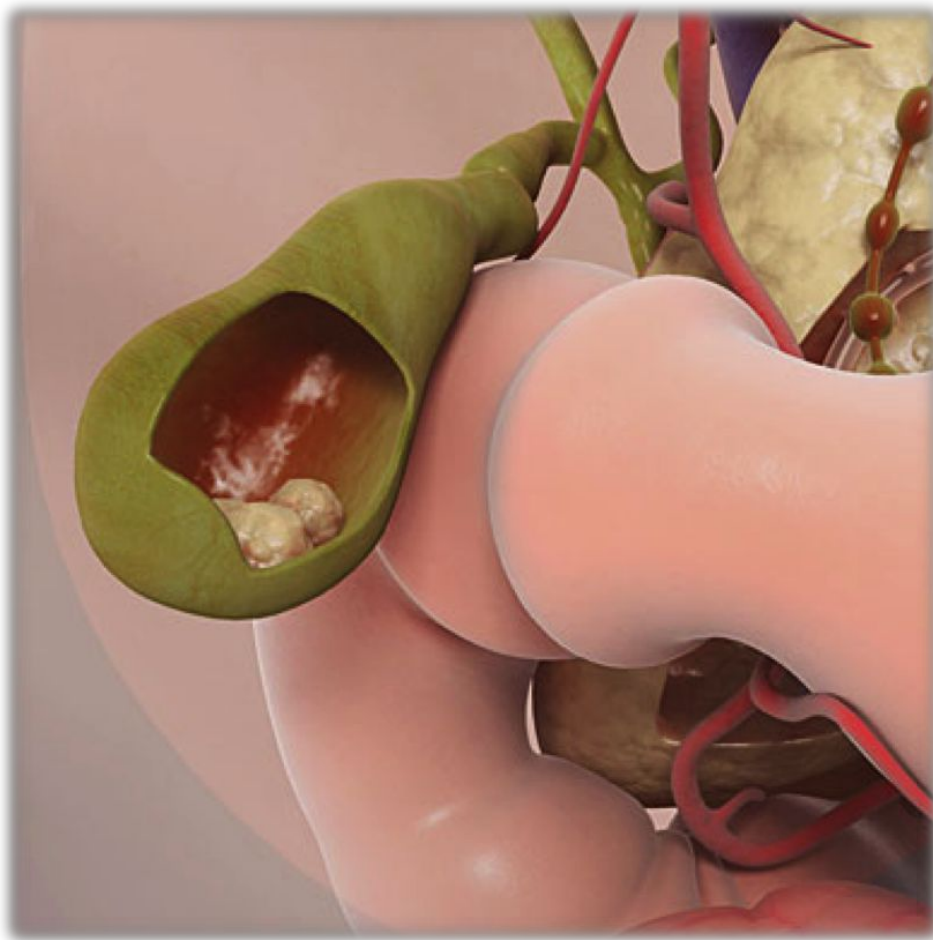


Cholecystitis



Objectives:

1. Pathology and pathogenesis of cholecystitis.
2. Recognize the predisposing factors of cholecystitis.
3. Describe the different types of cholecystitis.
4. Understand the pathogenesis of acute and chronic cholecystitis.

Important note: Please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: [Pathology Edit](#).

Cholelithiasis “Gallstones”

- **80% are silent** “free of biliary pain or stone complications”.
- Symptoms appear if there’s an obstruction due to small stone that would move with secretion of bile to → neck of gallbladder.

Type :

1. Cholesterol stones:

2. 80% of cases of gallstones (**most common**)
3. Stones contains more than 50% of crystalline cholesterol monohydrat.

Risk Factors:

- Demography: northern Europeans, North and South Americans, Native Americans, Mexican Americans.
- **Female gender.**
 - Female sex hormones (estrogen).
 - Pregnancy.
 - Oral contraceptives.
- Advancing age (40).
- Obesity and metabolic syndrome.
- Rapid weight reduction.
- Gallbladder stasis.
- Inborn disorders of bile acid metabolism.
- Hyperlipidemia syndrome.

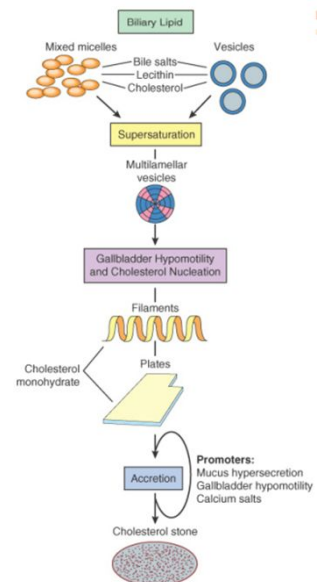
Pathogenesis:

- When cholesterol concentrations exceed the solubilizing capacity of bile (super saturation), cholesterol can no longer remain dispersed and nucleates into solid cholesterol monohydrate crystals.

Cholesterol gallstones formation involves four simultaneous defects:

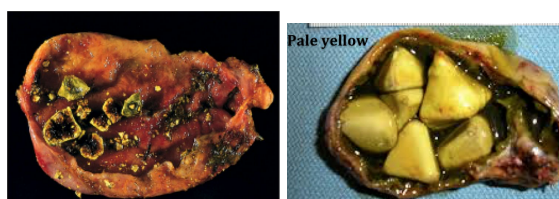
Hepatocellular hypersecretion of cholesterol → 1- **Supersaturation** of bile with cholesterol → 2- Gallbladder **hypomotility** → Promotes nucleation typically around a calcium salt crystal nidus → 3- Cholesterol nucleation in bile is accelerated → 4- **Mucus hypersecretion** in the gallbladder → traps the crystals, permitting their aggregation into stones.

- Prolonged fasting, pregnancy (risk factor → Hypomotility) , rapid weight loss, total parenteral nutrition, and spinal cord injury also promote stone formation.



Morphology:

Pale yellow, round to ovoid to multifaceted, and have a finely granular, hard external surface. Stones composed largely of cholesterol are **radiolucent**, only 10% to 20% of cholesterol stones are radiopaque.



4. Pigment stones

- 20% bilirubin calcium salts.
- 80% of cases of gallstones (**most common**)
- Stones contains more than 50% of crystalline cholesterol monohydrate.

Risk Factors:

- Demography: Asians more than Westerners, rural more than urban.
- **Chronic hemolytic syndromes.**
- Biliary infection.
- Gastrointestinal disorders:
 - Ileal disease (e.g., Crohn disease), ileal resection or bypass.
 - Cystic fibrosis with pancreatic insufficiency.

Pathogenesis: unconjugated bilirubin + calcium = Precipitation of calcium bilirubin salts

Based on:

1. The presence of unconjugated bilirubin (poorly soluble in water) such as chronic hemolytic conditions.
2. Precipitation of calcium bilirubin salts such as infection of the biliary tract with:
 - *Escherichia coli*.
 - *Ascaris lumbricoides*.
 - Liver fluke *Opisthorchis sinensis*.

Morphology:

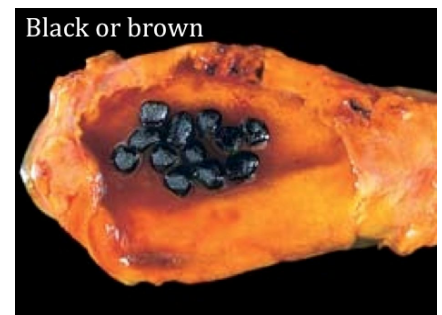
"**Black**" pigment stones are found in sterile gallbladder.

"**Brown**" pigment stones are found in **infected** intrahepatic or extrahepatic bile ducts.

Both are soft and usually multiple.

Brown stone are greasy.

Because of calcium carbonates and phosphates, approximately 50% to 75% of black stones are **radiopaque**.

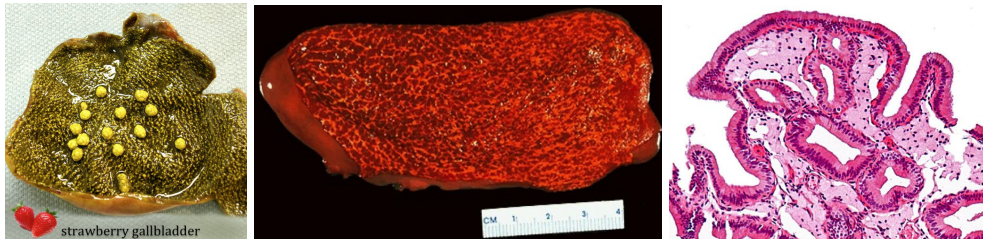


Cholesterolosis:

This is another condition associated with excessive cholesterol, in which cholesterol is in lamina propria trapped in macrophages → forming foamy cells

An incidental finding usually associated with cholelithiasis.

Cholesterol hypersecretion by the liver promotes excessive accumulation of cholesterol esters within the lamina propria of the gallbladder. The mucosal surface is studded with minute yellow flecks, producing the “**strawberry gallbladder**”



Clinical Features of gallstones:

- 70% to 80% of patients are **asymptomatic**.
- Symptoms: Colicky upper quadrant pain, which tends to be excruciating.
- Pain is localized to right upper quadrant or epigastrium that may **radiate to the right shoulder** or the back.
- It usually follows a fatty meal which forces a stone against the gall bladder outlet leading to increased pressure in the gall bladder causing pain.
- It is usually due to **obstruction** of bile ducts by passing stones.

Complications of gallstones:

1. Empyema¹.
2. Perforation.
3. Fistula.
4. Inflammation of the biliary tree (**cholangitis**).
5. Obstructive cholestasis.
6. Pancreatitis (Obstruction of bile duct → pancreatic enzymes accumulate → get activated early → Pancreatitis).
7. Occasionally, a large stone may erode directly into an adjacent loop of small bowel, generating intestinal obstruction (“gallstone ileus²”). Complete or partial small-bowel obstruction occurs when one or more gallstones erode through the gallbladder or biliary duct into the GI tract, creating a cholecysto-enteric fistula.
8. Most notable is the increased risk for carcinoma of the gallbladder.

The larger the calculi, the less likely they are to enter the cystic or common ducts to produce obstruction; it is the very **small stones**, that are the more dangerous.


¹ Collection of pus in a cavity in the body

² Obstruction of the gastrointestinal tract by a gallstone

CHOLECYSTITIS

Inflammation of the gallbladder may be acute, chronic, or acute superimposed on chronic. It almost always occurs in association with gallstones.

Acute Cholecystitis:



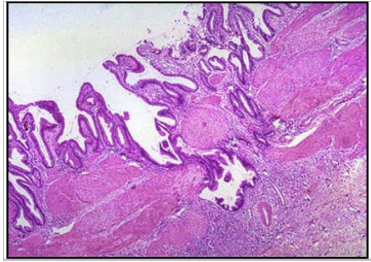
Type	Calculous	Acalculous
Definition	Obstruction of the neck or cystic duct.	Occurs in the absence of gallstones . Due to severe underlying condition.
Pathogenesis	Results from chemical irritation and inflammation of the obstructed gallbladder. These events occur in the absence of bacterial infection; only later in the course may bacterial contamination develop.	Generally in severely ill patient . <ul style="list-style-type: none"> - Postoperative. - Severe trauma. - Severe burns. - Multisystem organ failure. - Sepsis. - Postpartum state (after giving birth).
Morphology	<ul style="list-style-type: none"> ● Gallbladder is usually enlarged and tense. ● Serosal covering is frequently layered by fibrin in severe case → Exudate ● Bile is cloudy to turbid → contain fibrin + pus + hemorrhage. (When the contained exudate is pure pus the condition is referred to as → Empyema of the gallbladder. - Mild cases: gallbladder wall is thickened, edematous and hyperemic. - Severe cases: It's transformed to green-black → necrotic organ called → gangrenous cholecystitis with perforation. 	
Clinical Features	<ul style="list-style-type: none"> • Progressive right upper quadrant or epigastric pain. • Mild fever. 	
	May appear with remarkable suddenness and constitute an acute surgical emergency or may present with mild symptoms that resolve without medical intervention.	<ul style="list-style-type: none"> • More insidious, since symptoms are obscured by the underlying conditions precipitating the attacks. • A higher proportion of patients have no symptoms referable to the gallbladder. • The incidence of gangrene and perforation is much higher than in calculous cholecystitis.

Chronic cholecystitis

- Chronic cholecystitis may be a sequel to repeated bouts of mild to severe acute cholecystitis, but in many instances, it develops in the apparent absence of antecedent attacks.
- It is associated with **cholelithiasis** in over 90% of cases.
- The symptoms of calculous chronic cholecystitis are similar to those of the acute form and range from biliary colic to indolent right upper quadrant pain and epigastric distress.
- Patients often have **intolerance to fatty food**, belching and postprandial epigastric distress, sometimes include nausea and vomiting.

Morphology

The morphologic changes in chronic cholecystitis are extremely variable and sometimes minimal.

Gross	Microscopic	
	 <p>Rokitansky-Aschoff sinuses Outpouchings of the mucosal epithelium through the wall</p>	
<p>Gall bladder may be:</p> <ol style="list-style-type: none"> 1. Contracted (fibrosis). 2. Normal in size. 3. Enlarged (from obstruction). 4. The <u>wall</u> is variably thickened. 	<ul style="list-style-type: none"> - The degree of inflammation is variable.(mainly lymphocytes) - Outpouchings of the mucosal epithelium through the wall (Rokitansky-Aschoff sinuses) may be quite prominent. - Extensive dystrophic calcification within the gallbladder wall may yield a porcelain gallbladder, notable for a markedly increased incidence of associated cancer. - Xanthogranulomatous cholecystitis abundant lipid filled macrophages - an atrophic, chronically obstructed gallbladder may contain only clear secretions, a condition known as hydrops of the gallbladder. 	

Complications of acute and chronic cholecystitis:

1. Bacterial superinfection with cholangitis or sepsis.
2. GB perforation & local abscess formation.
3. GB rupture with diffuse peritonitis.
4. Biliary enteric fistula with drainage of bile into adjacent organs, and potentially gallstone-induced intestinal obstruction (ileus)

5. Gallbladder cancer

Summary

	Cholesterol stones 80%. crystalline cholesterol monohydrate.	Pigment stones 20% bilirubin calcium salts
Risk factors	Age, Female, Obesity, Rapid weight reduction, Gallbladder stasis.	<ul style="list-style-type: none"> - Chronic hemolytic syndromes. - Biliary infection. - Gastrointestinal disorders:
Pathogenesis	<ul style="list-style-type: none"> - Supersaturation of bile with cholesterol. - Gallbladder hypomotility. - Mucus hypersecretion in the gallbladder. 	<p>Based on:</p> <ol style="list-style-type: none"> 1. The presence of unconjugated bilirubin (poorly soluble in water) such as chronic hemolytic conditions. 2. Precipitation of calcium bilirubin salts such as infection of the biliary tract with: <ul style="list-style-type: none"> - <i>Escherichia coli</i>. - <i>Ascaris lumbricoides</i>. - Liver fluke <i>Opisthorchis sinensis</i>.
Morphology	Pale yellow stones composed largely of cholesterol are radiolucent , only 10% to 20% of cholesterol stones are radiopaque.	Calcium carbonates 50% to 75% of black stones are radiopaque .
Cholesterosis	An incidental finding associated with cholelithiasis. Excessive accumulation of cholesterol esters within the lamina propria of the gallbladder " strawberry gallbladder ".	
Clinical features	<ul style="list-style-type: none"> • 70% to 80% of patients are asymptomatic. • Symptoms: Colicky right upper quadrant pain that may radiate to the right shoulder or the back. • It is usually due to obstruction of bile ducts by passing stones. 	
Complications	Empyema - Perforation - Fistula - Inflammation of the biliary tree (cholangitis) - Pancreatitis. Occasionally, a large stone may erode directly into an adjacent loop of small bowel, generating intestinal obstruction ("gallstone ileus").	

CHOLECYSTITIS

Inflammation of the gallbladder may be acute, chronic, or acute superimposed on chronic. It almost always occurs in association with gallstones.

	Acute Cholecystitis		Chronic cholecystitis
	Calculous	Acalculous	
Type	Obstruction of the neck or cystic duct.	Occurs in the absence of gallstones .	Associated with cholelithiasis in over 90% of cases.
Pathogenesis	Results from chemical irritation and inflammation of the obstructed gallbladder.	Generally in severely ill patient . <ul style="list-style-type: none"> - Postoperative. - Severe trauma. - Severe burns. - Multisystem organ failure. - Sepsis. - Postpartum state (after giving birth). 	Sequel to repeated bouts of acute cholecystitis.
Clinical Features	<ul style="list-style-type: none"> • Progressive right upper quadrant or epigastric pain. • Mild fever. 	Symptoms are obscured by the underlying conditions precipitating the attacks.	The symptoms of calculous chronic cholecystitis are similar to those of the acute form and range from biliary colic to indolent right upper quadrant pain and epigastric distress. Patients often have intolerance to fatty food , belching and postprandial epigastric distress, sometimes include nausea and vomiting.
	sudden and constitute acute surgical emergency or may present with mild symptoms that resolve without medical intervention.		
Morphology	Gallbladder is usually enlarged and tense. Bright red to green-black → gangrenous (much higher in acalculous cholecystitis). Fibrin, Exudate, hemorrhage → Empyema .		It's extremely variable, but sometimes could be: <ul style="list-style-type: none"> •Contracted (fibrosis). •Normal in size. •Enlarged (from obstruction).
Complications	<ul style="list-style-type: none"> • Bacterial superinfection with cholangitis or sepsis. • GB perforation & local abscess formation. • GB rupture with diffuse peritonitis. • Biliary enteric fistula with drainage of bile into adjacent organs. 		

MCQs

1/ A 47-year-old woman presents with a 3-month history of vague upper abdominal pain after fatty meals, some abdominal distension, and frequent indigestion. Physical examination shows an obese woman (BMI = 30 kg/m²) with right upper quadrant tenderness. An ultrasound examination discloses multiple echogenic objects in the gallbladder. Which of the following metabolic changes is most likely associated with the formation of gallstones in this patient?

- (A) Increased hepatic cholesterol secretion
- (B) Decreased serum albumin
- (C) Increased bilirubin uptake by the liver
- (D) Increased hepatic calcium secretion

2/ For the patient described in Question 1, which of the following is a common complication?

- (A) Bile peritonitis
- (B) Chronic passive congestion of the liver
- (C) Confluent hepatic necrosis
- (D) Extrahepatic biliary obstruction

3/ A 45-year-old, mildly obese woman presents with a 1-week history of upper abdominal pain, fever, shaking chills, and occasional vomiting. Physical examination shows severe right upper quadrant tenderness. . An ultrasound examination of the abdomen reveals a normal appearing liver and bile duct and thickening of the wall of the gallbladder. Which of the following is the most likely diagnosis?

- (A) Acute cholecystitis
- (B) Acute pancreatitis
- (C) Adenocarcinoma of the gallbladder
- (D) Adenocarcinoma of the pancreas

Answers: 1- A 2- D 3- A

SAQs

1/What are risk factors for the development of pigment gallstones?

Cirrhosis, chronic hemolytic anemias (such as patients with sickle cell anemia), bacterial contamination of the biliary tree, and chronic parasitic biliary infections are recognized risk factors for the development of pigment stones.

2/What are the pathobiological mechanisms leading to the development of acute calculous cholecystitis?

Acute calculous cholecystitis is due to irritation and inflammation of the gallbladder wall when there is obstruction of bile outflow. Lysolecithin, a hydrolytic product of biliary lecithin produced with bile stasis, is toxic to the gallbladder mucosa. Bile salts are also toxic. Prostaglandins contribute to further damage. Furthermore, inflammation and distention of the gallbladder lead to increased luminal pressure, which compromises blood flow to the wall.

3/In addition to cholecystitis what are the complications arising from cholelithiasis?

However, stones can cause colicky pain, acute and chronic cholecystitis, empyema of the gallbladder, gallbladder perforation or fistula, gallstone ileus, choledocholithiasis with ascending cholangitis and possible liver abscesses, obstructive cholestasis, and pancreatitis.

4/ what is the main symptom which people with gallbladder stone present with?

Asymptomatic (silent)

5/ in which case we might see a strawberry gallbladder?

Cholesterosis

6/ what is the term used to describe the necrotic green-black gallbladder?

Gangrenous cholecystitis.

7/What do the laboratory tests of elevated alkaline phosphatase with a conjugated hyperbilirubinemia indicate?

An elevated alkaline phosphatase with a conjugated hyperbilirubinemia is suggestive of obstructive jaundice due to choledocholithiasis.

8/A 47-year-old woman presents with a 3-month history of vague upper abdominal pain after fatty meals, some abdominal distension, and frequent indigestion, Physical examination shows an obese woman with right upper quadrant tenderness, An ultrasound examination discloses multiple echogenic objects in the gallbladder, The opened gallbladder is shown in the image. What is the diagnosis?



Chronic cholecystitis due to longstanding cholelithiasis.

For any suggestions or questions please don't hesitate to contact us on: Pathology434@gmail.com

Twitter: @Pathology434

Ask us: www.ask.fm/Pathology434

GOOD LUCK !!

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ريم لبني
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