

PATHOLOGY AND PATHOGENESIS OF CHOLECYSTITIS

Made by:

Pathology Team:

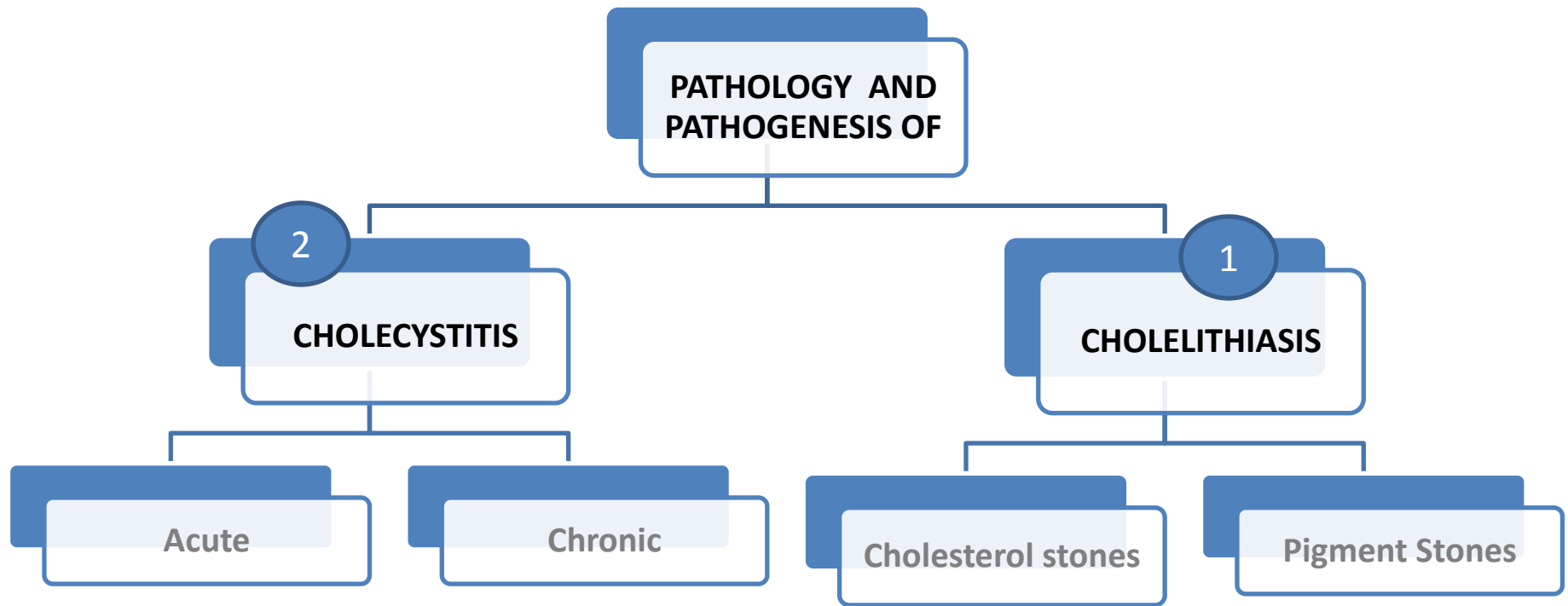
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N.B: RED !! → Important Point

STAR !! → Important Slide



Disorders of the Gallbladder

CHOLELITHIASIS (GALLSTONES)

- Majority of gallstones (>80%) are "silent", and most individuals remain free of biliary pain or stone complications for decades.
- There are two main types of gallstones:
 - About 80% are cholesterol stones, containing more than 50% of crystalline cholesterol monohydrate.
 - The remainder are composed predominantly of bilirubin calcium salts and are designated pigment stones.

Prevalence and Risk Factors

Demography: distribution in the world

Cholesterol Stones (اي شي مظلل بالاحمر بالجدول مهم more in female)

Demography: Northern Europe, North and South America, Native Americans, Mexican Americans

Advancing age

Female sex hormones

Female gender

Oral contraceptives

Pregnancy

Obesity

Rapid weight reduction

Gallbladder stasis

Inborn disorders of bile acid metabolism

Hyperlipidemia syndromes

Pigment Stones اي مرض يسبب انتاج اكبر للبيليروبين - more in rich countries

Demography: Asian more than Western, 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

1st: Pathogenesis of Cholesterol Stones

- Cholesterol is rendered soluble in bile by aggregation with water-soluble bile salts and water-insoluble lecithins, both of which act as detergents.
- *When cholesterol concentrations exceed the solubilizing capacity of bile (supersaturation), cholesterol can no longer remain dispersed (scattered or circulated) and nucleates into solid cholesterol monohydrate crystals.*

Pathogenesis of Cholesterol Stones

- *Cholesterol gallstone formation involves four simultaneous (Happening at the same time) defects:*
 - 1) *Supersaturation of bile with cholesterol is the result of hepatocellular hypersecretion of cholesterol.*
 - 2) *Gallbladder hypomotility ensues (to occur as a result). It promotes nucleation typically around a calcium salt crystal nidus.*
 - 3) *Cholesterol nucleation in bile is accelerated.*

Nidus: A point or place at which something originates, accumulates, or develops, as the center around which salts of calcium, uric acid, or bile acid form calculi

Pathogenesis of Cholesterol Stones

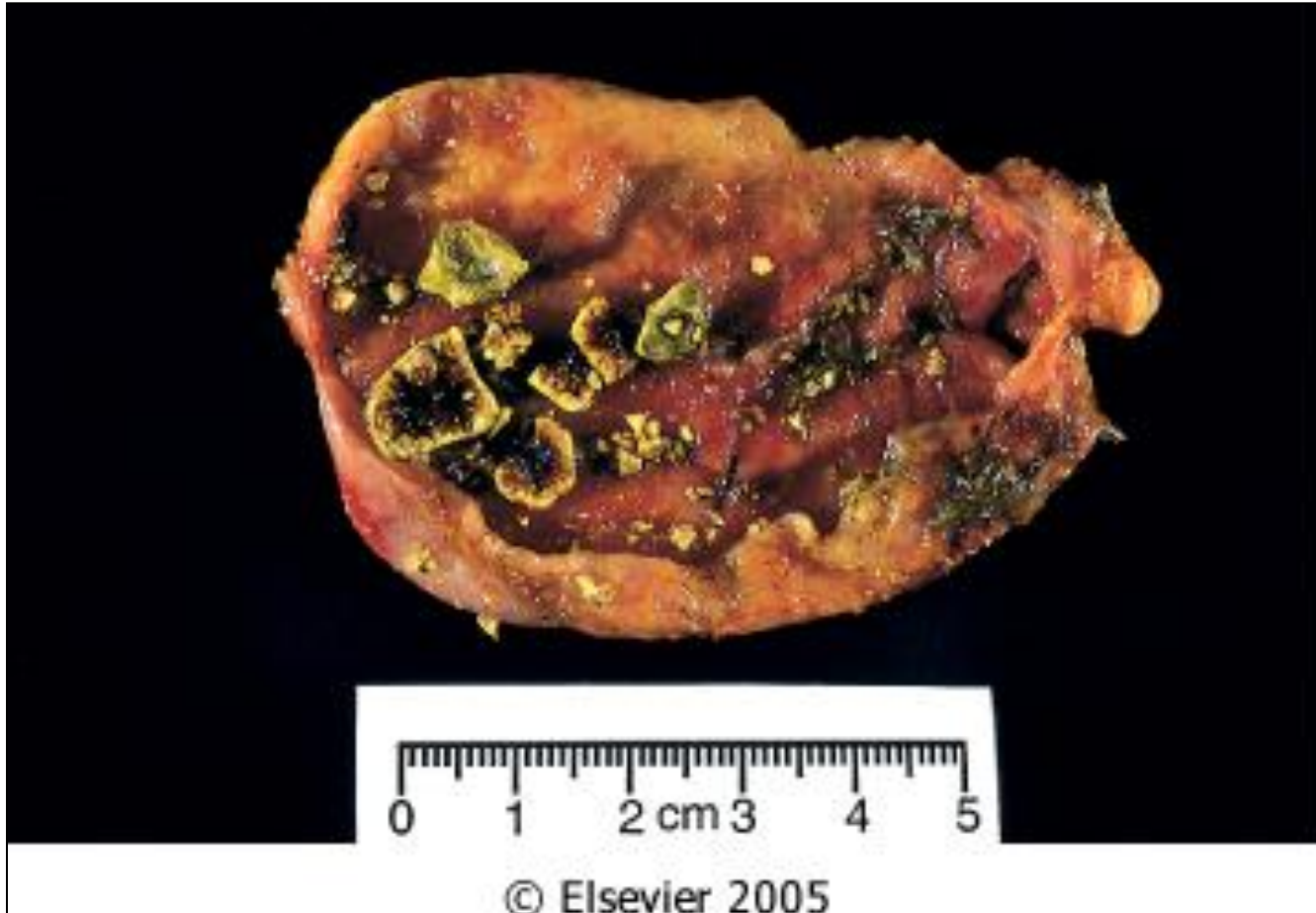
- 4) Mucus hypersecretion in the gallbladder traps the crystals, permitting their aggregation into stones.
- prolonged fasting, pregnancy, rapid weight loss, total parenteral nutrition ((no food passing through GI!)), and spinal cord injury also promote stone formation.

2nd: Pathogenesis of Pigment Stones

- Pathogenesis of pigment stones is based on the presence in the biliary tract of unconjugated bilirubin (which is poorly soluble in water) and precipitation of calcium bilirubin salts.
- Thus, infection of the biliary tract, as with *Escherichia coli* or *Ascaris lumbricoides* or by the liver fluke *Opisthorchis sinensis*, increases the likelihood of pigment stone formation.
- Chronic hemolytic conditions also promote formation of unconjugated bilirubin in the biliary tree.

Morphology

- 1- Cholesterol stones** arise exclusively in the gallbladder and are composed of cholesterol ranging from 100% pure (which is rare) down to around 50%.
- pale yellow, round to ovoid to faceted, and have a finely granular, hard external surface.
 - **Stones composed largely of cholesterol are radiolucent; only 10% to 20% of cholesterol stones are radio-opaque.**



Morphology

2- Pigment gallstones are black and brown.

- "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 radio-opaque.**



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Cholesterolosis

- An incidental finding, is **cholesterolosis**. 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 Cholesterolosis

- 70% to 80% of patients remain asymptomatic throughout their lives.
- Symptoms: spasmodic or "colicky" right upper quadrant pain (radiating to the right shoulder), which tends to be excruciating . It is usually due to obstruction of bile ducts by passing stones.

Colic is a form of pain which starts and stops abruptly.

Clinical Features

○ Complications of Cholesterolosis:

- Empyema تجمع الصديد
- Perforation
- Fistula
- Inflammation of the biliary tree (cholangitis)
- Obstructive cholestasis
- Pancreatitis (by small stones)

Clinical Features of Cholesterolosis

- 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, or "gravel," that are the more dangerous.** Occasionally, a large stone may erode directly into an adjacent loop of small bowel, generating intestinal obstruction (**"gallstone ileus"**).
- **Increased risk for carcinoma of the gallbladder**

CHOLECYSTITIS

- Means: Inflammation of the gallbladder.
- may be
 - acute
 - chronic
 - acute superimposed on chronic.
(chronic disease with acute attacks)
- It almost always occurs in association with gallstones.

1. Acute Cholecystitis

- *Acute calculous cholecystitis is an acute inflammation of the gallbladder, precipitated 90% of the time by obstruction of the neck or cystic duct.*

It is the primary complication of gallstones and the most common reason for emergency cholecystectomy.

- Acute acalculous cholecystitis occurs in the absence of gallstones, generally in severely ill patient. Most cases of occur in the following circumstances:
 - (1) the postoperative state after major, nonbiliary surgery;
 - (2) severe trauma (motor vehicle accidents, war injuries);
 - (3) severe burns;
 - (4) multisystem organ failure;
 - (5) sepsis;
 - (6) prolonged intravenous hyperalimentation;
 - (7) the postpartum state.

Calculous : describing a substance that has the hardness of stone.

Acalculous: The opposite meaning without stones

Acute Cholecystitis: Pathogenesis.

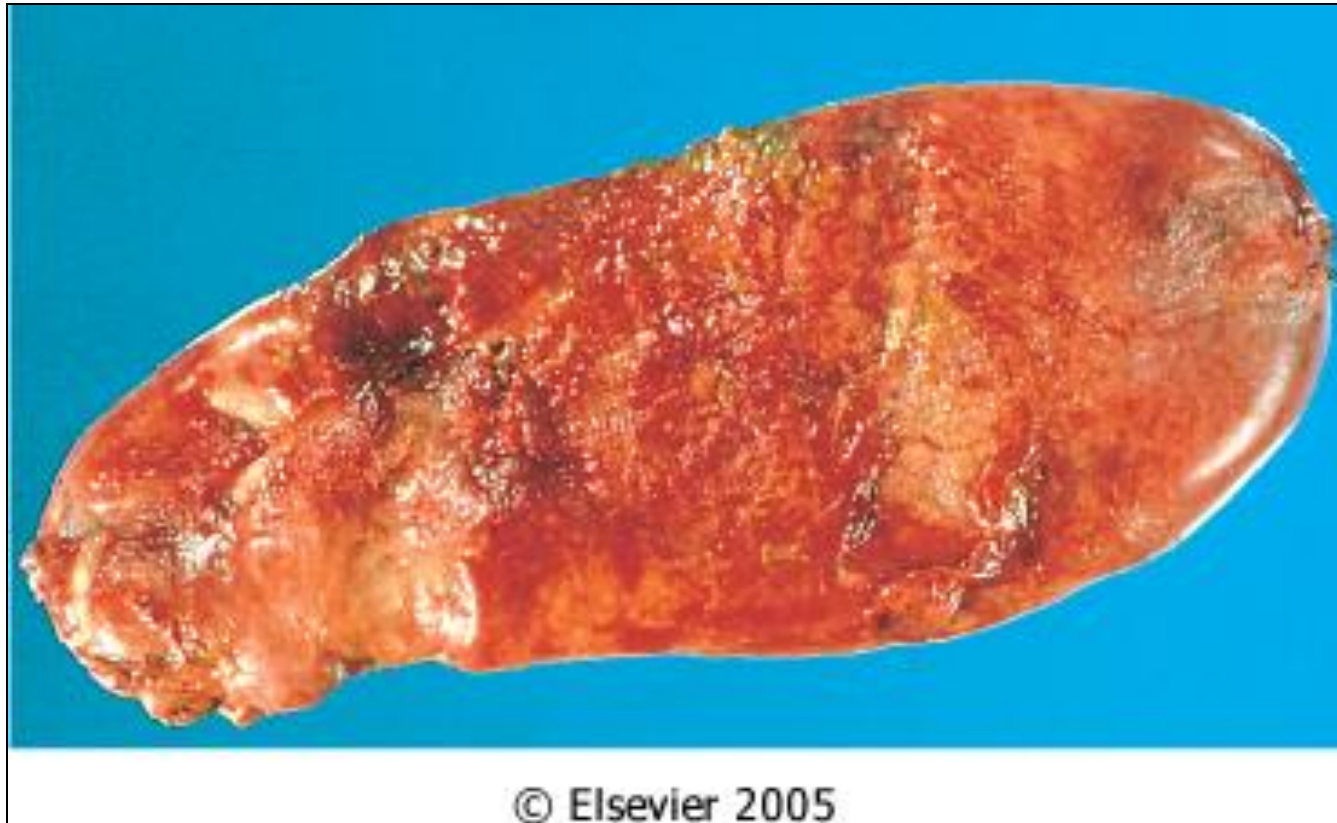
- **Acute Calculous cholecystitis**:
results from **chemical irritation and inflammation** of the obstructed gallbladder.
These events occur in the absence of bacterial infection; only later in the course may bacterial contamination develop.

Acute Cholecystitis: Morphology

- In **acute cholecystitis**, the gallbladder is usually **enlarged** and tense, and bright red to green-black. The serosal covering is frequently layered by fibrin and, in severe cases, by exudate.
- There are no morphologic differences between acute acalculous and calculous cholecystitis, except for the absence of macroscopic stones in the former (acalculous). In the latter instance (calculous), an **obstructing stone is usually present in the neck of the gallbladder or the cystic duct.**

Acute Cholecystitis: Morphology

- The gallbladder lumen is filled with a cloudy or turbid bile that may contain fibrin and frank pus, as well as hemorrhage. When the contained exudate is virtually pure pus, the condition is referred to as **empyema of the gallbladder**.
- In mild cases, the gallbladder wall is thickened, edematous, and hyperemic (having a large volume of blood in any given place in the body).
- In more severe cases, it is transformed into a green-black necrotic organ, termed **gangrenous cholecystitis**, with small-to-large perforations.



Acute Cholecystitis: Clinical Features

- Progressive right upper quadrant pain(**radiating to the right shoulder**) or epigastric pain, frequently associated with mild fever, anorexia, tachycardia, sweating, and nausea and vomiting. The upper abdomen is tender. Most patients are free of jaundice
- ***Acute calculous cholecystitis*** may appear with remarkable suddenness and constitute an acute surgical emergency or may present with mild symptoms that resolve without medical intervention.

Acute Cholecystitis: Clinical Features

- Clinical symptoms of **acute acalculous cholecystitis** tend to be more insidious (**dangerous**), since symptoms are obscured by the underlying conditions precipitating the attacks (**remember the 7 conditions mentioned earlier**). 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.

2.Chronic cholecystitis

- Chronic cholecystitis may be a sequel (a result of) to repeated bouts (attacks) 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.

Chronic cholecystitis

- 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, and postprandial epigastric distress, sometimes include nausea and vomiting.

Biliary colic: (blockage by a gallstone of the common bile duct or cystic duct)
postprandial : means after eating a meal

Chronic Cholecystitis: Morphology

- The morphologic changes in chronic cholecystitis are extremely variable and sometimes minimal.
- Gall bladder may be **contracted** (fibrosis), **normal in size or enlarged** (from obstruction). The wall is variably thickened. Stones are frequent.

Chronic Cholecystitis: Morphology

- On histology, the degree of inflammation is variable. Outpouchings of the mucosal epithelium through the wall (**Rokitansky-Aschoff sinuses**) << (no dysplasia) may be quite prominent.
- Rarely, extensive **dystrophic calcification** within the gallbladder wall may yield:
porcelain gallbladder بسبب زياده ترسب الكالسيوم – مهمه جدا , notable for a markedly increased incidence of associated cancer.
- **Xanthogranulomatous cholecystitis** is also a rare condition in which the gallbladder is shrunken, nodular, fibrosed and chronically inflamed with abundant lipid filled macrophages.
- Finally, an atrophic, chronically obstructed gallbladder may contain only clear secretions, a condition known as **hydrops of the gallbladder**.



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Complications: Acute And Chronic Cholecystitis

- Bacterial superinfection with cholangitis or sepsis
- GB (gall bladder) perforation & local abscess formation
- GB rupture with diffuse peritonitis
- Biliary enteric (cholecystenteric) fistula with drainage of bile into adjacent organs, and potentially gallstone-induced intestinal obstruction (ileus)
- Aggravation of pre-existing medical illness, with cardiac, pulmonary, renal, or liver decompensation