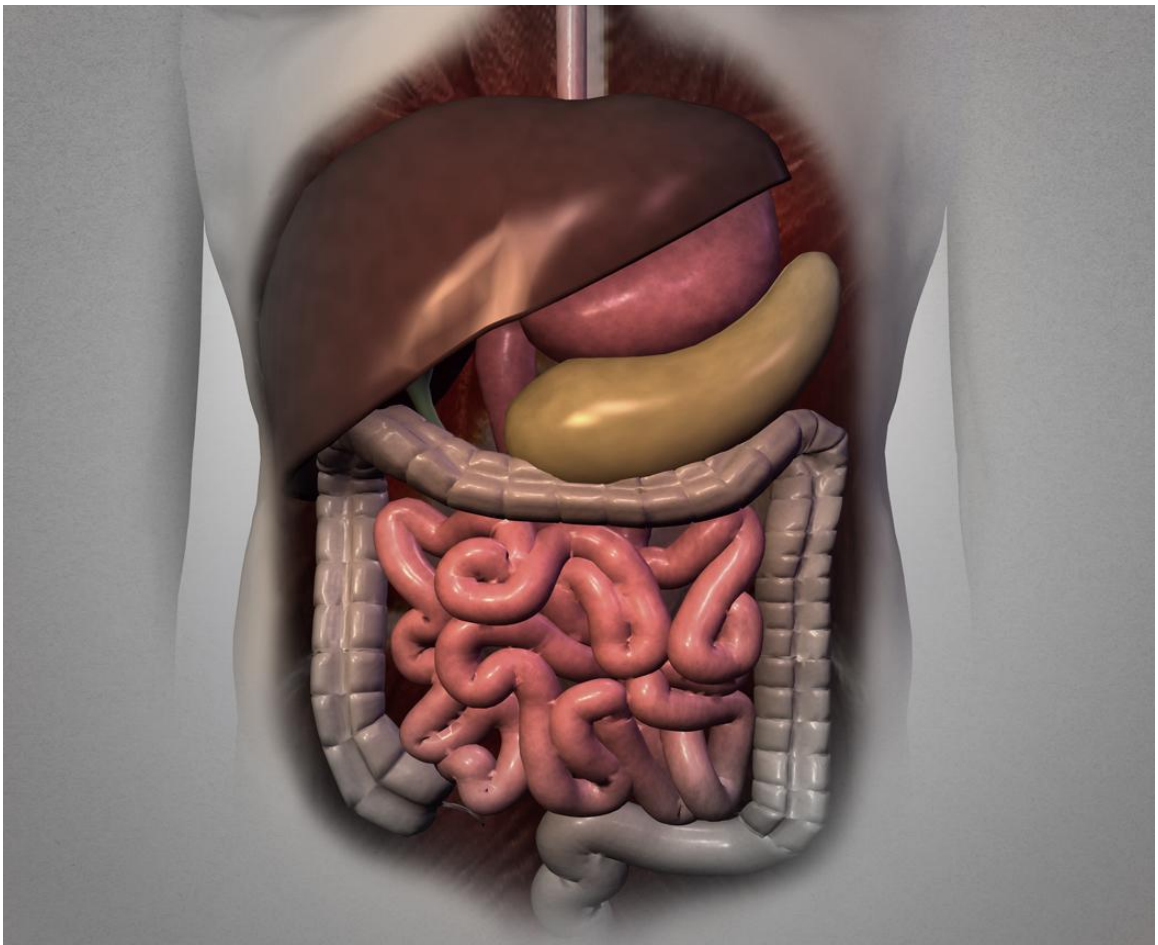

GIT Block

Physiology Team 431

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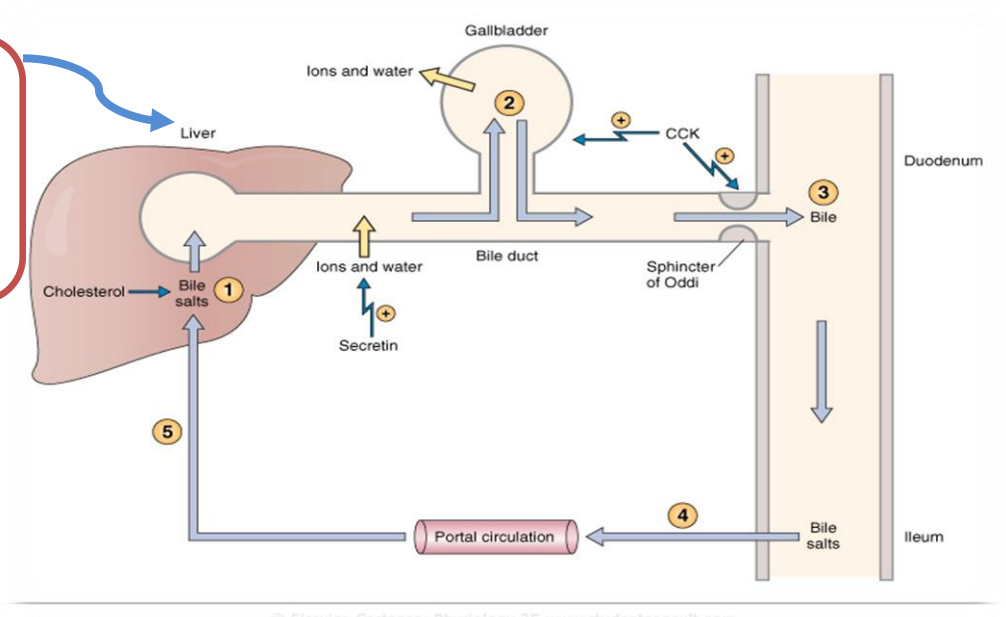
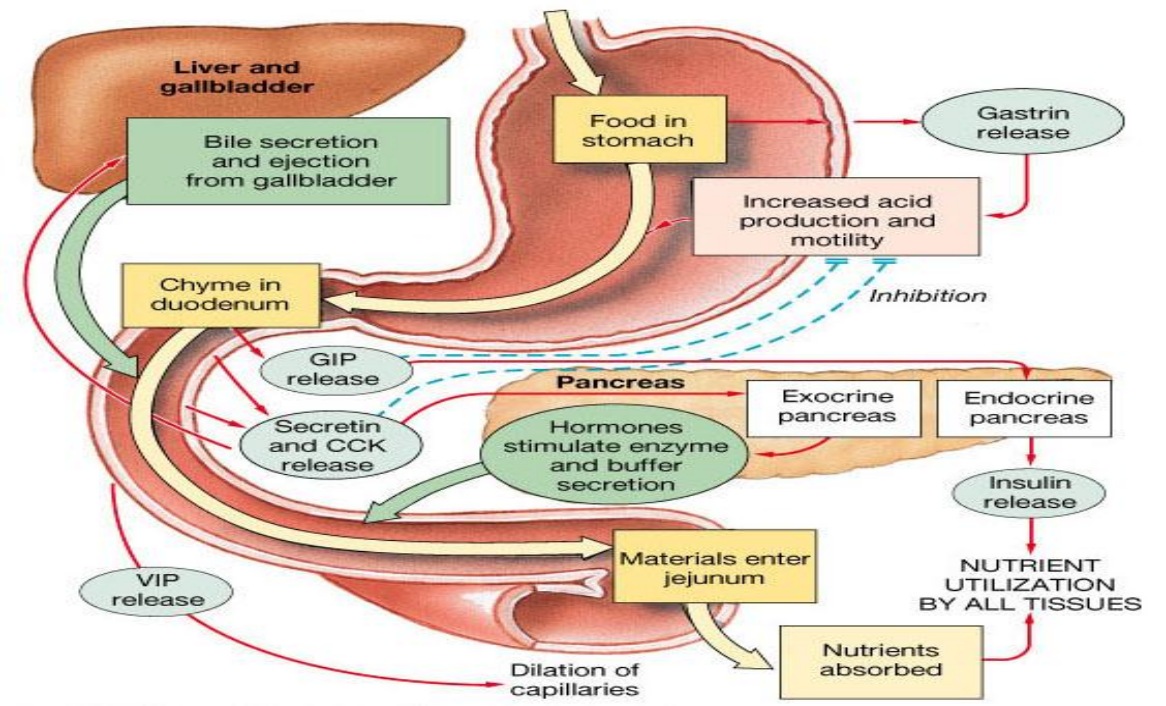
Female slides

Bile acids (bile salts):

- **Bile secretion is primarily regulated by a feedback mechanism, with secondary hormonal and neural controls:**
  - **The major determinant of bile acid synthesis is its concentration in hepatic portal blood (feedback control)**
  - **CCK, Secretin and estrogen (hormonal control)**
  - **Parasympathetic and sympathetic nerves supply the biliary system:**
    - ✓ **Parasympathetic (vagal): stimulation results in contraction of the gallbladder and relaxation of the sphincter of Oddi, as well as increased bile formation.**
    - ✓ **Bilateral vagotomy: results in reduced bile secretion after a meal, suggesting that the parasympathetic nervous system plays a role in mediating bile secretion.**
    - ✓ **By contrast, stimulation of the sympathetic nervous system results in reduced bile secretion and relaxation of the gallbladder.**

Secretion and enterohepatic circulation of bile salts





Q.What are the types of the bile acid

Q.What is the bile acid?

- **Bile acids** are formed in the liver from cholesterol. During the conversion, hydroxyl groups and a carboxyl group are added to the steroid nucleus.
- **Bile acids** are classified as primary or secondary. The hepatocytes synthesize the primary bile acids, which include cholic acid and chenodeoxycholic acid.
- **Bile acids** are secreted as conjugates of taurine or glycine. (the conjugation take place in the hepatocyte)
- When **bile** enters the GI tract, bacteria present in the lumen act on the primary bile acids and convert them to secondary bile acids by dehydroxylation. Cholic acid is converted to deoxycholic acid and chenodeoxycholic acid to lithocholic acid.

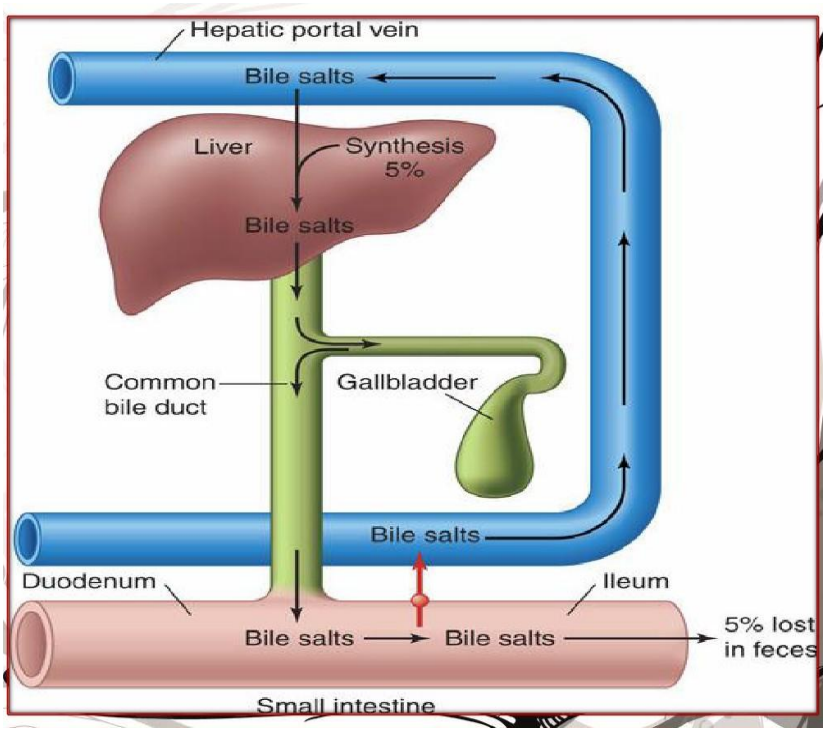
- **BUT** At a neutral pH (at bile duct or lumen of duodenum), the bile acids are mostly ionized (not like in hepatocyte) and are referred to as bile salts. Conjugated bile acids ionize more readily than the unconjugated bile acids and, thus, usually exist as salts of various cations (e.g., sodium glycocholate and potassium). (sodium and potassium are the usual salt that we have in the lap)
- Bile salts are much more polar than bile acids and have greater difficulty penetrating cell membranes (but that does not mean that we don't have bile salt back to the portal circulation, there is transporter mechanism carry the bile salt back to the portal circulation). Consequently, the small intestine absorbs bile salts much more poorly than bile acids (but there is some absorption). This property of bile salts is important because they play an integral role in the intestinal absorption of lipid. Therefore, it is important that the small intestine absorb bile salts only after all of the lipid has been absorbed.(which is usually take place in the illume)
- Bile acids are amphipathic that is having both hydrophilic & hydrophobic domains and tend to form molecular arrangement called micelles.
- In bile acid micelle, the hydrophobic side of bile acid faces inside & away from water. The hydrophilic surface faces outward towards the water.
- Bile acid micelles form when the conc. of bile acids exceed a certain limit (critical micelle conc.). Above this conc., any additional bile acid will join the micelle.
- Normally bile acid conc. in bile is much greater than critical micelle conc.

About 20-30 g of bile acids are poured into the duodenum /day.

♠ In the intestine, some of bile acids are deconjugated and dehydroxylated in the 7 α position by intestinal bacteria that normally colonize in the digestive tract.

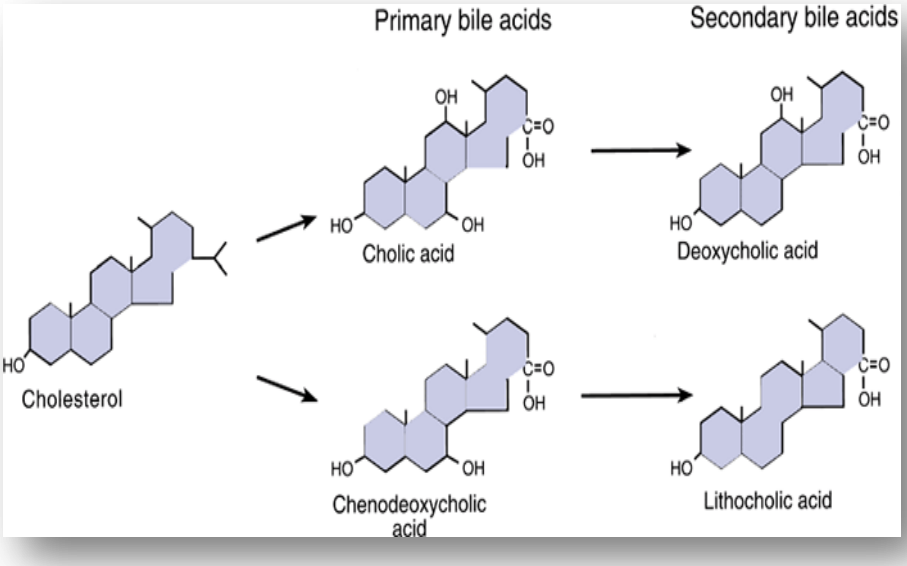
♠ Dehydroxylation results in the production of secondary bile acids. Cholic acid is converted to deoxycholic acid and chenodeoxycholic acid to lithocholic acid.

♠ On reaching the terminal ileum, 90 % of bile acids are absorbed and reach the liver through the portal vein.



- About 0.2-0.6 g of bile acids are lost in feces daily (15-35% of total bile acid pool)). These are replaced by new synthesis in liver so that thetotal bile acid pool is maintained constant at 2 - 4 g.
- Since the amount of bile acids poured into the duodenum each day is 20-30 g, the daily turnover of total bile acid pool through the enterohepatic circulation must be 6-10 times

Function of Bile Salts in Fat Digestion and Absorption



Bile acids are formed from cholesterol in the liver. Bile acids are conjugated with the amino acids glycine and taurine in the liver. At neutral pH, the bile acids are mostly ionized and referred to as bile salts.

- They have a detergent action (emulsifying) on the fat particles in the food which decreases the surface tension of the particles.
- They help in the absorption of fatty acids, monoglycerides, cholesterol, and other lipids from the intestinal tract.

Enterohepatic Circulation of Bile Salts. Bile Salts Are Recycled Between the Small Intestine and the Liver

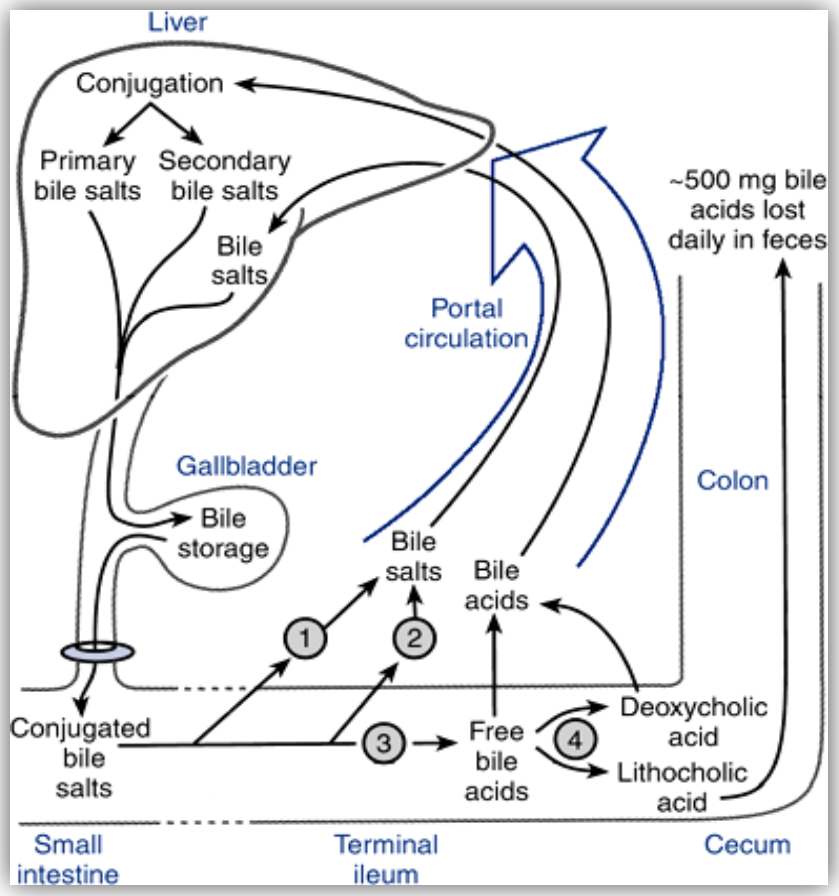
❖ The enterohepatic circulation of bile salts is the recycling of bile salts between the small intestine and the liver. The total amount of bile acids in the body, primary or secondary, conjugated or free, at any time is defined as the total bile acid pool.

- In healthy people, the bile acid pool ranges from 2 to 4 g.
- The enterohepatic circulation of bile acids in this pool is physiologically extremely important. By cycling several times during a meal, a relatively small bile acid pool can provide the body with sufficient amounts of bile salts to promote lipid absorption.

- N.B: Excess amount of bile acids entering the colon may result in diarrhea
- In a light eater, the bile acid pool may circulate three to five times a day; in a heavy eater, it may circulate 14 to 16 times a day.
- The intestine is normally extremely efficient in absorbing the bile salts by carriers located in the distal ileum.
- Inflammation of the ileum can lead to their malabsorption and result in the loss of large quantities of bile salts in the feces.
- Depending on the severity of illness, malabsorption of fat may result.

- Bile salts in the intestine lumen are absorbed via four pathways:

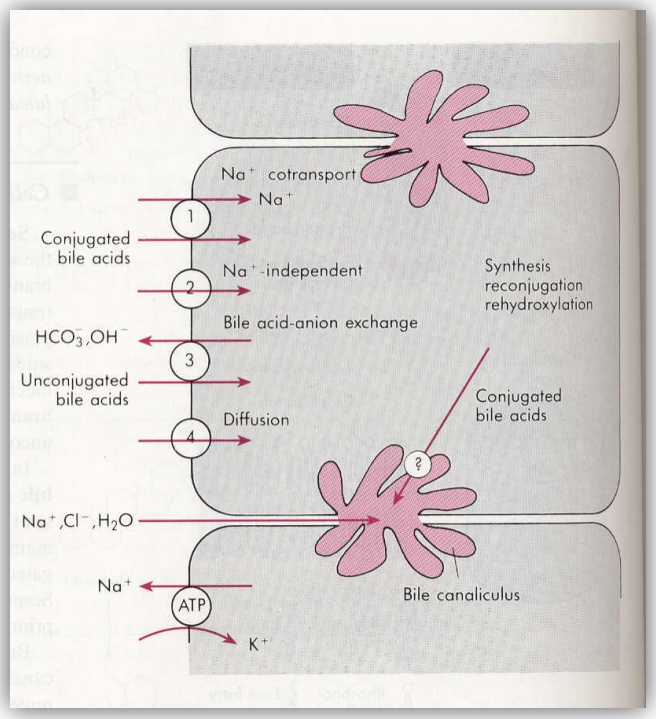
1. Passive diffusion.
2. An active carrier-mediated process.
3. De-conjugation of bile salts to bile acids .
4. Transforming the primary bile acids to secondary bile acids .



- Absorbed bile acids are carried away from the intestine in the portal blood, mostly bound to albumins.
- N.B: In the small intestine, cholic acid is absorbed faster than chenodeoxycholic acid, and primary bile acids are absorbed better than secondary bile acids.
- Some unconjugated bile acids are absorbed passively in the colon and reach the liver through portal vein.

Absorption of bile acids or bile salt back into hepatocytes

1. An active carrier-mediated process
2. Facilitated diffusion
3. Bile acid-HCO3 or OH exchange
4. Passive diffusion (very little)



- Hepatocytes extract bile acids, essentially clearing the bile acids from the blood in a single pass through the liver. In the hepatocytes, most deconjugated bile acids are reconjugated & some 2ry bile acids are rehydroxylated.
- The reprocessed bile acids, together with newly synthesized bile acids, are secreted into bile.

Functions of bile acid

1.Digestion of fats:- Bile salts have a detergent action that help fat digestion by decreasing fat surface tension resulting in emulsification of fats into small particles. This increase the surface area upon which the digestive enzymes will act.

2.Absorption of fats:- Bile salts combine with fats to form micelles (water soluble compounds) from which fatty acids,monoglycerides, cholesterol, and other lipids can be absorbed from the intestinal tract. Without the presence of bile salts in intestinal tract up to 40% of lipids are lost into the stools (steatorrhea).

3.bile acids are essential for absorption of fat soluble vitamins (A, D, E and K).

4.In the colon bile acids inhibit reabsorption of water & electrolytes, stimulate intestinal motility, prevent constipation & may cause diarrhea.

5.In the liver, bile salts are important for stimulating bile secretion and flow (choleretic action). They also take part in the formation of micells whichrender cholesterol soluble in bile.
6.Bile acids have a –ve feedback effect on the release of CCK from its cells in the upper intestine & thus contribute to the regulation of pancreatic secretion & the discharge of bile into intestine.
7.They have a –ve feedback effect on the synthesis of cholesterol by the intestinal mucosal cells.
8.Anti putrifactive: Bile acids have no direct anti septic effect but they prevent putrifaction by absorption of fat. In their absence undigested fats cover the protein particles & hinder their digestion.

Cholesterol secretion in bile

- 1-2g of cholesterol appears in bile per day. specific function is known for cholesterol in the bile & it is presumed that it is simply a byproduct of bile salt formation & secretion.
- is water insoluble; it is solubilized byincorporation in micelles along with the bile acids & phospholipid.

micelles remain stable so long as the concentration of bile acids, phospholipids & cholesterol remain within certain limits.
the relative concentration of any of the constituents alters, e.g. if bile contains more cholesterol than can be solubilized, (bile is supersaturated with cholesterol), cholesterol may be precipitated out of solution.people who produce bile with a high conc. of cholesterol, cholesterol gallstones may form in the gall bladder.

Types of gallstones

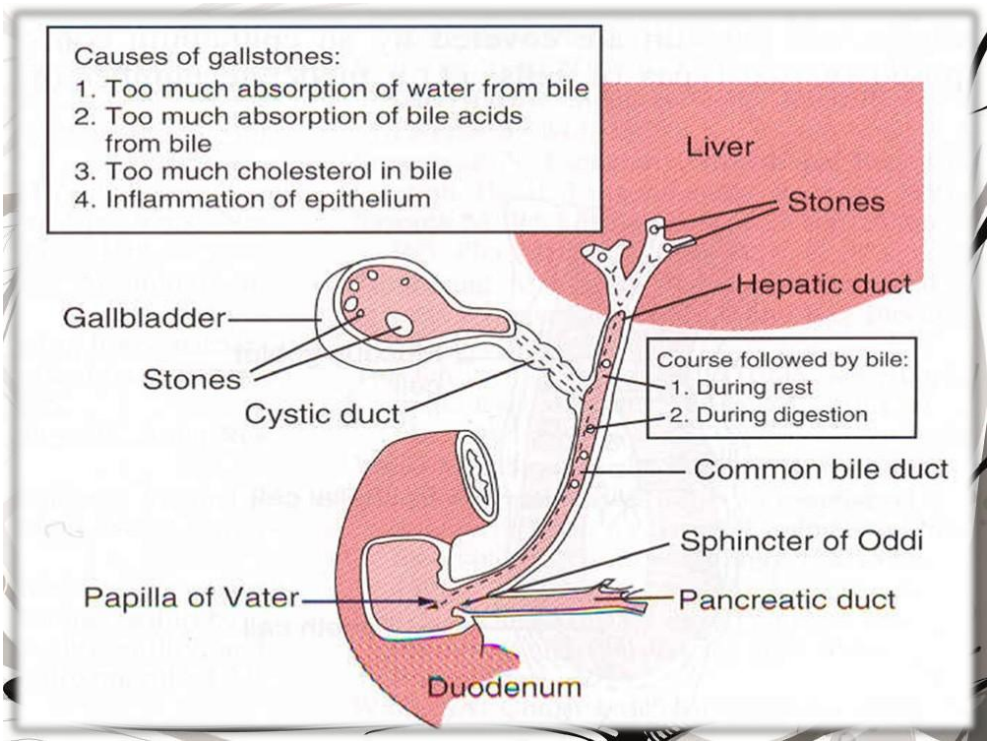
Gall stones may be formed in the gall bladder or bile ducts.

The commonest 2 types are:

1.Cholesterol stones:

under abnormal conditions the cholesterol may precipitate resulting in formation of cholesterol gallstones. The causes may be:

- Too much absorption of water from the bile.
- Too much absorption of bile salts & lecithin from bile.
- Too much secretion of cholesterol in bile.
- Inflammation of the epithelium of the gall bladder that often results from chronic infection which changes the absorptive characteristics of gall bladder mucosa allowing excessive absorption of water & bile salts that are necessary to keep cholesterol in solution.



2.Calcium bilirubinate stones:

The main constituent is calcium salt of unconjugated bilirubin.
In liver diseases, bile may contain elevated levels of unconjugated bilirubin. Individuals with liver disease have an increased incidence of forming bile pigment stones.

Gallstones risk factors

Female, Fat, Forty, Fertile , Oral contraceptives , Obesity , Rapid weight loss, (gastric bypass pts) , Fatty diet , diabetes mellitus , Prolonged fasting , Ileal resection , Hemolytic states , Cirrhosis , Bile duct stasis (biliary stricture, congenital cysts, pancreatitis, sclerosing cholangitis) , Vagotomy , Hyperlipidemia.

Gallstones pathogenesis

Gallstones due to imbalance rendering cholesterol & calcium salts insoluble.

o Pathogenesis of cholesterol gallstones involves:
(1) cholesterol supersaturation in bile
(2) crystal nucleation
(3) stone growth.

o Black pigment stones: contain Ca++ salts, following hemolytic conditions or cirrhosis, found in the gallbladder.

o Brown pigment stones: Asians, contain Ca++ palmitate, found in bile ducts, following biliary dysmotility and bacterial infection.

Effect of cholecystectomy

bile(not the gall bladder) is essential for digestion.
After removal of the gall bladder bile empties slowly but continouslly to the intestine allowing digestion of fats sufficient to maintain good health & nutrition.
Only high fat meals need to be avoided

Questions

1- Which one of the following conditions is associated with increased incidence of gall stones formation?

A. Male gender
B. Malnutrition
C. Increased gall bladder motility
D. Obesity

2- In patient with chronic hemolytic anemia, which one of the following stone types is predominantly seen in the gall bladder?

A. Cholesterol stones
B. Calcium oxalate stones
C. black pigment stones
D. Urate stones

3- Which one of the following is not function of bile acid

A. Digestion of fats
B. Absorption of fats
C. Stimulate reabsorption of water and electrolyte In the colon
D. Stimulating bile secretion

Answers

1- D
2- C
3- C