# Secretory Functions of the Alimentary Tract

**Pancreas & liver**

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# Pancreas

| Type of Secretion | Daily Volume (ml) | pH |
|---|---|---|
| Saliva | 1000 | 6.0-7.0 |
| Gastric secretion | 1500 | 1.0-3.5 |
| Pancreatic secretion | 1000 | 8.0-8.3 |
| Bile | 1000 | 7.8 |
| Small intestine secretion | 1800 | 7.5-8.0 |
| Brunner's gland secretion | 200 | 8.0-8.9 |
| Large intestinal secretion | 200 | 7.5-8.0 |
| Total | 6700 | |

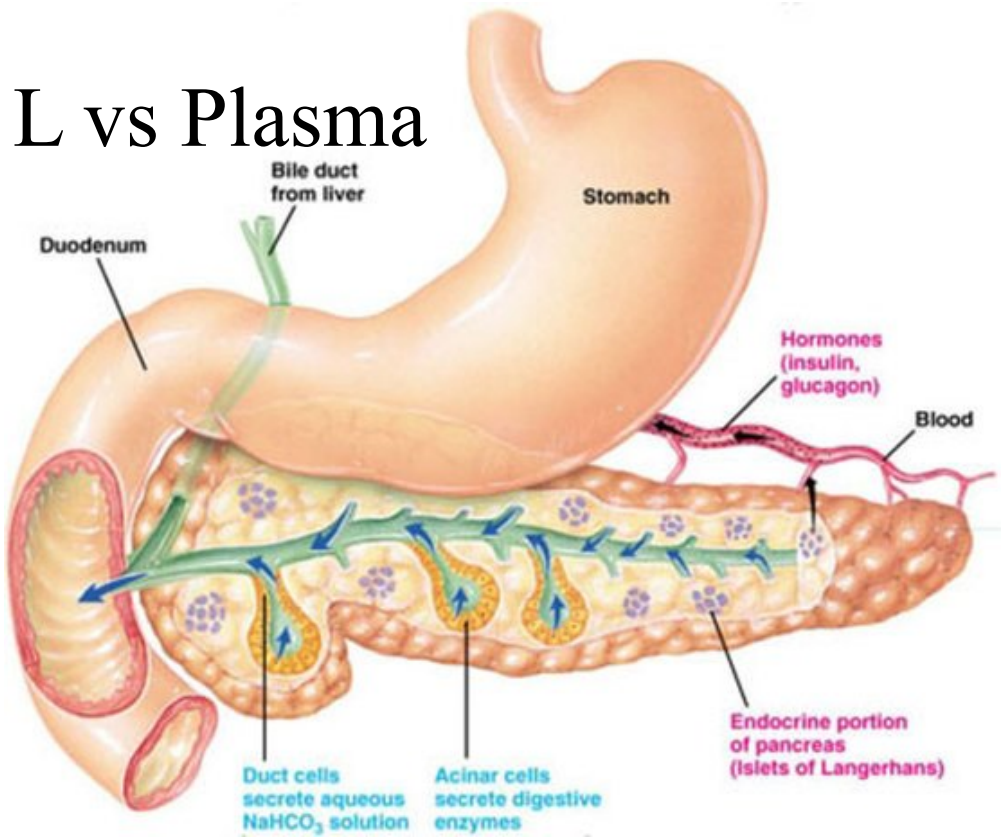
## Function

- **Exocrine function**
  - Digestive enzymes for all food types
  - Bicarbonate solution to neutralize acid chyme & prevent duodenal mucosa damage

- **Endocrine function**
  - Secrete insulin

# Internal Structure of Pancreas

- Compound gland with structure similar to salivary gland
- Acini - grape-like clusters of cells that store and secrete digestive enzymes
- Ducts - secrete bicarbonate 110-150 mEq/ L vs Plasma HCO3 24 mEq/L.
  Ducts unite →Wirsung duct.
  Wirsung duct joins common bile duct to form ampulla of Vater→D



# Nerve supply to pancreas

- Sympathetic →splanchnic nerve
- Parasympathetic → vagus nerve

# Pancreatic digestive enzymes for proteins

| Protein digestion pancreatic enzymes | |
|---|---|
| **Enzyme** | **Action** |
| Trypsin | Cleaves proteins to polypeptides<br>Converts caseinogen in milk into casein (Curdling of milk)<br>Activates other pancreatic enzymes |
| Chymotrypsin | Cleaves proteins to polypeptides<br>Converts caseinogen in milk into casein (faster than trypsin) |
| Carboxypolypeptidase | Cleaves polypeptides to amino acids |

# Pancreatic digestive enzymes for Fats

| Fat digestion pancreatic enzymes | |
|---|---|
| **Enzyme** | **Action** |
| Pancreatic lipase<br>activity needs bile salts & colipase | TG→ fatty acids + monoglycerides<br>Responsible for 80% fat digestion<br>Defect: steatorrhea |
| Cholesterol esterase | Cholesterol esters → cholesterol & fatty acid |

# Pancreatic digestive enzymes for carbohydrates

| Carbohydrates digestion pancreatic enzymes | |
|---|---|
| **Enzyme** | **Action** |
| Pancreatic amylase | Release of disaccharides and a few trisaccharides from starch, glycogen, & other carbohydrate (except cellulose). |

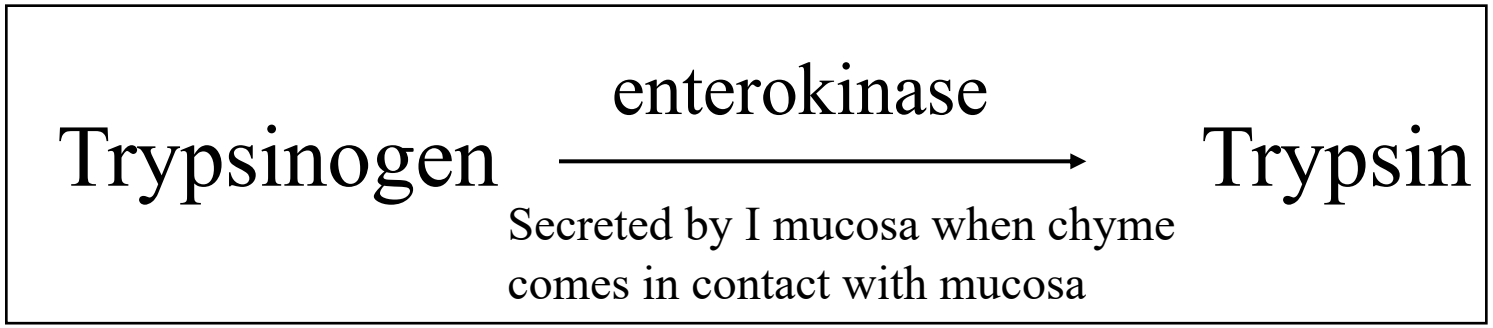
| Enzyme | Activator | Acts on (substrate) | End products |
|---|---|---|---|
| Trypsin | Enterokinase<br>Trypsin | Proteins | Proteoses and polypeptides |
| Chymotrypsin | Trypsin | Proteins | Polypeptides |
| Carboxypeptidases | Trypsin | Polypeptides | Amino acids |
| ✓ Nucleases | Trypsin | RNA and DNA | Mononucleotides |
| ✓ Elastase | Trypsin | Elastin | Amino acids |
| ✓ Collagenase | Trypsin | Collagen | Amino acids |
| Pancreatic lipase | Alkaline medium | Triglycerides | Monoglycerides and fatty acids |
| Cholesterol ester hydrolase | Alkaline medium | Cholesterol ester | Cholesterol and fatty acids |
| ✓ Phospholipase A | Trypsin | Phospholipids | Lysophospholipids |
| ✓ Phospholipase B | Trypsin | Lysophospholipids | Phosphoryl choline and free fatty acids |
| ✓ Colipase | Trypsin | Facilitates action of pancreatic lipase | – |
| ✓ Bile-salt-activated lipase | Trypsin | Phospholipids | Lysophospholipids |
| | | Cholesterol esters | Cholesterol and fatty acids |
| | | Triglycerides | Monoglycerides and fatty acids |
| Pancreatic amylase | – | Starch | Dextrin and maltose |

# Why Doesn't the Pancreas Digest Itself?

1. Pancreatic proteolytic enzymes are stored and secreted in **inactive** form
   - Trypsinogen → trypsin
   - Chymotrypsinogen → chymotrypsin
   - Procarboxypeptidase → carboxypeptidase
   - Activated only after they are secreted into the intestinal tract.

2. Trypsin inhibitor is present in cells

# Activation of Proteolytic Enzymes




- Trypsin - autocatalytic activation - activates
  - trypsinogen
  - chymotrypsinogen,
  - procarboxypeptidase

# Trypsin Inhibitor

- Enzyme precursors stored in cells along with trypsin inhibitor
  - Trypsin inhibitor prevents formation of trypsin

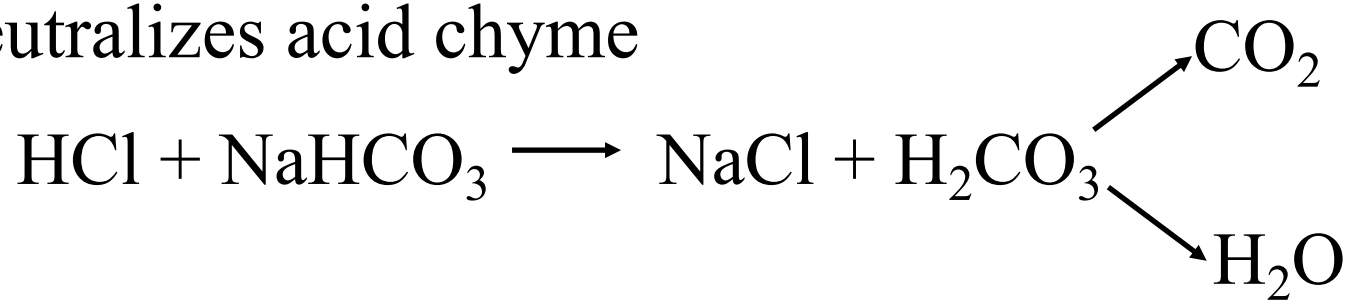
    - in acini
    - in ducts
  - Acute pancreatitis -

    - a primary lack of trypsin inhibitor
    - not enough trypsin inhibitor is present

# Bicarbonate neutralizes acidic chyme

- **Secretin** stimulates HCO3
- HCO3 Function:

➢ Neutralizes acid chyme

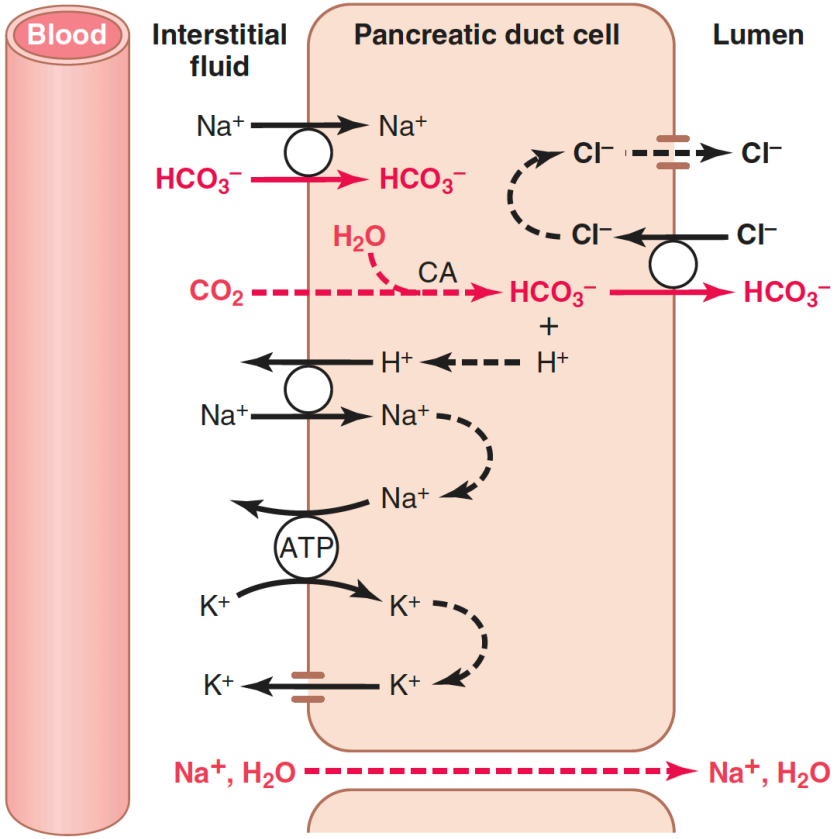


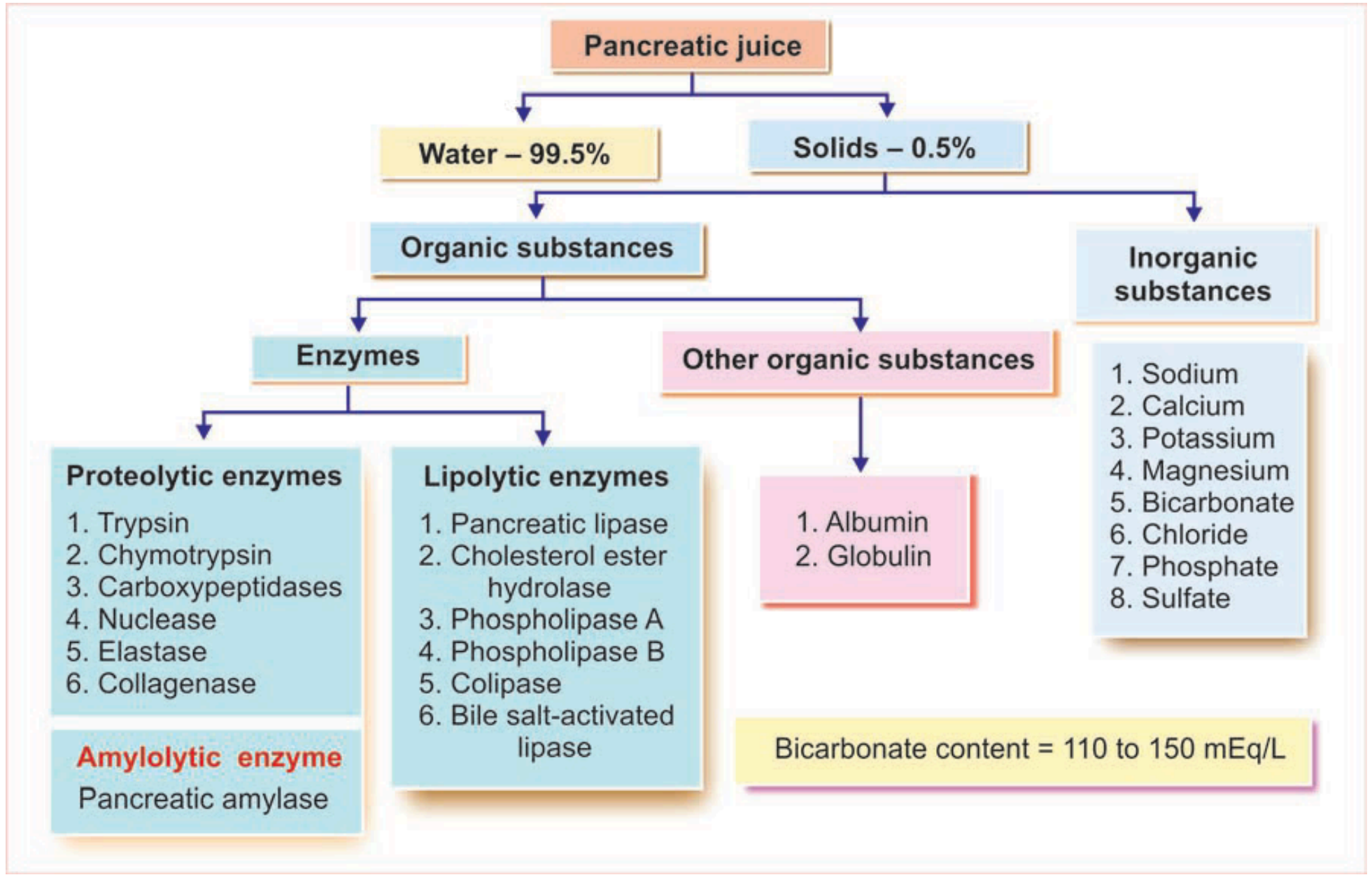

➢ Creates optimal conditions (pH = 7-8) for digestive enzymes

# Model of bicarbonate secretion

1. $CO_2$ combines with $H_2O$ in presence of carbonic anhydrase in cell
2. Carbonic acid dissociates into $HCO_3^-$ and $H^+$
3. $H^+$ are transported through basolateral membrane by **secondary transport mechanism** that requires $Na^+$ gradient. $Na^+$ gradient is established by usual $Na^+$ - $K^+$ ATPase pump.
4. $HCO_3^-$ moves out of cell in exchange for $Cl^-$ (Rate of $HCO_3^-$ secretion is dependent upon luminal [$Cl^-$])
5. $Na^+$ moves down electrochemical gradient.
6. H2O moves into lumen establishing osmotic equilibrium.

- Pancreatic juice is always isotonic.

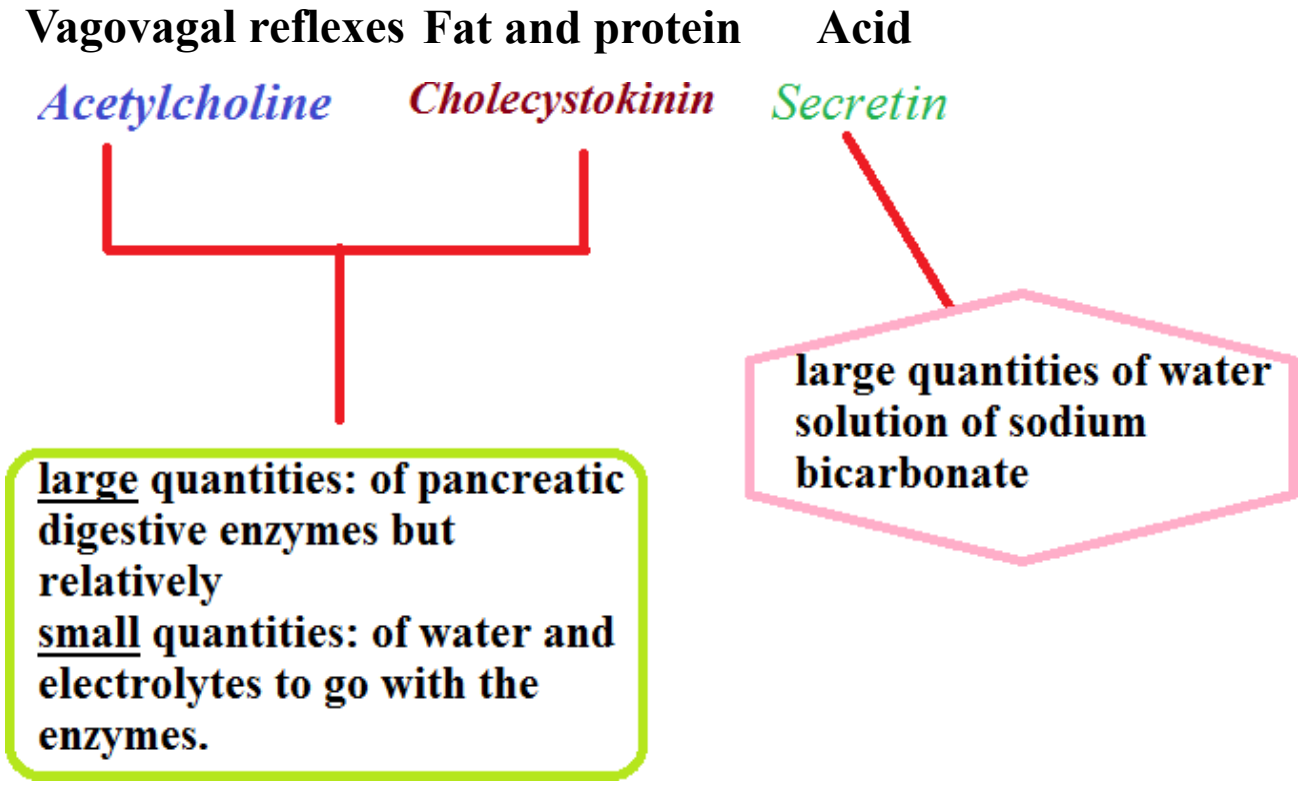



Pancreatic juice
Water – 99.5%
Solids – 0.5%
Organic substances
Inorganic substances
Enzymes
Other organic substances
1. Sodium
2. Calcium
3. Potassium
4. Magnesium
5. Bicarbonate
6. Chloride
7. Phosphate
8. Sulfate
Proteolytic enzymes
1. Trypsin
2. Chymotrypsin
3. Carboxypeptidases
4. Nuclease
5. Elastase
6. Collagenase
Lipolytic enzymes
1. Pancreatic lipase
2. Cholesterol ester hydrolase
3. Phospholipase A
4. Phospholipase B
5. Colipase
6. Bile salt-activated lipase
1. Albumin
2. Globulin
Amylolytic enzyme
Pancreatic amylase
Bicarbonate content = 110 to 150 mEq/L

# Effect of Secretion Rate on Ionic Composition of Pancreatic Juice

- Low secretion rates
  - [HCO3] is low
  - [Cl] is high
- High secretion rates
  - [HCO3] is high
  - [Cl] is low
- Na and K concentrations always same as plasma

# Regulation of pancreatic secretion




**Hormones Inhibiting Pancreatic Secretion**

1. Pancreatic polypeptide (PP) secreted by PP cells in islets of Langerhans of pancreas
2. Somatostatin secreted by D cells in islets of Langerhans of pancreas
3. Peptide YY secreted by intestinal mucosa
4. Peptides like ghrelin and leptin

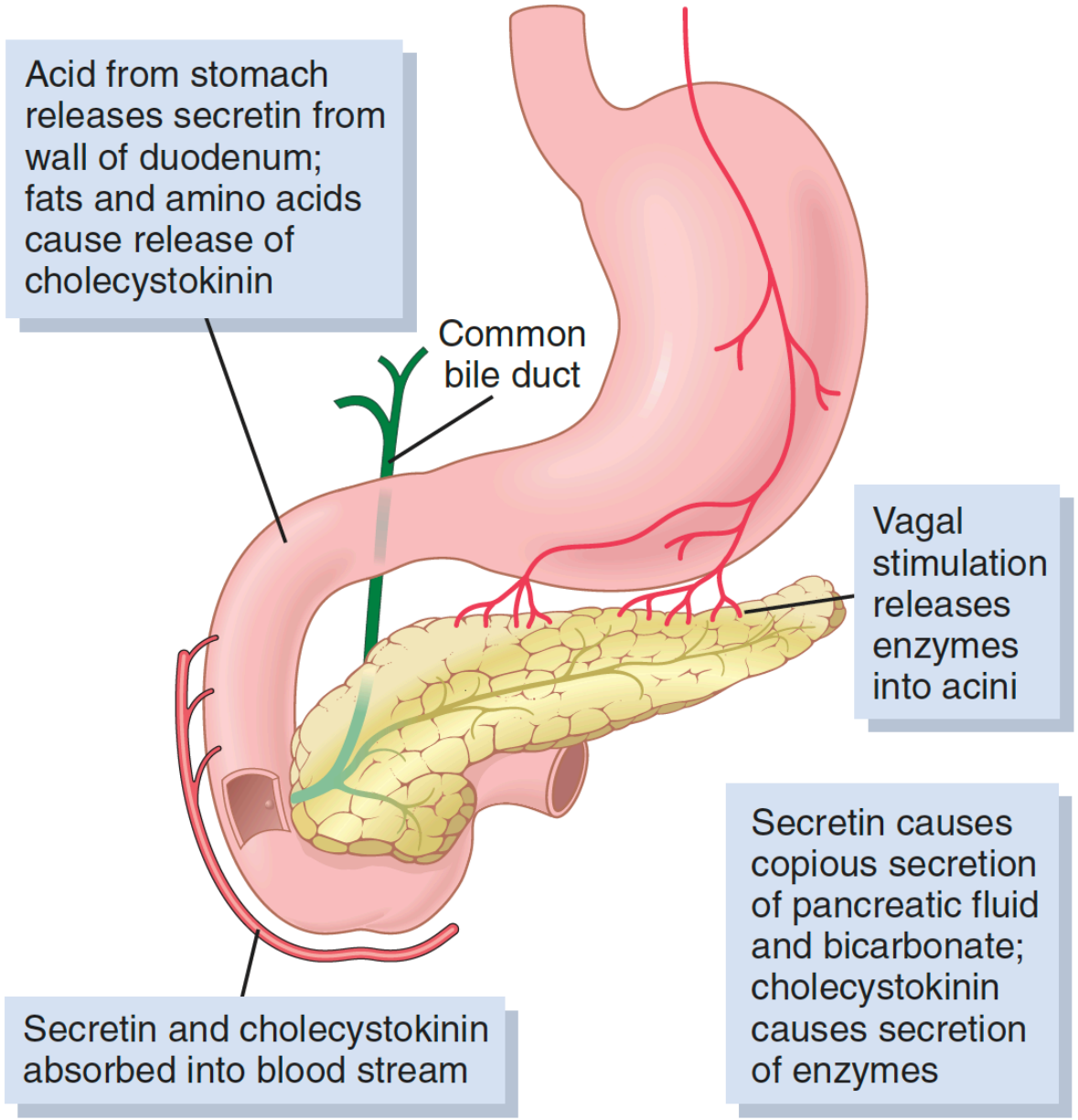



**Figure 65-10.** Regulation of pancreatic secretion.

# Phases of Pancreatic Secretion

- Cephalic (20%)
- Gastric (5-10%)

} Both phases mediated by vagus; low H2O & electrolytes, high enzyme secretion

- Intestinal (70-80%)
  - acid → secretin → $HCO_3^-/H_2O$
  - fat/protein → CCK → enzymes
  - acid/fat/protein → vagovagal Ach → enzymes

- CCK and acetylcholine both potentiate the effects of secretin on $H_2O$ and $HCO_3^-$ secretion.

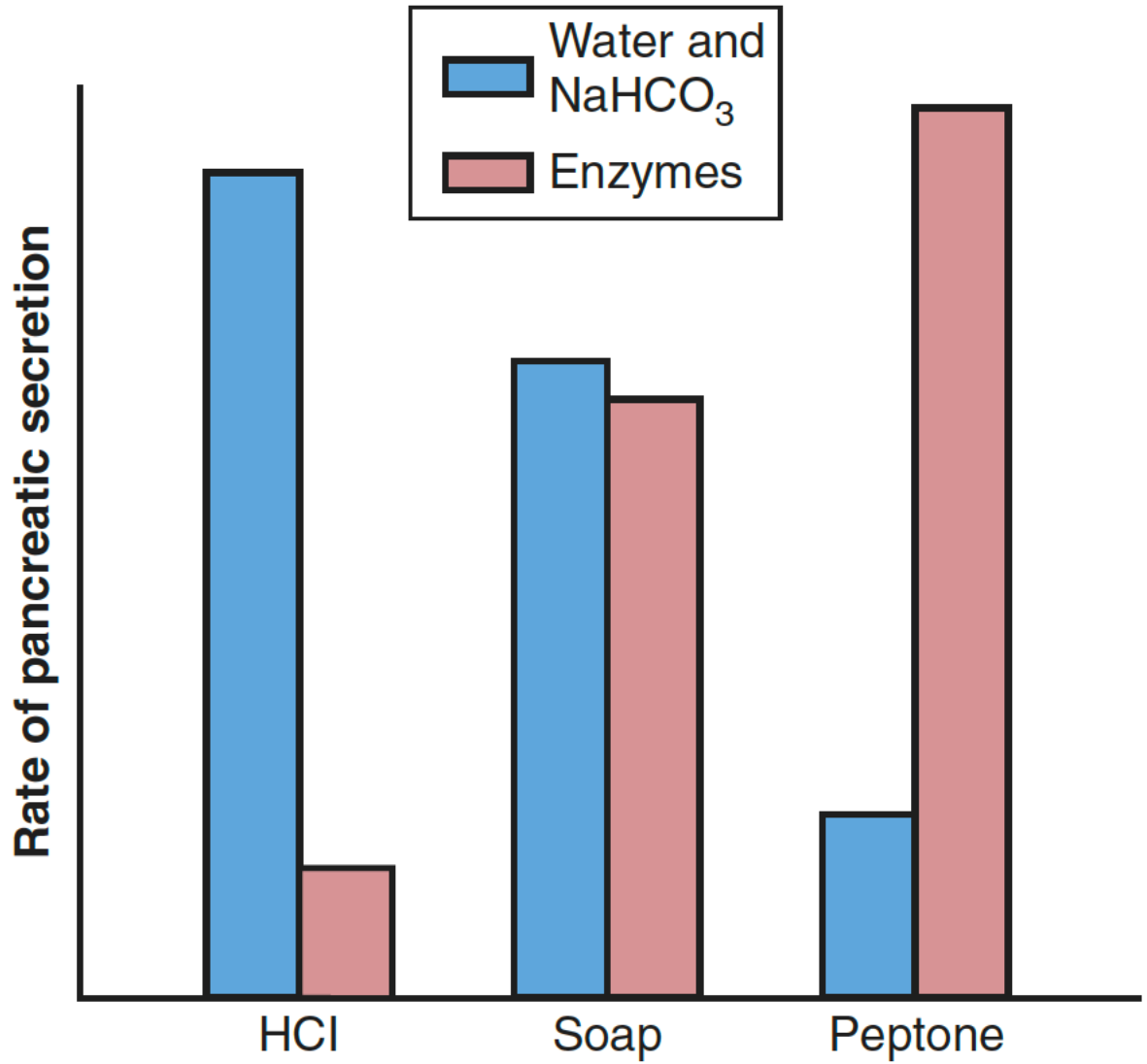
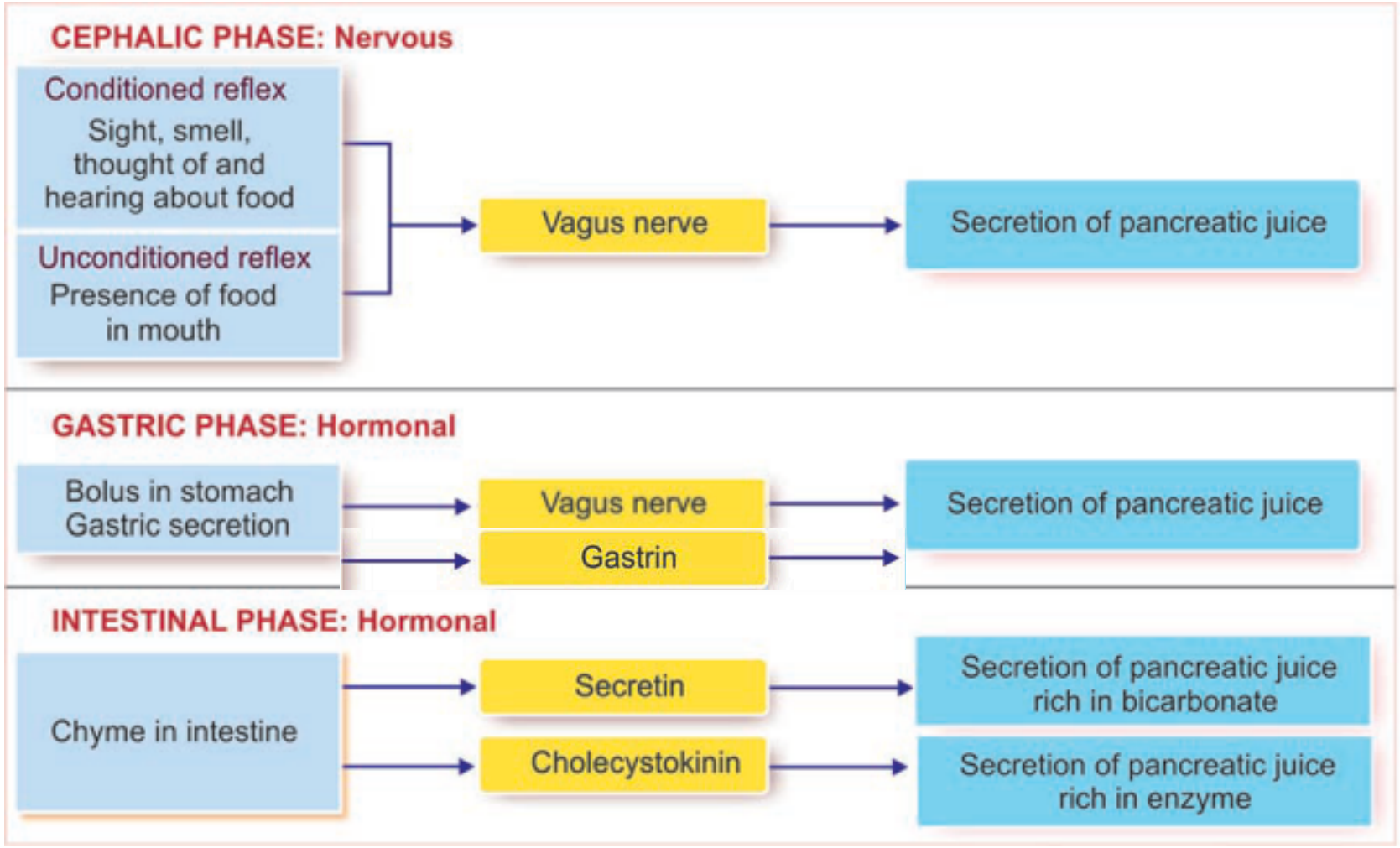


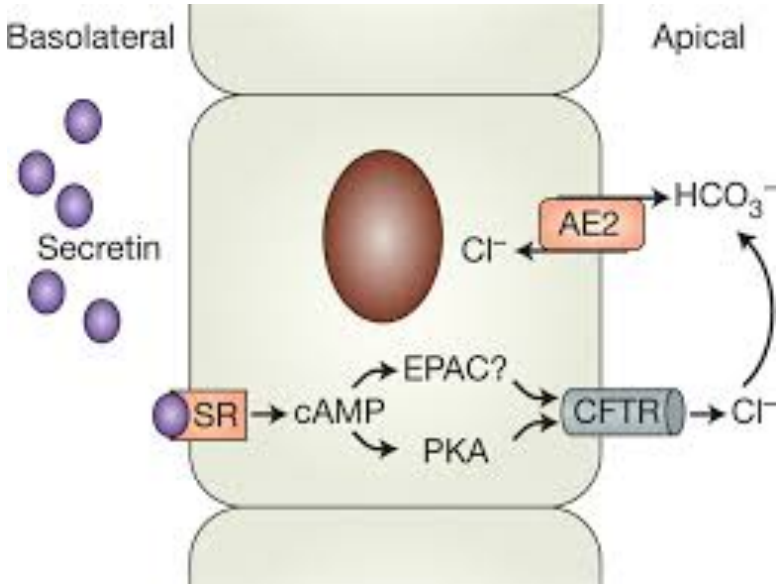

**Figure 65-9.** Sodium bicarbonate *($NaHCO_3$)*, water, and enzyme secretion by the pancreas, caused by the presence of acid *(HCl)*, fat (soap), or peptone solutions in the duodenum.

# Phases of Pancreatic Secretion



# Pancreatic $HCO_3^-$ Output (Secretin) Response to Duodenal Acidification

- Secretin is present in inactive form, prosecretin, in S cells (D & J)
- Released when pH < 4.5 →pancreas to secrete large quantities of fluid containing high [HCO3] (up to 145 mEq/L) & low [Cl]
- Secretin - acts to open Cl channels & thus increase secretion of HCO3
- Below pH = 3, secretin release is maximal in segment of D. Further release of secretin depends upon area of SI affected. (Maximal HCO3 response is 30 mEq/hr)
- During meal pH rarely < 3.5 or 4.0.



# Bile secretion by the liver

- **Liver function:**
- Liver cells synthesize about 6 g of bile salts/day.
- Bile secretion -600 -1000  ml/day.

- **Bile acids functions**:
  - Fat digestion and absorption
  - Excretion of bilirubin (hemoglobin destruction by-product) and excess cholestrol.

# Fat digestion and absorption

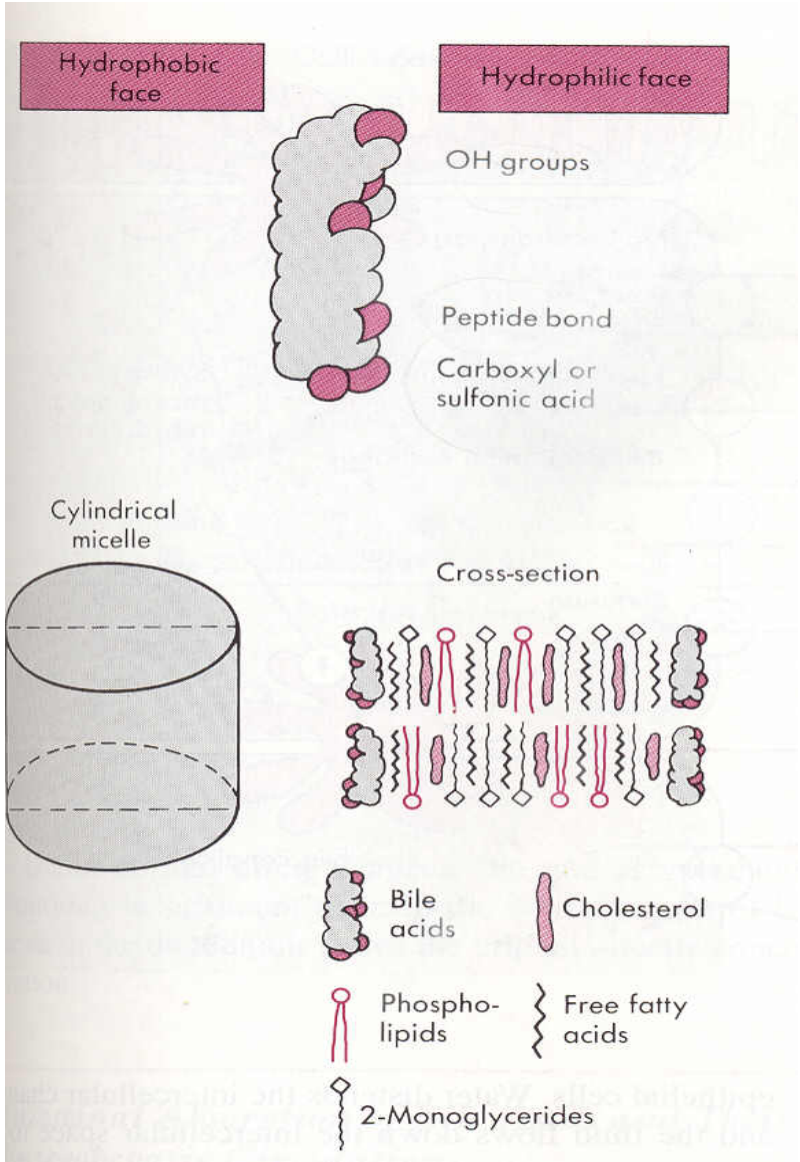
- *Fat digestion and absorption by means of:*

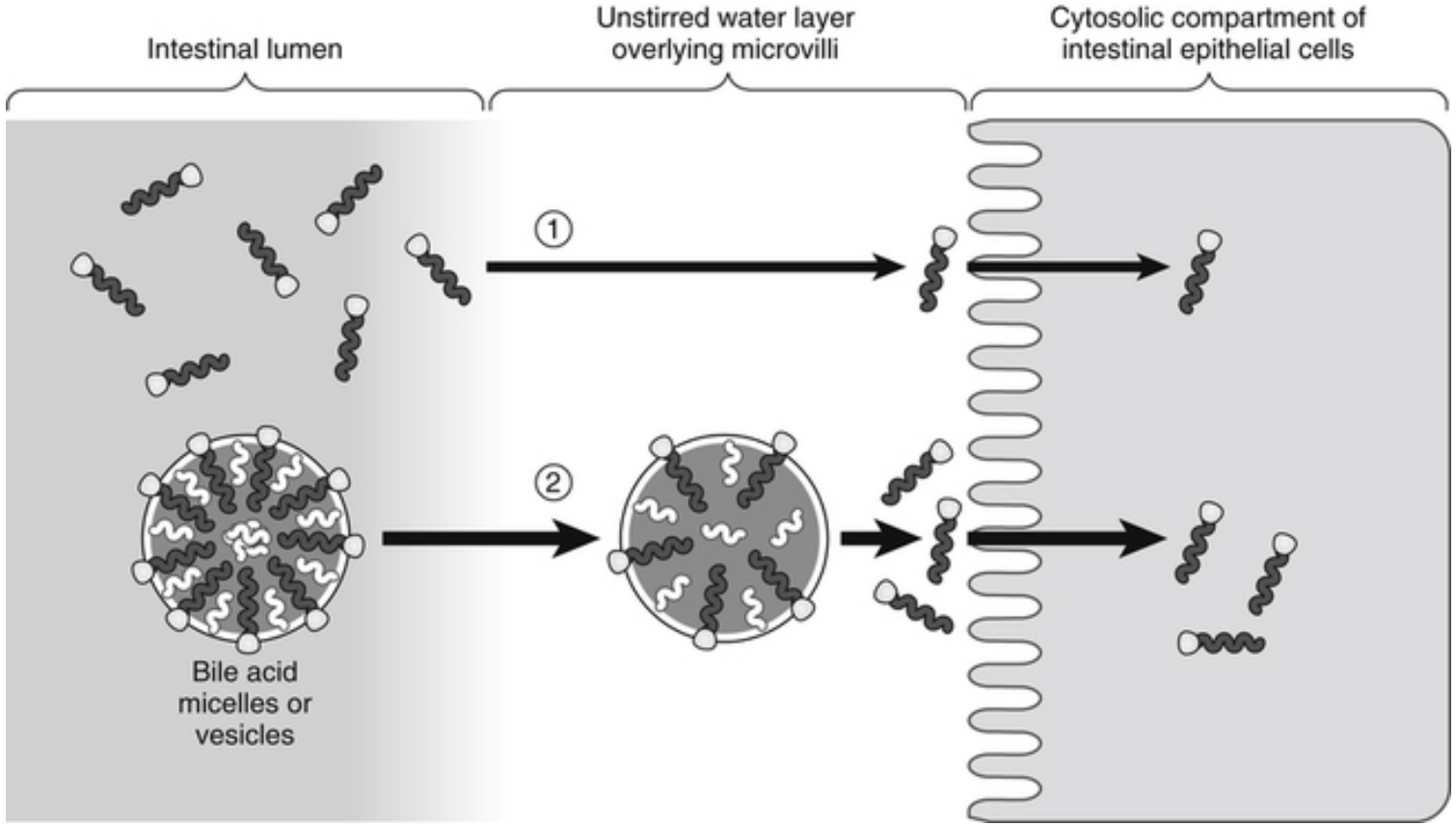
(1) Emulsification (detergent function) of large fat particles into many minute particles→ surface of which can be attacked by lipase enzymes

(2) Aid in absorption of digested fat end products (fatty acids, monoglycerides, cholesterol, other lipids by forming **micelle**) sthrough I mucosal membrane.

- ✓ Micelles are semisoluble in chyme because of electrical charges of bile salts
- ✓ No bile salts, about 40% of ingested fats are lost into feces →metabolic deficit.

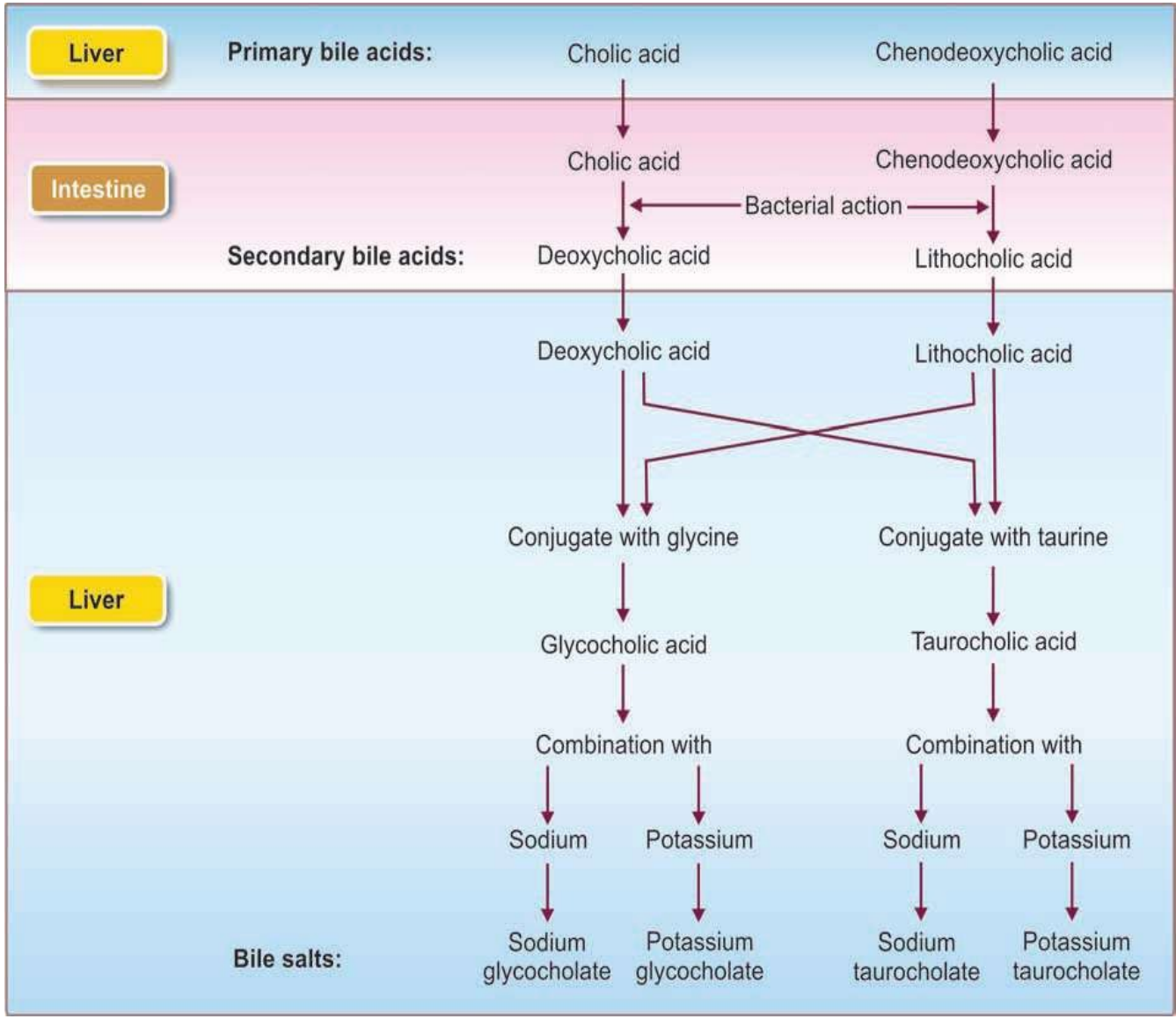
# Micelles Formation



## Function of bile salts in fat digestion and absorption

- ✓ Precursor of the bile salts is **cholesterol**.
- ✓ Cholesterol is present in diet / synthesized in liver cells during fat metabolism.
- ✓ Cholesterol is first converted to cholic acid or chenodeoxycholic acid in about equal quantities.
- ✓ These acids in turn combine principally with **glycine** and to a lesser extent with taurine to form glyco- and tauro-conjugated bile acids.
- ✓ The salts of these acids, mainly Na salts, are then secreted in the bile.

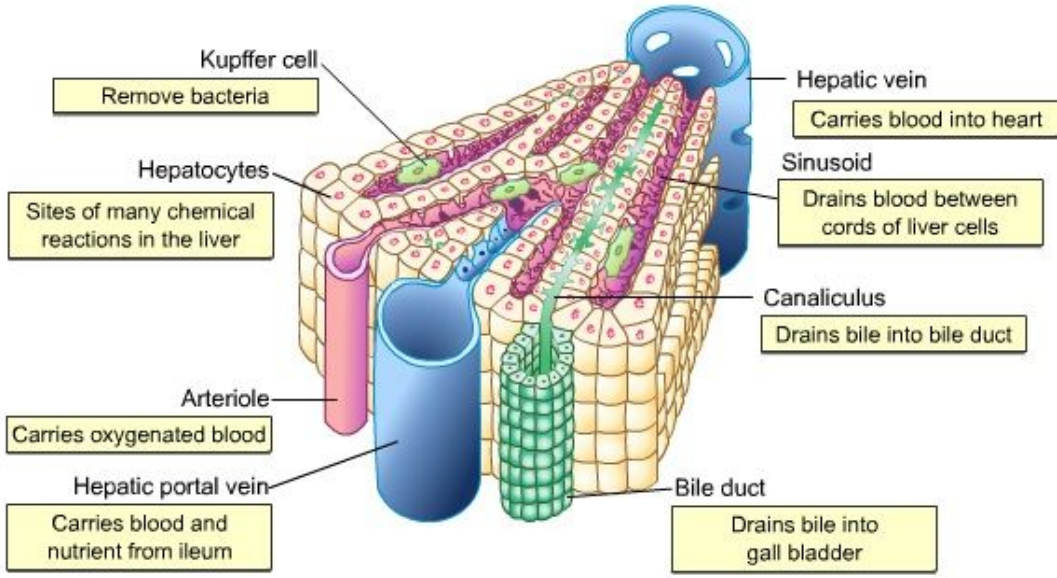


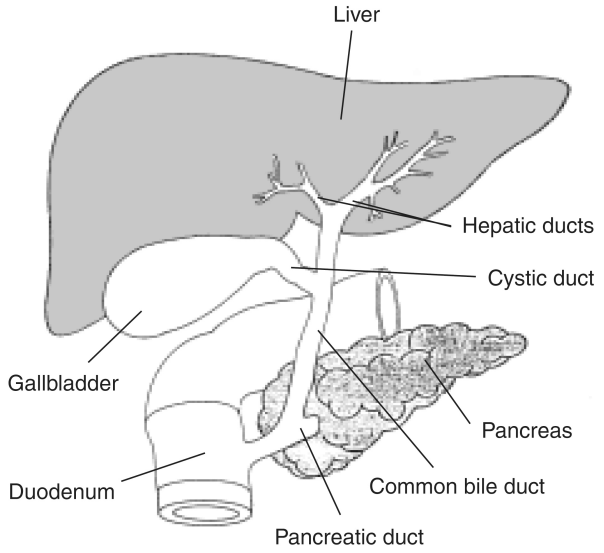
## Physiologic anatomy of biliary secretion:

- Bile is secreted in two stages by the liver:

1 Hepatocytes (large amounts of bile acids, cholesterol, & other organic constituents) →bile canaliculi between hepatic cells.

2 Directly into D (BD-HD) / stored in GB (CD)



**Physiologic anatomy of biliary secretion:**

- Second portion of liver secretion is added to the initial bile by epithelial cells lining ductules and ducts.
- Watery solution of Na & $HCO_3$
- Sometimes increases total quantity of bile 100%.
- Stimulated by **secretin** to supplement $HCO_3$ in pancreatic secretion (for neutralizing gastric acid)

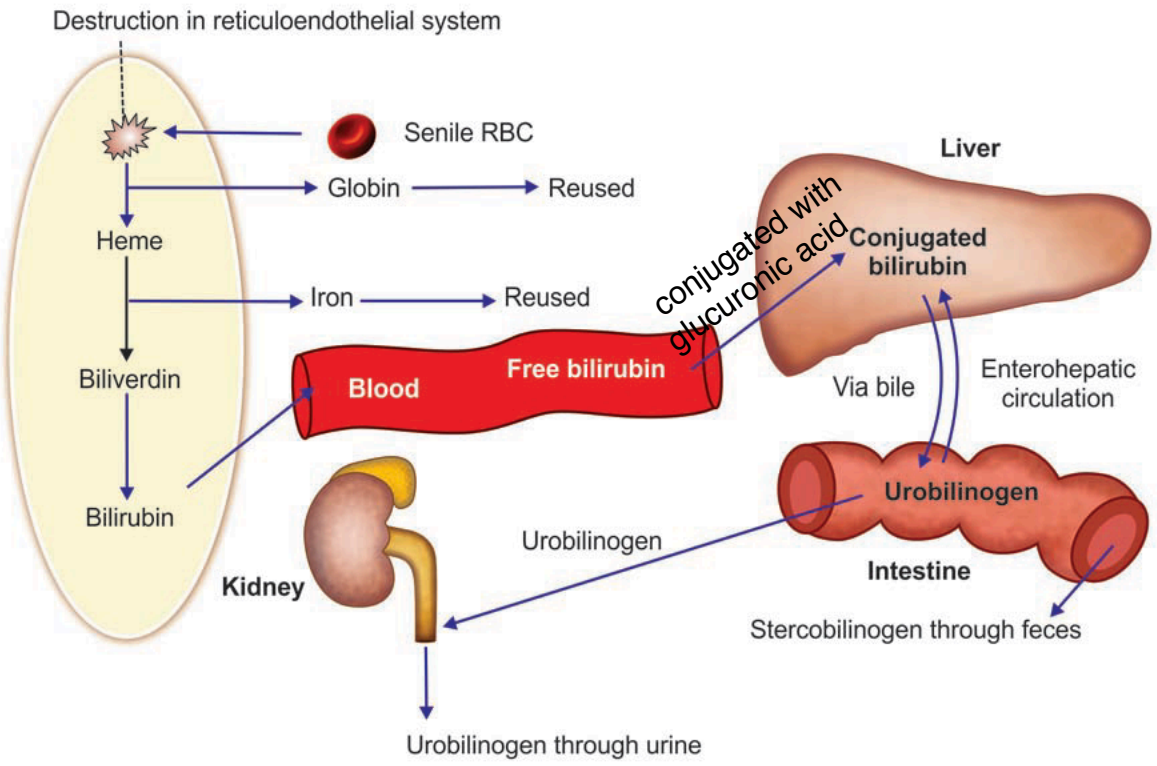
# BILE PIGMENTS

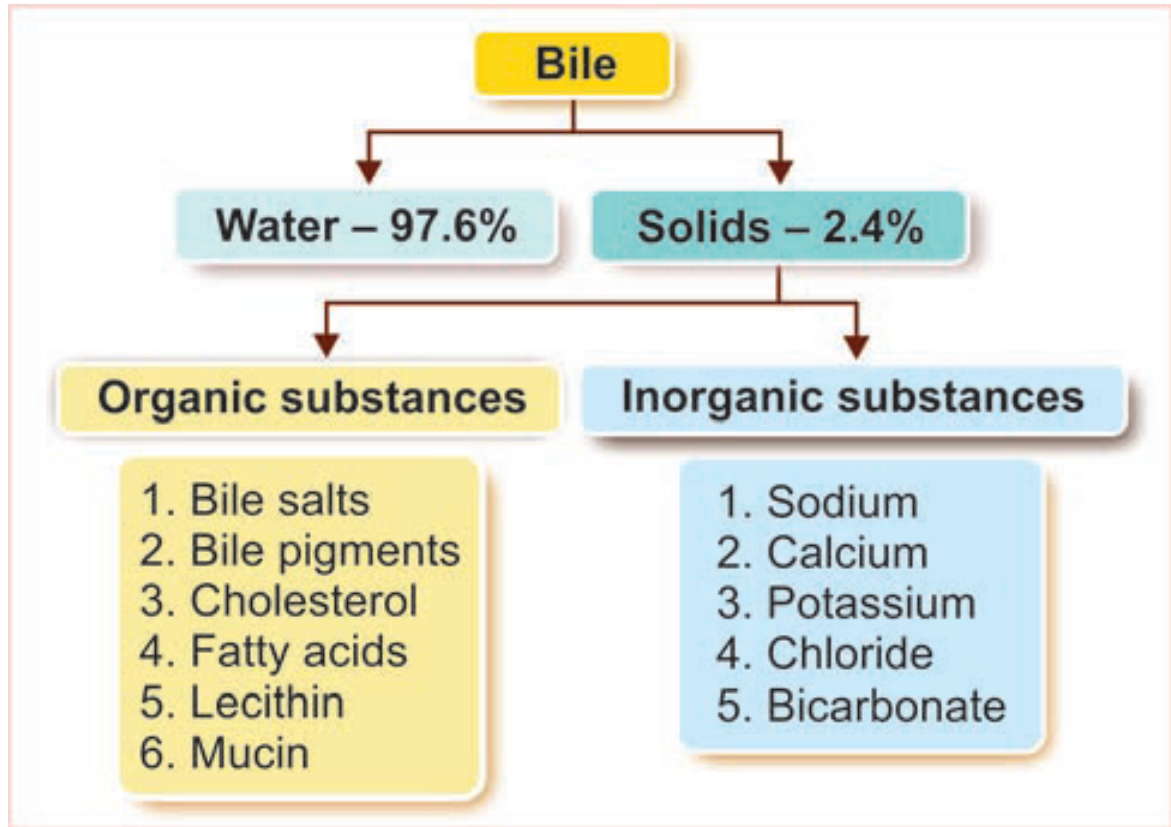
Bilirubin and biliverdin

bilirubin is the major bile pigment in human beings.
Bile pigments are formed during the breakdown of hemoglobin (destroyed RBCs)

Normal bilirubin (Total bilirubin) content in plasma is 0.5-1.5 mg/dL.

- > 1mg/dL→hyperbilirubinemia.
- > 2 mg/dL →jaundice occurs.




Bile
Water – 97.6%
Solids – 2.4%
Organic substances
Inorganic substances
1. Bile salts
2. Bile pigments
3. Cholesterol
4. Fatty acids
5. Lecithin
6. Mucin
1. Sodium
2. Calcium
3. Potassium
4. Chloride
5. Bicarbonate

# Storing and Concentrating Bile in GB

- Bile secreted continually by liver.
- Most of secreted bile is stored in GB until it is needed in D.
- Maximum volume capacity of GB is 30-60 ml
- 12 hr bile secretion is about 450 ml →can be stored in GB due to continous absorption of $H_2O$, Na, Cl, other electrolyte by epithelial mucosa of GB

# Storing and Concentrating Bile in GB

- Absorption is caused by active transport of Na, followed by secondary absorption of Cl, H2O, & others.
- The concentrated bile contain bile salts, cholesterol, lecithin, and billirubin.
- Bile is normally concentrated up to 5 fold or as much as 15 – 20 folds

# Composition of Bile

**Table 65-2** Composition of Bile

| Substance | Liver Bile | Gallbladder Bile |
|---|---|---|
| Water | 97.5 g/dl | 92 g/dl |
| Bile salts | 1.1 g/dl | 6 g/dl |
| Bilirubin | 0.04 g/dl | 0.3 g/dl |
| Cholesterol | 0.1 g/dl | 0.3 to 0.9 g/dl |
| Fatty acids | 0.12 g/dl | 0.3 to 1.2 g/dl |
| Lecithin | 0.04 g/dl | 0.3 g/dl |
| $Na^+$ | 145 mEq/L | 130 mEq/L |
| $K^+$ | 5 mEq/L | 12 mEq/L |
| $Ca^{++}$ | 5 mEq/L | 23 mEq/L |
| $Cl^-$ | 100 mEq/L | 25 mEq/L |
| $HCO_3^-$ | 28 mEq/L | 10 mEq/L |

Not absorbed

# Cholecystokinin Stimulates GB Emptying

1. GB begins to empty (30 min) after fatty meals comes to D.

2. GB emptying is rhythmical contractions of the gallbladder wall + Simultaneous relaxation of sphincter of Oddi.
3. Most potent stimulus for GB contractions is CCK
4. Acetylcholine-secreting nerve fibers from both the vagi and the intestinal ENS have **less** effect on GB contraction.

5. When significant quantities of fat are present, GB empties completely in about 1 hour.

Choleretics=Substances increase the secretion of bile from liver

i. Acetylcholine
ii. Secretin
iii. Cholecystokinin
iv. Acid chyme in intestine
v. Bile salts

Cholagogue=agent increases release of bile into intestine by contracting gallbladder

i. Bile salts
ii. Calcium
iii. Fatty acids
iv. Amino acids
v. Inorganic acids

All these substances stimulate the secretion of cholecystokinin

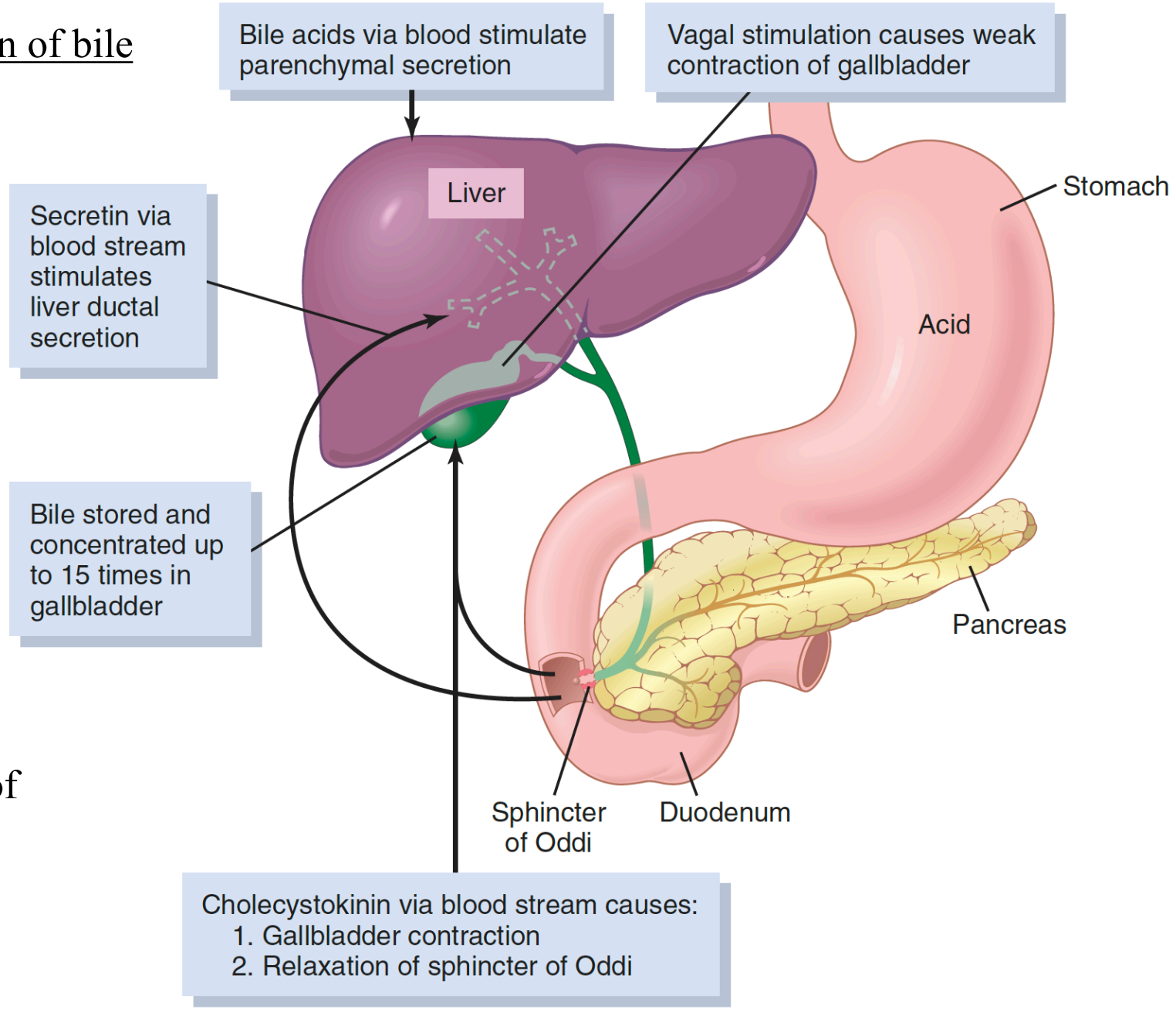
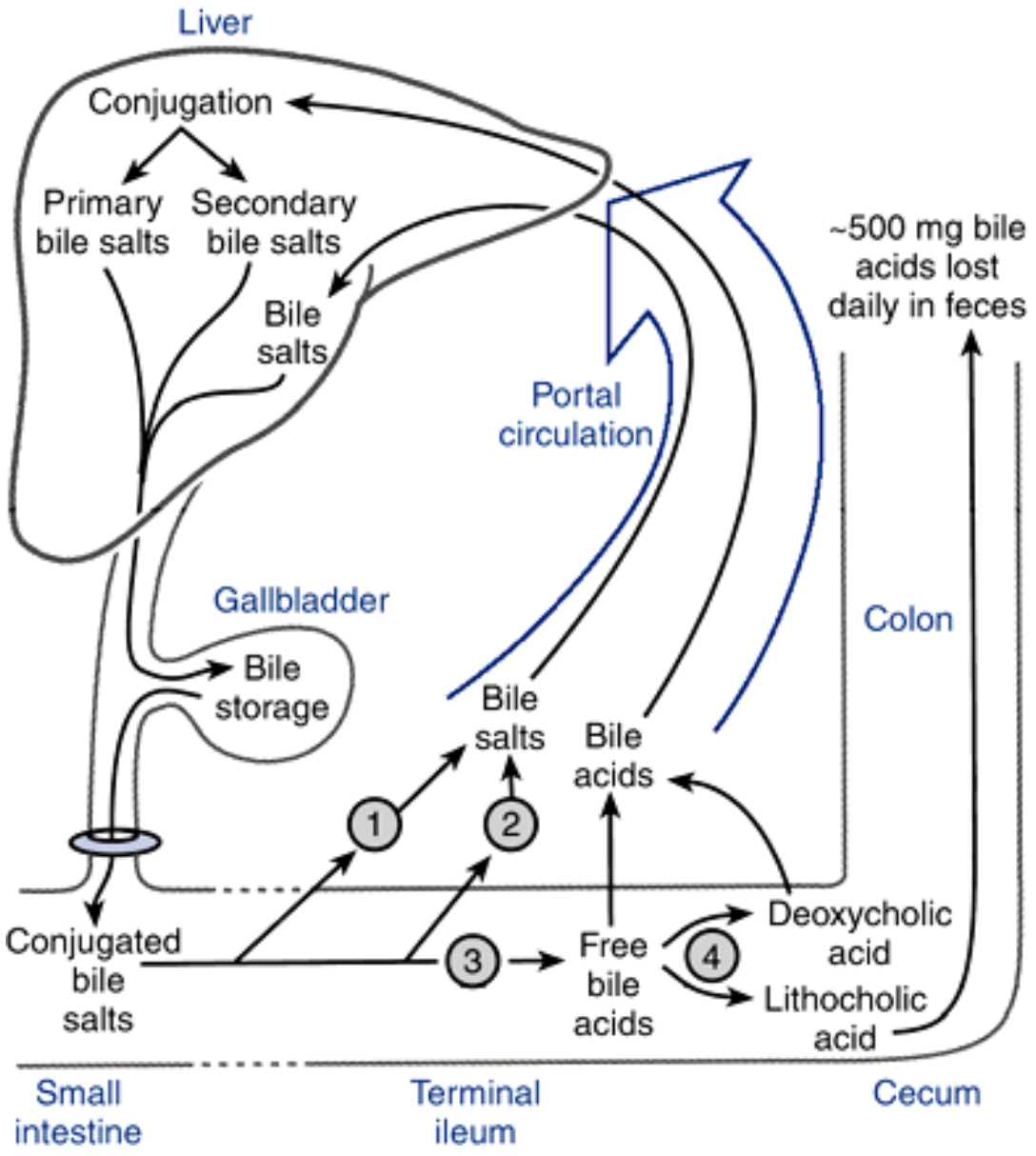



**Figure 65-11.** Liver secretion and gallbladder emptying.

## Enterohepatic Circulation of Bile Salts

- 94% of bile salts are reabsorbed into blood
- from SI
- ½ → by diffusion through mucosa (early portions of SI)
- ½ → active transport process through I mucosa in distal ileum.

- Enter portal blood and pass back to the liver.



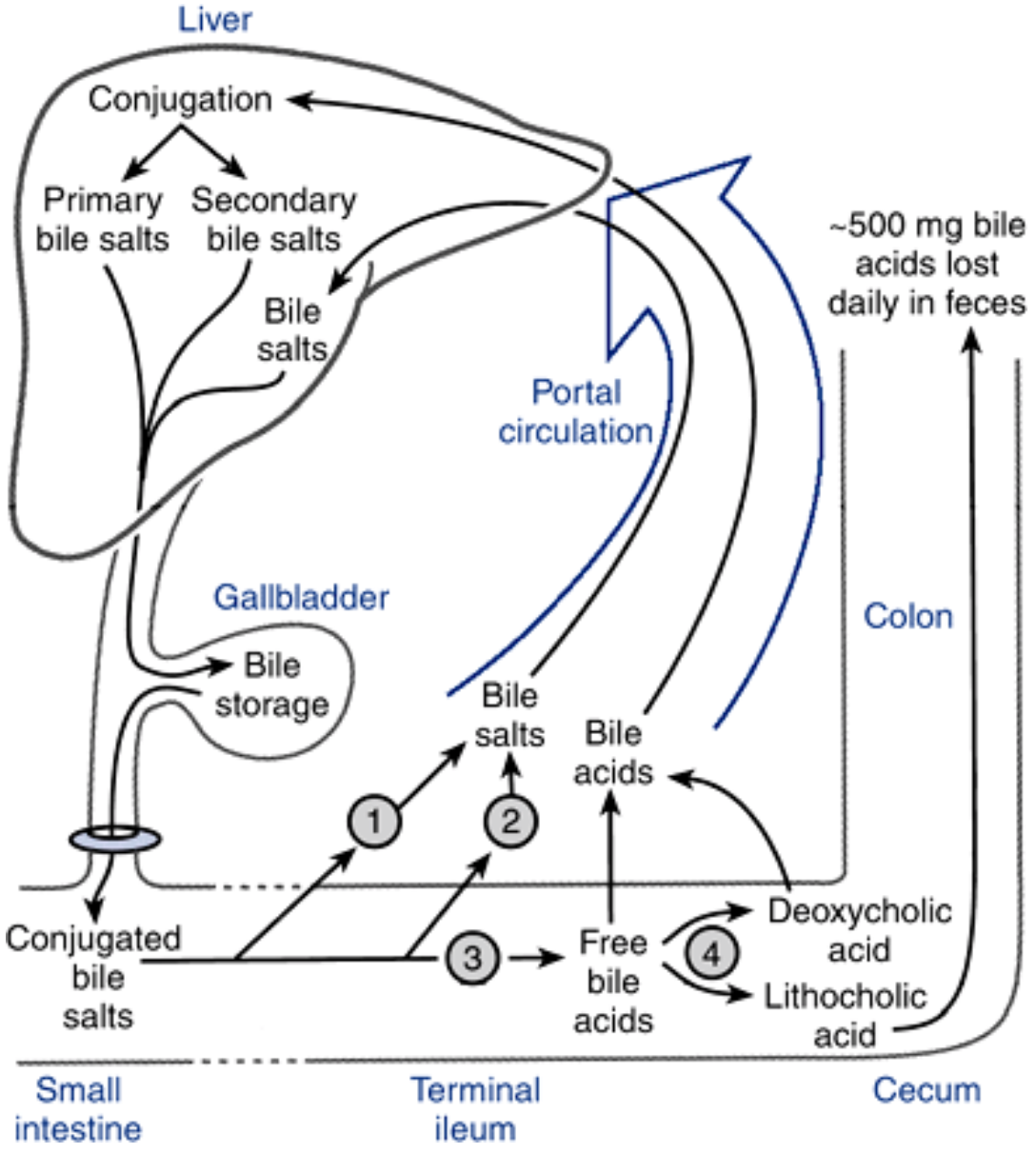
**Enterohepatic Circulation of Bile Salts**.

- Salts are absorbed almost entirely back into hepatic cells & resecreted into bile.

- Small quantities of bile salts lost into feces → replaced by new amounts formed by liver cells.
- 
- Quantity of bile secreted by liver is dependent on availability of bile salts

- Bile fistula → liver increases production of bile salts 6-1 0-fold → ↑ bile secretion

- Secretin ↑ bile secretion (↑ NaHCO3)



1,2-Inflammation of the gallbladder epithelium

3-high-fat diet

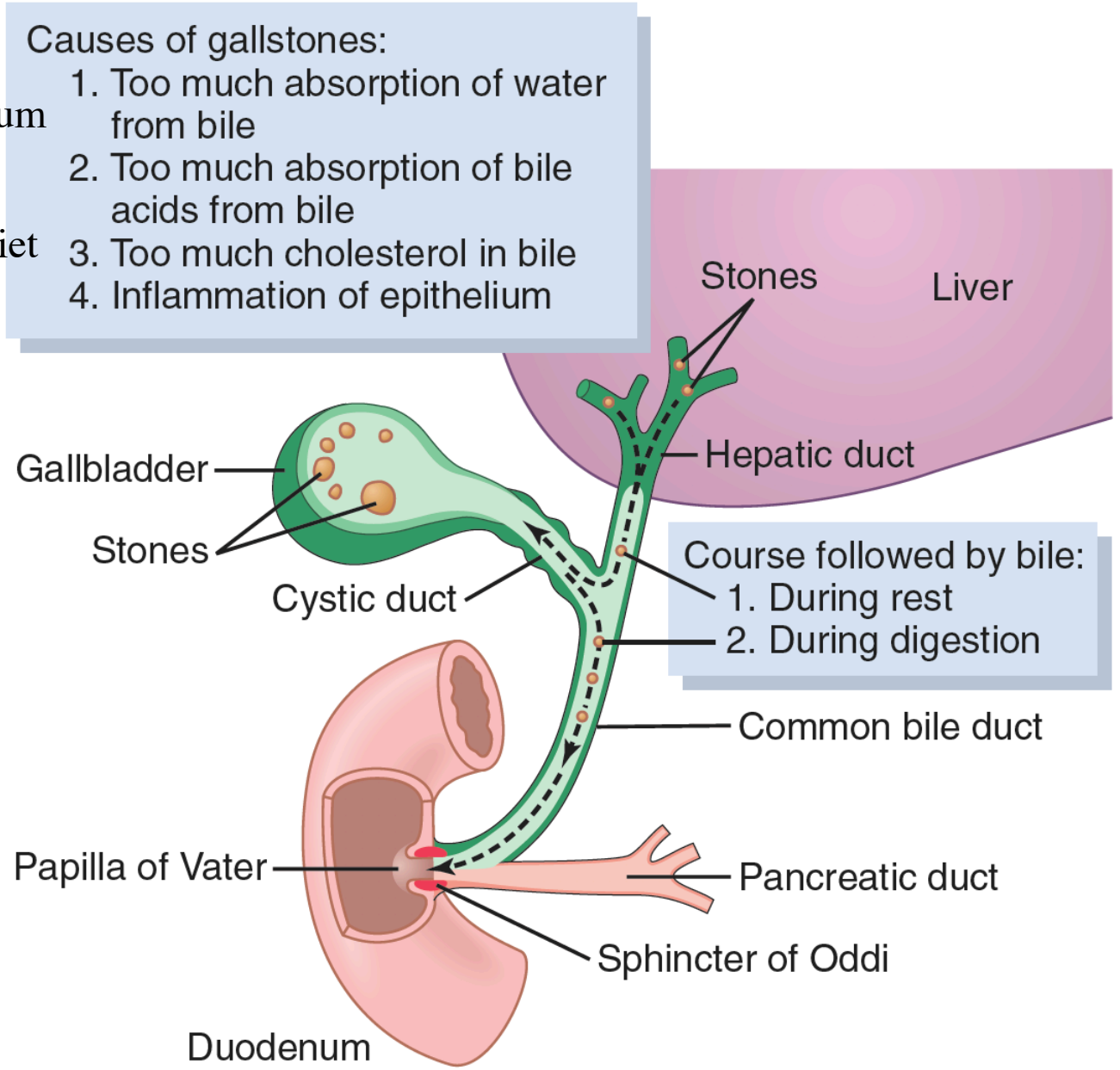



**Figure 65-12.** Formation of gallstones.