

Biochemical Aspects of Bile Acids and Salts

GNT block

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Objectives

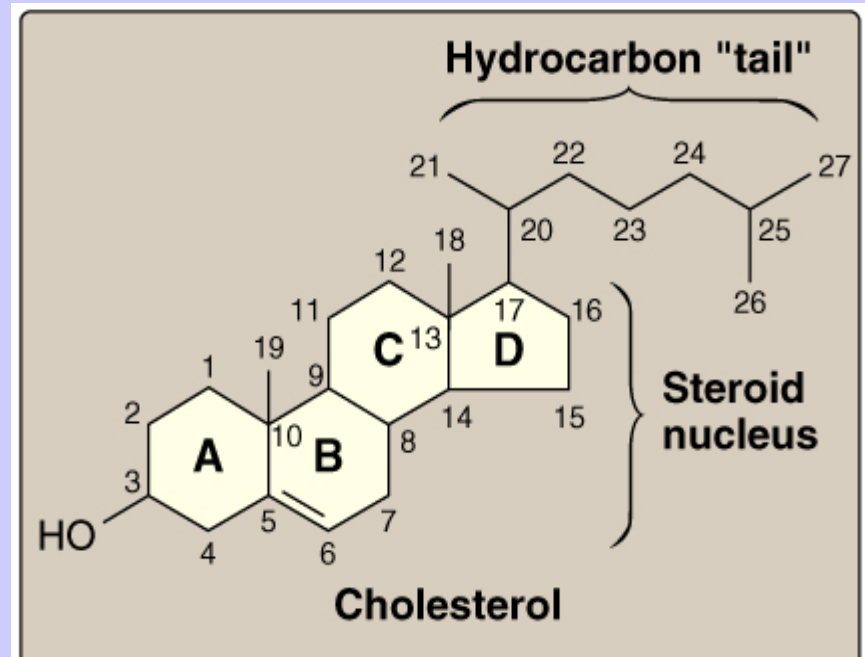
- Structure of primary bile acids and salts
- Structure of secondary bile acids and salts
- Functions of bile salts
- Enterohepatic circulation
- Malabsorption syndrome
- Cholelithiasis

Cholesterol

Cholesterol (27 C) is the:

Parent steroid compound

Precursor of bile acids and salts



Primary Bile Acids

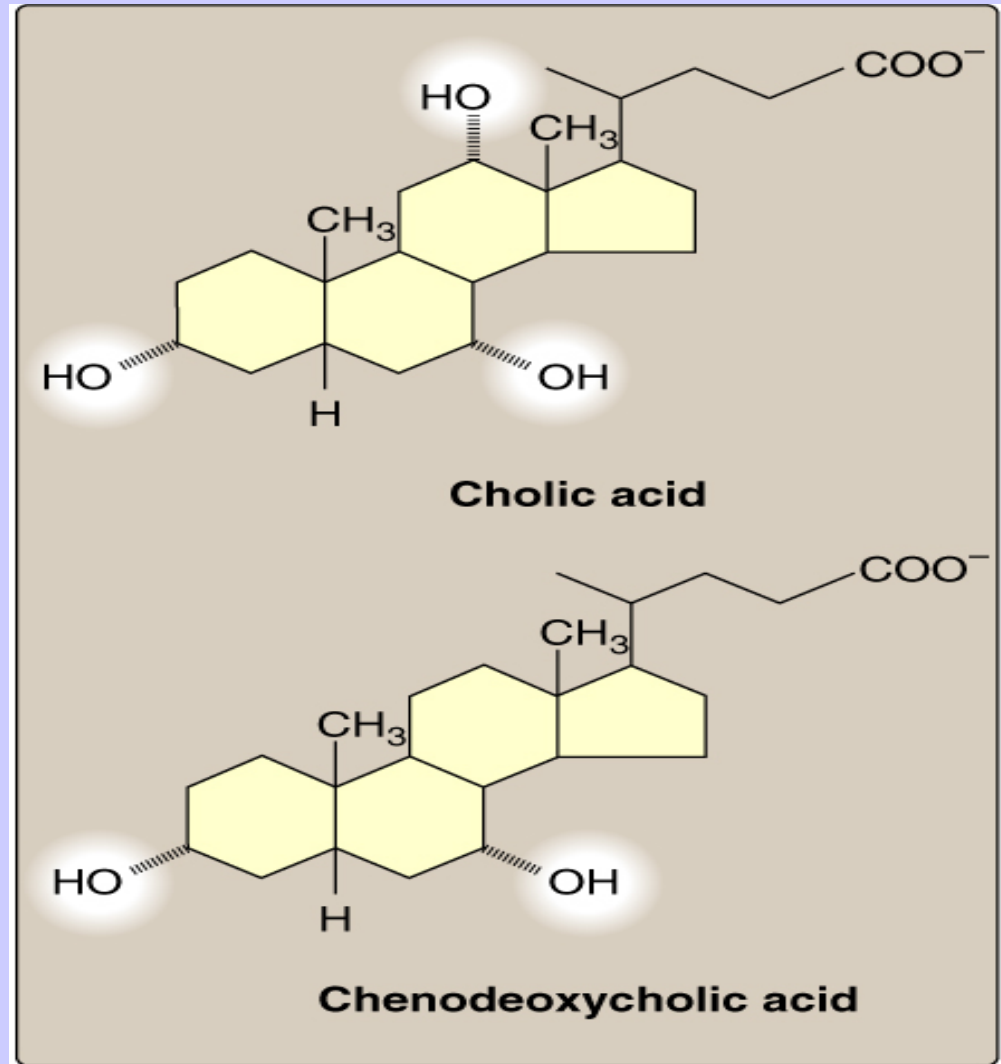
Primary bile acids (24 C):

Amphipathic

-COOH at side chain

Cholic acid: 3 OH

Chenodeoxycholic: 2 OH



Hepatic Synthesis of Bile Acids

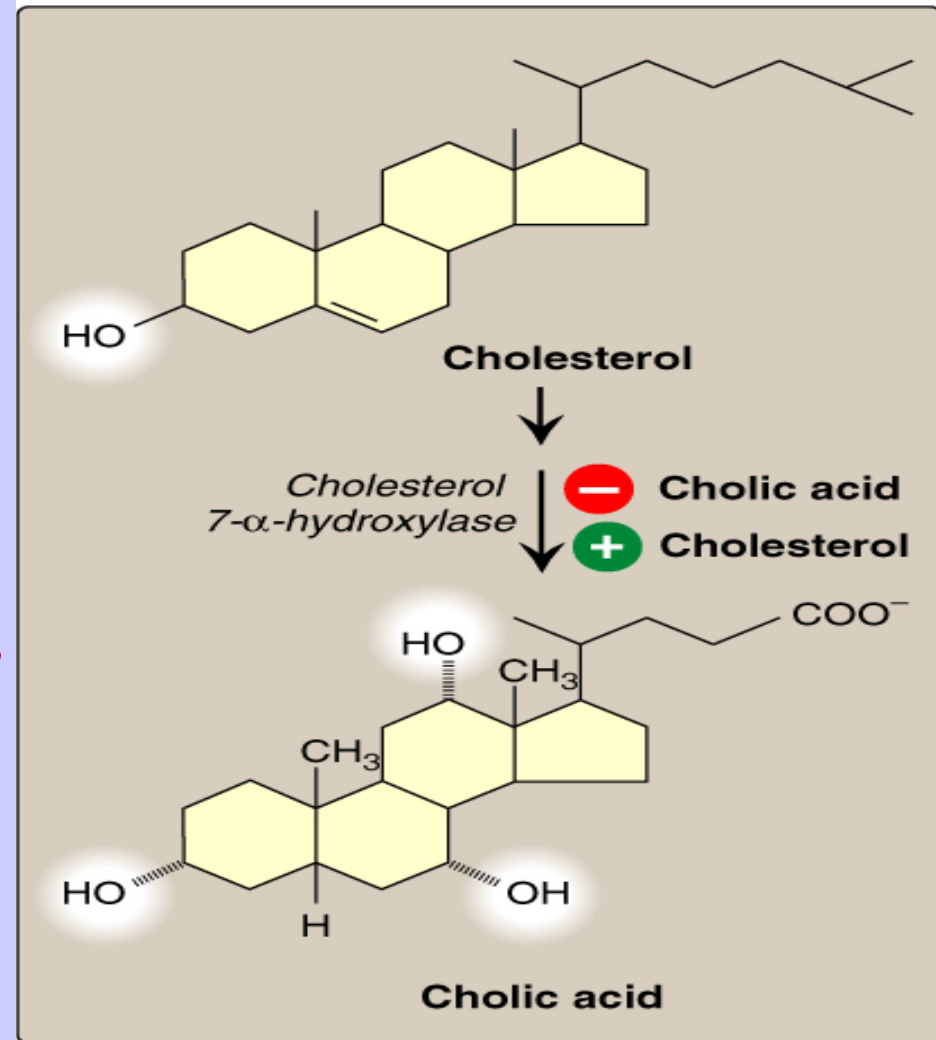
The rate-limiting step is catalyzed by:

Cholesterol 7- α -hydroxylase

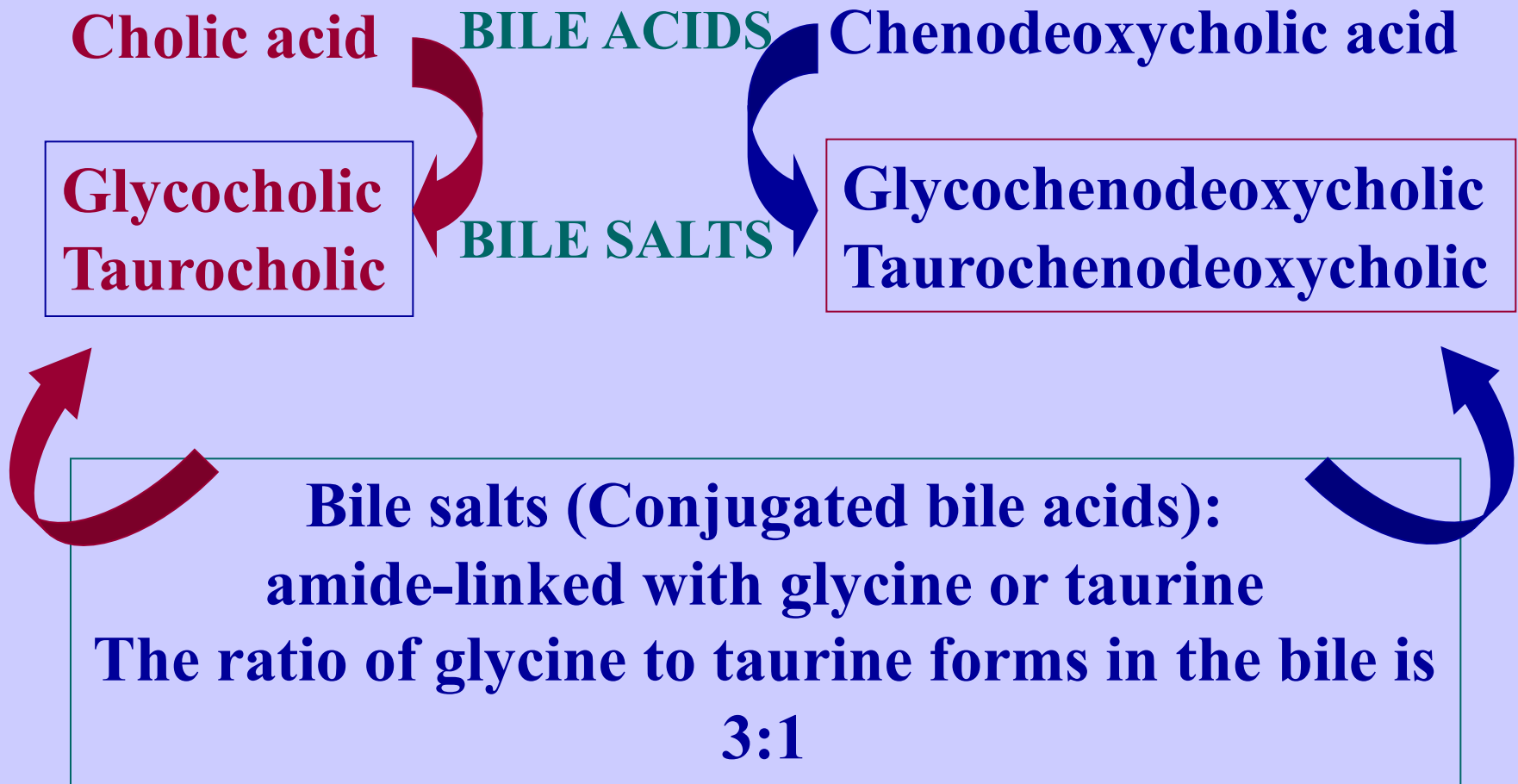
Regulation:

Down-regulated by end products (bile acids) “Enzyme repression”

Up-regulated by cholesterol “Enzyme induction”



Primary Bile Acids and Salts

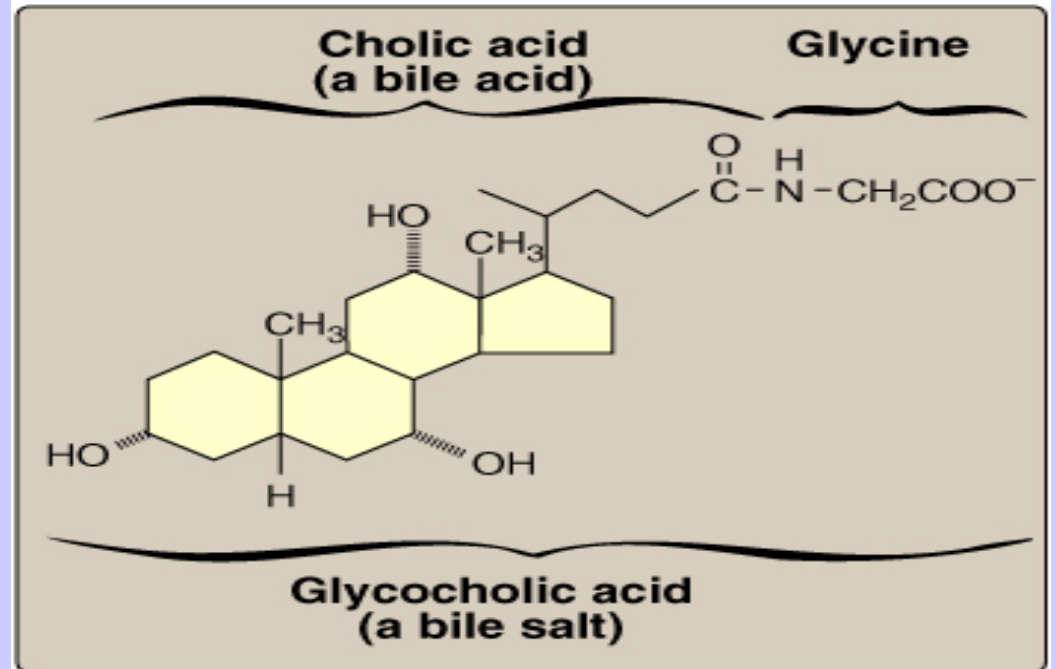


Bile Salts

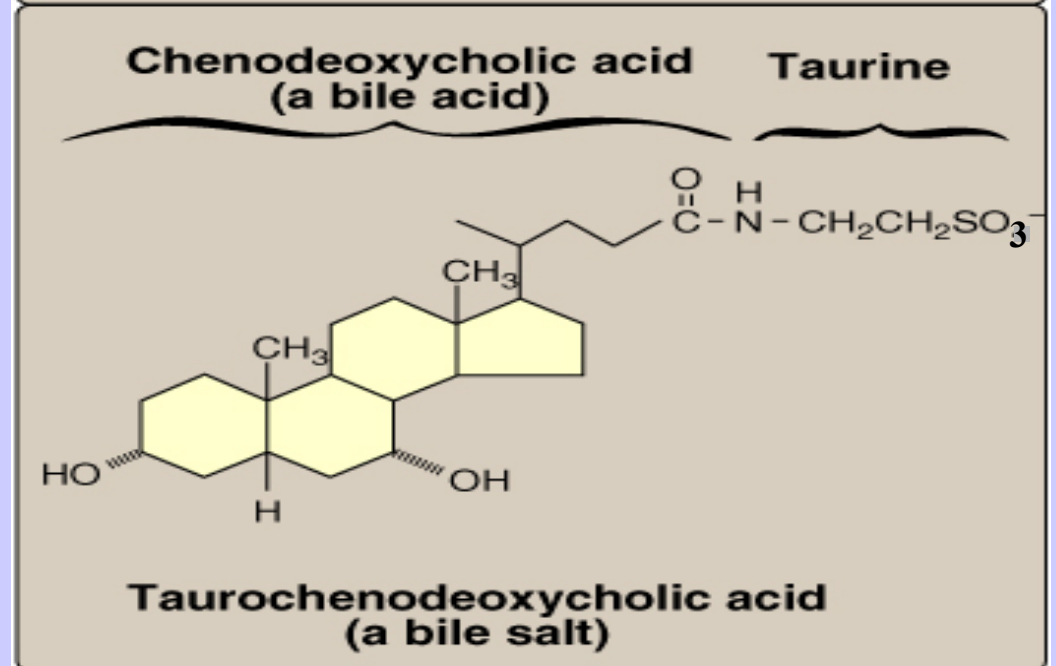
- **Addition of glycine or taurine results in the presence of fully ionized groups at pH 7.0:**
 - COOH of glycine &**
 - SO₃ of taurine**
 - (hence, its name as bile salts e.g., Sodium or potassium glycocholate)**
- **More effective detergent than bile acids**
- **Only bile salts, but not acids, found in bile**

Bile Salts

Na or K Glycocholate



Na or K Taurochenodeoxycholate



Hormonal Control of Bile Secretion

Stimulus:

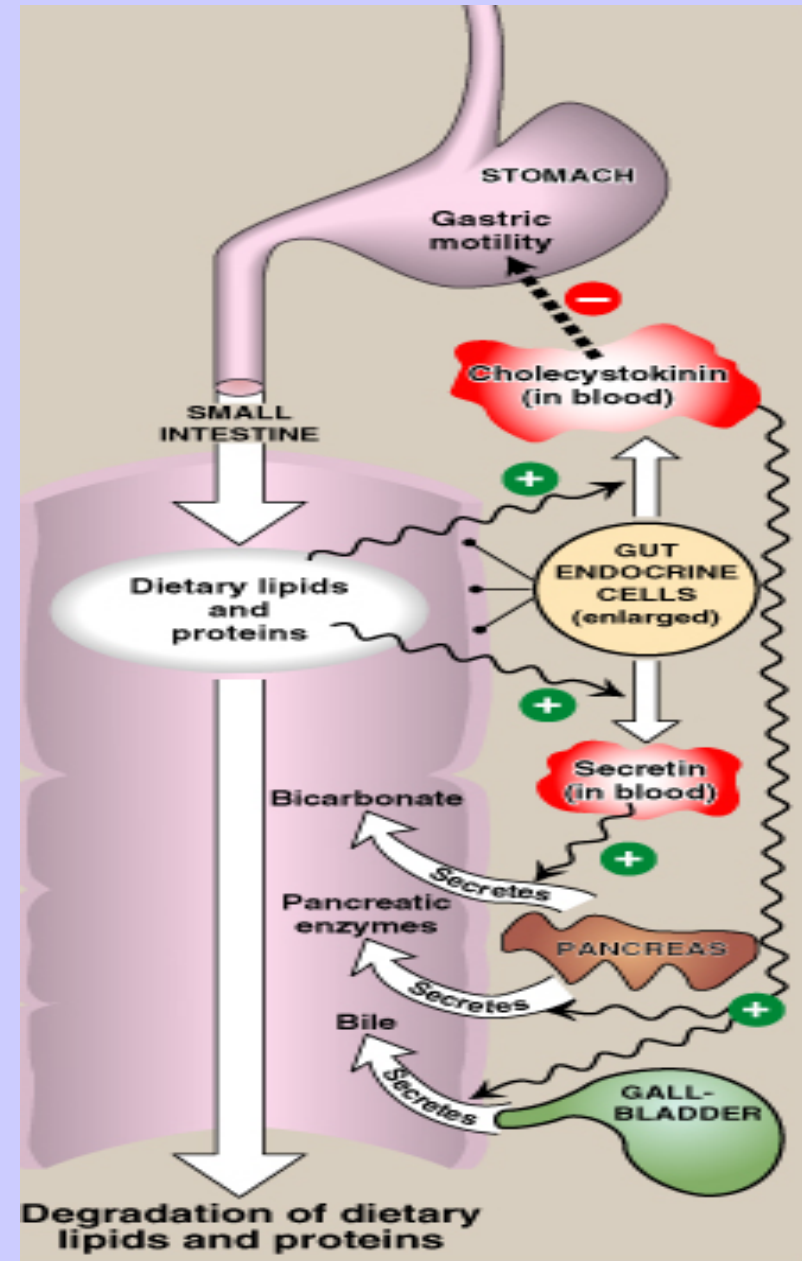
Undigested lipids and partially digested proteins in duodenum

Hormone from gut cells:

Cholecystokinin (CCK)

Responses:

1. Secretion of pancreatic enzymes
2. Bile secretion
3. Slow release of gastric contents



Functions of Bile Salts

- Important for cholesterol excretion:
 1. As metabolic products of cholesterol
 2. Solubilizer of cholesterol in bile
- Emulsifying factors for dietary lipids, a prerequisite step for efficient lipid digestion
- Cofactor for pancreatic lipase and PLA2
- Facilitate intestinal lipid absorption by formation of mixed micelle

Emulsification of Dietary Lipids in Duodenum: Role of Bile Salts

- Emulsification increases the surface area of lipid droplets, therefore the digestive enzymes can effectively act.
- **Mechanisms:**
 1. Mechanical mixing by peristalsis
 2. **Detergent effect of bile salts:**

Bile salts interact with lipid particles and aqueous duodenal contents, stabilizing the particles as they become smaller, and preventing them from coalescing.

Absorption of Lipids by Intestinal Mucosal Cells: Role of Bile salts

Mixed micelles:

Disc-shaped clusters of amphipathic lipids.

Arranged with their hydrophobic groups on the inside and their hydrophilic groups on the outside.

Micelle includes end products of lipid digestion, **bile salts** and fat-soluble vitamins

Note: Short- and medium-chain fatty acids do not require mixed micelle for absorption by intestinal cells

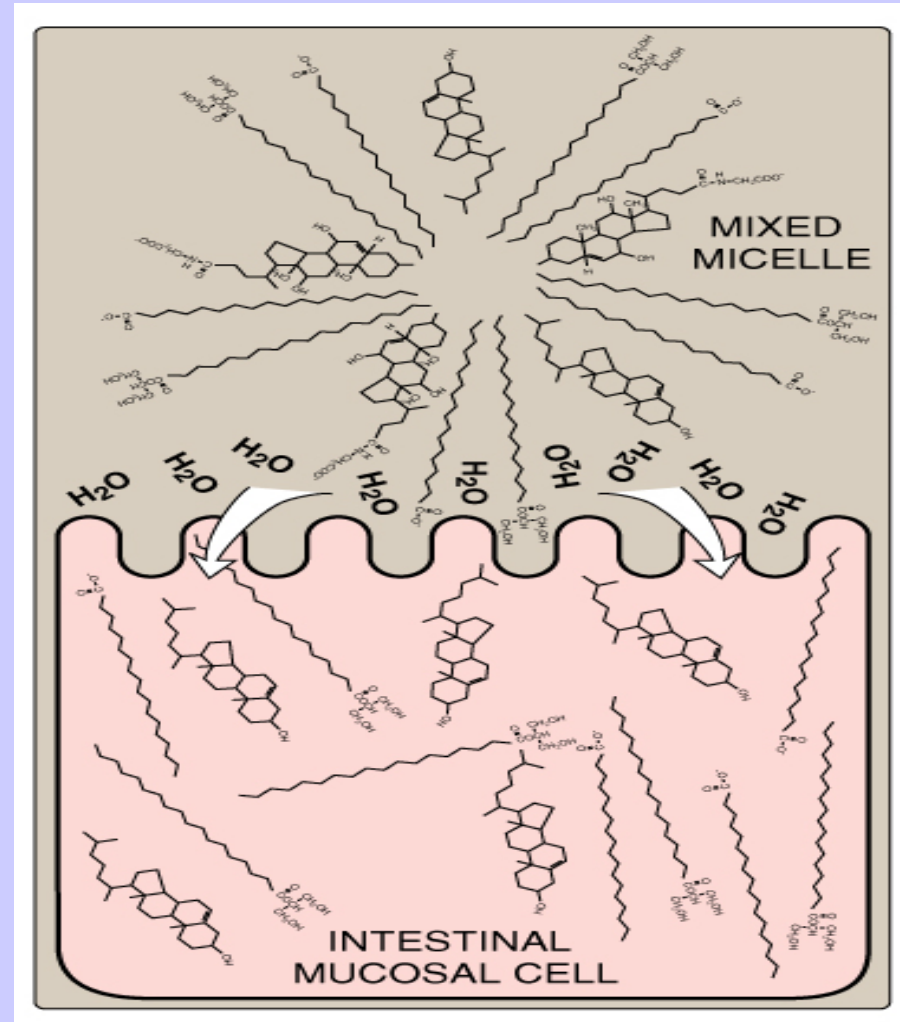
The Role of Bile Salts in Absorption of Lipids by Intestinal Cells

Mixed Micelle Formation:

Bile salts

End products of lipid digestion

Fat-soluble vitamins



Secondary Bile Acids

Bile salts **Glyco- or Tauro-cholate** **-Chenodeoxycholate**

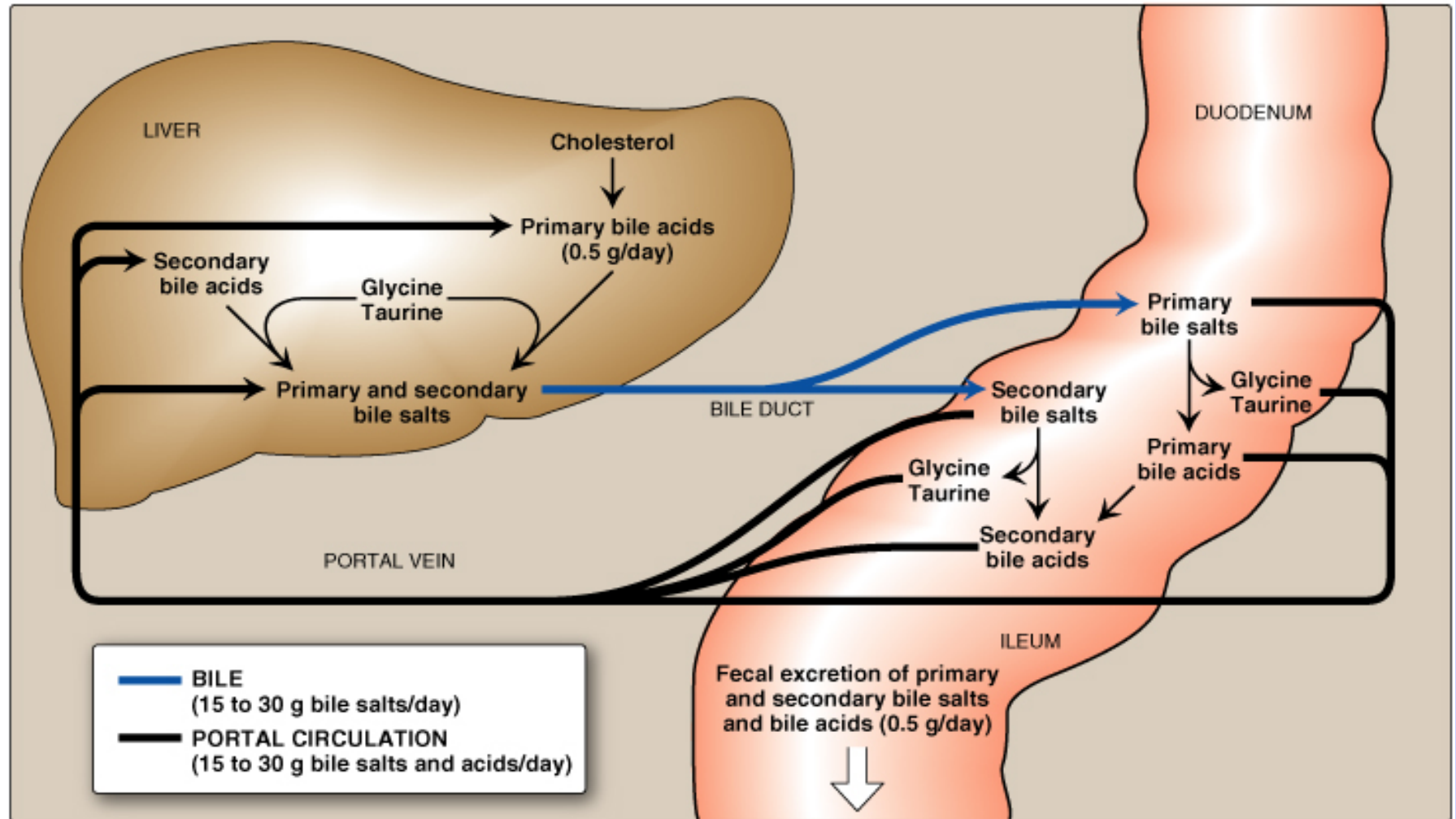
Glycine **Taurine** **Intestinal bacteria**

Bile acids **Cholic acid** **Chenodeoxycholic**

OH **Intestinal bacteria**

2° Bile acids **Deoxycholic acid** **Lithotomic**

Enterohepatic Circulation



Enterohepatic Circulation

CONT'D

Cholestyramine: Bile acid sequestrants

It binds to bile acids in the gut,
preventing their reabsorption &
Promoting their excretion

It is used for treatment of hypercholesterolemia



Dietary fiber:

It binds to bile acids, increasing their excretion

Maldigestion / Malabsorption of Lipids

Decreased bile secretion by:

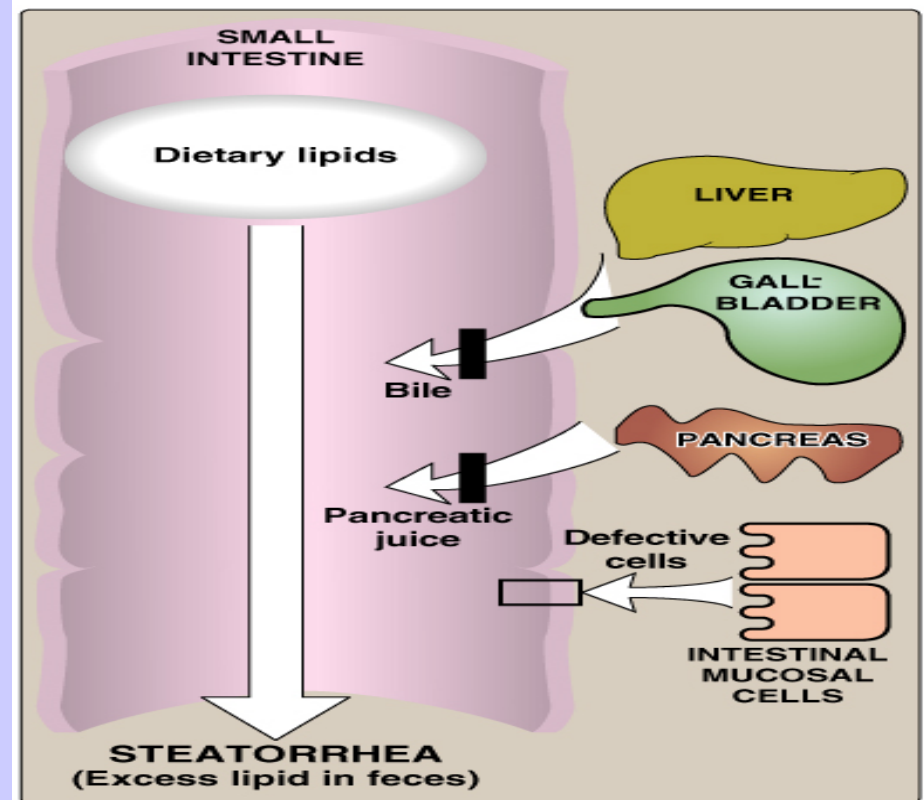
Liver diseases:

e.g., Hepatitis or cirrhosis

Gall bladder diseases:

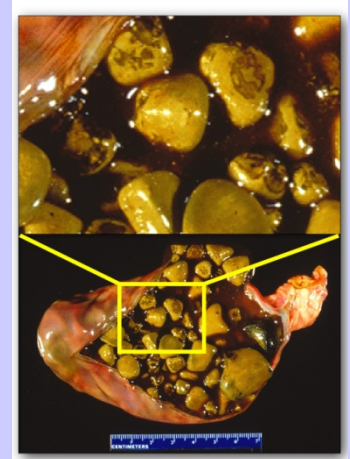
e.g., Gall stones

➔ Malabsorption of lipids



Cholelithiasis

Cholesterol Gallstone Disease



Causes:

↓ Bile salts in bile:

Biliary tract obstruction

(interferes with enterohepatic circulation)

Hepatic dysfunction (↓ synthesis)

↑ Biliary cholesterol excretion

Treatment:

- **Bile acid replacement therapy**
- **Surgical**

Thank you