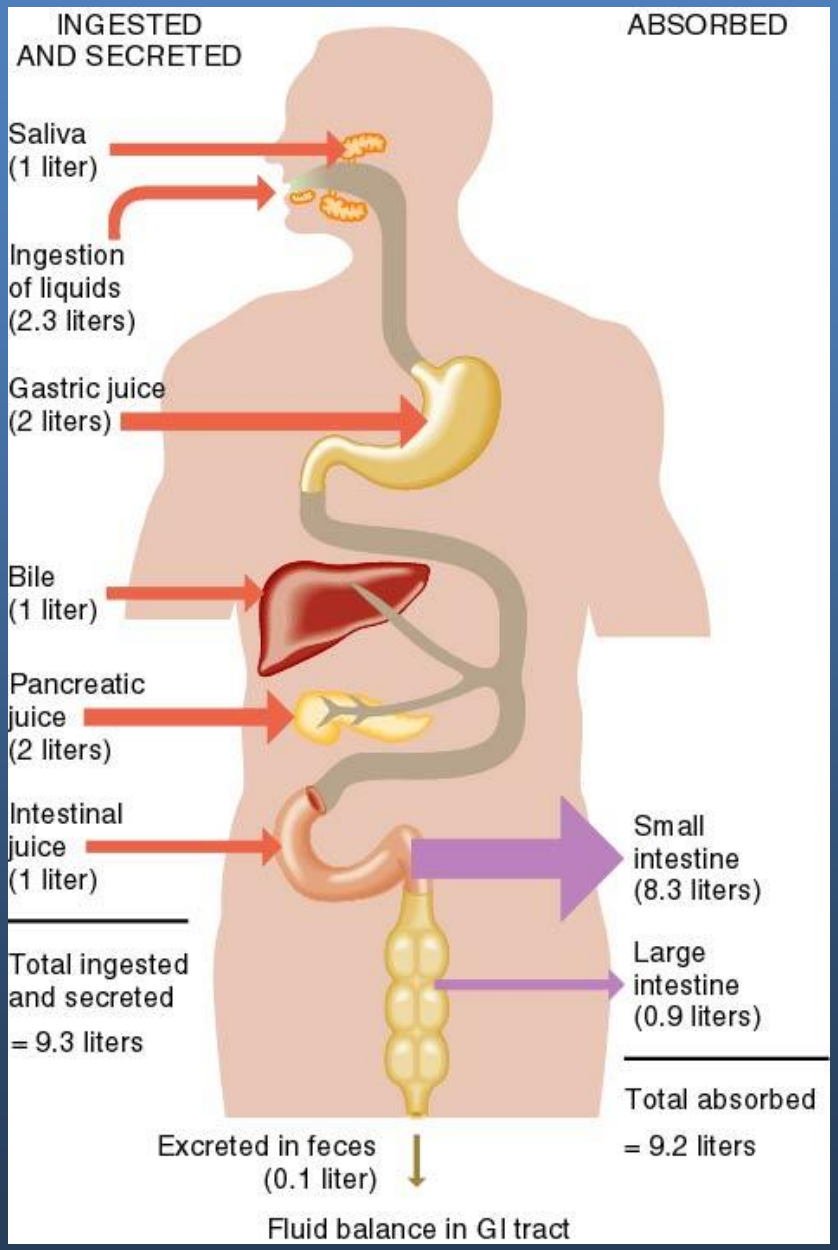
Gastrointestinal Physiology

Secretion

Fig. 24.26


INGESTED AND SECRETED
ABSORBED
Saliva (1 liter)
Ingestion of liquids (2.3 liters)
Gastric juice (2 liters)
Bile (1 liter)
Pancreatic juice (2 liters)
Intestinal juice (1 liter)
Total ingested and secreted = 9.3 liters
Small intestine (8.3 liters)
Large intestine (0.9 liters)
Total absorbed = 9.2 liters
Excreted in feces (0.1 liter)
Fluid balance in GI tract

Functions

Provided by secretory glands which serve 2 functions:

- Digestive enzymes.
- Lubrication and protection of the mucosa.

Types of secretory structures

The types of secretory glands:

- Single-cell secretory glands (goblet cells).

- Pits that represent invaginations of the epithelium in the submucosa in small intestine are known as crypts of Lieberkühn.

- Complex glands : in stomach and duodenum.

- Organs: salivary, pancreas and liver. Located outside the tubular structure of the GI.

Control of secretion

Neural Control

ENS:

ANS:

Parasympathetic:

Sympathetic:

- **moderate increase →**
- **it reduces secretion by reducing blood → flow.**

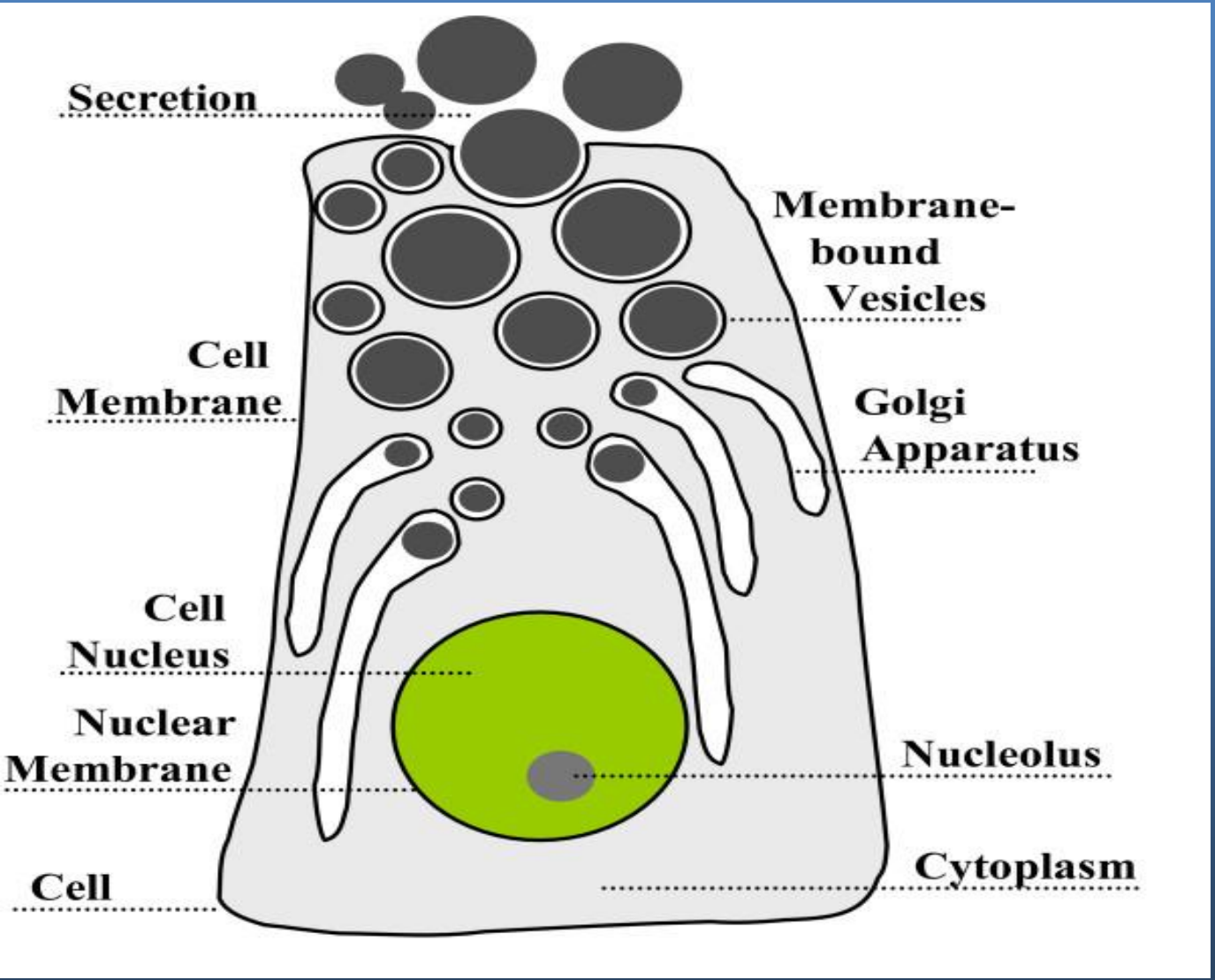
Hormonal regulation

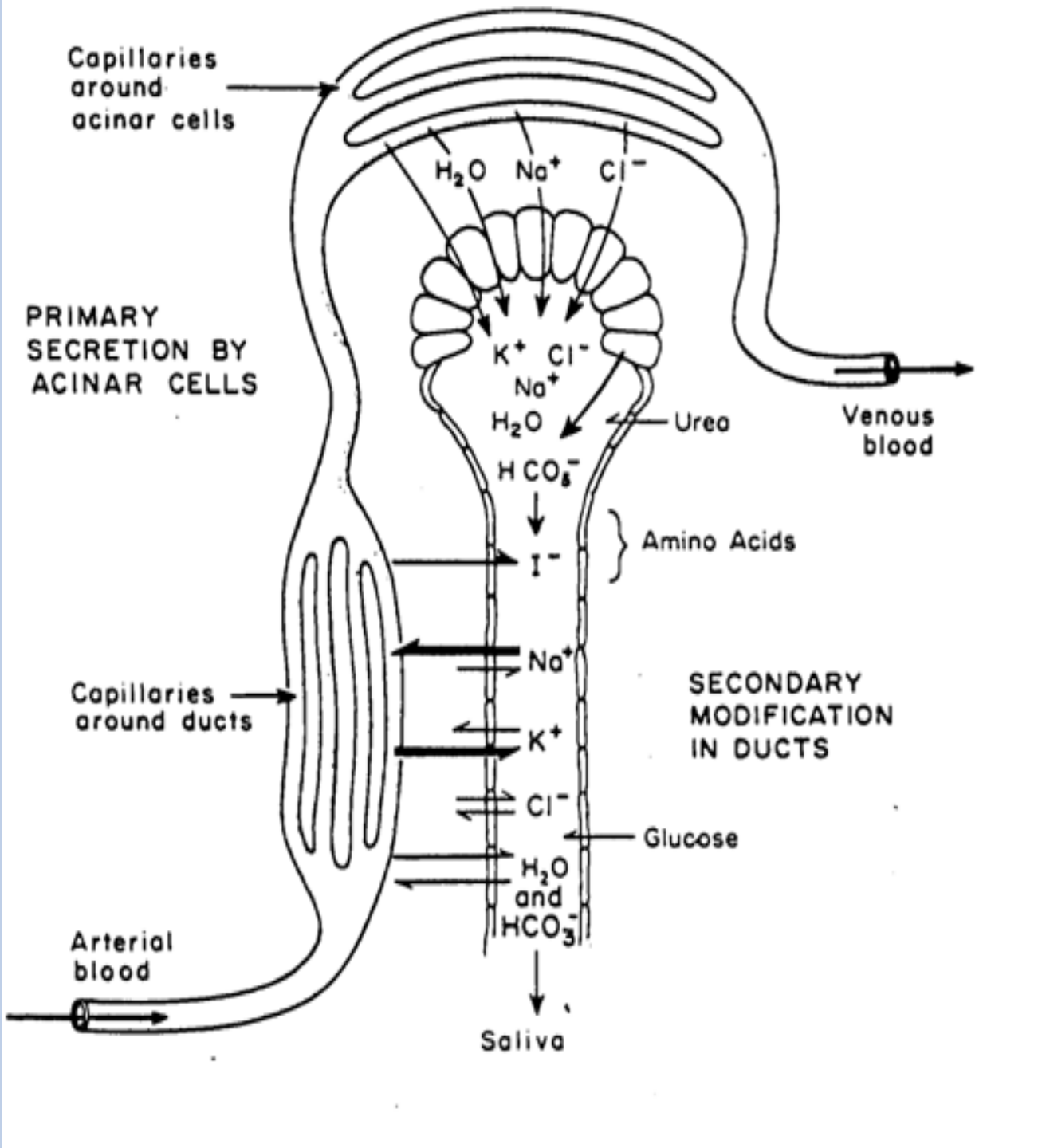
Some hormones are secreted by the presence of food or other local changes in the digestive organs.

Salivary Secretions

Salivary Glands

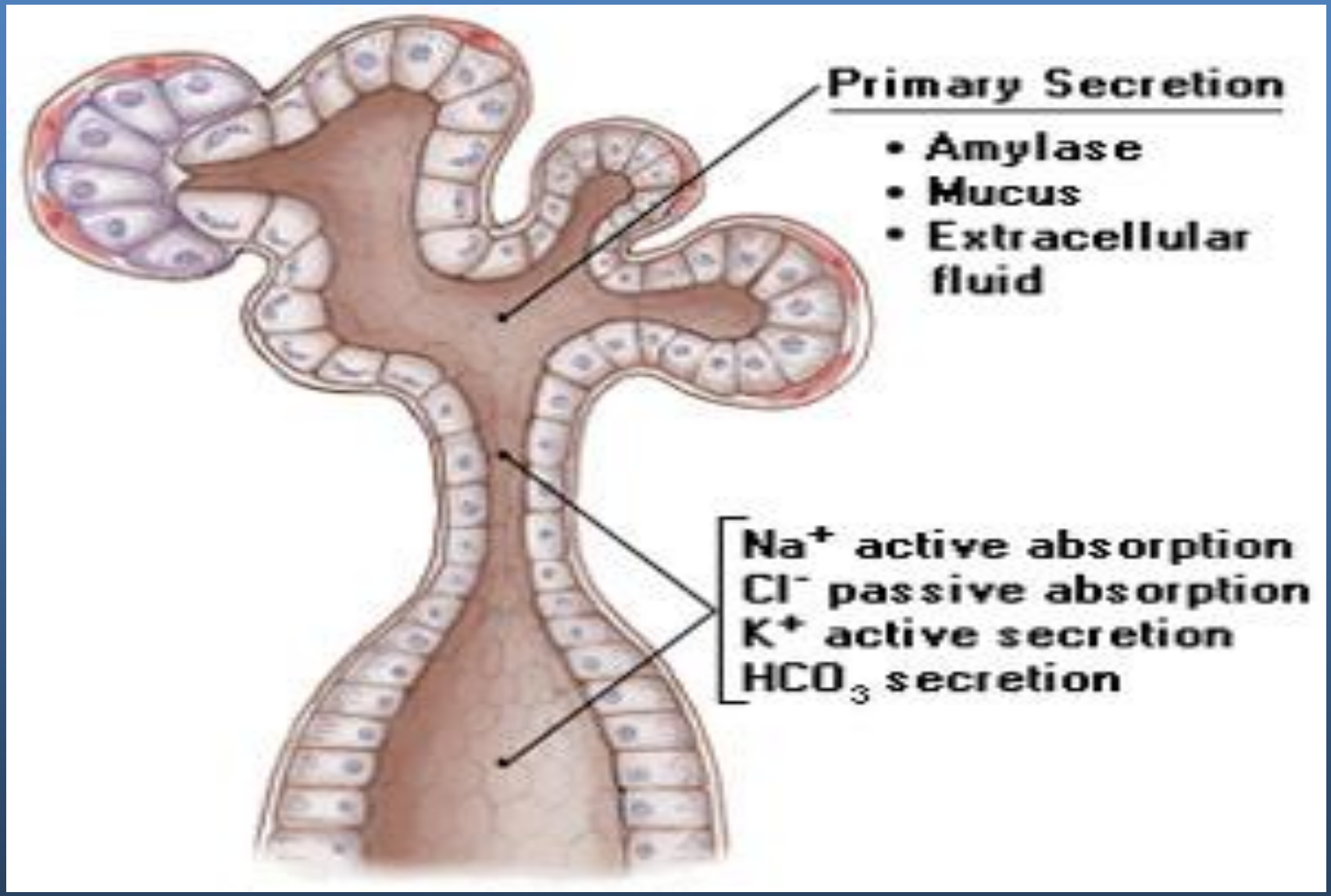
Name of Gland	Type of Saliva	% of Total Saliva Secreted
Submandibular	Mucous-serous	70
Parotid	Serous	25
Sublingual	Mucous	5

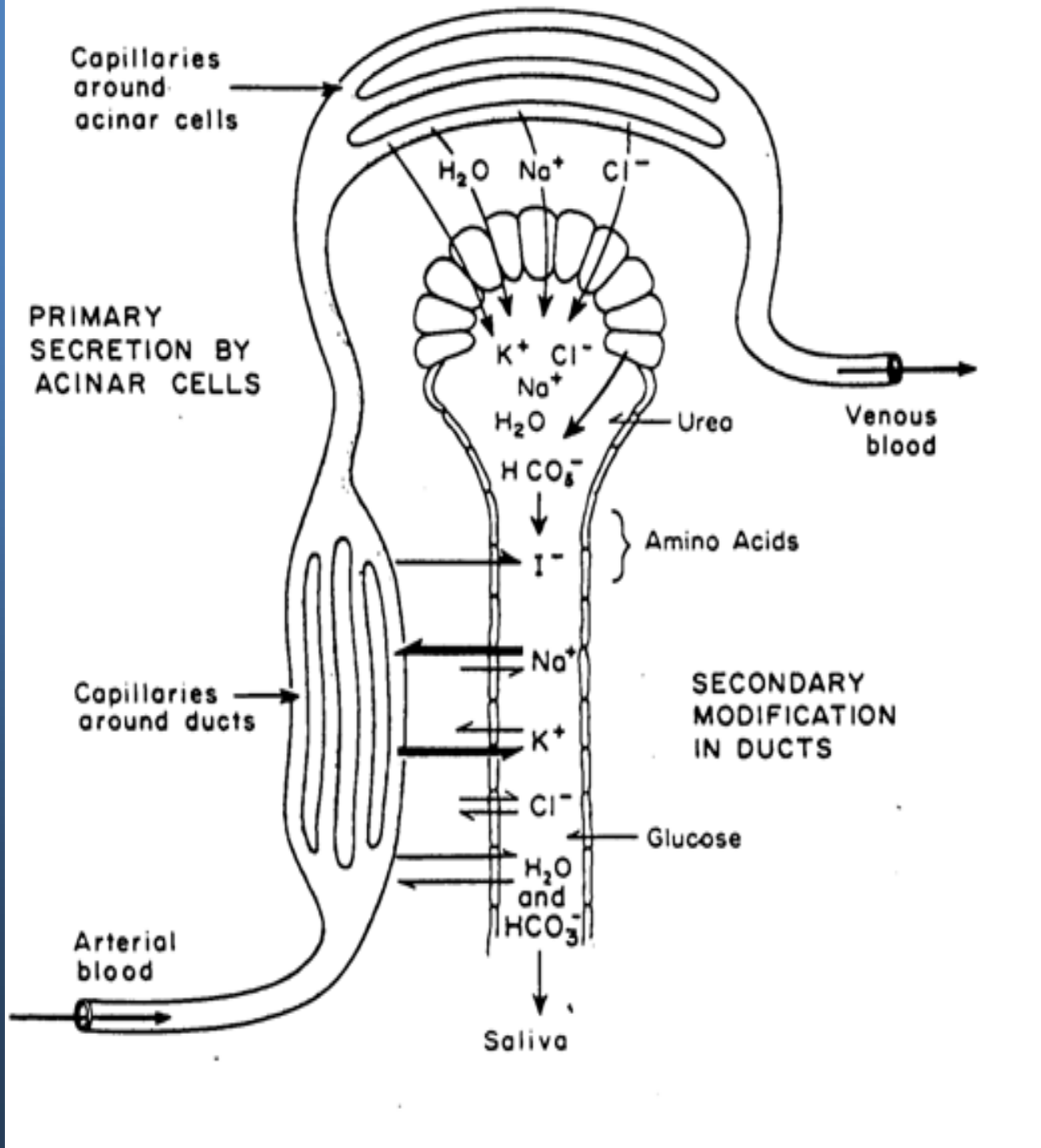

Secretion
Membrane-
bound
Vesicles
Cell
Membrane
Golgi
Apparatus
Cell
Nucleus
Nuclear
Membrane
Nucleolus
Cell
Cytoplasm


Capillaries around acinar cells
H_2O Na^+ Cl^-
PRIMARY SECRETION BY ACINAR CELLS
K^+ Cl^-
Na^+
H_2O
Urea
Venous blood
HCO_3^-
I^-
Amino Acids
Capillaries around ducts
Na^+
K^+
SECONDARY MODIFICATION IN DUCTS
Cl^-
Glucose
H_2O and HCO_3^-
Arterial blood
Saliva

Mechanism of Secretion

- **Active transport of Cl-** at the basal portion of the membrane.
- Increase in negativity of membrane potential which **attract the positive ion (Na+).**
- Increase osmotic pressure inside the cell >> **pull water inside** >> increase hydrostatic pressure.
- This increase results in **minute ruptures at the lumenal part** of the membrane which causes flushing of water,


Primary Secretion
• Amylase
• Mucus
• Extracellular fluid
Na^+ active absorption
Cl^- passive absorption
K^+ active secretion
HCO_3 secretion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Capillaries around ducts
Na^+
SECONDARY MODIFICATION IN DUCTS
K^+
Cl^-
Glucose
H_2O and HCO_3^-
Arterial blood
Saliva

Changes in Composition in Final Saliva

↓ the Na+ and Cl- concentration to the 1/10 of their plasma concentration

↑ 7 folds increase in K+ concentration.

↑ HCO3- concentration also increases 2-3 times.

Rate of Secretion

The amount of salivary secretion is about 1500ml/day.

Resting secretion rate 0.025-0.5ml/min (during basal conditions).

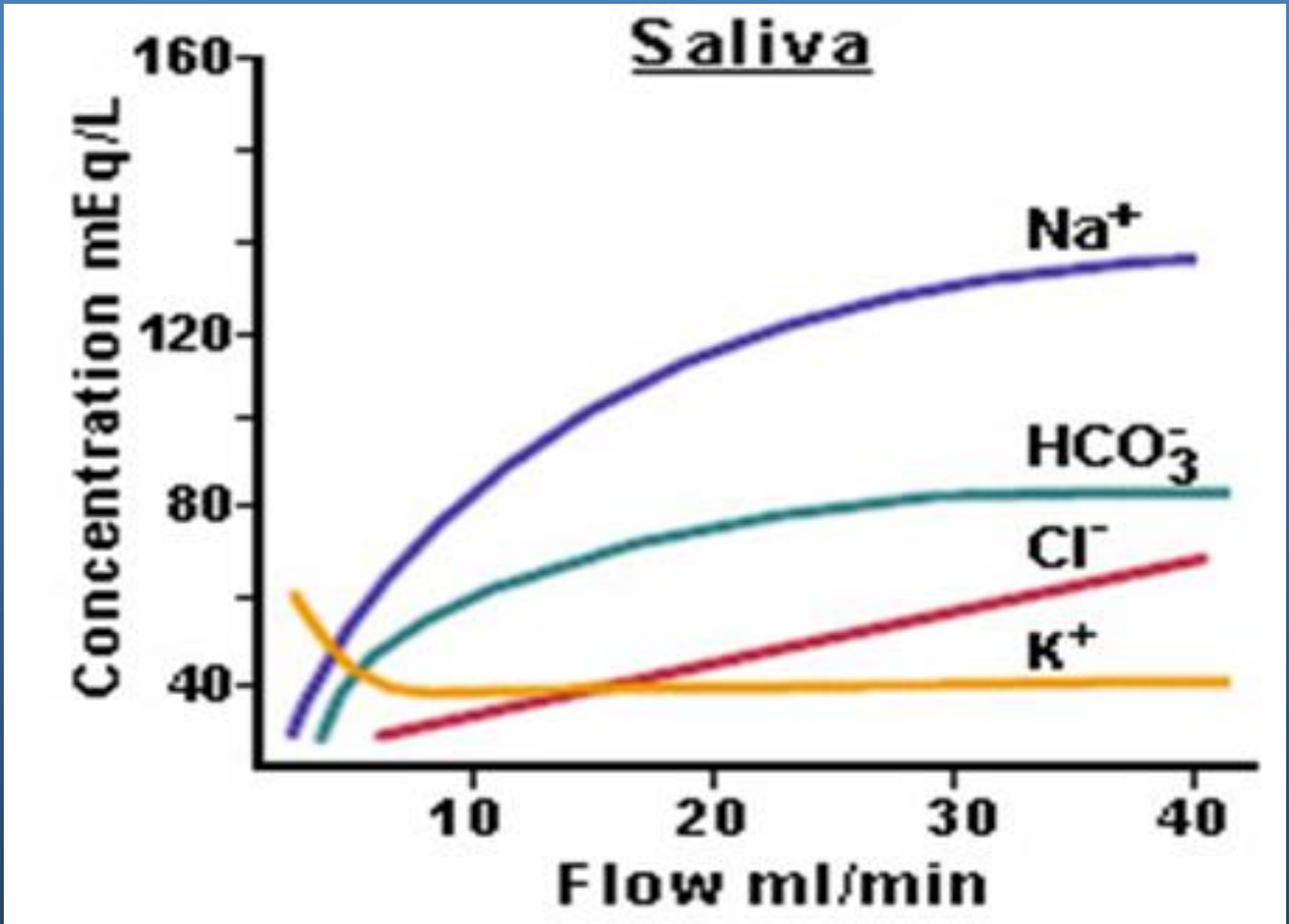
The pH = 7.0

DURING MAXIMAL STIMULATION

The primary saliva increasing 20 folds.

- Flow rate of saliva is increased

PH=8


Saliva
160
120
80
40
Concentration mEq/L
Na+
HCO3-
Cl-
K+
10
20
30
40
Flow ml/min

Control of salivary Secretion

Autonomic nervous system.

- Both sympathetic and parasympathetic increase salivation but by different mechanisms

- **parasympathetic** increase water and electrolyte secretion.

- **Sympathetic** increase mucin synthesis.

→An increase in the sympathetic activity reduces salivation

Control of salivary Secretion

Aldosterone:

Salivation is increased by:

- **Unconditioned** salivary reflex (dental procedures).
- **Conditioned** salivary reflex (learned – response).

Functions of Saliva

- Saliva begins **digestion** of carbohydrates in the Saliva begins digestion of carbohydrates in the mouth:

Amylase that breaks polysaccharide into maltose (disaccharide consists of 2 glucose).

- **Facilitate swallowing** by:

Moistening the food particles.

Lubrication

Functions of Saliva

- Antibacterial actions:

Lysozyme: an enzyme that lyses or destroys certain bacteria.

- Oral hygiene

keeping mouth and teeth clean by the constant flow and secretion of

IgA which helps in the destruction of bacteria

Functions of Saliva

- Solvent for molecules that stimulate taste buds.
- Aids speech.
- Bicharbonate neutralizes acids

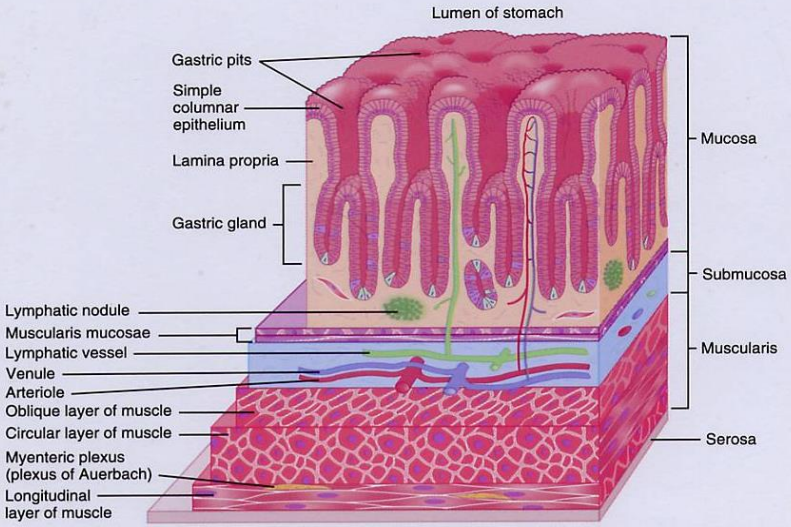
  →preventing cari

Esophageal secretion

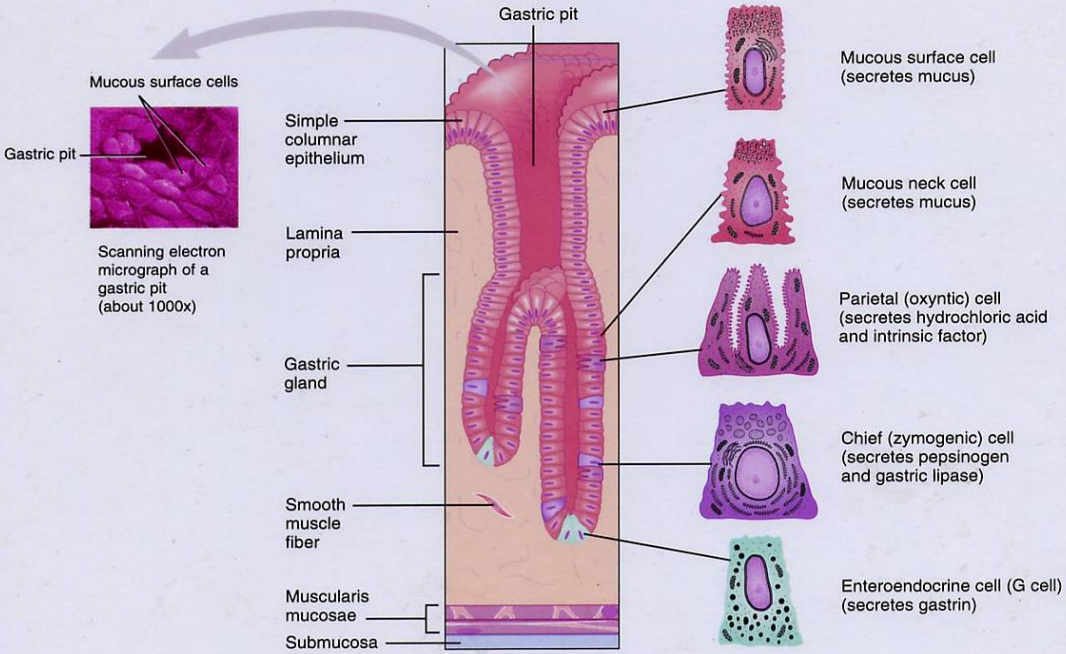
- Simple mucus glands and solitary cells (mucoid character) help in lubrication and protection.

- Compound mucus glands near the esophago-gasrtic junction and protect the esophagus from reflux.

Gastric Secretions



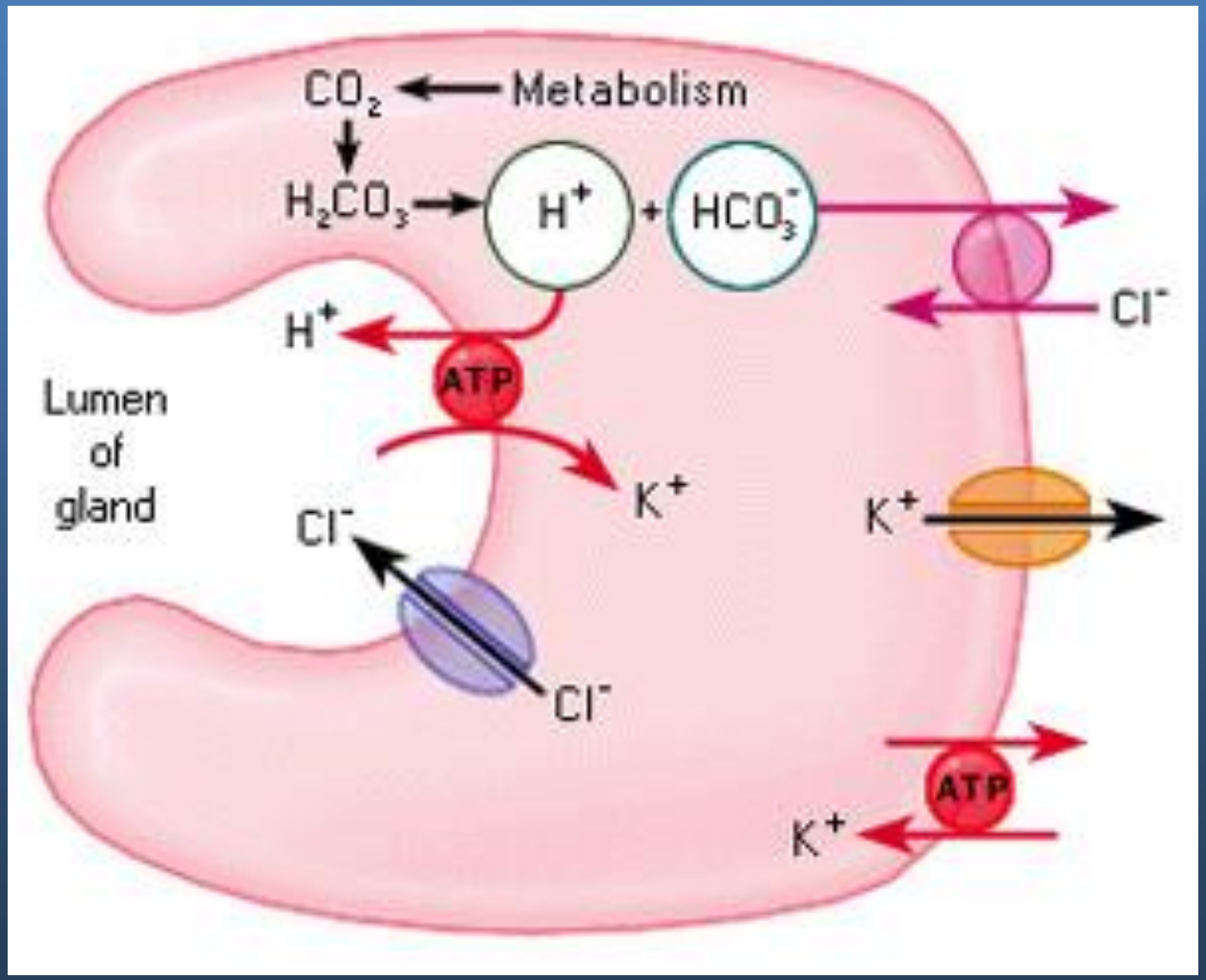
(a) Three-dimensional view of layers of the stomach



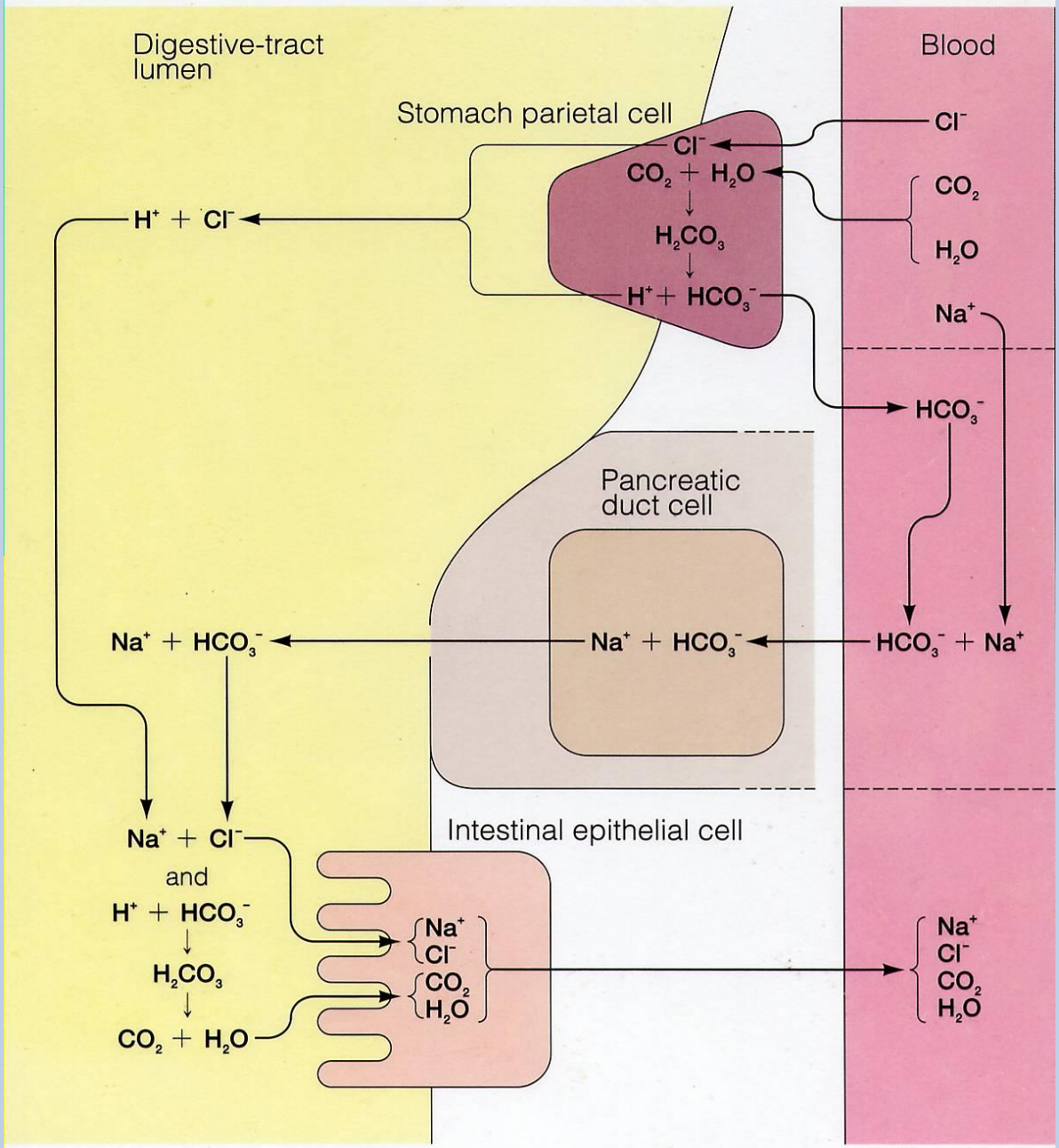
(b) Sectional view of the stomach mucosa showing gastric glands

Histology of the Stomach: Layers of the Stomach and the Stomach Mucosa, Fig# 24.12a-b

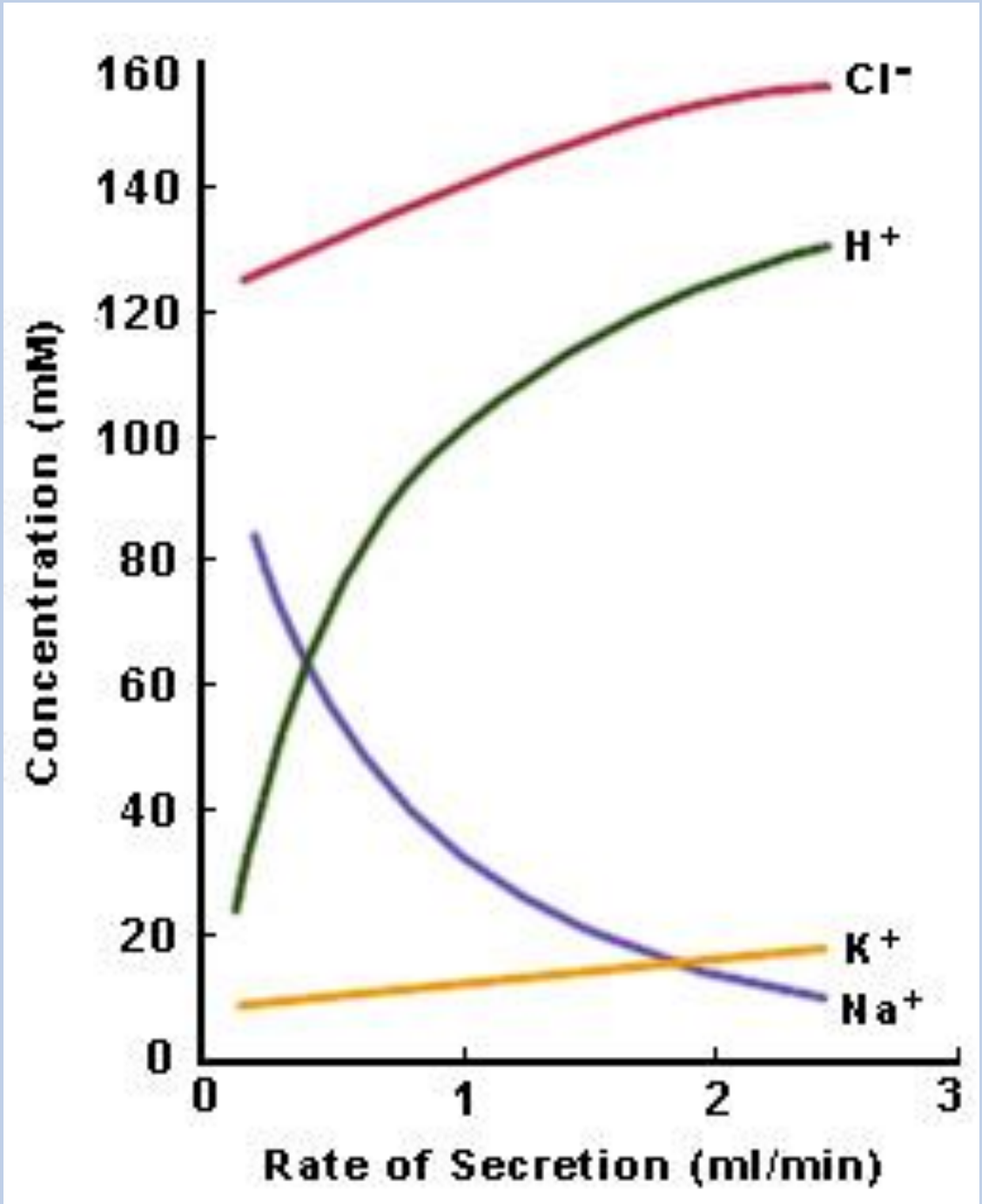
Mechanism of HCl Secretion

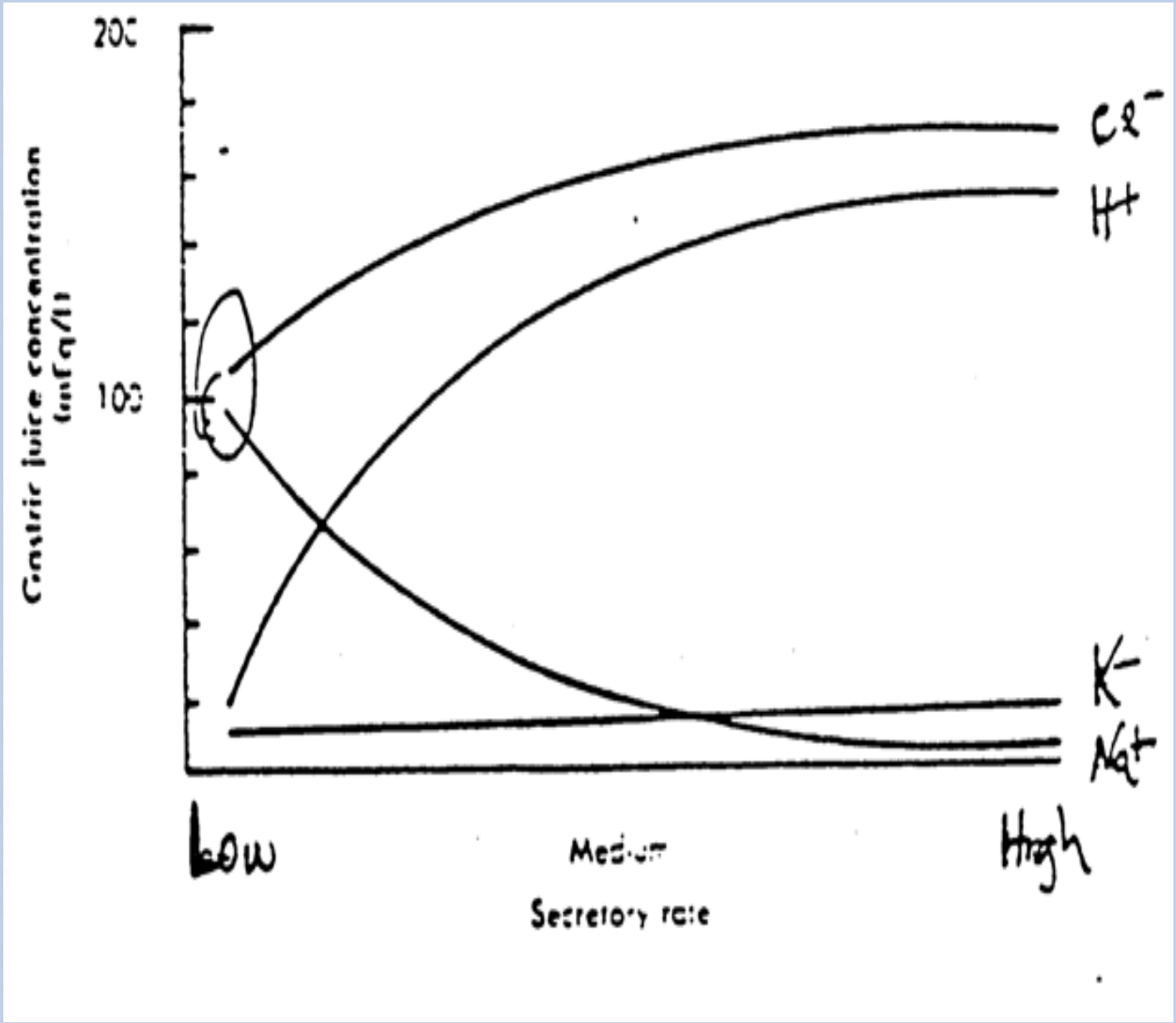


Biochemical Balance Among the Stomach, Pancreas, and Small Intestine



Acetate 158 (Figure 16-30)


160
140
120
100
80
60
40
20
0
Concentration (mM)
Cl⁻
H⁺
K⁺
Na⁺
0
1
2
3
Rate of Secretion (ml/min)


200
100
Gastric juice concentration (mEq/l)
Cl⁻
H+
K+
Na+
Low
Medium
High
Secretory rate

Functions of HCl

- Conversion of pepsinogen to pepsin
- Helps in the decomposition of connective tissue.
- Defense (killing most microorganisms ingested with food).

Secretion of pepsinogen

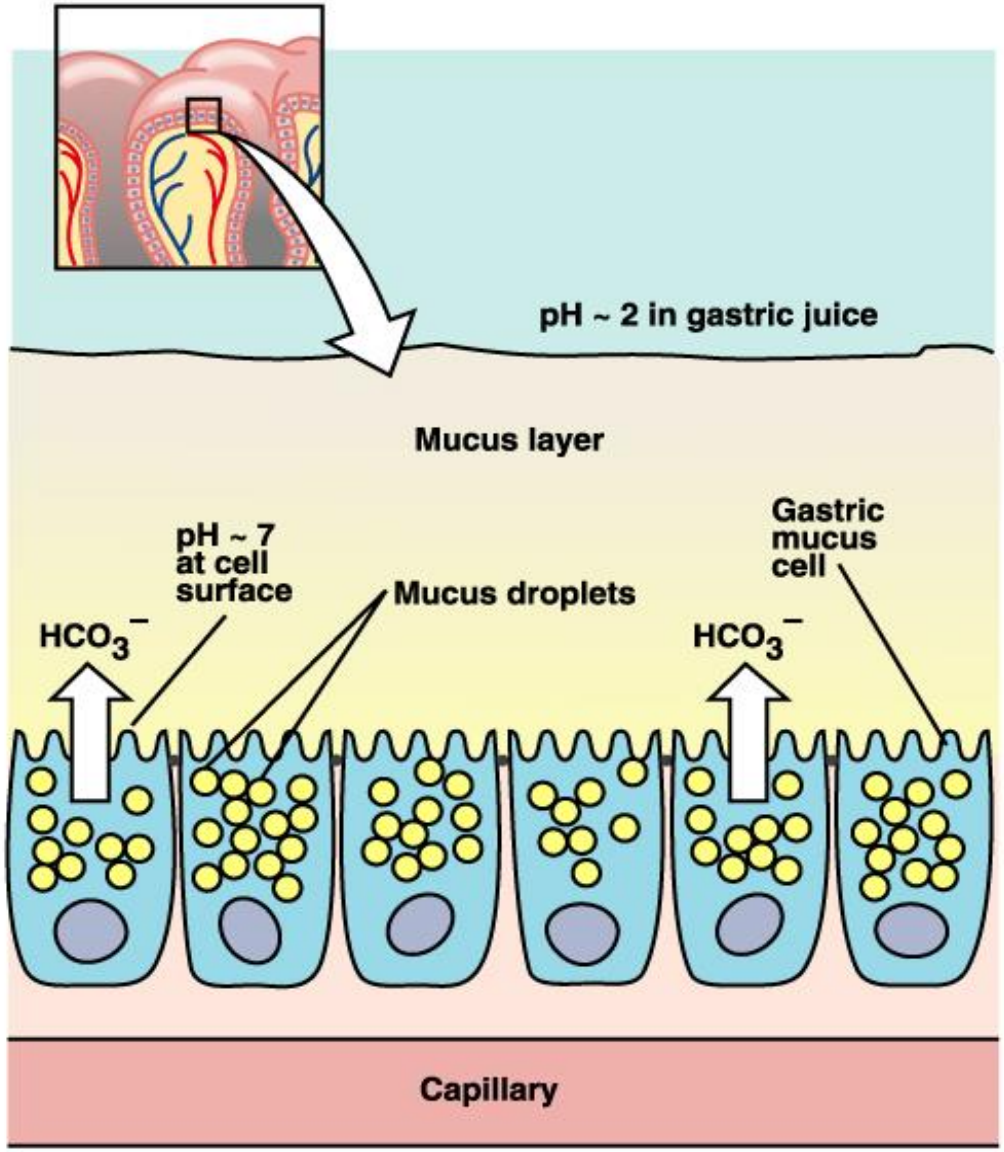
Secreted by peptic (chief) and mucos cells.

- Optimal activity at pH (1.8-3.5).

Function:

- Pepsin cleaves the peptide linkage protein →into smaller peptide fragments.

Mucus secreting cells



Mucus secreting cells

Function:

- Lubricating functions.
- Protect the mucosa from the chemical injury by:
  - Preventing the activity of the proteolytic enzymes to act on the mucosa
  - Neutralizing HCl by its alkaline character.

Gastrin Secretion

Secreted by G cells

stimulated by:

- gastric distention.
- presence of proteins in chyme.
- vagal stimulation.

Functions:

- Increases HCl and pepsinogen secretion.
- trophic effect on gastric mucosa to maintain growth of mucosal cells.

Secretion of Intrinsic factor

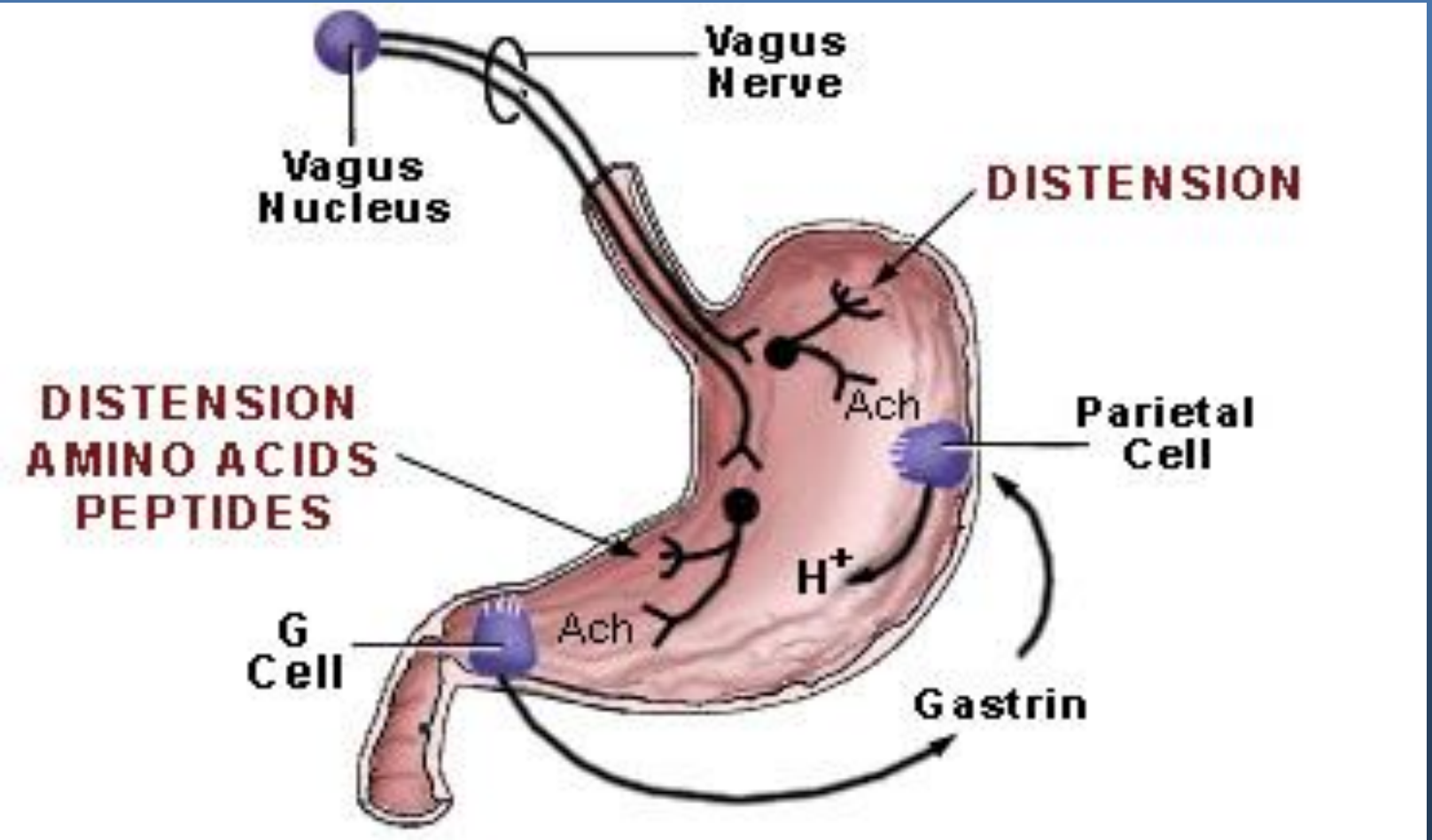
Is secreted by parietal cells (**oxyntic cells**).

Essential for B12 absorption

Control of Gastric Secretion

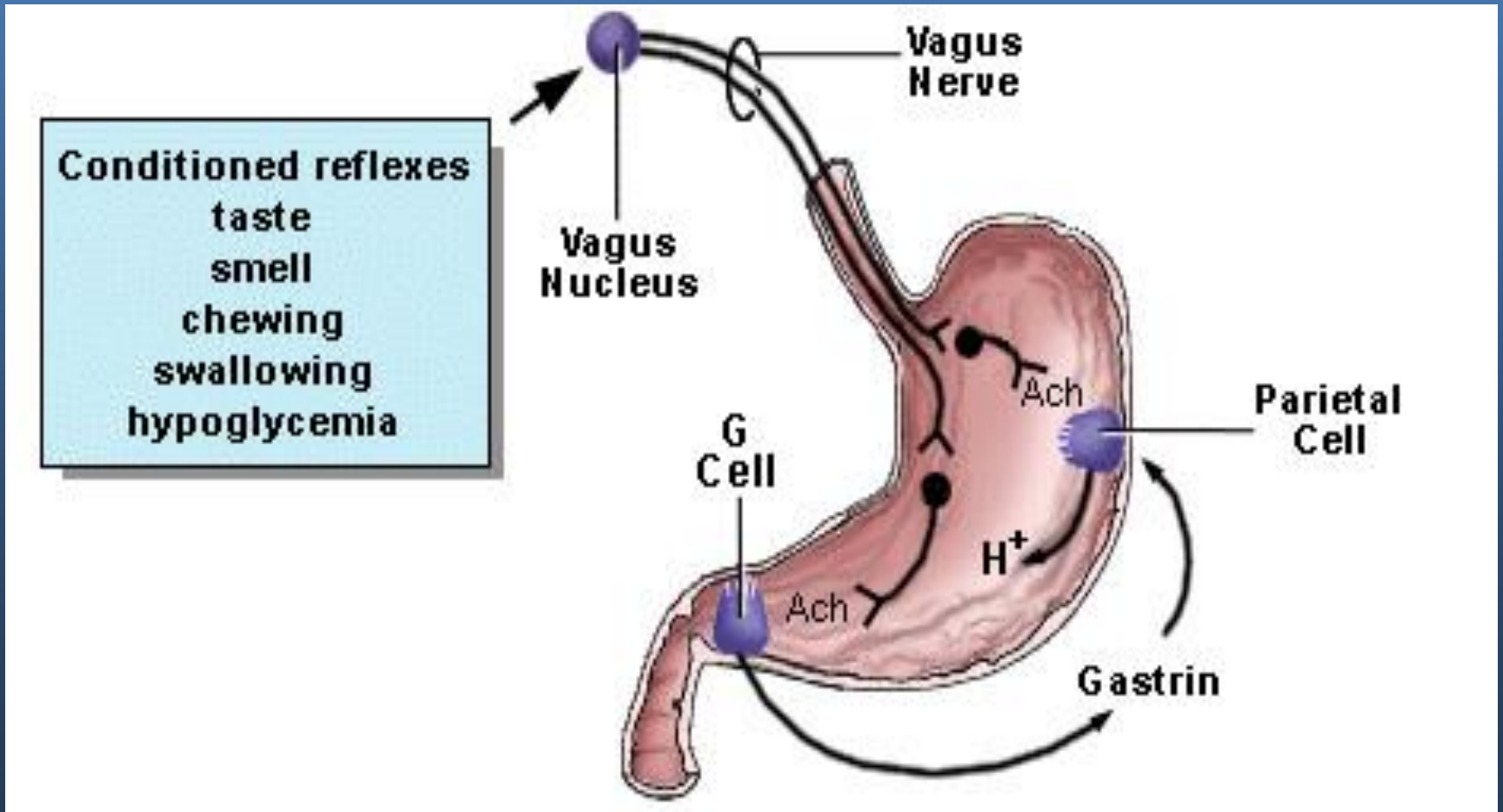
Neural Control

ENS: Ach neurons → parietal and peptic cells.



Neural Control

ANS (**Parasympathetic**): vagal activation during cephalic and gastric phases (via long arc reflex)



Neural Control

ANS (**Parasympathetic**): vagal activation during cephalic and gastric phases (via long arc reflex)

- **enteric excitatory** neurons to release **Ach**.

- **enteric neurons** → enterochromaffin-like cells →**Histamine**.

- **enteric neurons** that release GRP → Gastrin Releasing Peptide → G Cells→ **Gastrin.**

Control of Gastric Secretion

Hormonal control

Gastrin → parietal cells →increase HCl secretion.

Gastrin stimulate CCK-B receptor on oxyntic cells to secrete HCl.

This receptor can also be activated by CCK (cholecystokinin).

Control of Gastric Secretion

Paracrine

Histamine (secreted by enterochromaffin-like cells) → H2 receptors on parietal cells → increased cAMP → increased HCl secretion.

Somatostatin (SS) → SS receptors on parietal cells decrease cAMP → decrease HCl secretion.

Role of HCl in controlling secretion

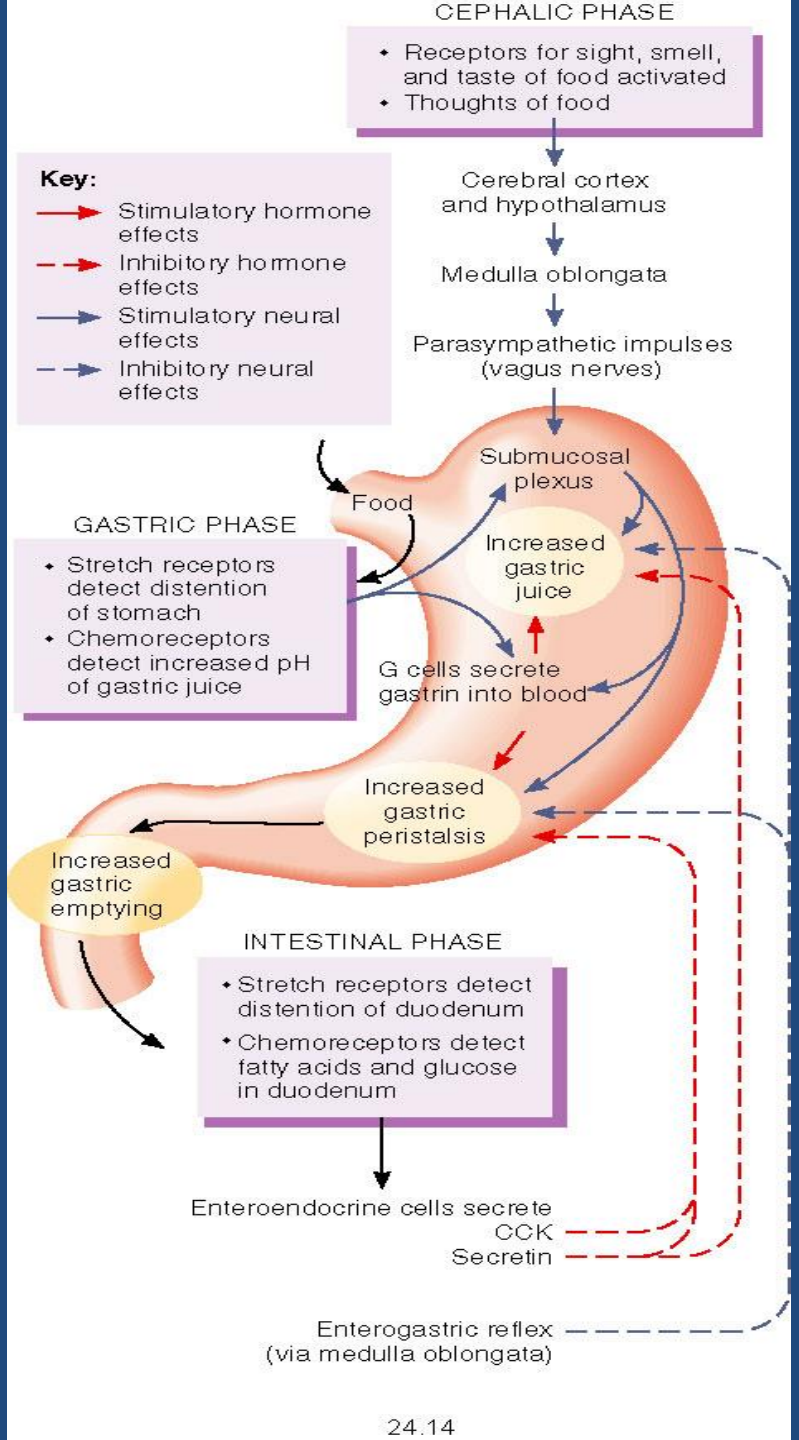
- HCl acts indirectly by initiating enteric reflexes that causes an increase in pepsinogen secretion by peptic cell.

- **Excess of acids**
- causes feed back inhibition of gastric secretions by 2 ways:
    * Reduction of gastrin release
    * Initiation of inhibitory reflexes.

This maintains the pH from falling below 3.

Summary of Control

- Cephalic phase
- Gastric phase
- Intestinal phase



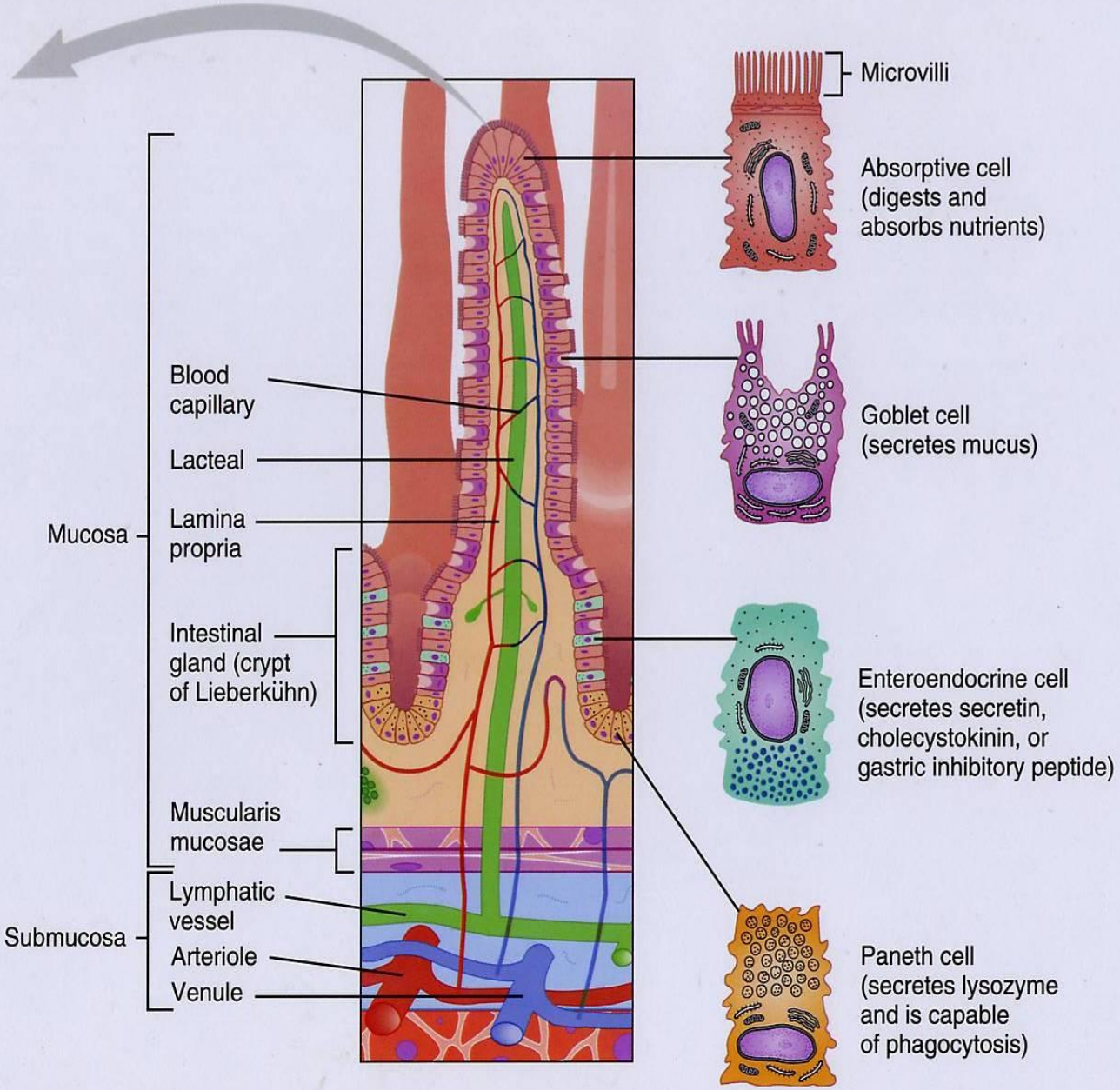
3 phases of control of gastric secretions

- Cephalic phase: stimuli before food reaching the stomach via parasympathetic NS
- Gastric phase: Food in stomach
  - Distension and the presence of proteins local and long reflexes increased gastric secretion.
  - Caffeine and alcohol also stimulate acid secretions

via ENS, ANS and Hormones

- Intestinal phase:
  - Excitatory
  - Inhibitory

Intestinal Secretions



Enlarged Villus Showing Lacteal, Capillaries and Intestinal Gland, Fig# 24.23b

Small Intestinal Secretions

(1500ml/day)

- Cells of mucosal epithelium secrete mucus, water and electrolytes.

Tubular glands (crypts of Leiberkuhn) secrete serous secretion.

Small Intestinal Secretions

Regulation

Neural mechanisms (mediated by Ach and VIP.

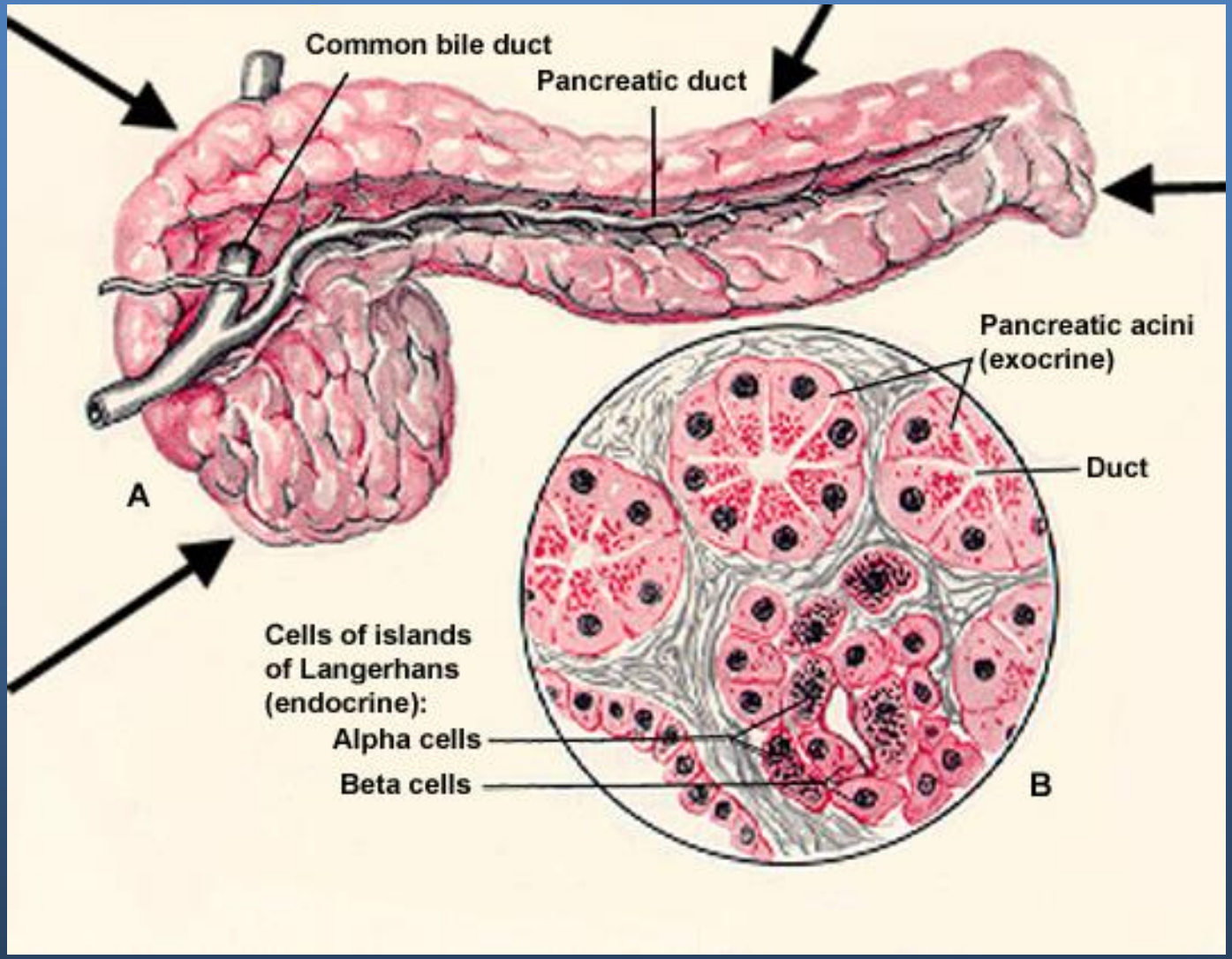
Hormonal:

Secretin: increases duodenal secretion.

Colonic secretions

- Mostly mucus secretion
- Small amount of serous secretions which is high in K+ and HCO3-.

Pancreatic Secretions

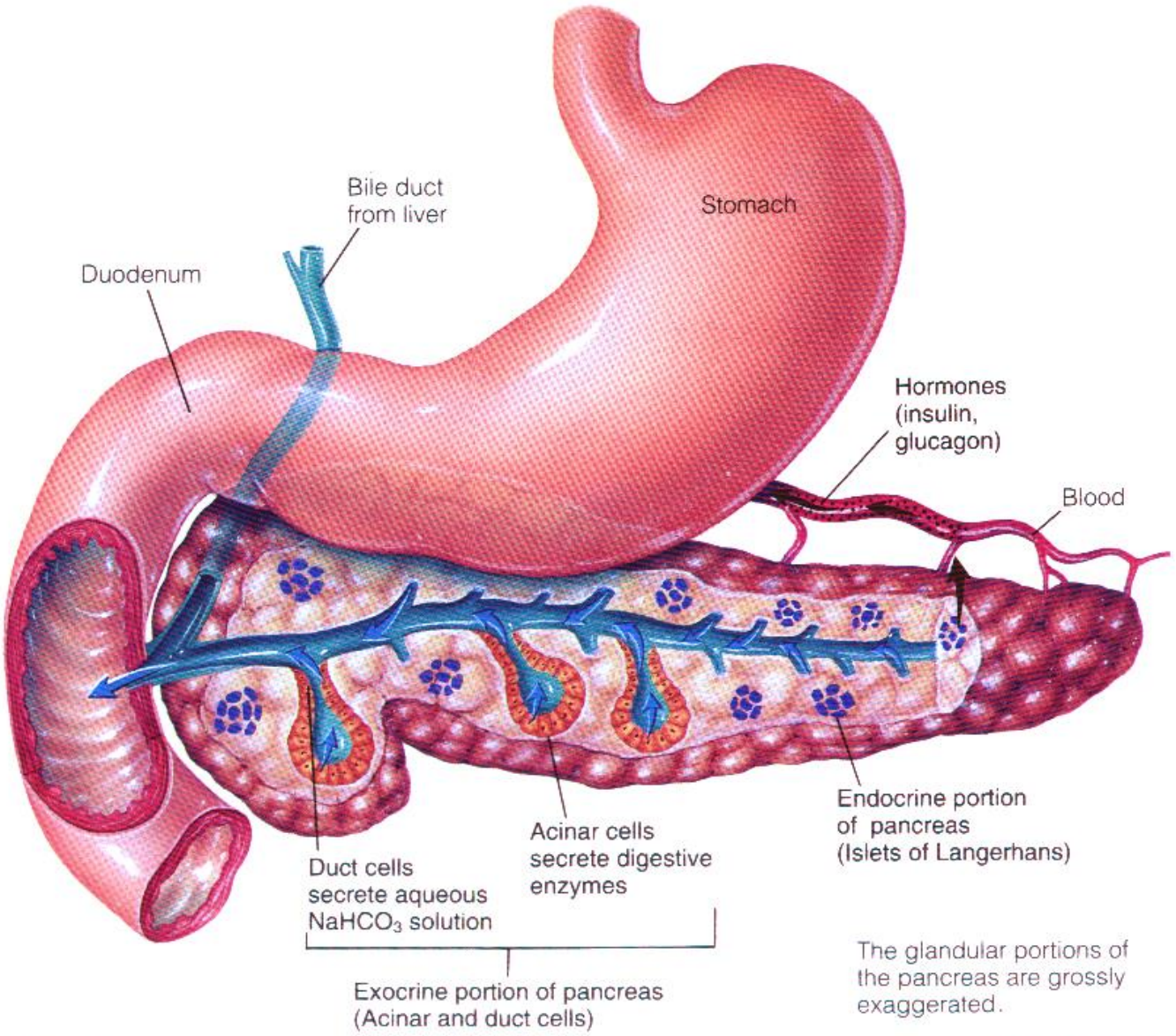

Common bile duct
Pancreatic duct
A
Pancreatic acini
(exocrine)
Duct
Cells of islands
of Langerhans
(endocrine):
Alpha cells
Beta cells
B

Exocrine portion

- Enzymes: secreted by acinar cells.

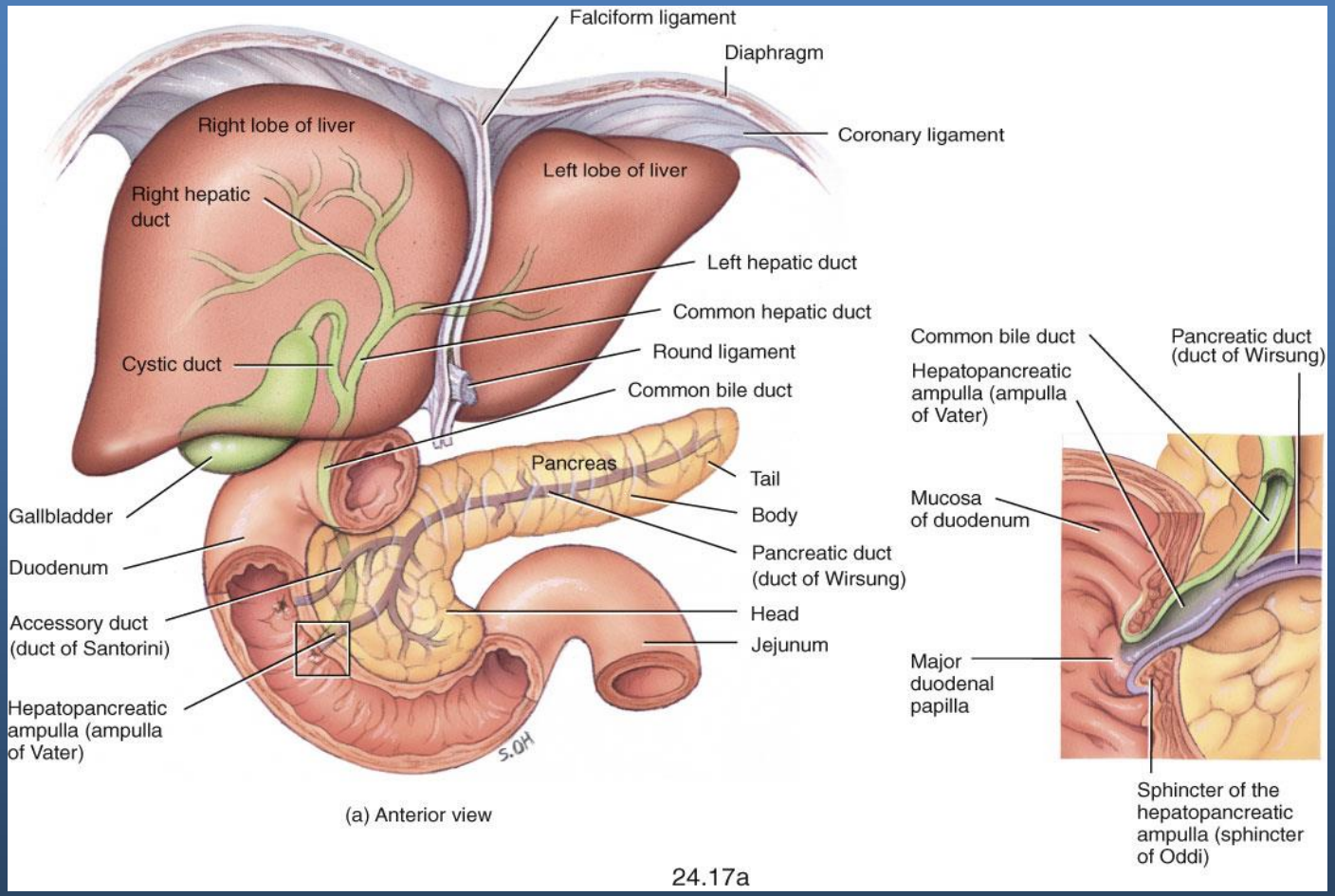
- Water and bicarbonate are secreted by duct cells.

Schematic Representation of Exocrine and Endocrine Portions of the Pancreas



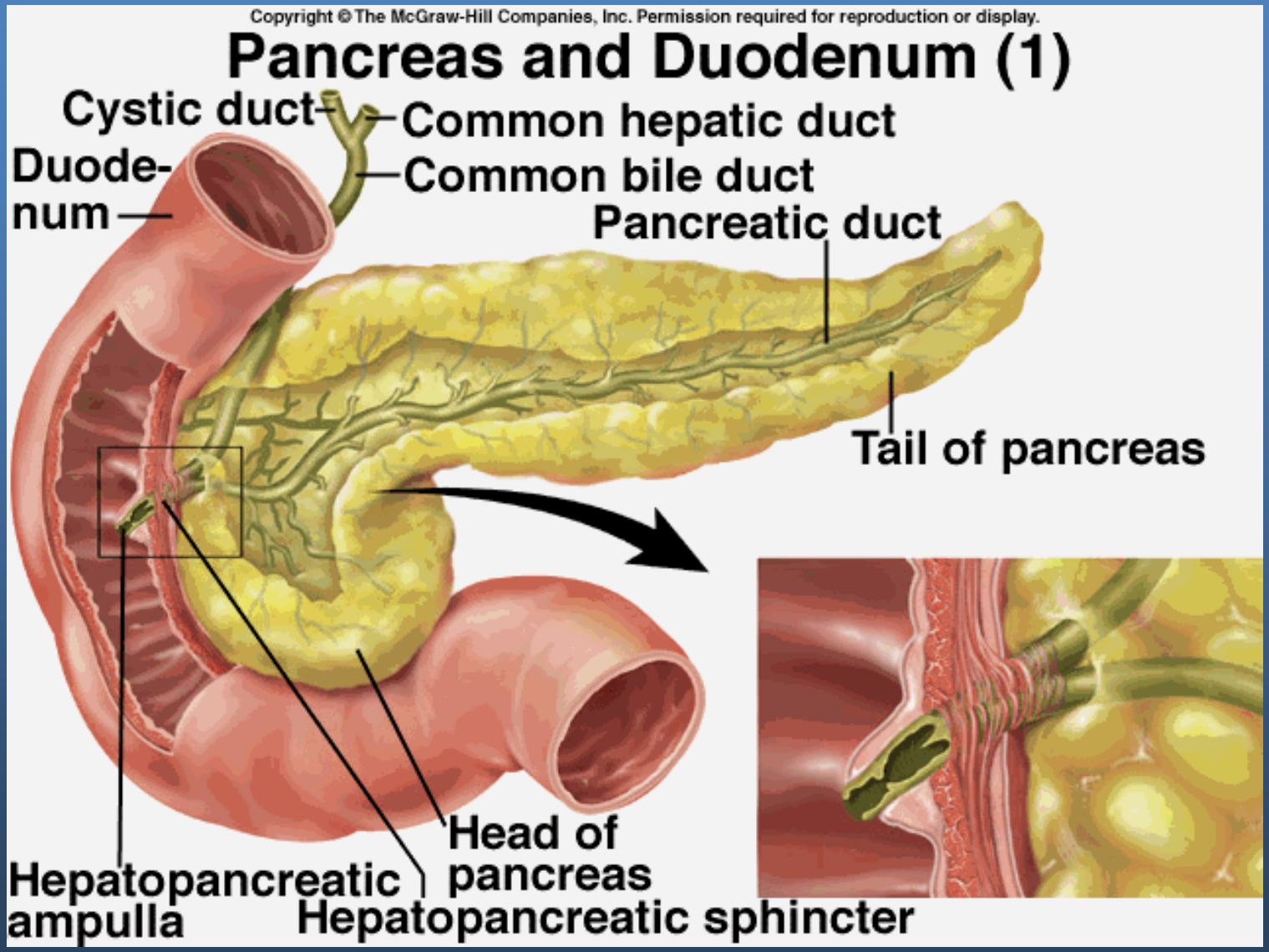
Acetate 148 (Figure 16-16)

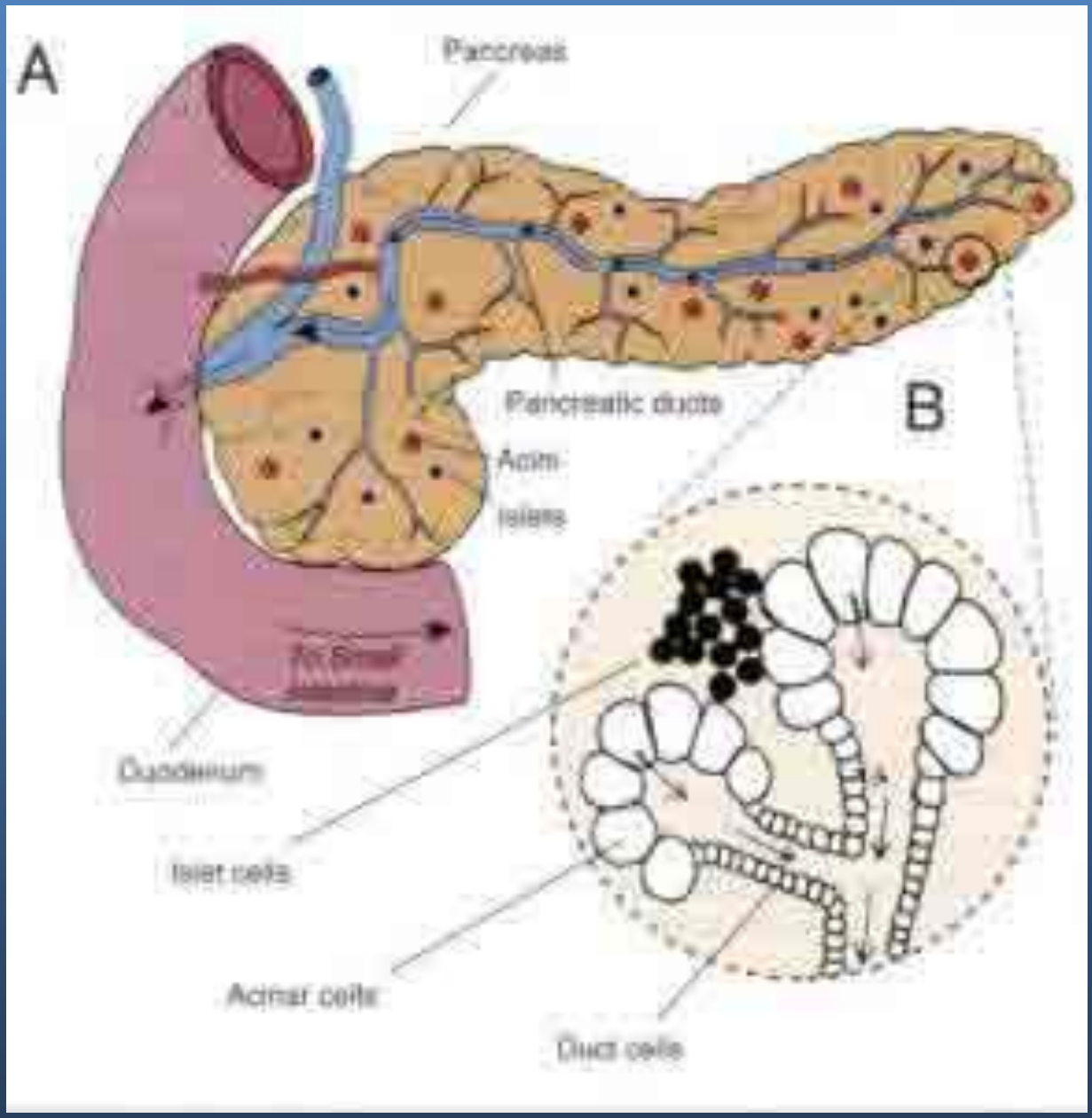
Fig. 24.17a



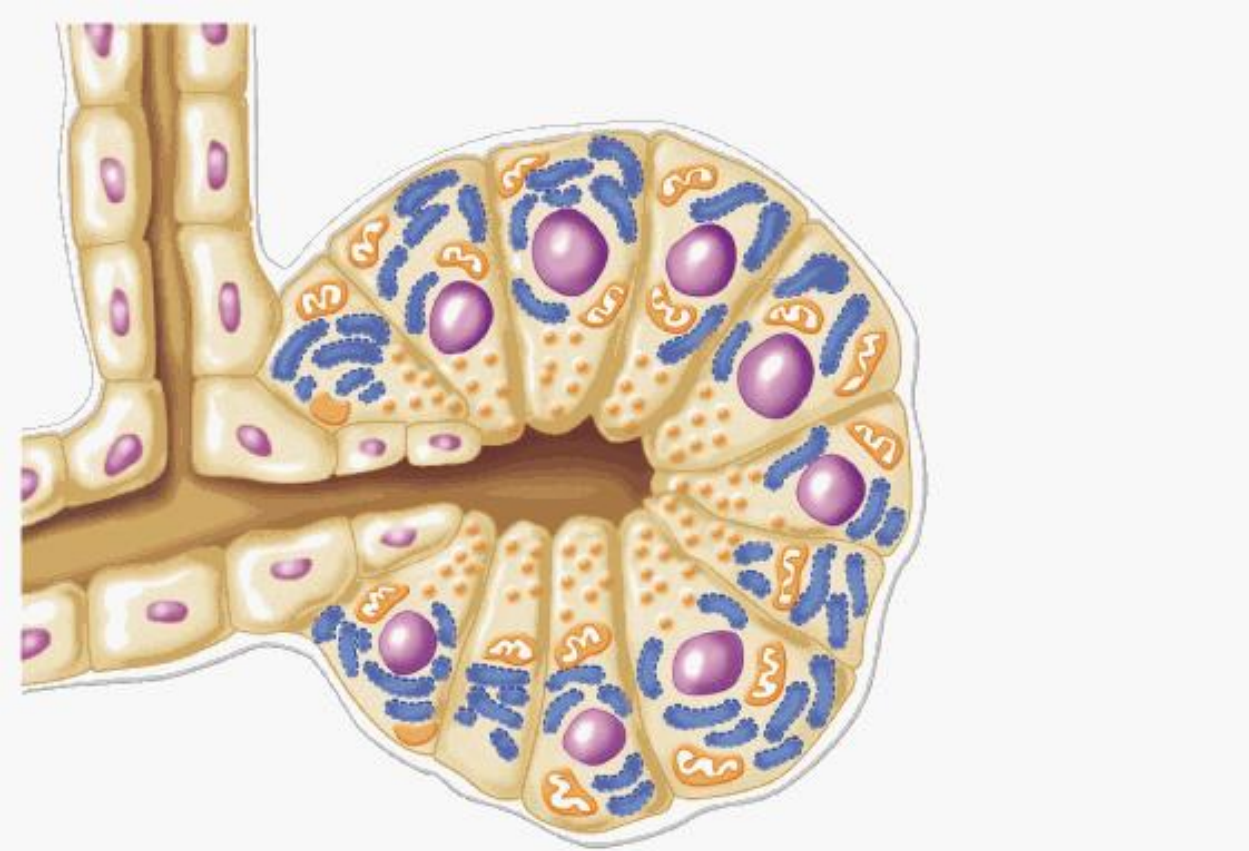
24.17a

Pancreas and Duodenum (1)




A
Pancreas
Pancreatic ducts
B
Acini
Islets
Duodenum
Islet cells
Acinar cells
Duct cells

Enzyme Secretion by acinar cells



(a)

Protelytic enzymes:

- **Trypsin (ogen):** activated by **enterokinase** from the duodenum acts as (endopeptidase. As long as this enzyme is in pancreas remains inactive by trypsin inhibitor.
- **Chemotrypsin(ogen):** activated by trypsin and acts as endopeptodase.
- **(Pro) carboxypeptidase:** activated by trypsin and acts as exopeptidase.

Enzyme for Digestion of Carbohydrates

Pancreatic amylase:

secreted as active enzyme to convert

Starch (polysaccharide) → disaccharides.

Lipolytic enzymes

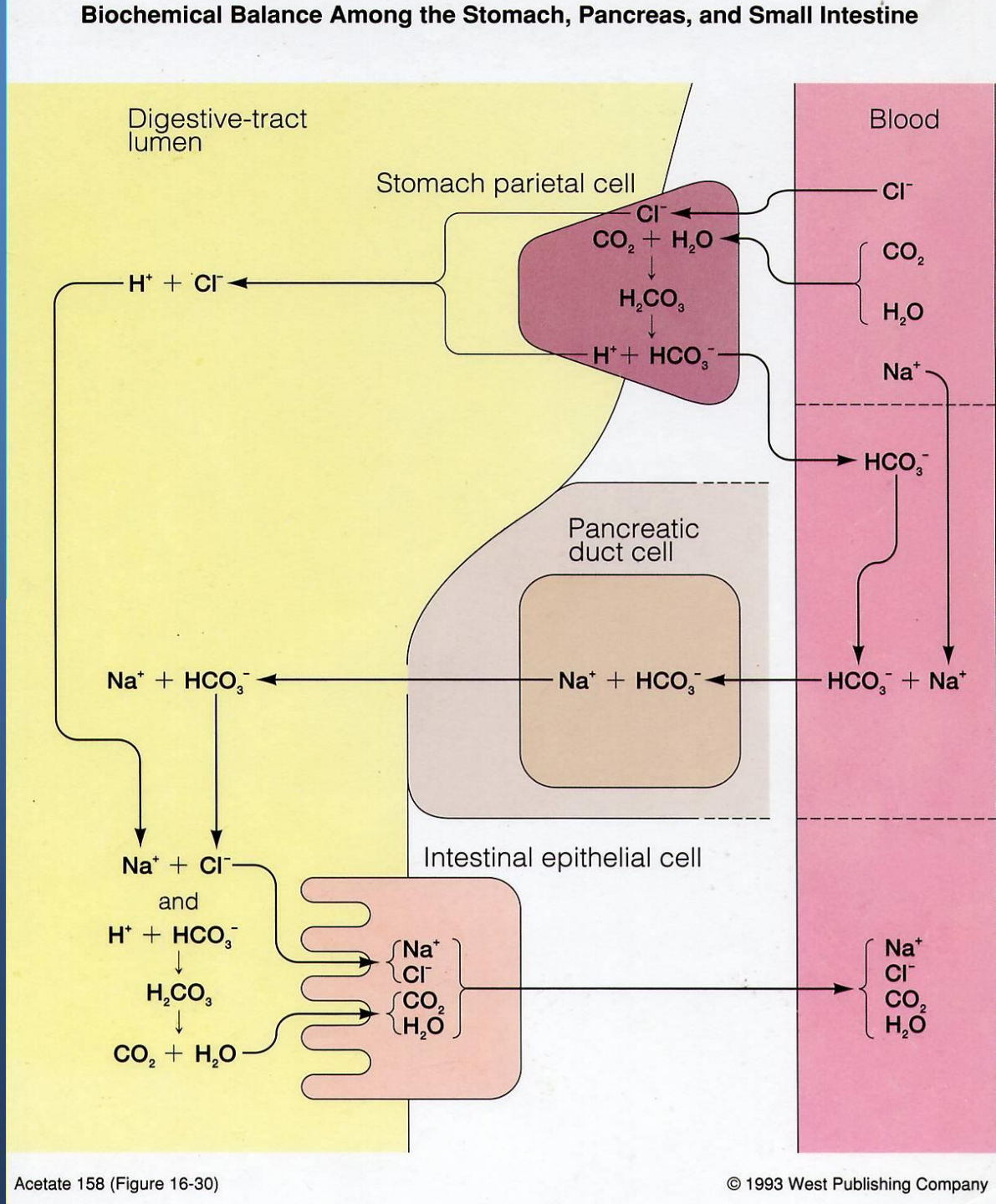
- **Lipase** that split

Triglycerides → monglyceride + free fatty acids.

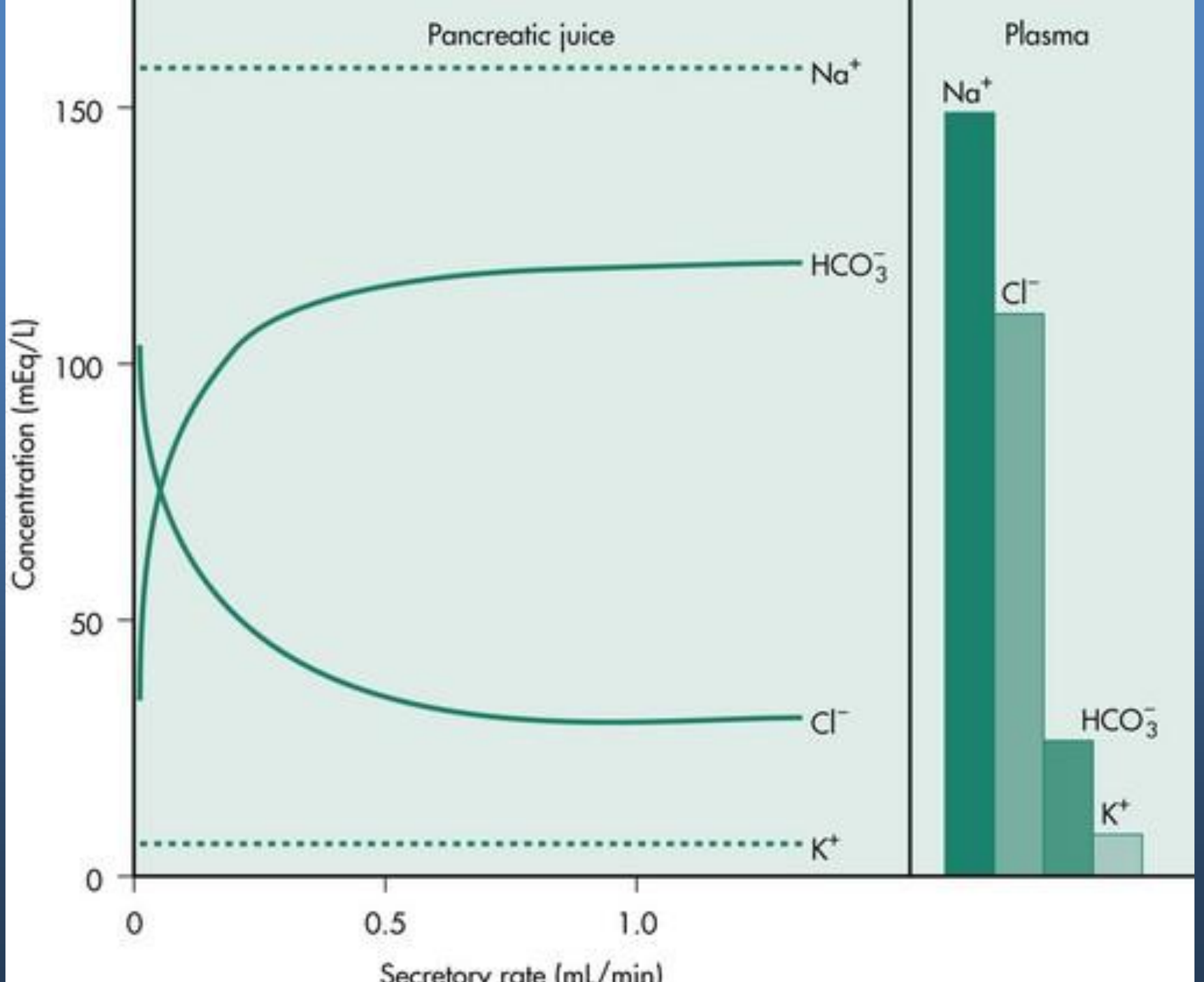
Their activity requires an oil/water interface, bile salts (secreted by liver) and other co-lipase secreted by the pancreas.

- **Phospholipase.**
- **Cholesterol ester hydroxylase.**

Water and bicarbonate secretion by duct cells.

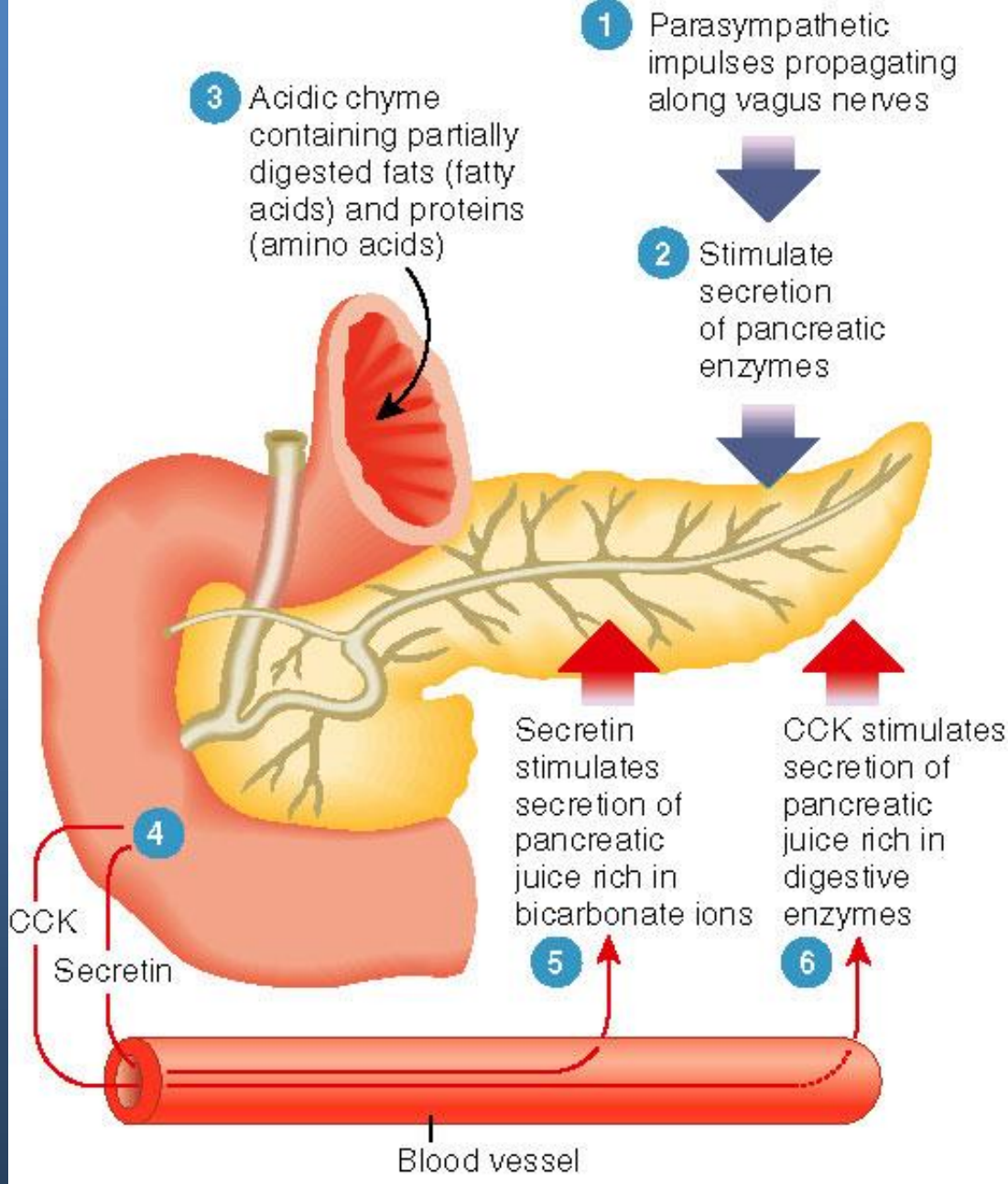


Acetate 158 (Figure 16-30)


Pancreatic juice
Plasma
Na+
HCO3−
Cl−
K+
Concentration (mEq/L)
150
100
50
0
0
0.5
1.0
Secretory rate (ml/min)

Control of pancreatic secretion:

- Neural
- Hormonal



24.18

Neural Control

- **Parasympathetic:**

  Vagal stimulation → enteric nervous system→ release of Ach, VIP, and GRP (Gastrin releasing peptide).

- **Sympathetic:** indirect inhibition via vasoconstriction

Hormonal Control

- **Secretin** (duodenal mucosa) → blood → ductal cells → increase water and HCO3- secretion.

-**CCK (Cholecystokinin):**

*→CCK-A receptors (acinar cells) → enzyme secretion.

*→vago-vagal reflex to stimulate enzyme secretions.

Hormonal Control

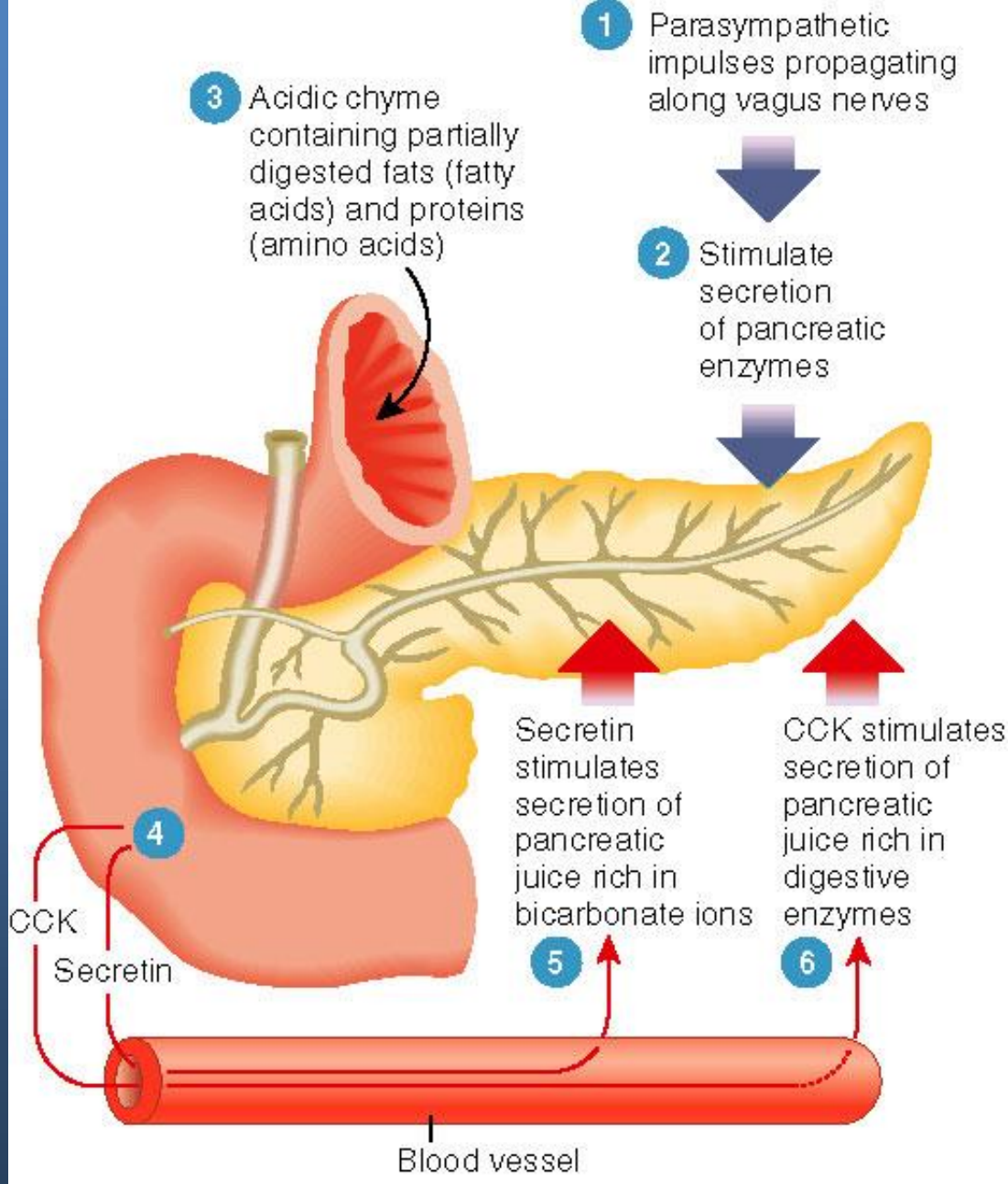
- **Pancreatic polypeptide:** inhibits the release of enzymes by its inhibitory effect

  *- Inhibits Ach release from enteric nervous system.

  *- Inhibits vagal output of the CNS.

Control of pancreatic secretion:

- Cephalic phase
- Gastric phase
- Intestinal phase



24.18

3 phases of control of pancreatic secretions

Cephalic phase: sight, smell, taste or hearing.

Mediated by vagus.

Gastric phase: Distension.

Mediated by vagus.

Intestinal phase: Aminoacids (aa), Fatty acids, H+, Distension.

Mediated by CCK, secretin, enteropancreatic reflexes, other hormones.

Liver Secretions

Liver functions

- Metabolic processing: Process all nutrients after their absorption.
- Detoxification of body wastes, hormones, drugs, and other foreign bodies.
- Synthesis of plasma proteins, including clotting factors (their synthesis requires vit. K), hormone transporters.
- Storage organ of glycogen, iron (ferritin), copper, and vitamines.
- Removal of bacteria and foreign materials by reticuloendothelial cells (Kupffer cells).
- Excretion of cholesterol and bilirubin.

Bile secretion

- Bile acts as detergent to emulsify lipids and make them soluble.

Bile is composed of **bile salts**, water & - electrolytes, cholesterol, phosphlipids and wastes intended for excretion, (bilirubin).

Liver functions

- Metabolic processing: Process all nutrients after their absorption.
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- Storage organ of glycogen, iron (ferritin), copper, and vitamines.
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- **Excretion of cholesterol and bilirubin.**

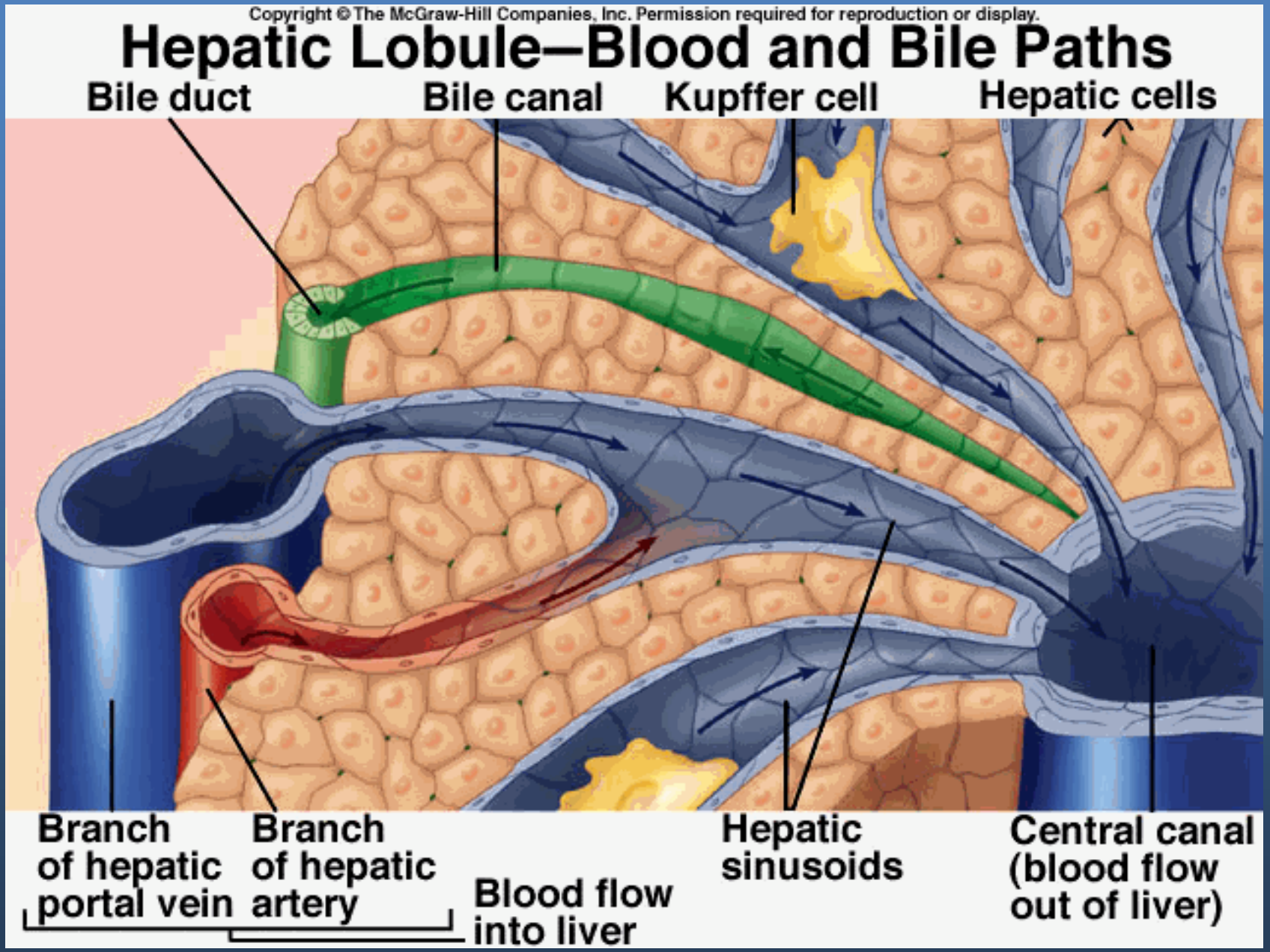
Excretion of bilirubin in the bile

Bilirubin results from the catabolism of hemoglobin → Heme + Globin

Heme ring → iron + biliverdin

Biliverdin → bilirubin secreted with bile as conjugated (glucoronide, sulfate, other substances).

Hepatic Lobule—Blood and Bile Paths



bilirubin

Bilirubin (by bacterial action) → urobilinogen → reabsorbed and secreted in urine (urobilin).

Or in feces →stercobilin.

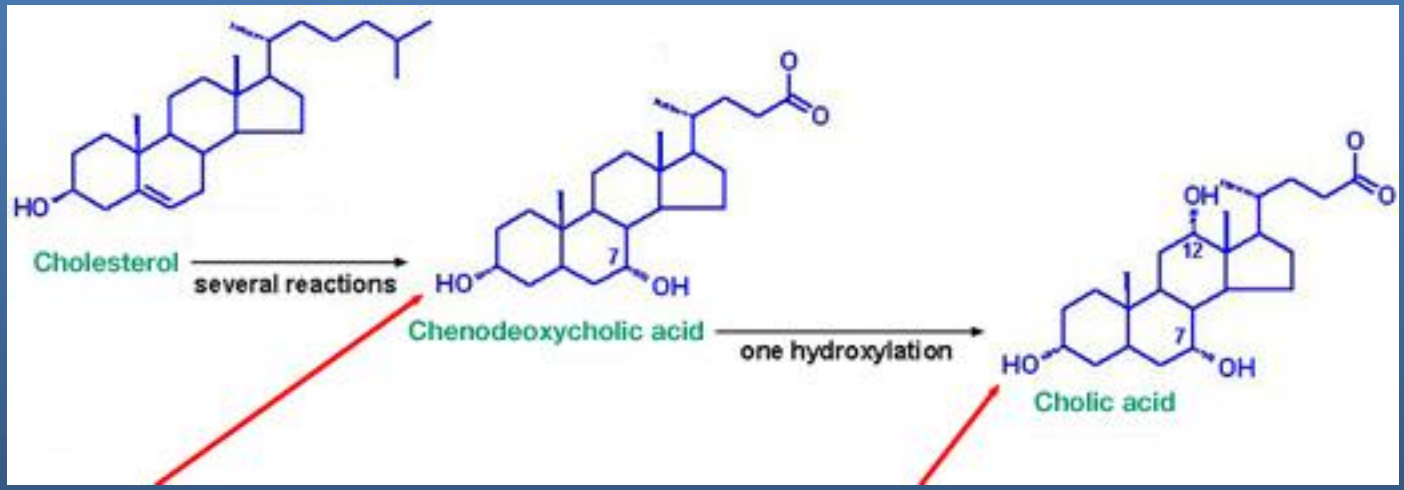
Jaundice is cause by large quantity of bilirubin in the extracellular space.

Bile formation

- Bile salts are synthesized by the liver, concentrated in the gallbladder and modified in the lumen.

-Synthesized as primary bile acids from cholesterol (*cholic* and *chenodeoxycholic acid*)

Bile salts

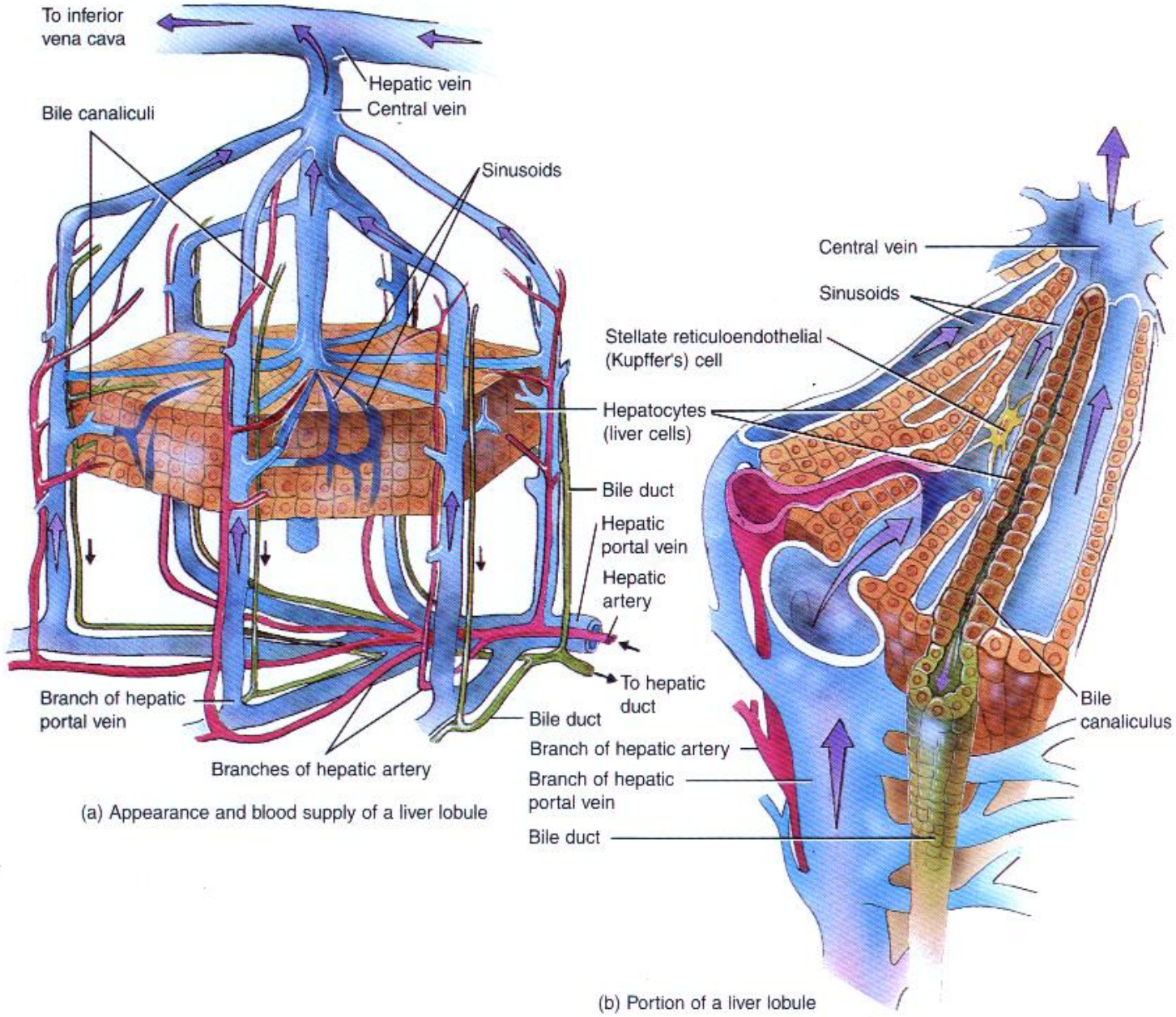


Bile acids → Conjugated to Glycine or Taurine

→ Bile salts

Bile

- Between meals, bile →gallbladder where it is stored. The epithelium of the gallbladder removes water and electrolytes → 5-20 fold concentration of bile.



Histology of the Liver, Fig# 24.19a-b

Hepatic Lobule—Blood and Bile Paths

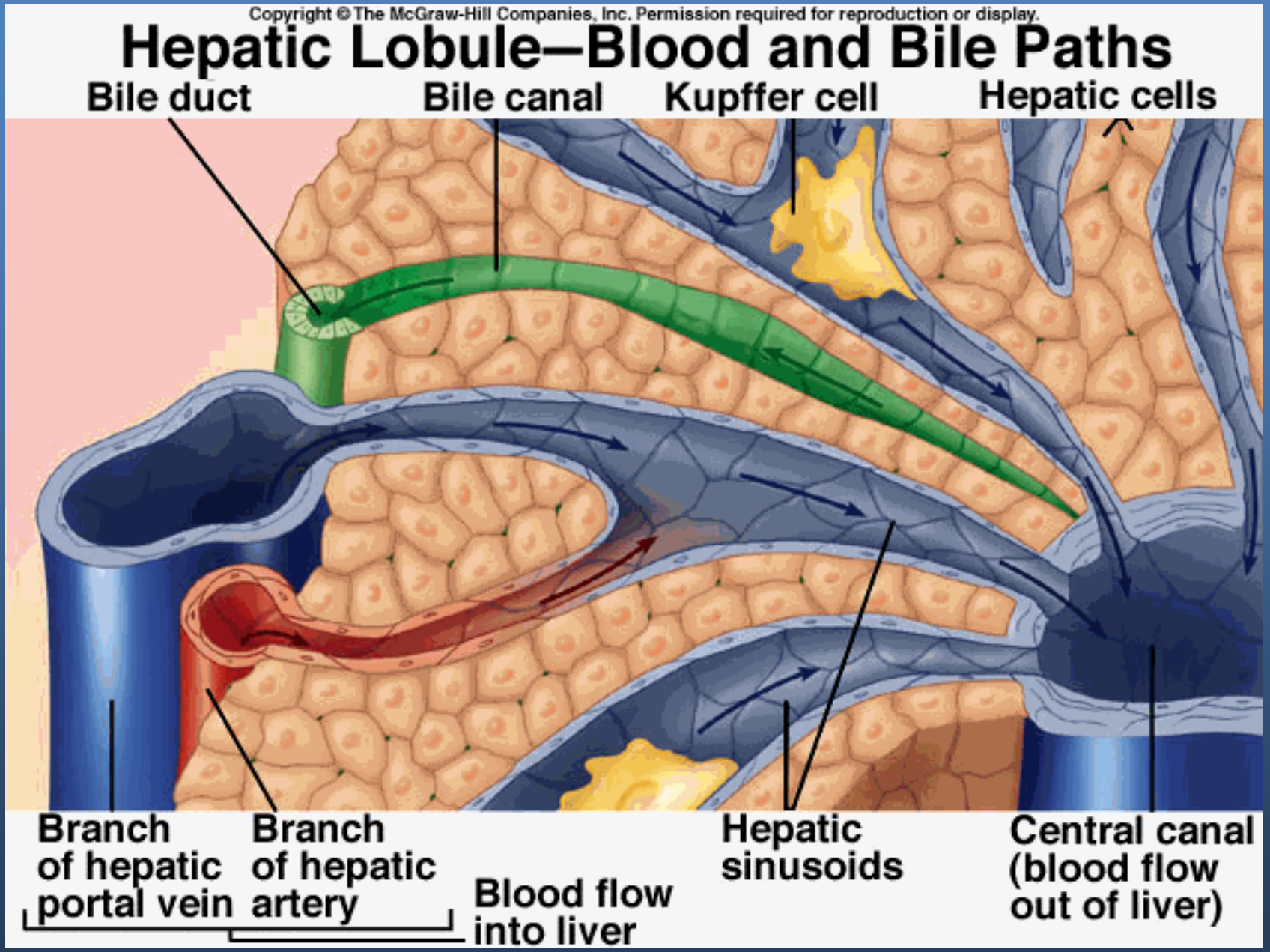
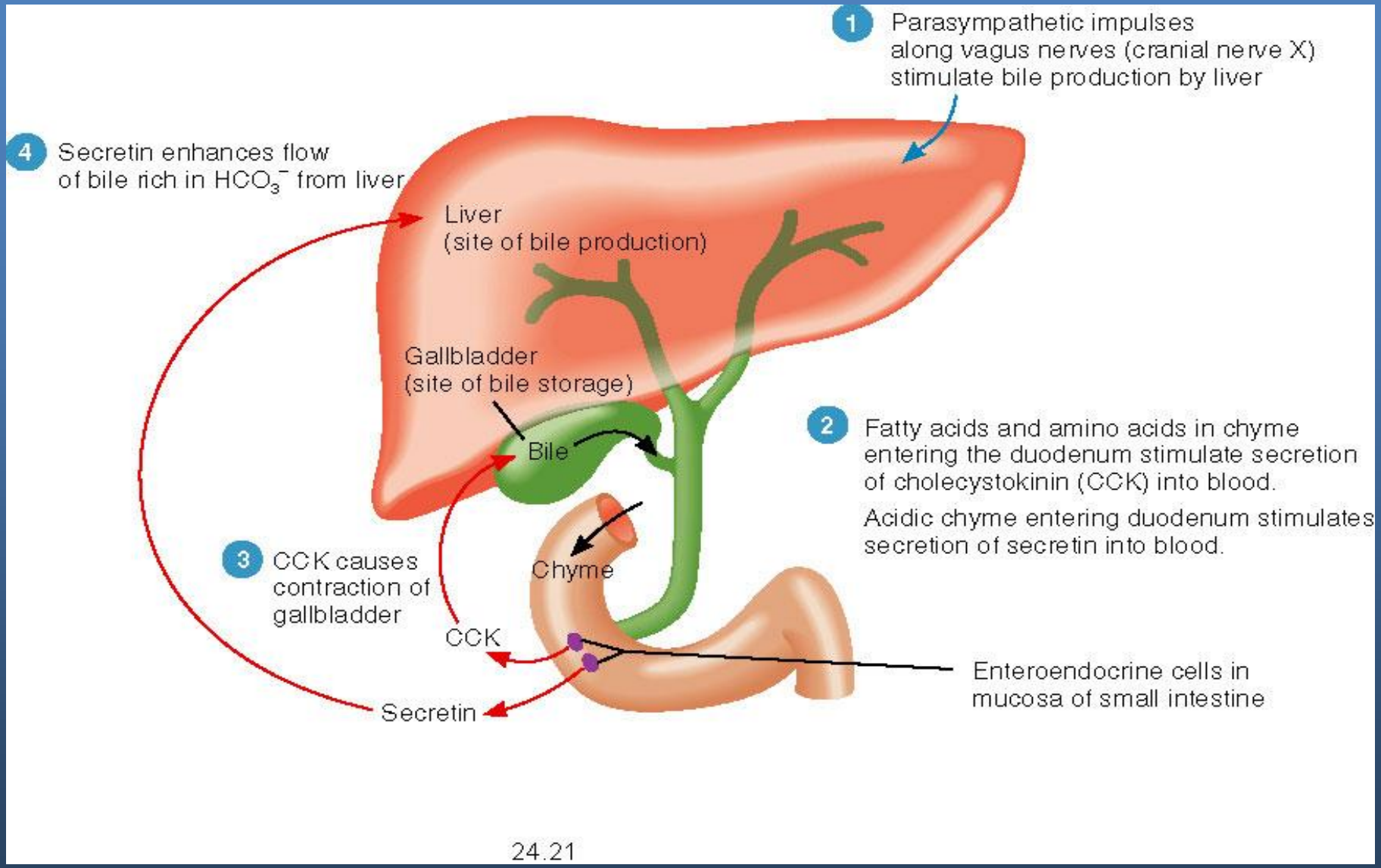
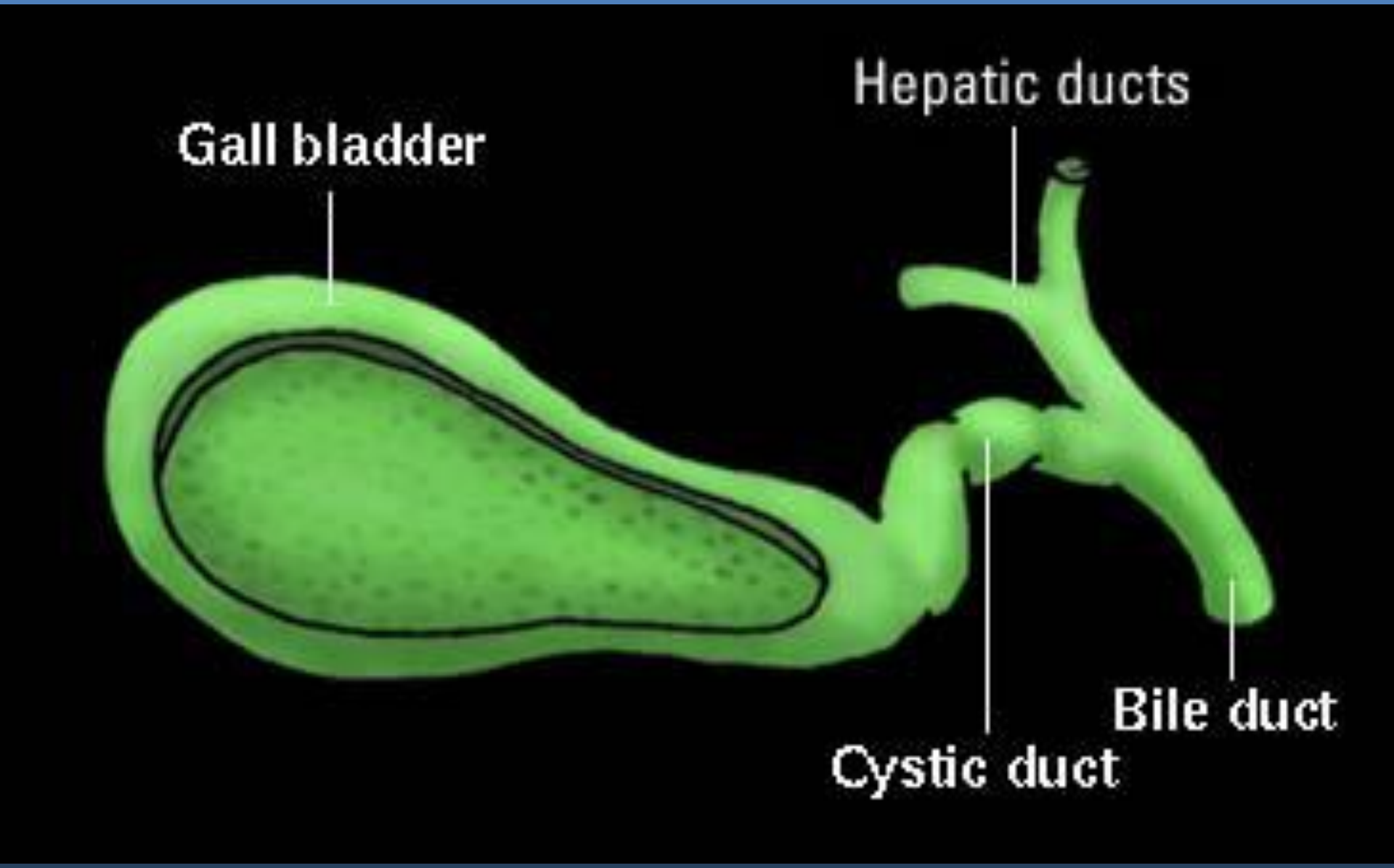


Fig. 24.21

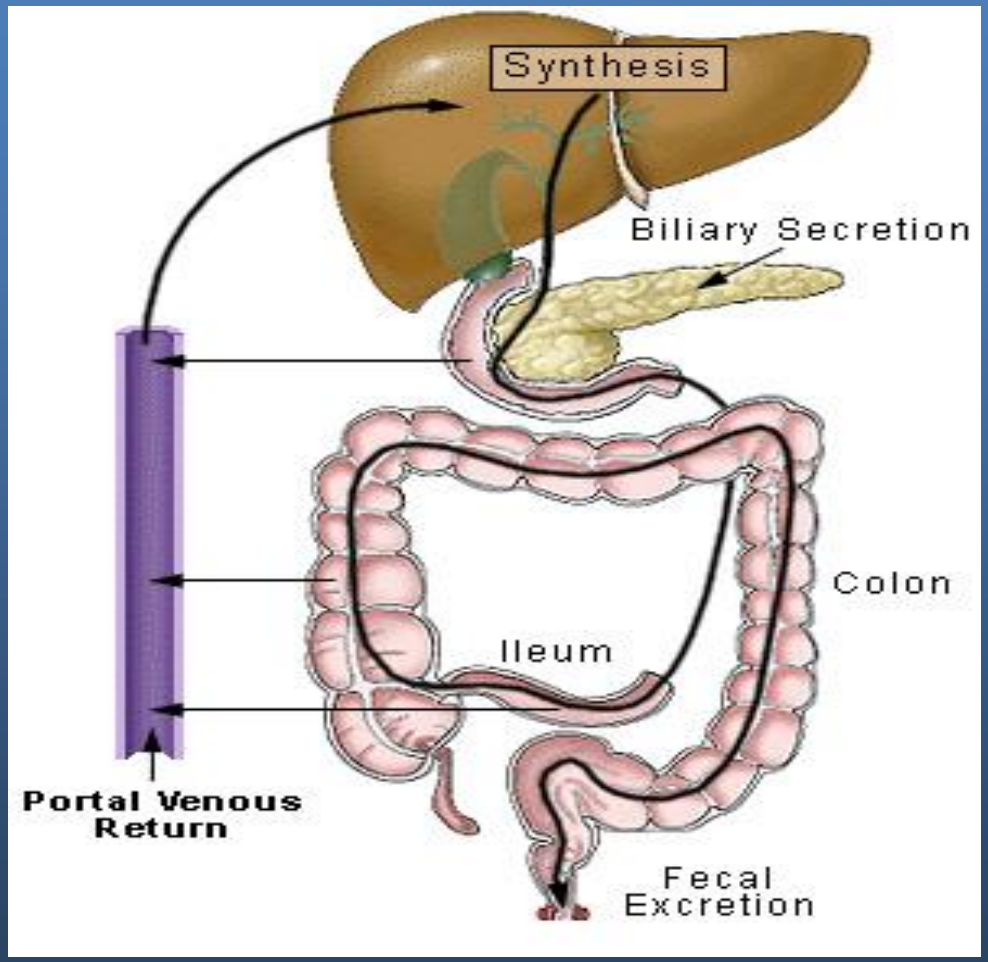


24.21


Hepatic ducts
Gall bladder
Bile duct
Cystic duct

	LIVER BILE	GALLBLADDER BILE
Water	97.5 gm/dl	92 gm/dl
Bile Salts	1.1 gm/dl	6 gm/dl
Bilirubin	0.04 gm/dl	0.3 gm/dl
Chlolesterol	0.1 gm/dl	0.3 to 0.9 gm/dl
Fatty Acids	0.12 gm/dl	03 to 1.2 gm/dl
Lecithin	0.04 gm/dl	0.3 gm/dl
Na^+	145 mEq/liter	130 mEq/liter
K^+	5 mEq/liter	12 mEq/liter
Ca^{++}	5 mEq/liter	23 mEq/liter
Cl^-	100 mEq/liter	25 mEq/liter
HCO_3^-	28 mEq/liter	10 mEq/liter

Enterohepatic circulation



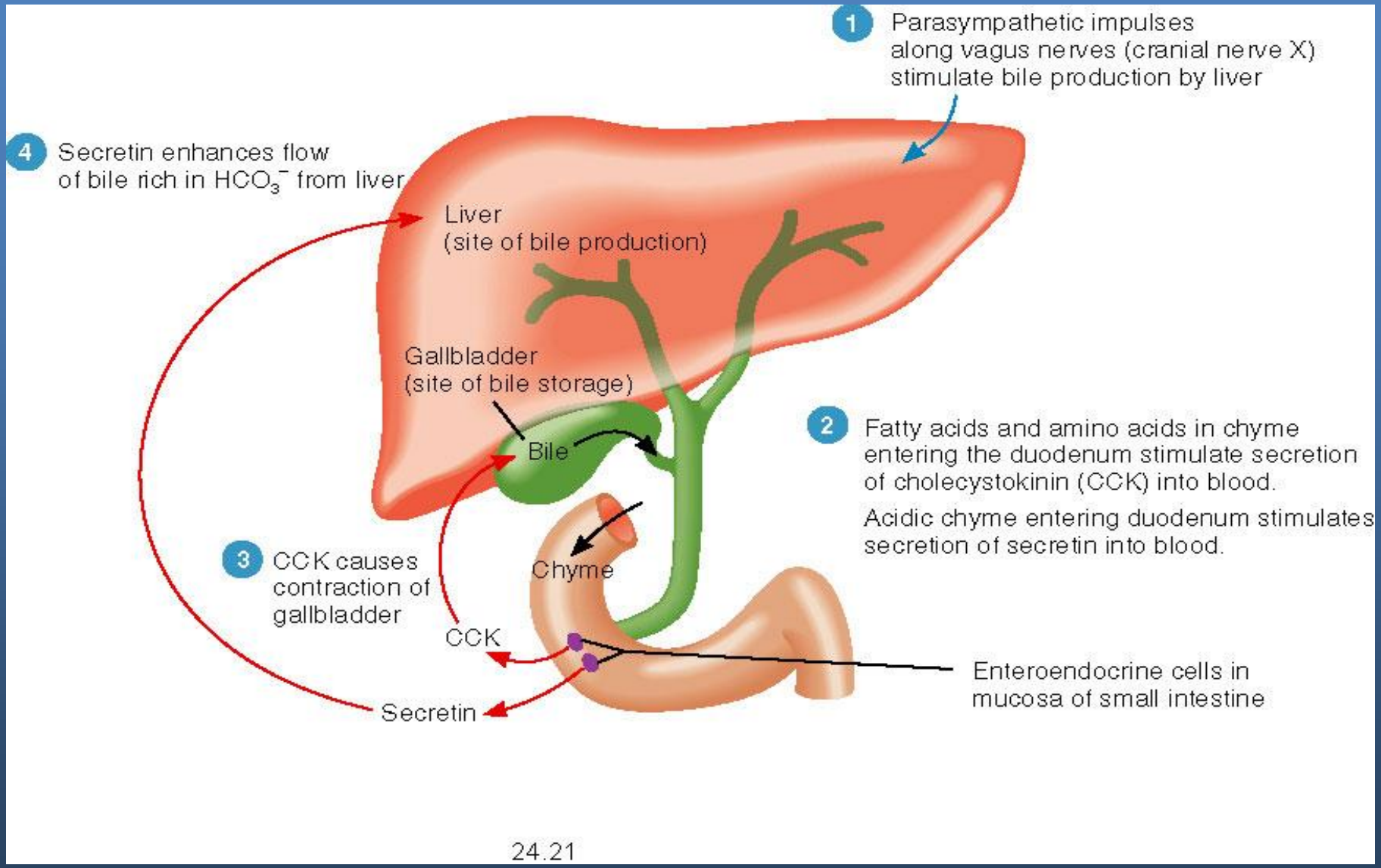
Modification in the intestine

Modified to secondary bile acid:

Cholic acid → deoxycholic acid.

Chenodeoxycholic acid → lithocholic acid

Fig. 24.21



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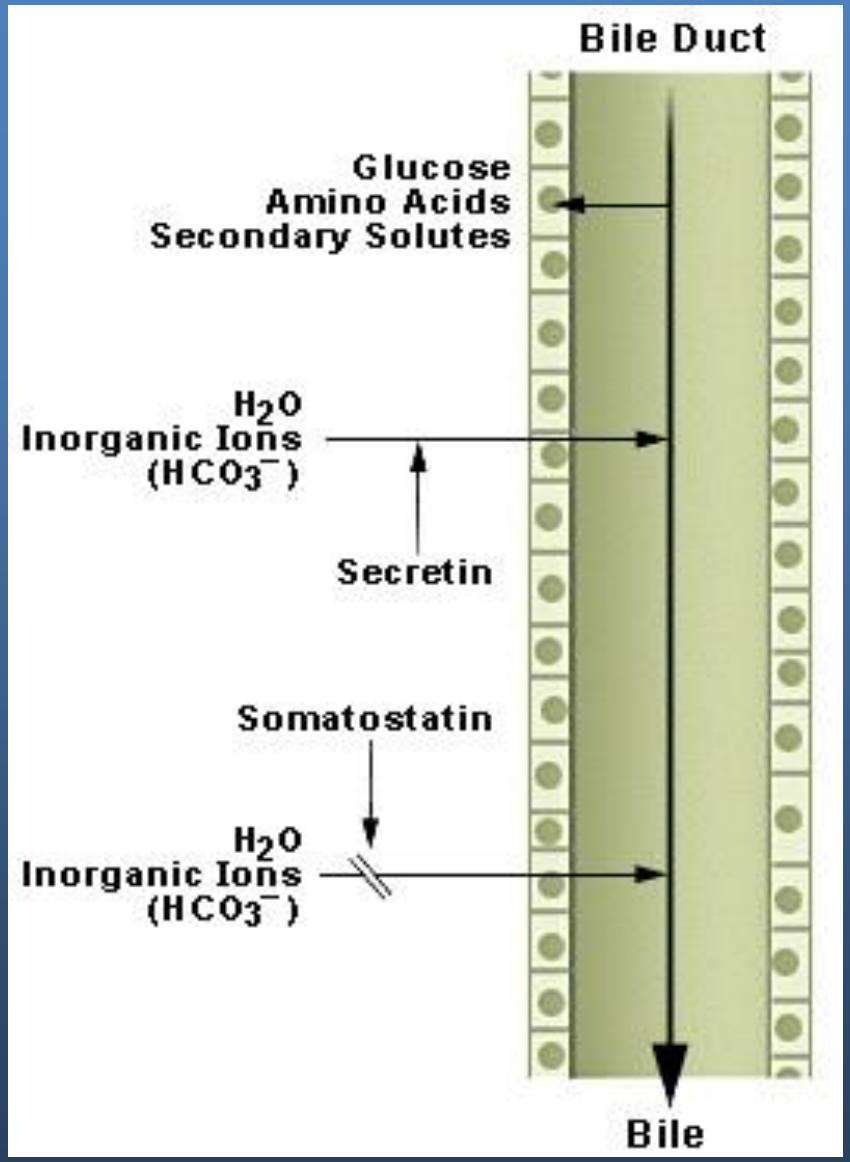
Bile Duct
Glucose
Amino Acids
Secondary Solutes
H_2O
Inorganic Ions
(HCO_3^-)
Secretin
Somatostatin
H_2O
Inorganic Ions
(HCO_3^-)
Bile