Biochemical Aspects of Bile Acids and Salts

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Objectives

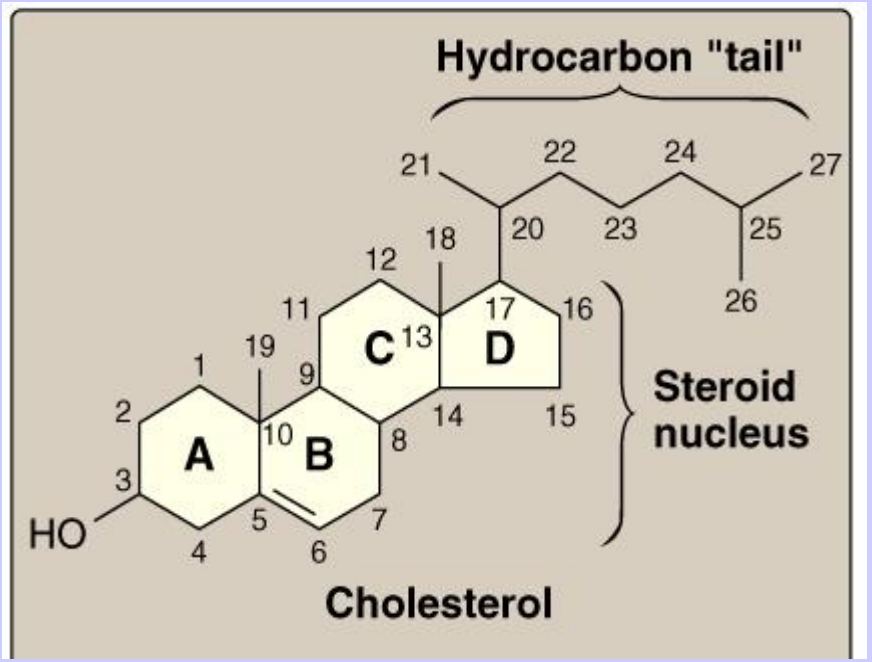
- Structure of primary bile acids and salts
- Structure of secondary bile acids and salts
- Functions of bile salts
- Enterohepatic circulation
- Malabsorption syndrome
- Cholelithiasis

Cholesterol

Cholesterol (27 C) is the:

Parent steroid compound

Precursor of bile acids and salts



Primary Bile Acids

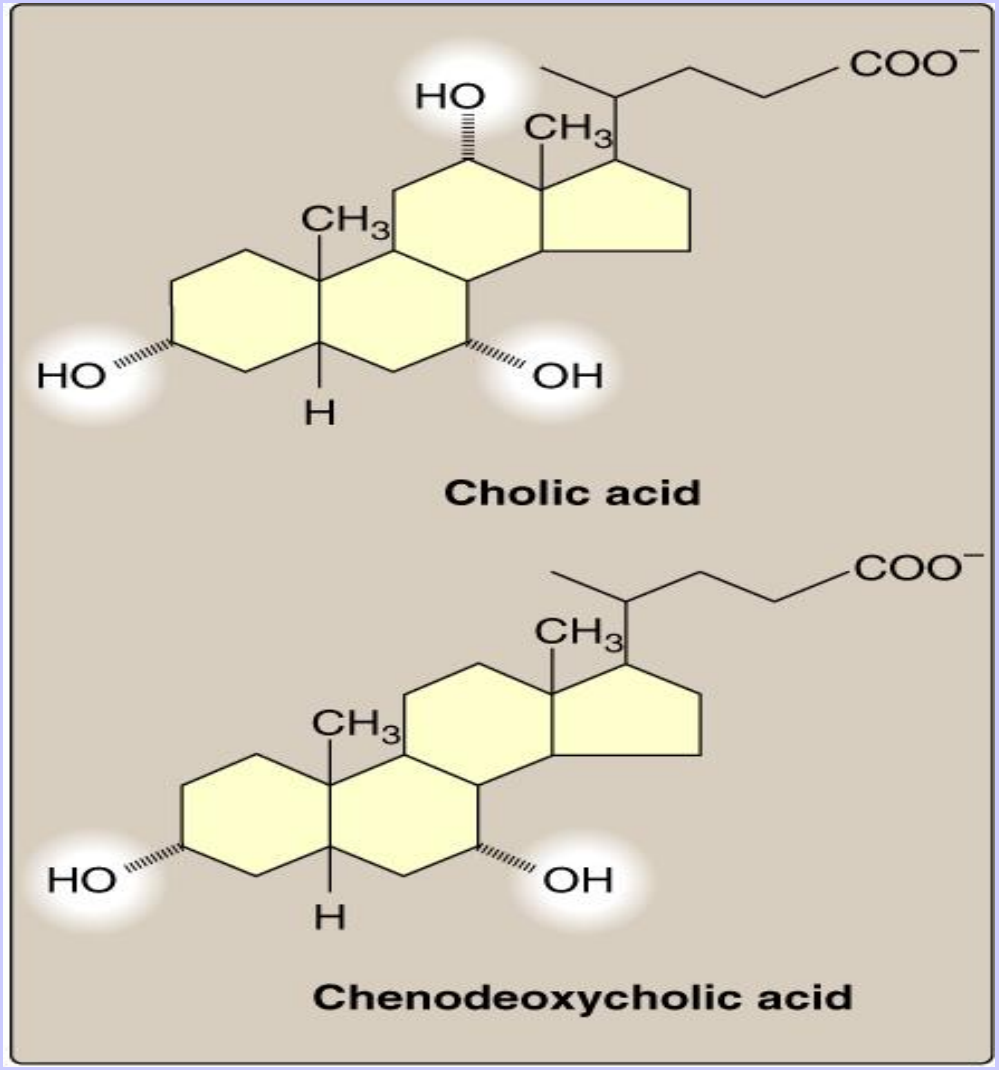
Primary bile acids (24 C):

Amphipathic

-COOH at side chain

Cholic acid: 3 OH

Chenodeoxycholic: 2 OH



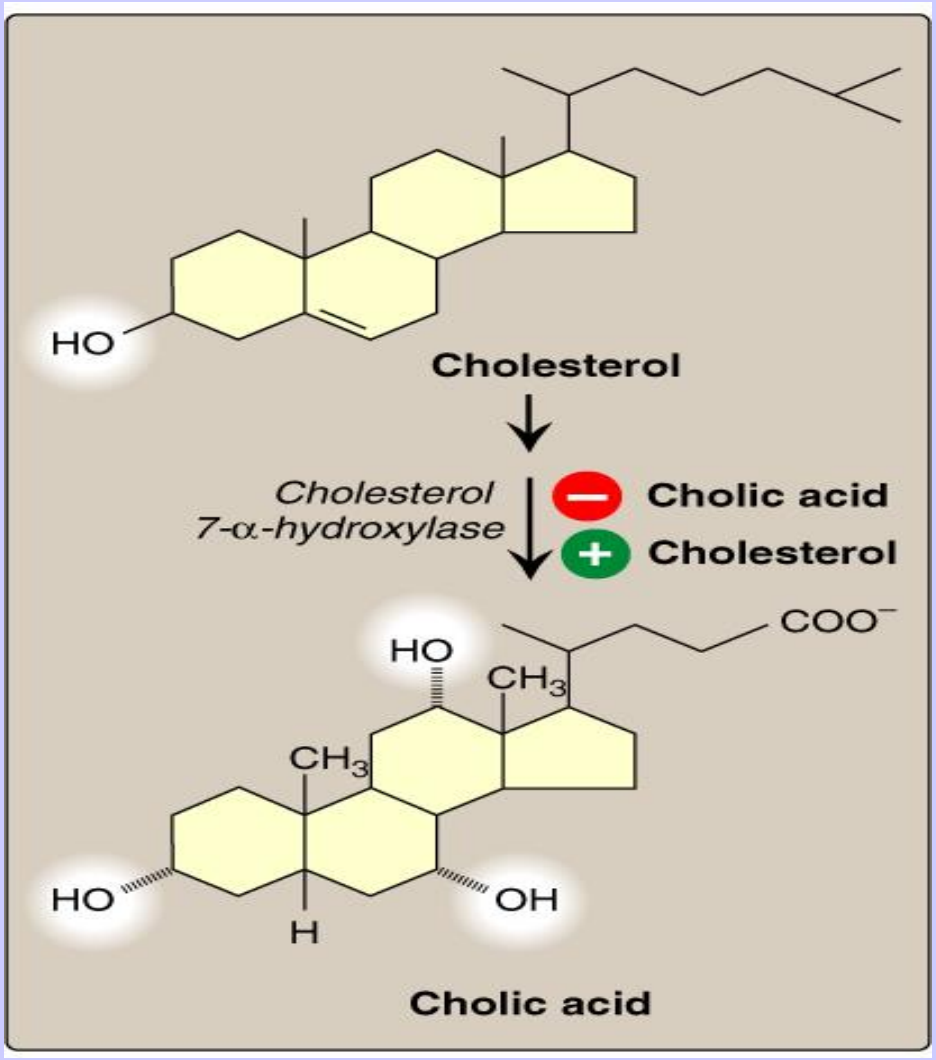
Hepatic Synthesis of Bile Acids

The rate-limiting step is catalyzed by:

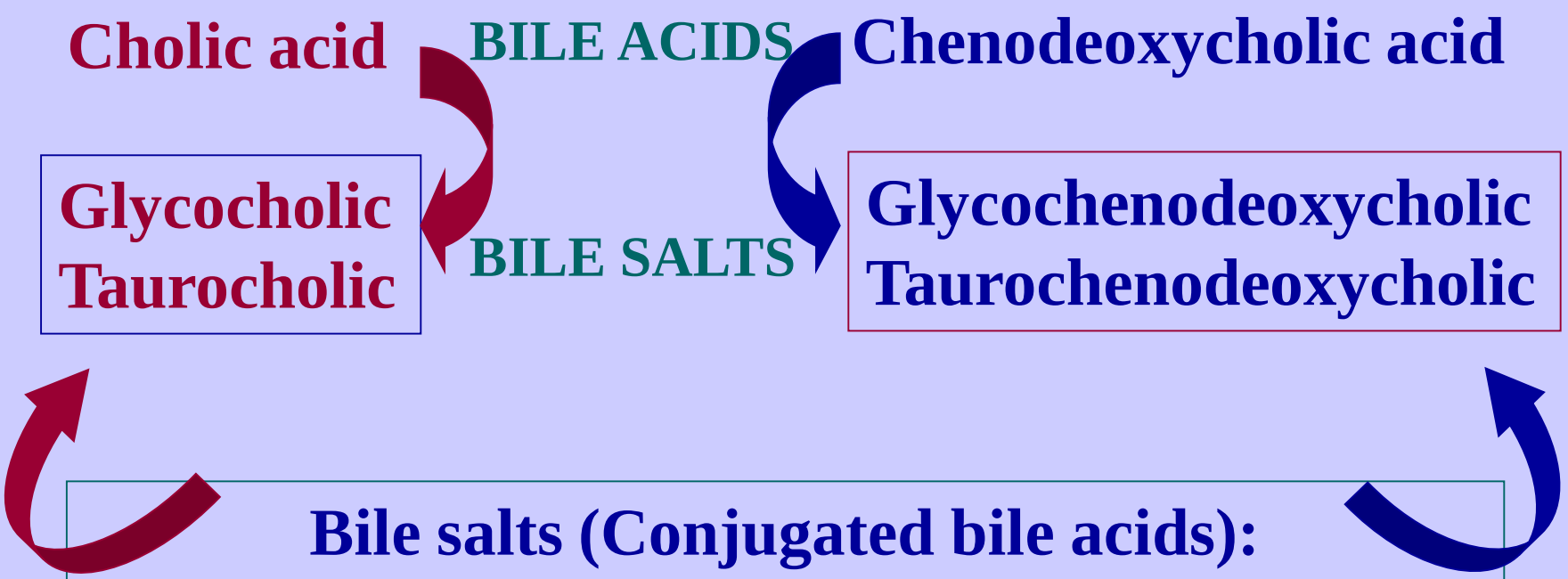
Cholesterol 7-α-hydroxylase

Regulation:
Down-regulated by end products (bile acids) "Enzyme repression"

Up-regulated by cholesterol "Enzyme induction"



Primary Bile Acids and Salts



Bile salts (Conjugated bile acids):
amide-linked with glycine or taurine
The ratio of glycine to taurine forms in the bile is 3:1

Bile Salts

- **Addition of glycine or taurine results in the presence of fully ionized groups at pH 7.0:**

  -COOH of glycine &
  -SO_3 of taurine
  (hence, its name as bile salts e.g., Sodium or potassium glycocholate)

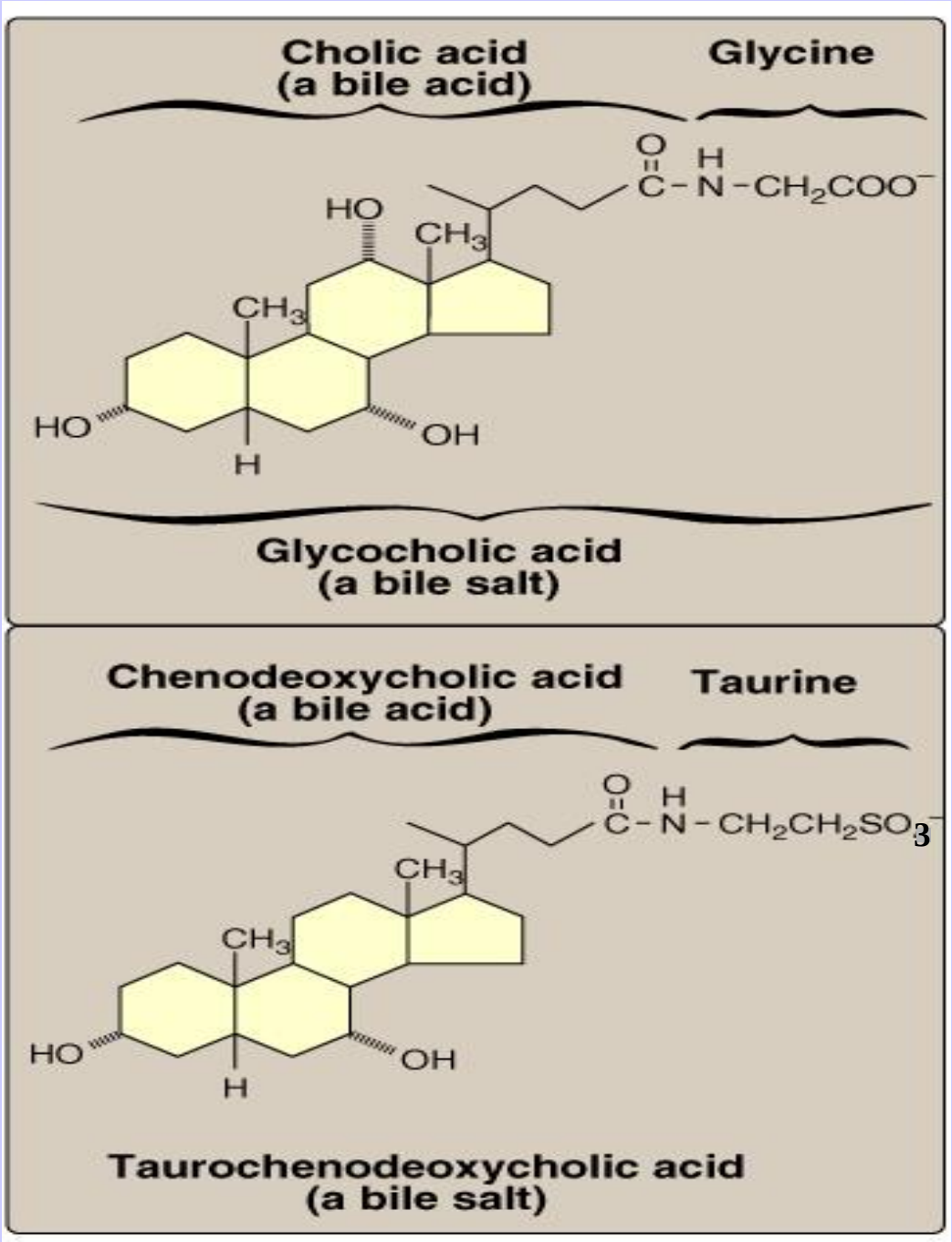
- **More effective detergent than bile acids**

- **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:

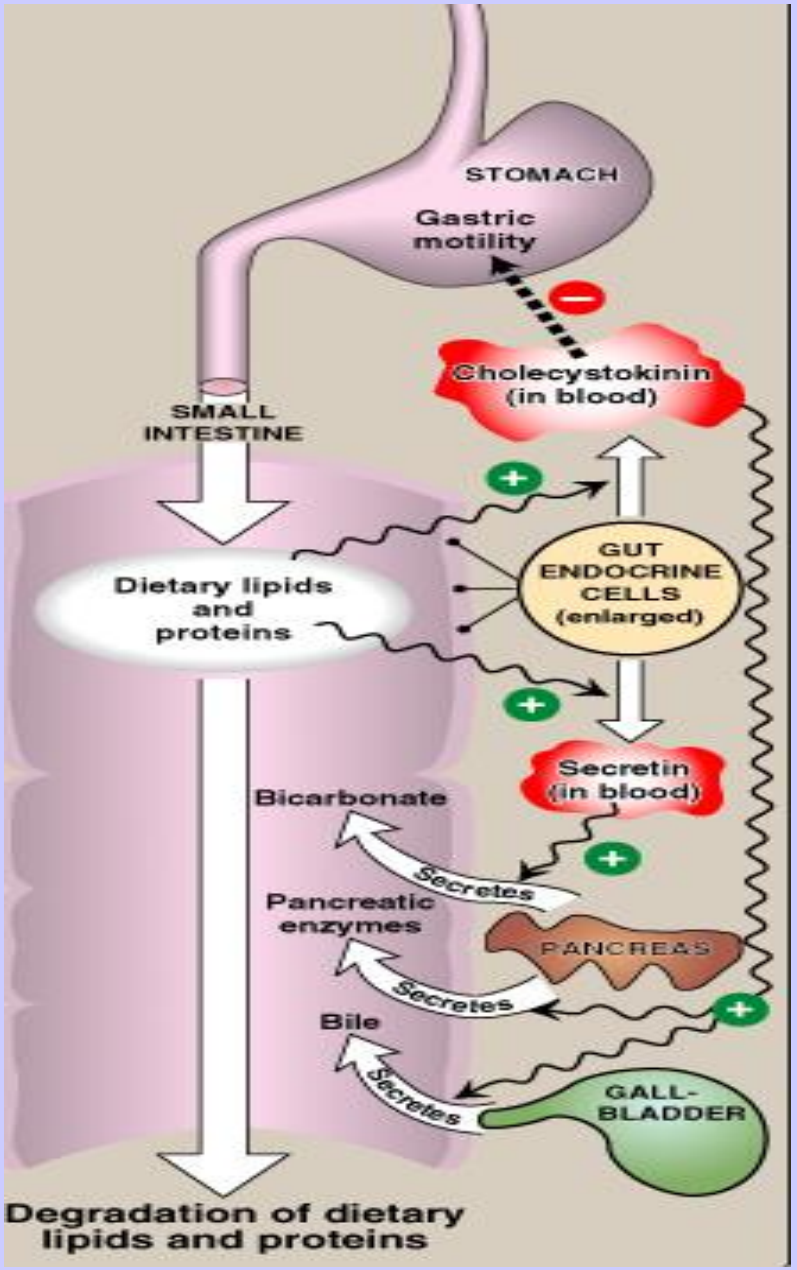
Undigested lipids and partially digested proteins in duodenum

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.

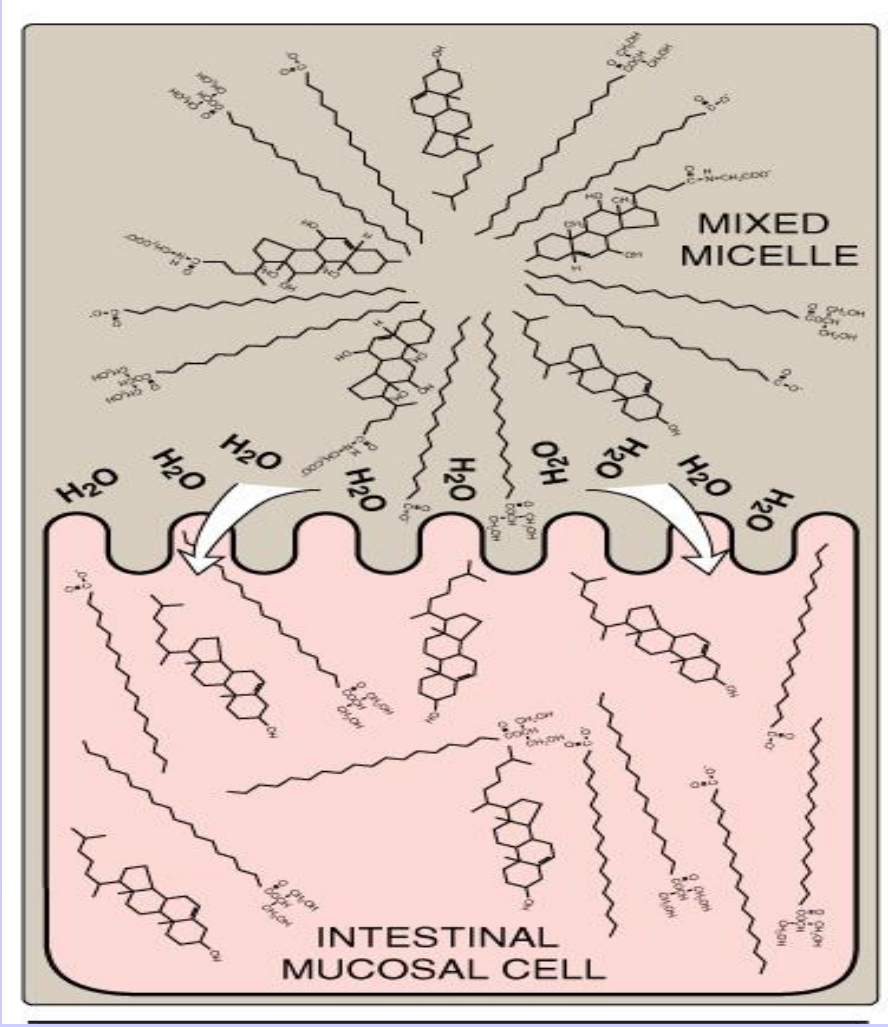
Micelle includes end products of lipid digestion, bile salts and fat-soluble vitamins

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

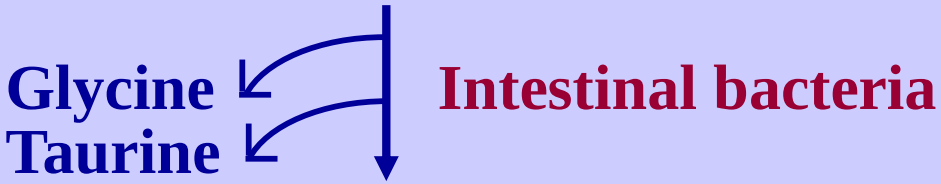
Mixed Micelle Formation:

- Bile salts
  - End products of lipid digestion
  - Fat-soluble vitamins



Secondary Bile Acids

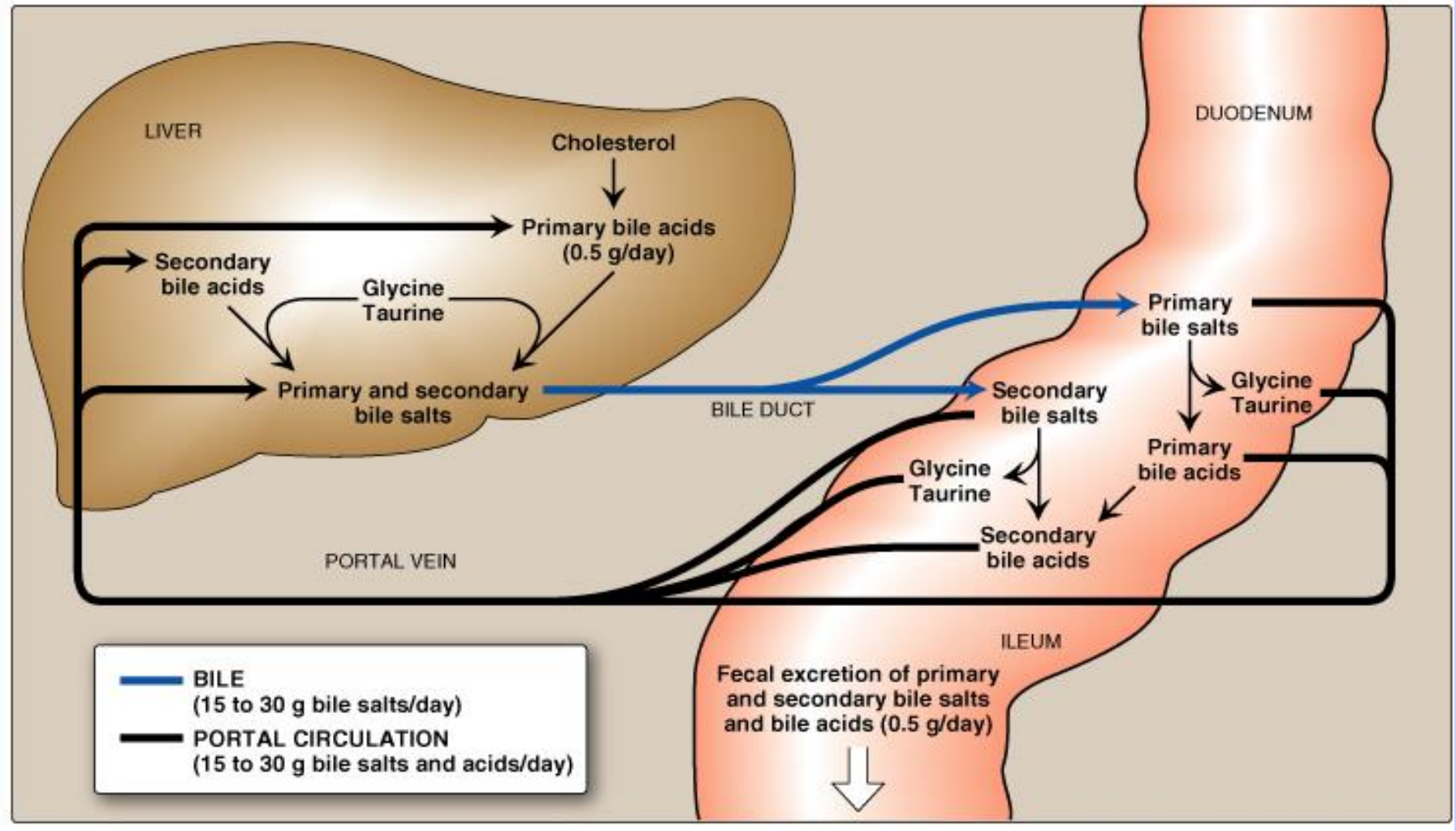
Bile salts	Glyco- or Tauro-cholate	-Chenodeoxycholate



Bile acids	Cholic acid	Chenodeoxycholic

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

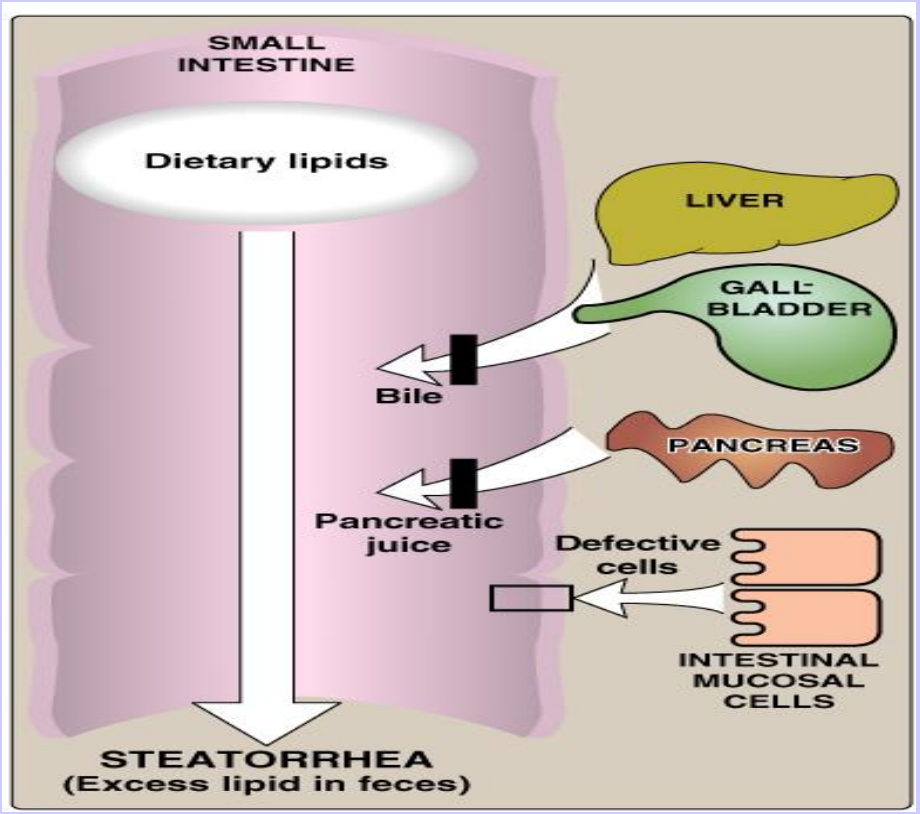
Maldigestion / Malabsorption of Lipids

Decreased bile secretion by:

Liver diseases:
e.g., Hepatitis or cirrhosis

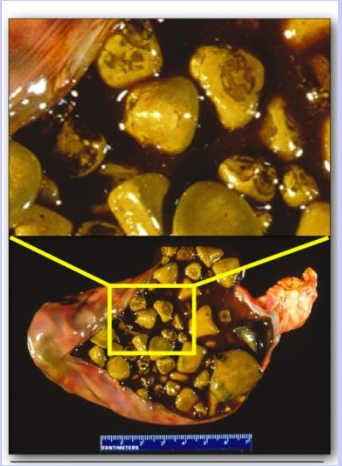
Gall bladder diseases:
e.g., Gall stones

→ Malabsorption of lipids



Cholelithiasis

Cholesterol Gallstone Disease



Causes:

↓ Bile salts in bile:

Biliary tract obstruction

(intereferes with enterohepatic circulation)

Hepatic dysfunction (↓ synthesis)

↑ Biliary cholesterol excretion

Treatment:

- Bile acid replacement therapy
- Surgical

Thank you