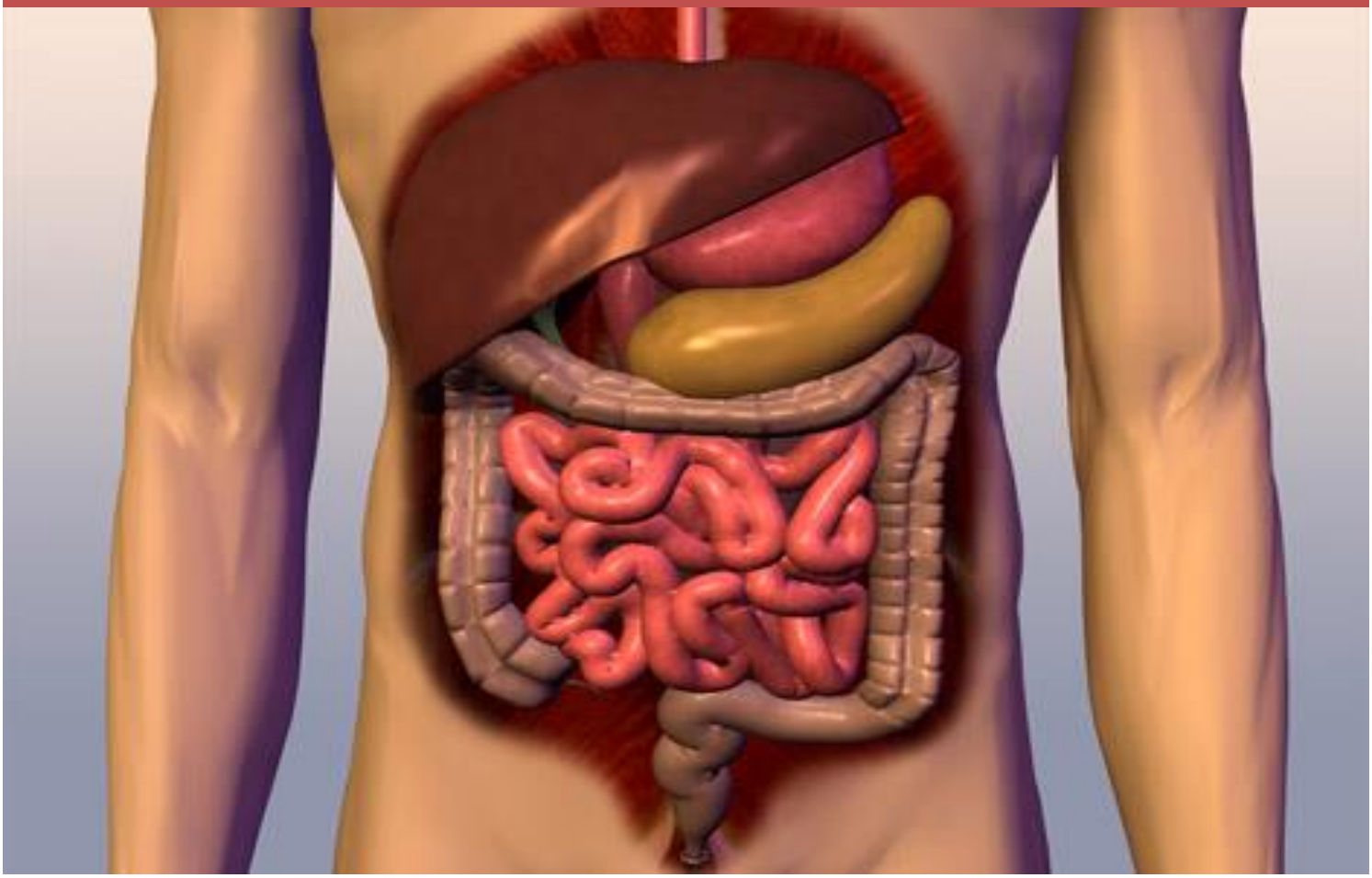


Lecture 13

Cholecystitis

*432 **Pathology** Team*

***Done By: Abdulrahman** Al-Zahrani*

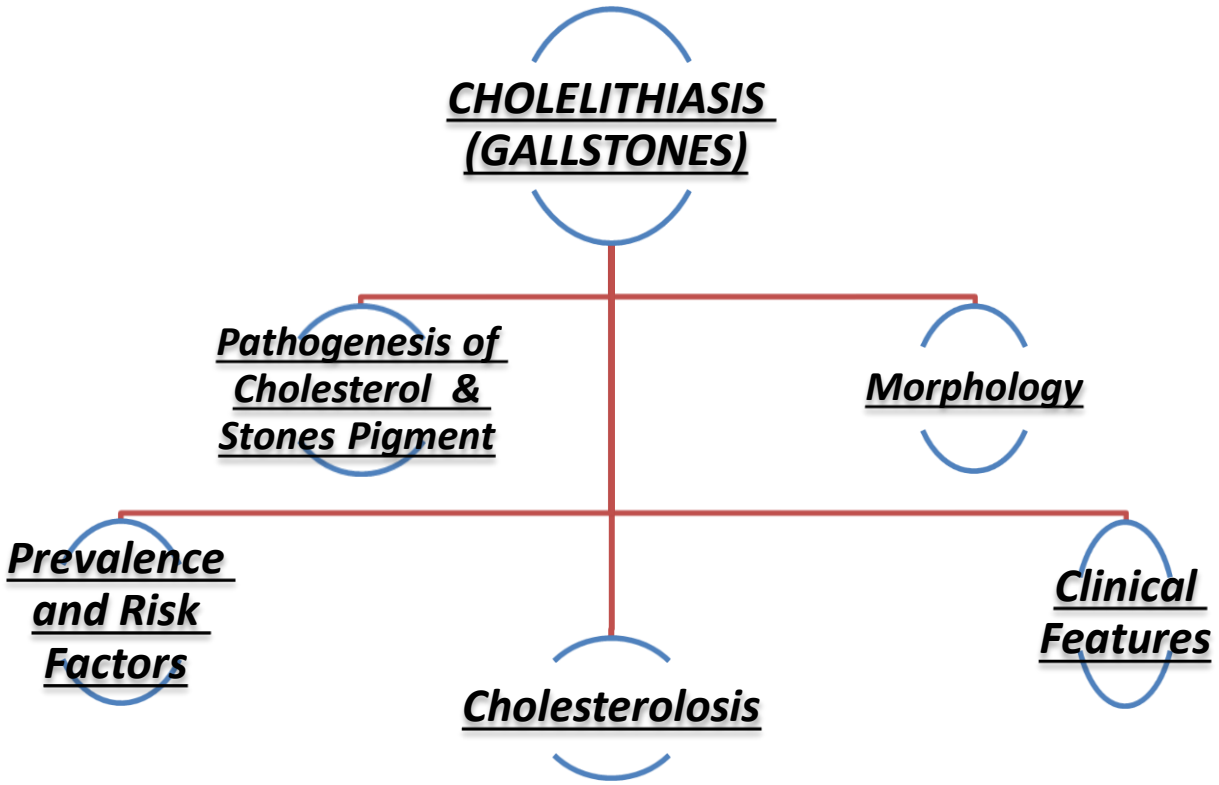
***Reviewed By: Raghad** Al-Motlaq*

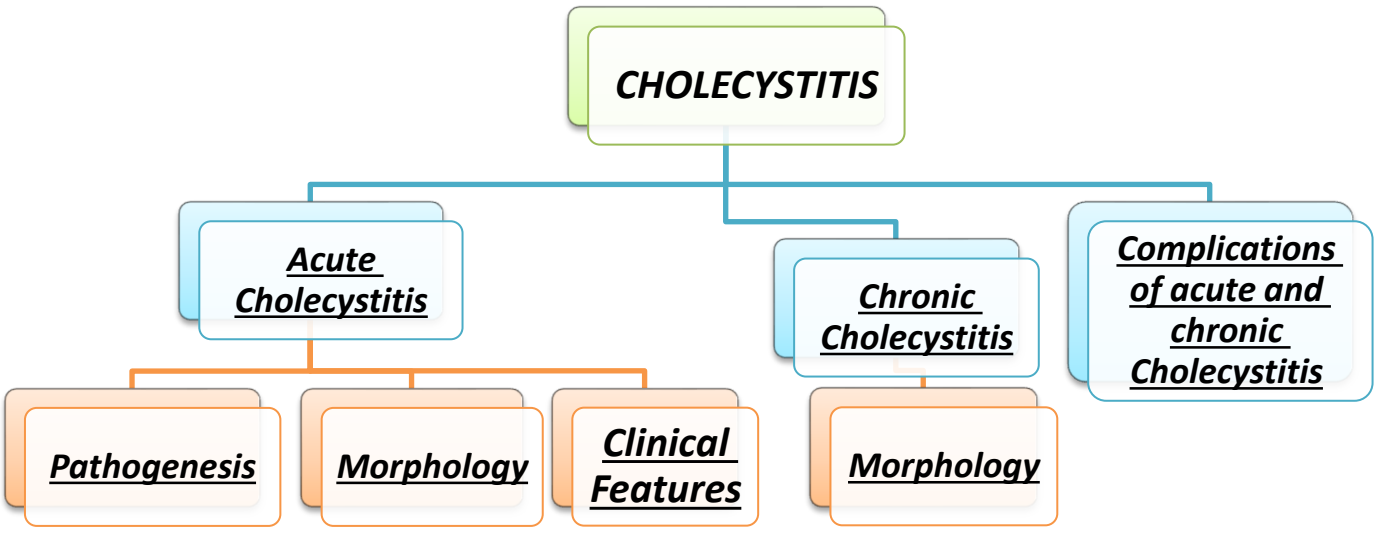
GIT Block

Color Index: Female notes are in Green. Male notes are in Blue. Red is important. Orange is explanation.

Pathology and Pathogenesis of Cholecystitis

Mind Map: *The lecture is formed of two parts: Cholelithiasis & Cholecystitis.*





Disorders of the Gallbladder *CHOLELITHIASIS (GALLSTONES)*

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 ***pigment stones*** *(composed predominantly of bilirubin calcium salts and are designated)*.

Prevalence and Risk Factors:

Cholesterol Stones

- **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. (There will be dehydration and increase cholesterol levels)**
- **Gallbladder stasis.**
- **Inborn disorders of bile acid metabolism.**
- **Hyperlipidemia syndromes.**

To summarize Any increase in cholesterol levels could be a risk factor.

Pigment Stones

- **Demography: Asian more than Western, rural more than urban.**
- **Chronic hemolytic syndromes. (most common)**
- **Biliary infection.**
- **Gastrointestinal disorders: ileal disease (e.g., Crohn disease), ileal resection or bypass, cystic fibrosis with pancreatic insufficiency.**

REMEMBER: **The most important risk is the five Fs. *Female*, *Fair* (white women), *Fat* (overweight); *Forty* (age near or above 40), *Fertile* (premenopausal- increased estrogen is thought to increase cholesterol levels in bile and decrease gallbladder contractions)**

Pathogenesis of Cholesterol Stones:

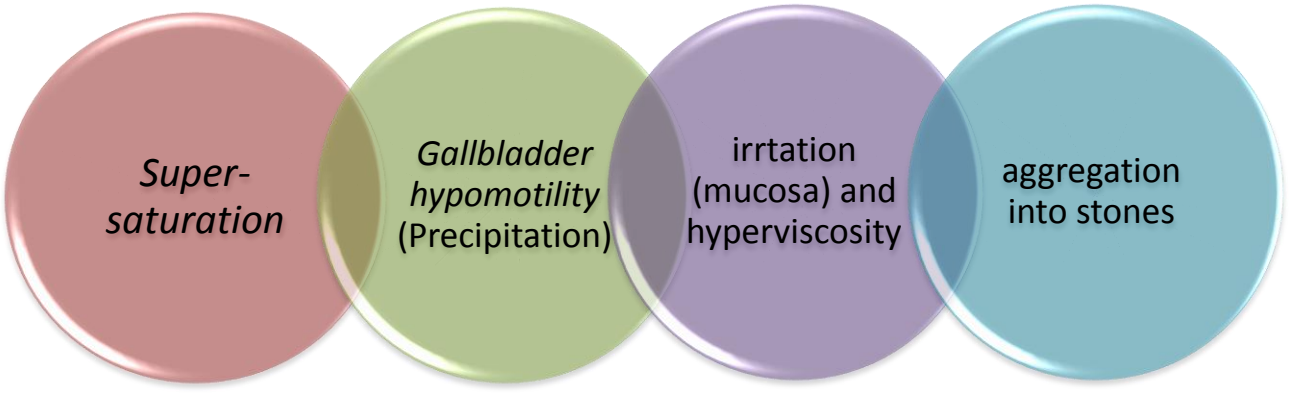
Bile formation is the only significant pathway for elimination of excess cholesterol. Cholesterol is rendered soluble in bile by aggregation with water-soluble bile salts and water-insoluble lecithins, both of which act as detergents. *When cholesterol concentrations exceed the solubilizing capacity of bile (super-saturation) [lead to stasis], cholesterol can no longer remain dispersed and nucleates (accumulates) into solid cholesterol monohydrate crystals.*

***Cholesterol gallstone formation involves four simultaneous defects*:**

1) *Supersaturation of bile with cholesterol is a result of hepatocellular hypersecretion of cholesterol.*
2) *Gallbladder hypomotility ensues (stasis).* It promotes nucleation (ترسب) 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.

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:

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 (when it contains calcium because it absorbs all the beams and reflex nothing. Like in bones).

Cholesterol gallstones.
Mechanical manipulation during laparoscopic cholecystectomy has caused fragmentation of several cholesterol gallstones, revealing interiors that are pigmented because of entrapped bile pigments. The gallbladder mucosa is reddened and irregular as a result of coexistent acute and chronic cholecystitis.

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.**

Pigmented gallstones.
Several faceted black gallstones are present in this otherwise unremarkable gallbladder removed from a patient who had a mechanical mitral valve prosthesis, leading to chronic intravascular hemolysis.

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" (projection like) gallbladder.

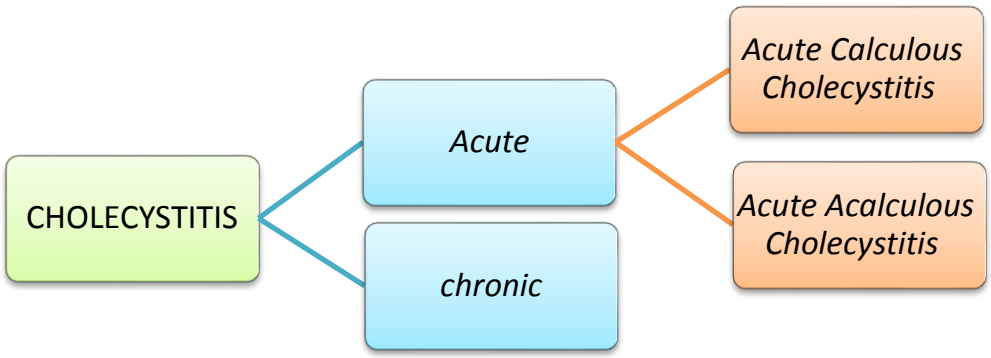
Clinical Features:

- 70% to 80% of patients remain asymptomatic throughout their lives.
- Symptoms: spasmodic or "colicky مغص" right upper quadrant pain, which tends to be excruciating. It is usually due to **obstruction** of bile ducts by passing stones.
- More severe complications include empyema*, perforation, fistulae, inflammation of the biliary tree (cholangitis), and obstructive cholestasis or pancreatitis with ensuing problems.
- 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.

***REMEMBER:**
Empyema: is a collection of pus within a naturally existing anatomical cavity

CHOLECYSTITIS

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



I. Acute Cholecystitis:

Acute ***Calculous*** **(with stone)** *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. (Sometimes patients' need surgery, but most of the time they don't)

Acute ***Acalculous*** **(without stone)** *Cholecystitis* occurs in the absence of gallstones, generally in severely ill patient. Most cases of occur in the following circumstances:

- ✓ The postoperative state after major, non-biliary surgery.
- ✓ Severe trauma (motor vehicle accidents, war injuries).
- ✓ Severe burns.
- ✓ Multisystem organ failure.
- ✓ Sepsis.
- ✓ Prolonged intravenous hyperalimentation.
- ✓ The postpartum state.

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.

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. In the latter instance, an obstructing stone is usually present in the neck of the gallbladder or the cystic duct.
- 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.
- In more severe cases, it is transformed into a green-black necrotic organ, termed **gangrenous cholecystitis**, with small-to-large perforations.

NOTE: ***Acute Cholecystitis*** **usually comes with edema while** ***Chronic Cholecystitis*** **comes with fibrosis.**

II. 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 (تجشؤ) and postprandial (بعد الاكل) epigastric distress, sometimes include nausea and vomiting.

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.

- On histology, the degree of inflammation is variable. Outpouchings of the mucosal epithelium through the wall (***Rokitansky-Aschoff sinuses***) may be quite prominent.
- Rarely, extensive dystrophic calcification within the gallbladder wall may yield a ***porcelain gallbladder***, 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 with macrophages.
- Finally, an atrophic, chronically obstructed gallbladder may contain only clear secretions, a condition known as ***hydrops of the gallbladder.***

NOTE: *The histological difference between Acute and Chronic:*

Acute → neutrophils + fibroblast proliferation ---Chronic → fibroblast proliferation only

Clinical Features:

- ✓ Progressive right upper quadrant 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.
- ✓ Clinical symptoms of ***acute acalculous cholecystitis*** tend to be 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.

Complications of acute and chronic Cholecystitis:

- Bacterial superinfection with cholangitis or sepsis.
- Gallbladder perforation & local abscess formation.
- Gallbladder 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.

Summary From Robbins:

Diseases of the Gallbladder and Extrahepatic Bile Ducts

- Gallbladder diseases include cholelithiasis and acute and chronic cholecystitis.
- Gallstone formation is a common condition in Western countries. The great majority of the gallstones are cholesterol stones. Pigmented stones containing bilirubin and calcium are most common in Asian countries.
- Risk factors for the development of cholesterol stones are advancing age, female gender, estrogen use, obesity, and heredity.
- Cholecystitis almost always occurs in association with cholelithiasis, although in about 10% of cases it occurs in the absence of gallstones.
- Acute calculous cholecystitis is the most common reason for emergency cholecystectomy.
- Obstructive lesions of the extrahepatic bile ducts in adults can give rise to ascending infection (cholangitis) and secondary biliary cirrhosis.
- Infants born with congenital biliary atresia present with neonatal cholestasis and require liver transplantation for cure.

Questions

1/ A 47-year-old woman presents with a 3-month history of vague upper abdominal pain after fatty meals, some abdomi- nal distension, and frequent indigestion. Physical examination shows an obese woman (BMI = 30kg/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

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

- Asymptomatic (silent)

5/ in which case we might see a strawberry gall bladder?

- Cholesterolosis

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

- Gangrenous cholecystitis.

Answers:

1- A
2- D
3- A

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us: 432PathologyTeam@gmail.com