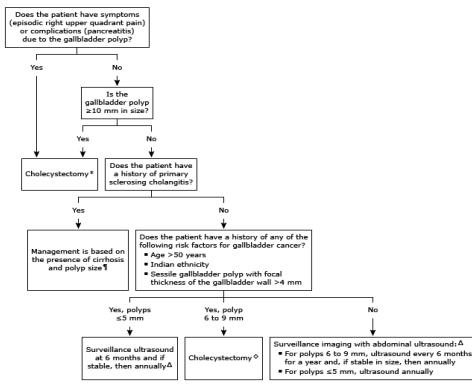
Cancer risk — Most gallbladder polyps are benign, and most benign polyps, with the exception of adenomas, have no malignant potential.

Established risk factors:

- Large polyps (≥ 1 cm)
- Primary sclerosing cholangitis (PSC)
- Indian ethnicity
- Age >50



Suggested approach to the management of gallbladder polyps in adults



Management and Surveillance of Gallbladder Polyps

- Gallbladder polyps ≥ 10 mm have an increased risk of malignancy, cholecystectomy is indicated.
- Cholecystectomy is indicated in patients with primary sclerosing cholangitis with gallbladder polyps >8 mm.
- In patients who are unable or unwilling to undergo cholecystectomy, we perform a surveillance ultrasound at 6 months and then annually if stable in size.
- An increase in size of >2 mm on imaging is likely to represent a clinically relevant increase in size and should prompt referral to a surgeon for cholecystectomy.



Gallbladder Cancer


- Gallbladder cancer is an uncommon but highly fatal malignancy; fewer than 5000 new cases are diagnosed each year in the United States.

Risk Factors:

- Gallstone disease
- Porcelain gallbladder
- Gallbladder polyps
- Primary sclerosing cholangitis
- Chronic infection
- Congenital biliary cysts
- Medications
- Obesity

Clinical presentation


- Vague abdominal complaints and systemic signs of anorexia and weight loss. Pruritis, jaundice, and scleral icterus



Gallbladder Cancer

Diagnosis


- **Ultrasound** has a high sensitivity for the detection of tumor at advanced stages.
- **Endoscopic ultrasound (EUS):** superior to conventional ultrasonography due to its ability to produce high-resolution imaging of the gallbladder from close proximity to the biliary tree.
- **CT scan** may be useful for detection of metastatic disease.
- **MRI** is helpful for visualizing gallbladder cancer extension to neighboring structures.



Gallbladder Cancer

Management

- **T1a:** Simple cholecystectomy.
- **T1b-2:** Once the tumor extends beyond the gallbladder mucosa and tumors invade the muscular layer (T1b – 2), treatment will involve surgical resection of the liver.
- **T3:** Invasion of the serosa, liver, and likely other adjacent organs represents advanced disease. Resection of involved adjacent bowel, stomach, pancreas, and/or liver to achieve margin clearance may be required.
- **T4:** refers to widespread disease via vascular invasion and/or metastases. Chemotherapy is the preferred treatment.




Functional Gallbladder Disorder

Functional gallbladder disorder is characterized by biliary pain in the absence of gallstones, sludge, microlithiasis, or microcrystal disease.

Pathophysiology:

- Gallbladder dysmotility is hypothesized to play a central role.
- Gallbladder dysmotility may result from an initial metabolic disorder (ie, bile supersaturated with cholesterol) which increases bile viscosity or a primary motility disorder in the absence.
- Abnormal gastric emptying and colonic transit, suggesting a possible generalized gastrointestinal motility disorder.



Functional Gallbladder Disorder


Diagnosis:
Rome IV criteria for functional gallbladder disorder require:

Biliary pain defined as pain in the epigastrium and/or RUQ that meets all of the following criteria:

- Builds up to a steady level and lasts at least 30 minutes
- Is severe enough to interrupt daily activities/lead to an ED visit
- Is not significantly (<20 percent) related to bowel movements or relieved by postural change, or acid suppression
- Absence of gallstones or other structural pathology

Criteria that are supportive of functional gallbladder disorder, but are not required, include:


- Low ejection fraction on scintigraphy
- Normal liver enzymes, conjugated bilirubin, and amylase/lipase



Functional Gallbladder Disorder

Management

- Patients may benefit from antispasmodics, neuromodulators, or ursodeoxycholic acid.
- Despite poorly defined criteria for which patients benefit from surgical management, cholecystectomy is performed in 20% of patients with functional gallbladder disorder.
- A response to cholecystectomy has been defined as resolution of symptoms lasting greater than 1 year after surgery.
- Overall, current guidelines do not recommend surgical treatment and recommend shared decision-making between the patient and clinician.



Key Points

- The gallbladder plays a fundamental role in the digestive process of fats by coordinating the storage and release of bile.
- The wide breadth of gallbladder disease is a reflection of the complex interaction of anatomic, genetic, and environmental factors.
- Acute cholangitis is a GI emergency requiring prompt recognition and treatment.
- Gallbladder polyps ≥ 10 mm have an increased risk of malignancy and laparoscopic cholecystectomy is indicated.
- Gallbladder cancer is often diagnosed intraoperatively at the time of cholecystectomy for cholelithiasis, an important issue is the screening of patients with symptomatic biliary tract disease for the possibility of coexisting GBC.



Thank you

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