Intestinal absorption

BY

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2025-2026

Digestion and Absorption of carbohydrates

[A] Digestion of carbohydrates:

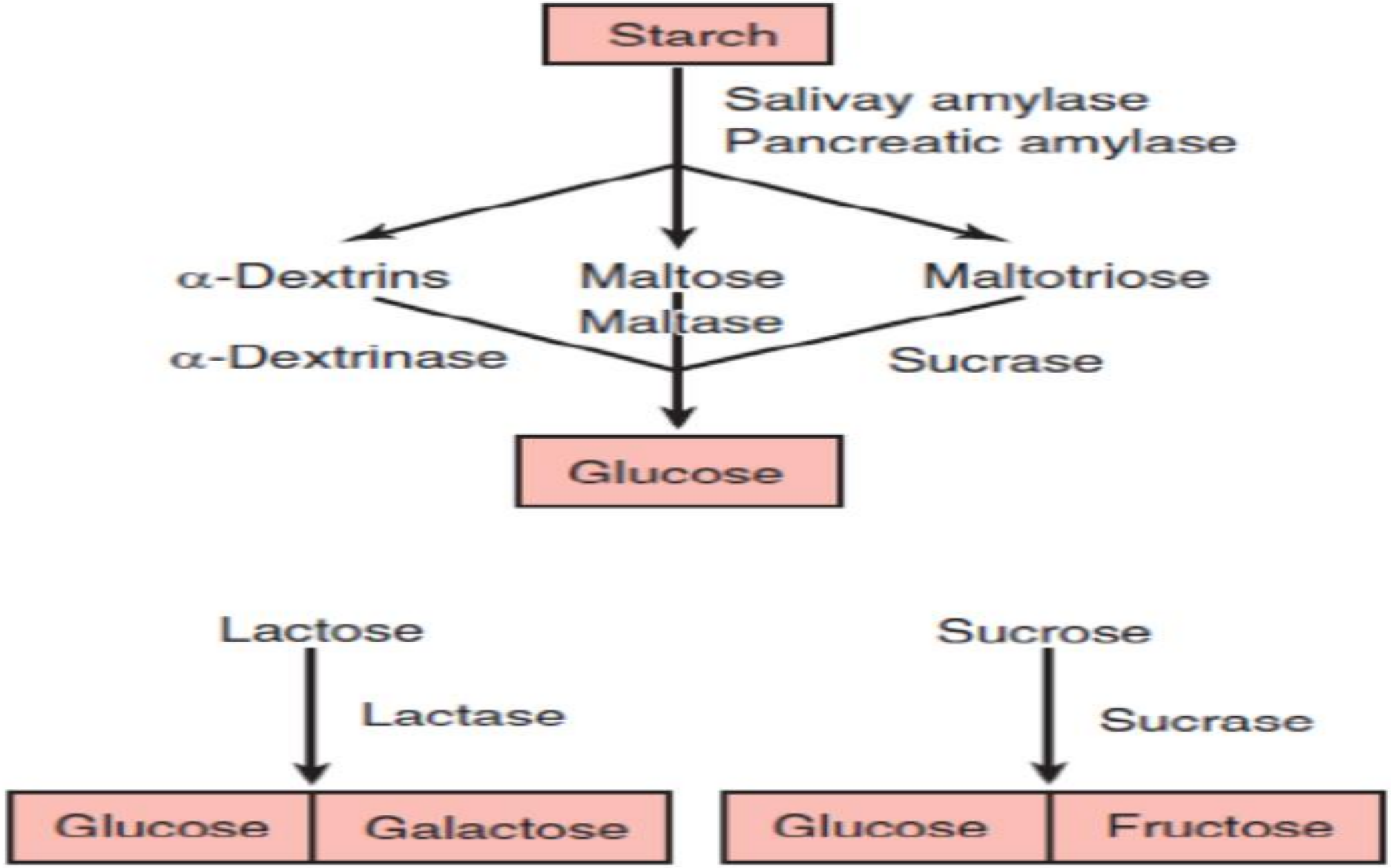
■ Only monosaccharides are absorbed. Carbohydrates must be digested to glucose, galactose and fructose for absorption to proceed.

a. α-Amylases (salivary and pancreatic) hydrolyze 1,4-glycosidic bonds in starch, yielding maltose, maltotriose and α-limit dextrins.

b. Maltase, α-dextrinase and sucrase in the intestinal brush border then hydrolyze the oligosaccharides to glucose.

c. Lactase & sucrase degrade their respective disaccharides to mono-saccharides.

- Lactase degrades lactose to glucose and galactose.
- Sucrase degrades sucrose to glucose and fructose.


Starch
Salivay amylase
Pancreatic amylase
α-Dextrins
Maltose
Maltotriose
Maltase
α-Dextrinase
Sucrase
Glucose
Lactose
Lactase
Glucose
Galactose
Sucrose
Sucrase
Glucose
Fructose

[B] Absorption of carbohydrates:

a) Glucose and galactose:

1. Na^+ –K^+ pump establishes a Na^+ concentration gradient from outside to inside the intestinal epithelial cell.

2. Glucose is absorbed by symport along with Na^+ [SGLT-1] by secondary active transport to inside cell.

3. Glucose moves out of the cell by facilitated diffusion [GLUT-2].

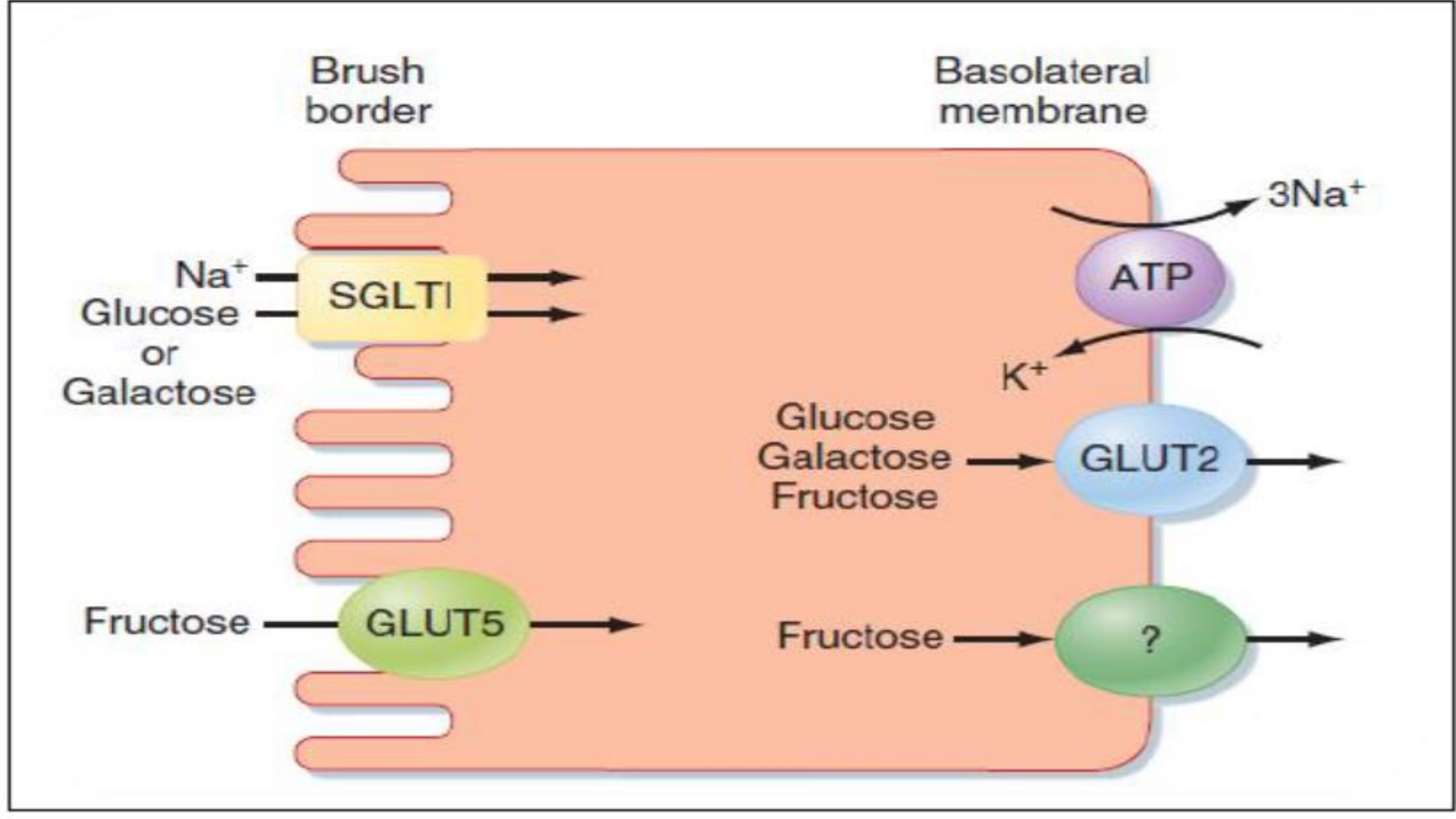
4. Glucose enters the capillary of an intestinal villus and is carried through the hepatic portal vein to the liver.

NB:

■ Poisoning the Na^+ –K^+ pump inhibits glucose & galactose absorption by dissipating the Na^+ gradient

b) Fructose:

- It is transported to inside intestinal cell by facilitated diffusion [GLUT-5].
- And then to the blood by facilitated diffusion


Brush border
Basolateral membrane
3Na+
ATP
K+
Na+
Glucose
or
Galactose
SGLTI
Glucose
Galactose
Fructose
GLUT2
Fructose
GLUT5
Fructose
?

[C] Clinical disorders of carbohydrate absorption:

■ **Lactose intolerance** results from the absence of brush border lactase and, thus, the inability to hydrolyze lactose to glucose and galactose for absorption.

- The undigested lactose (nonabsorbable) remains in the small intestine and is eventually delivered to the large intestine. Lactose in the large intestine acts as an osmotic particle that creates a gradient to draw water into the feces. This can lead to abdominal cramping and osmotic diarrhea when lactose is consumed.

- Lactose intolerance can be managed by avoiding lactose-containing foods (e.g., milk, ice cream) or by taking lactase supplements.

Digestion and absorption of proteins:

[A] Digestion of proteins:

 In the stomach:

- The enzyme pepsin breaks down proteins, producing shorter amino acid chains called polypeptides.

- Pepsin is secreted as pepsinogen by the chief cells of the stomach.

- Pepsinogen is activated to pepsin by gastric HCl.

 In the small intestine:

- Pancreatic proteases include trypsin, chymotrypsin, elastase, carboxypeptidase.

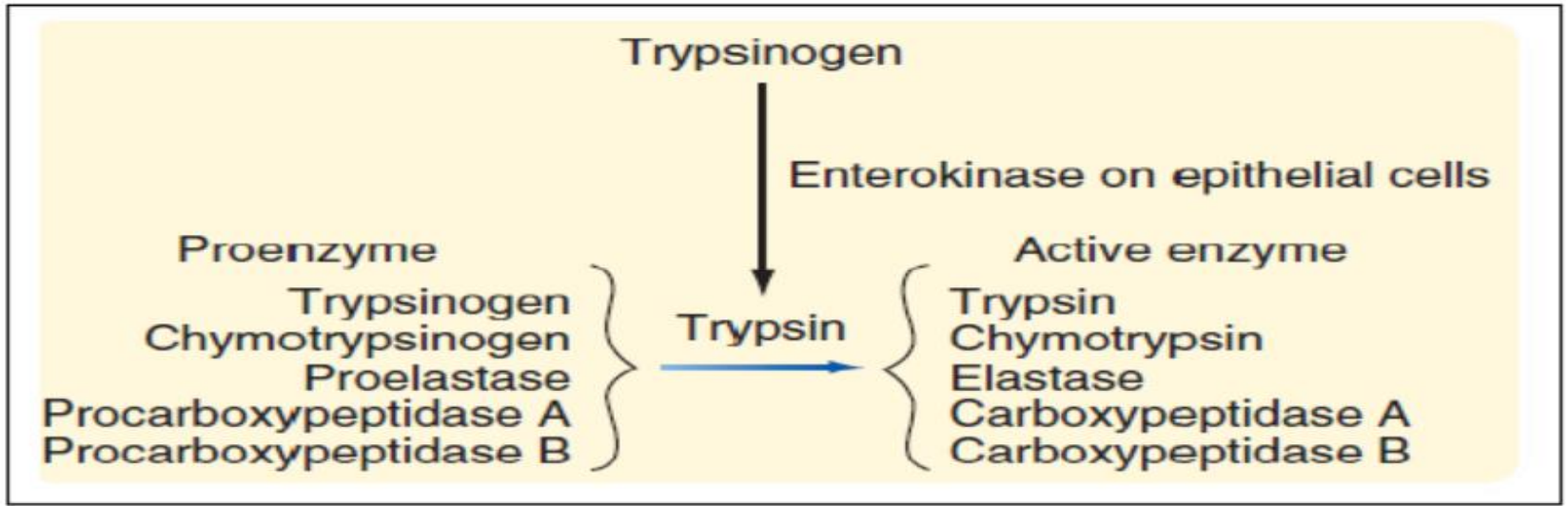
- They are secreted in inactive forms that are activated in the small intestine as follows:

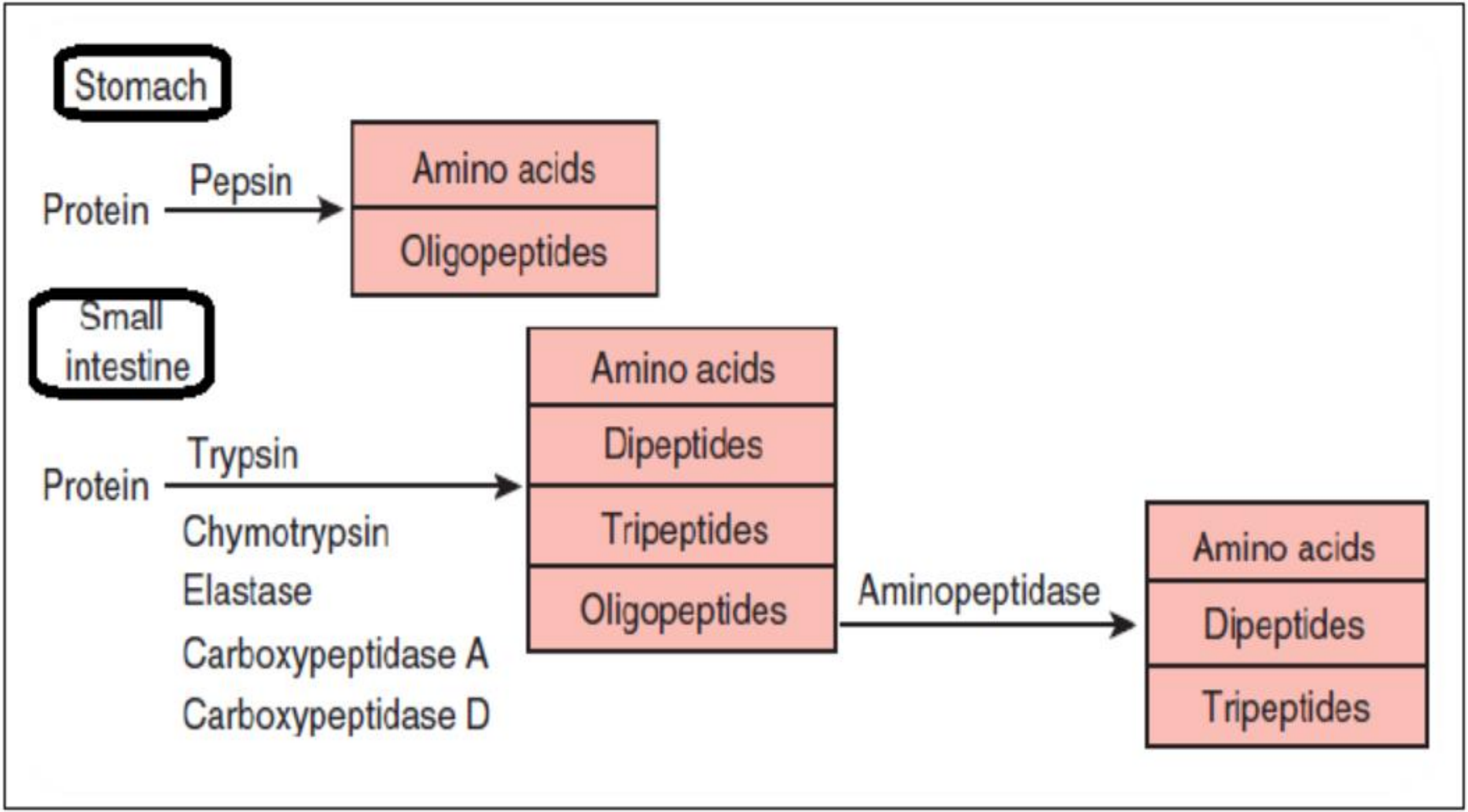
➢(1) Trypsinogen is activated to trypsin by a brush border enzyme, enterokinase.

➢(2) Trypsin then converts chymotrypsinogen, proelastase, & procarboxy-peptidase to their active forms. (Even trypsinogen is converted to more trypsin by trypsin).

- Trypsin, chymotrypsin & elastase are **endopeptidases** & continue the digestive process and produce small peptide chains.

- Carboxypeptidase and a brush border enzyme, aminopeptidase, are **exopeptidases** that finish protein digestion by cleaving amino acids from the carboxyl and amino ends of a polypeptide chain, respectively




Stomach
Protein
Pepsin
Amino acids
Oligopeptides
Small intestine
Protein
Trypsin
Chymotrypsin
Elastase
Carboxypeptidase A
Carboxypeptidase D
Amino acids
Dipeptides
Tripeptides
Oligopeptides
Aminopeptidase
Amino acids
Dipeptides
Tripeptides

[B] Absorption of proteins:

■ Digestive products of protein can be **absorbed as amino acids, dipeptides, and tripeptides** (in contrast to carbohydrates, which can only be absorbed as monosaccharides).

a) Free amino acids:

- 1. L-amino acids enter enterocytes by secondary active transport using Na^+-amino acid cotransporters.
- 2. There are four separate Na^+-amino acid cotransporters which handle either neutral, acidic, basic or imino amino acids.
- 3. The energy for this process is derived from a Na^+ gradient across the apical membrane which is created by Na^+K^+ ATPase located on the basolateral membrane.
- 4. The amino acids are then transported from cell to blood by facilitated diffusion.

b) Dipeptides and tripeptides:

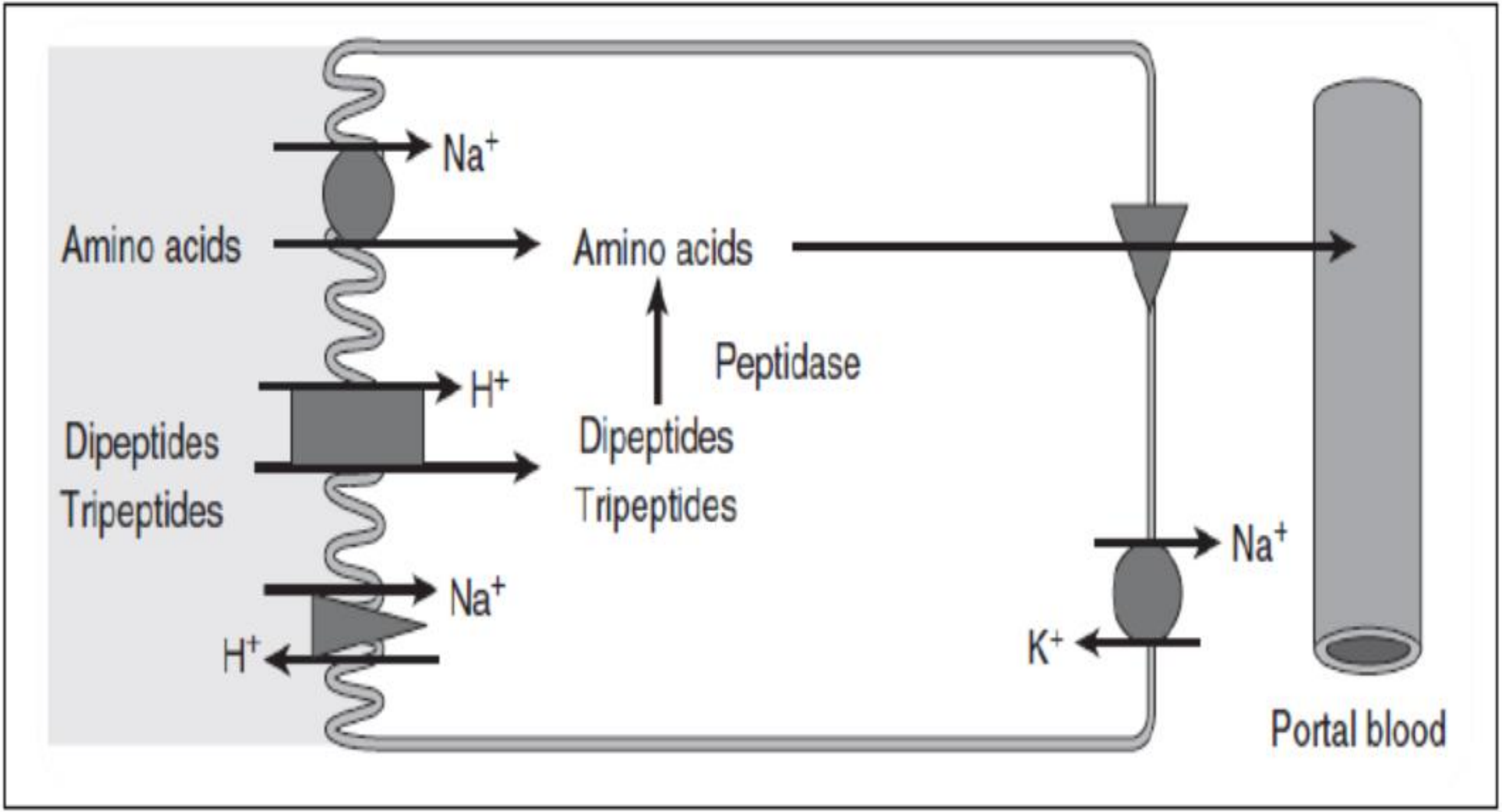
1. They are absorbed faster than free amino acids.

2. Dipeptides and tripeptides enter enterocytes by secondary active transport using H^+-dipeptide/tripeptide cotransporters.

3. The energy for this process is derived from an H^+ gradient across the apical membrane which is created by Na^+– H^+ exchanger located on the apical membrane.

4. After the dipeptides and tripeptides are transported into the intestinal cells, cytoplasmic peptidases hydrolyze them to amino acids.

5. The amino acids are then transported from cell to blood by facilitated diffusion.


Na+
Amino acids
Amino acids
Peptidase
H+
Dipeptides
Tripeptides
Dipeptides
Tripeptides
Na+
H+
Na+
K+
Portal blood

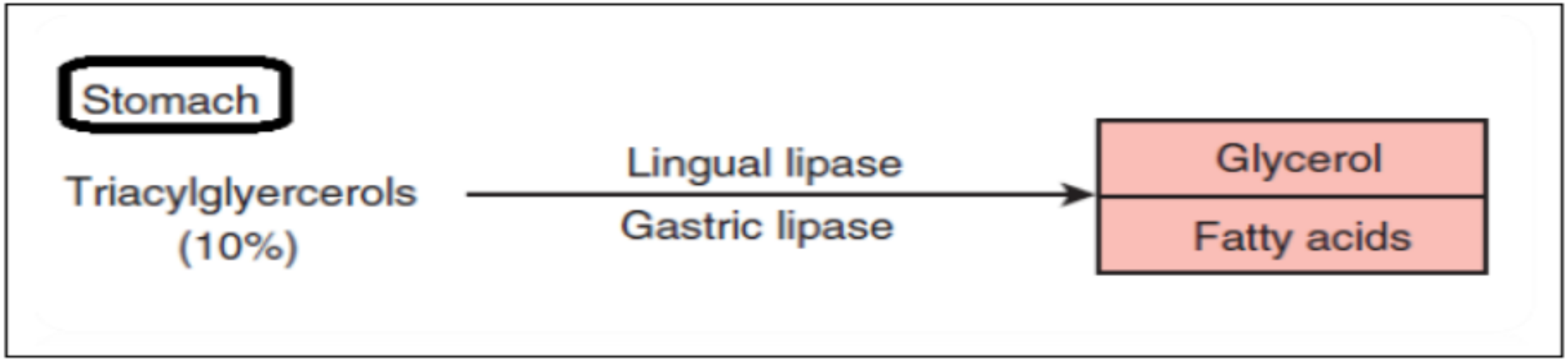
Digestion and absorption of lipids

[A] Digestion of lipids:

- Dietary fat is of both vegetable and animal origin. Mostly, it is in the form of neutral fat (triglycerides). It also includes small amounts of phospholipids, cholesterol, some free fatty acids, lecithin and cholesterol esters.

In the stomach:

- Lingual and gastric lipases initiate lipid digestion by hydrolyzing approximately 10% of ingested triglycerides to glycerol and free fatty acids.



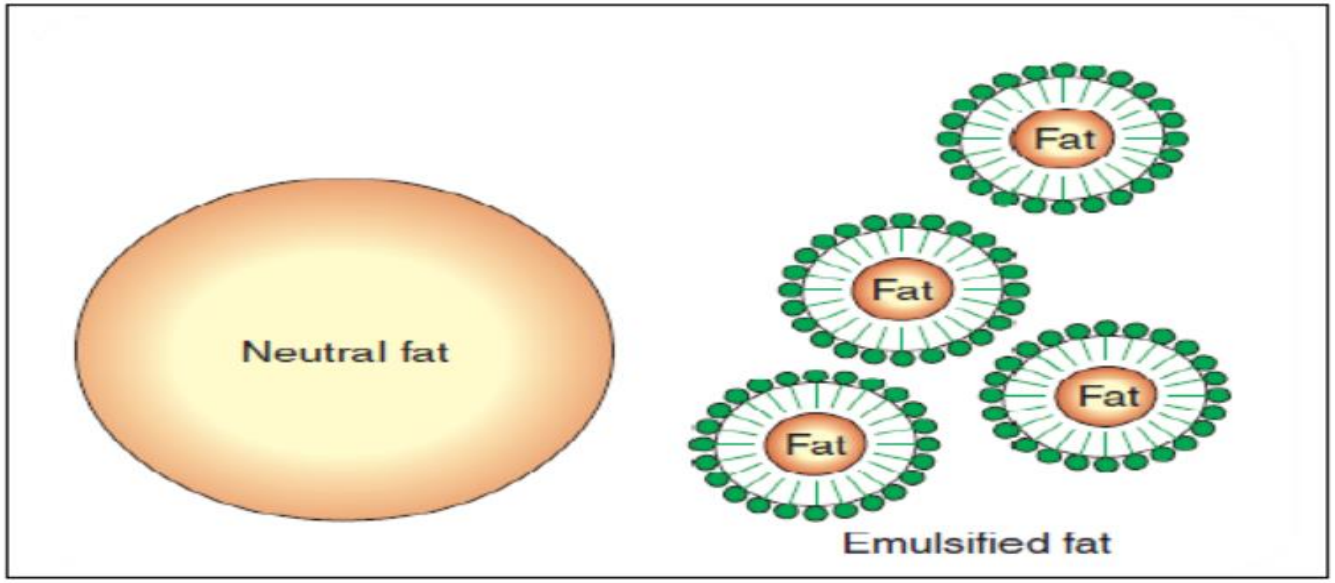
- **In the small intestine:**

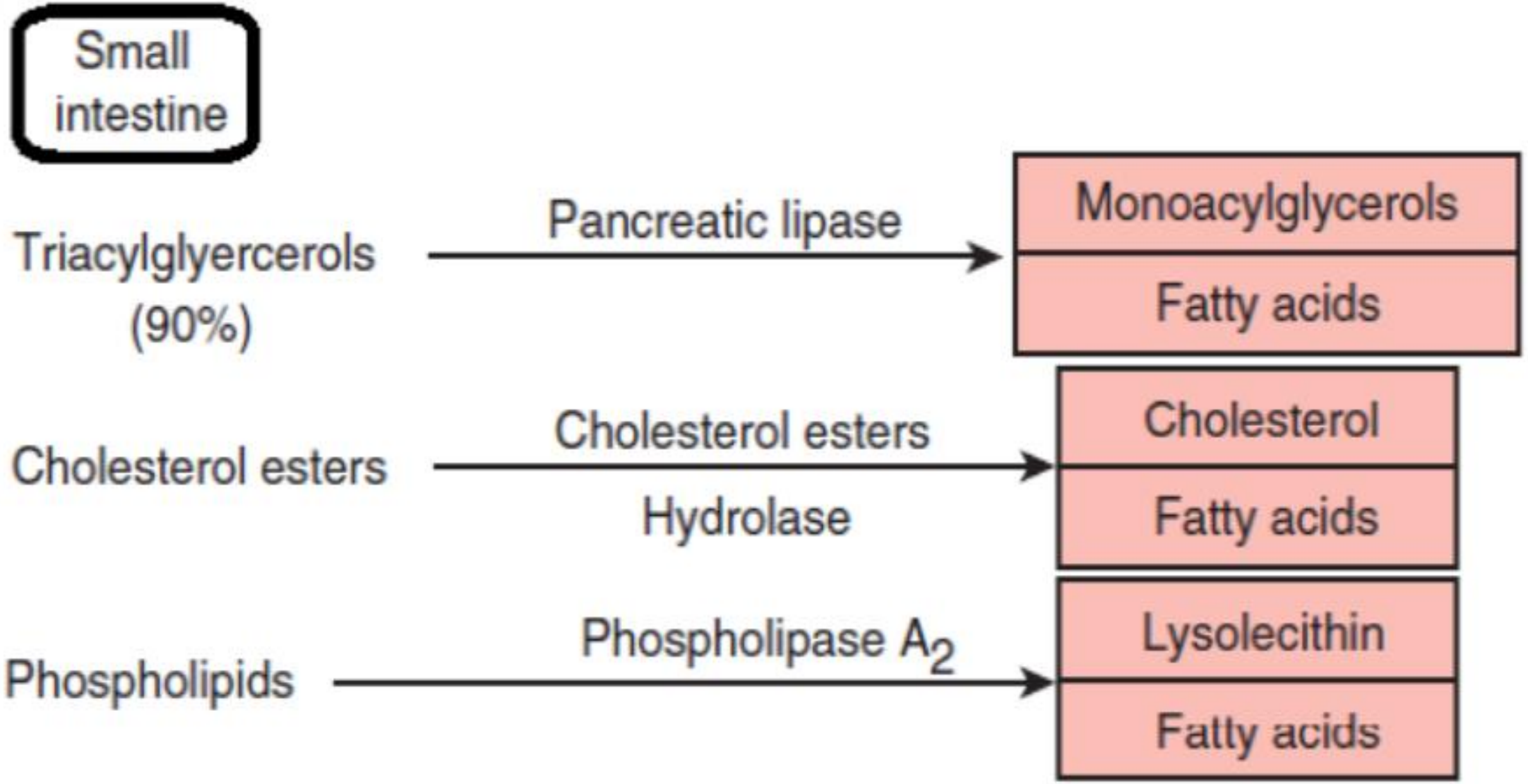
- Bile salts are secreted into the lumen of small intestine. These bile salts surround and **emulsify** dietary lipids. Emulsification produces small droplets of lipid dispersed in the aqueous solution of the intestinal lumen, creating a large surface area for the action of pancreatic enzymes (pancreatic lipase, cholesterol ester hydrolase, and phospholipase A2)

The **colipase**, a protein present in the pancreatic juice, displaces the bile salts from the fat droplet and allows the action of pancreatic lipase.

Pancreatic lipases hydrolyze lipids to fatty acids, monoglycerides, cholesterol, and lysolecithin.

The hydrophobic products of lipid digestion are solubilized in **micelles** by bile salts.



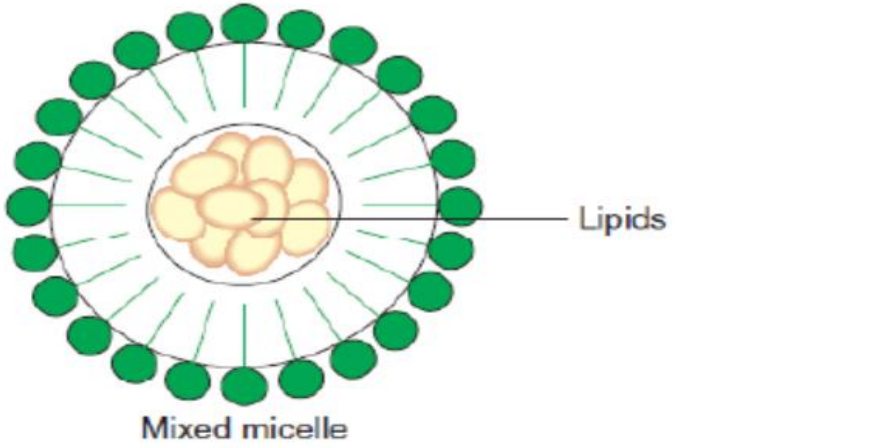

Small intestine
Triacylglyercerols (90%)
Pancreatic lipase
Monoacylglycerols
Fatty acids
Cholesterol esters
Cholesterol esters
Hydrolase
Cholesterol
Fatty acids
Phospholipids
Phospholipase A2
Lysolecithin
Fatty acids

Absorption of lipids:

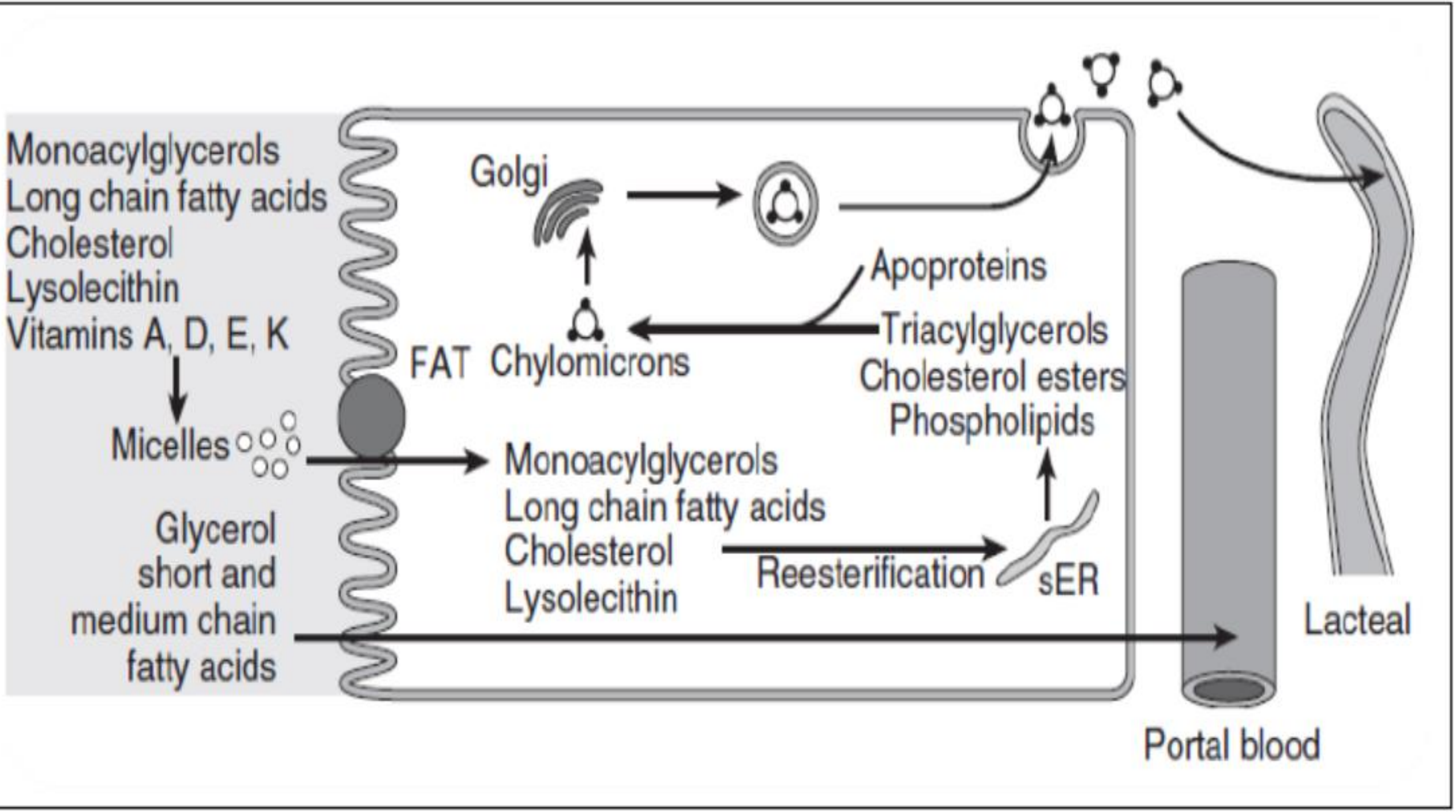
- Micelles bring the products of lipid digestion into contact with the absorptive surface of the intestinal cells. Then, fatty acids, monoglycerides, and cholesterol diffuse down their concentration gradients across the luminal membrane into the cells. Glycerol is hydrophilic and is not contained in the micelles.
- The bile salts are left behind in the intestinal lumen to be absorbed downstream in the ileum.
- Inside the intestinal epithelial cells, the products of lipid digestion are **reesterified** with free fatty acids on the smooth endoplasmic reticulum to form the original ingested lipids, triglycerides, cholesterol ester and phospholipids.

Inside the cells, the reesterified lipids are packaged with apoproteins in lipid-carrying particles called **chylomicrons**. The chylomicrons are packaged in secretory vesicles on the Golgi apparatus. The secretory vesicles migrate to the basolateral membranes, and there is **exocytosis** of the chylomicrons. Because chylomicrons are too large to enter the capillaries, they are transferred to **lymph vessels** and are added to the bloodstream via the thoracic duct.

- The hydrophilic product of lipid digestion (i.e., glycerol) along with short and medium chain fatty acids enter the intestinal epithelial cells directly by diffusion and exit the enterocyte by diffusion to enter portal blood.



Structure of a mixed micelle composed of lipids (monoglycerides, fatty acids, cholesterol) in the centre surrounded by bile salts.


Monoacylglycerols
Long chain fatty acids
Cholesterol
Lysolecithin
Vitamins A, D, E, K
Micelles
Glycerol
short and
medium chain
fatty acids
Golgi
FAT Chylomicrons
Apoproteins
Triacylglycerols
Cholesterol esters
Phospholipids
Monoacylglycerols
Long chain fatty acids
Cholesterol
Lysolecithin
Reesterification
sER
Lacteal
Portal blood

[C] Abnormalities of Lipid Digestion and Absorption (Causes of steatorrhea):

There are many steps in the normal process of lipid digestion or absorption: pancreatic enzyme secretion and function, bile acid secretion, emulsification, micelle formation, diffusion of lipids into intestinal epithelial cells, chylomicron formation, and transfer of chylomicrons into lymph.

An abnormality at any one of the steps will interfere with lipid absorption and result in **steatorrhea** (fat excreted in feces).

1) Pancreatic insufficiency:

Diseases of the exocrine pancreas (e.g., chronic pancreatitis and cystic fibrosis) result in failure to secrete adequate amounts of pancreatic enzymes including those involved in lipid digestion, pancreatic lipase and colipase, cholesterol ester hydrolase, and phospholipase A2. Undigested triglycerides are not absorbable and are excreted in feces.

2) Hypersecretion of gastrin:

Zollinger-Ellison syndrome (pancreatic tumor secretes large quantities of gastrin). Gastric H^+ secretion is increased and the duodenal pH is decreased. Low duodenal pH inactivates pancreatic lipase.

3) Deficiency of bile salts:

- Deficiency of bile salts interferes with the ability to form micelles, which are necessary for solubilization of the products of lipid digestion.
- Ileal resection (removal of the ileum) interrupts the enterohepatic circulation of bile salts, which then are excreted in feces rather than being returned to the liver.

4) Bacterial overgrowth:

- Bacterial overgrowth, which may lead to deconjugation of bile salts (removal of glycine and taurine from bile salts, converting them to bile acids).
- The bile acids are absorbed "too early" in the upper small intestine (before reaching the ileum), before micelle formation and lipid absorption are completed.

5) Decreased intestinal cells for absorption:

- In conditions such as tropical sprue, the number of intestinal epithelial cells is reduced, which reduces the microvillar surface area.

6) Failure to synthesize apoproteins:

Failure to synthesize Apoprotein B causes abetalipoproteinemia. In this disease, chylomicrons either do not form or are unable to be transported out of intestinal cells into lymph.

NB:

- **Bile salts** → help absorption of fat & fat soluble vitamins.
- **Intrinsic factor** → helps absorption of vitamin B12 in the terminal ileum.
- **Parathyroid hormone & vitamin D** → help absorption of calcium &phosphorus.
- **Aldosterone** → helps absorption of Na+, water & K+ secretion by the colon & to less extent by ileum.
- **Alcohol & some drugs** e.g. aspirin are absorbed from stomach.
- **Large intestine** can absorb water & electrolytes.

Iron absorption

Average daily intake of iron is 20 mg.

Iron is consumed in two forms:

a) Heme (meat) iron. B) Non heme (plant) iron.

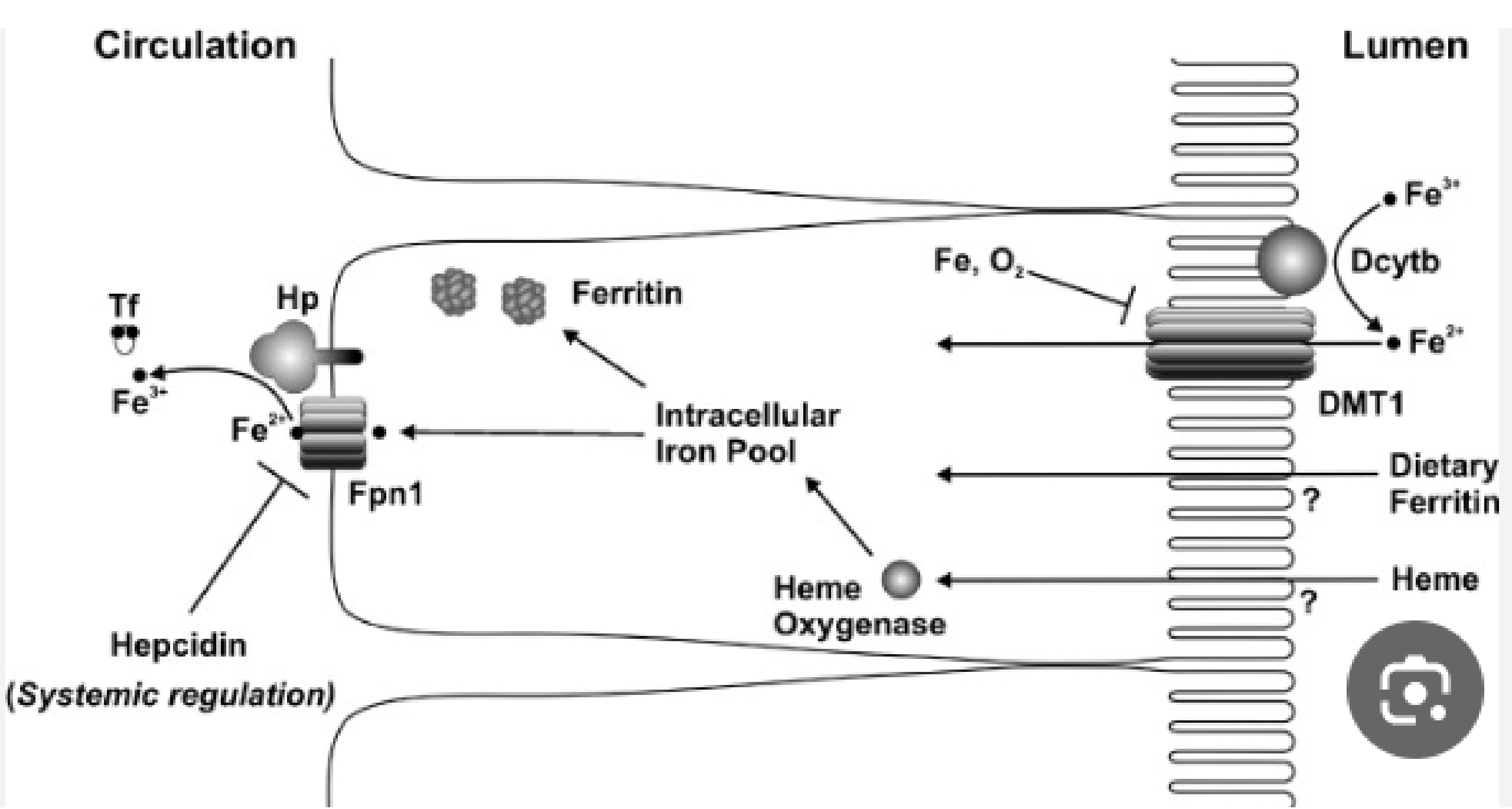
Non heme (plant) iron is in Fe^{+3} (ferric state). However ferric iron poorly absorbed & ferrous iron is better absorbed than it. So, ferric iron is reduced to ferrous in the stomach by HCl and vitamin C and also by surface enzymes like duodenal cytochrome B (Dcytb).

Ferric iron (Fe^{3+}) $\xrightarrow{\text{HCl \& Vitamin C}}$ Ferrous iron (Fe^{2+})

- Then, Fe^{2+} is transported to inside enterocyte (intestinal epithelial cells) via divalent metal transporter 1 (DMT1).

Heme iron is transported to inside enterocyte by a heme carrier protein 1 and then inside the enterocyte, heme iron is broken down by heme oxygenase into Fe^{2+}

- After that, Fe^{2+} is either stored inside the enterocyte in the form of ferritin (Apoferritin protein that combines with the ferrous iron to form ferritin) but the intestinal epithelial cells are sloughed after few days and iron is lost in the stool.
- Or, Fe^{2+} is transported at the basolateral border of enterocyte to the blood via ferroprotein.
- The blood containing transferrin protein which carries iron to bone marrow to form a part of R.B.Cs (hemoglobin) or to the liver to be stored.
- **Excessive oxalates, phytic acids and phosphates** in diet precipitate iron and decrease its absorption.
- **Hepcidin hormone** which is produced by liver, regulates iron absorption and prevents iron over load in the body through its binding to ferroprotein and degradation of it


Circulation
Lumen
Tf
Hp
Ferritin
Fe, O2
Dcytb
Fe3+
Fe3+
Fe3+
Fe2+
DMT1
Intracellular
Iron Pool
Dietary
Ferritin
?
Fpn1
Heme
Oxygenase
Heme
?
Hepcidin
(Systemic regulation)

Calcium absorption

Intestinal calcium absorption occurs via two main mechanisms:

1) **Transcellular active transport**: active process, occurs in the duodenum during low calcium intake.

2) Paracellular passive diffusion: passive process, occurs throughout the intestine during high calcium intake.

Transcellular transport involves.

a. Calcium enters the apical side of the enterocyte from the intestinal lumen through calcium channels.

b. Intracellular Diffusion: The absorbed calcium is bound to Calbindin, which ferries it across the cytosol, preventing high intracellular concentrations that could disrupt cellular processes.

c. Calcium is transported out of the cell across the basolateral membrane into the bloodstream, a process mediated by plasma membrane calcium ATPase (PMCA1b).

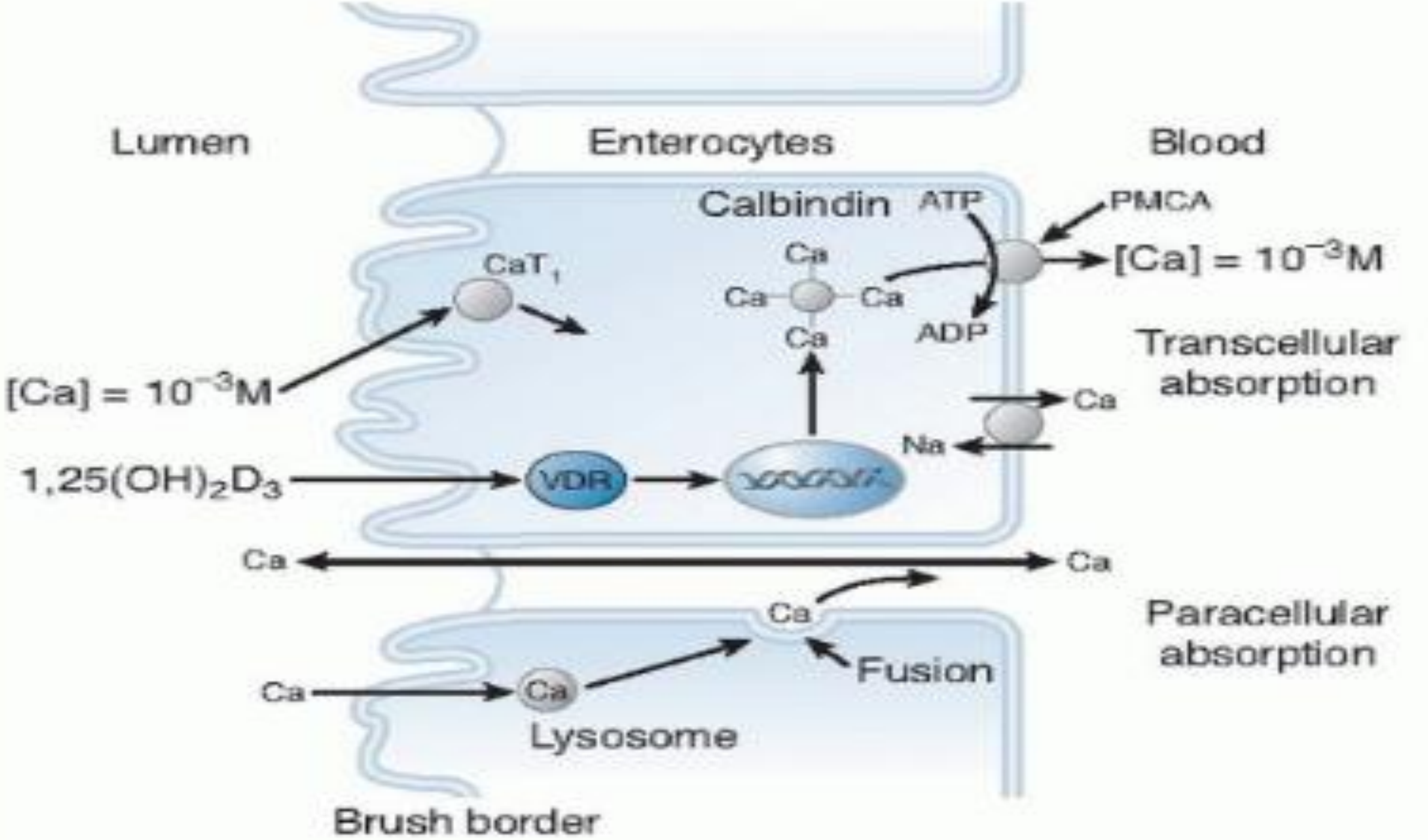
Vitamin D: Regulates the expression of all three components of transcellular transport (calcium channels, calbindin, and PMCA)

Paracellular Passive Transport

- This process is the primary pathway for calcium absorption when dietary calcium intake is high.
- Calcium moves between epithelial cells through tight junctions by the electrochemical gradient where higher luminal calcium concentration is present.
- It is largely independent of vitamin D.
- It occurs all along the small intestine, but more in the ileum.

Factors affect Ca absorption:

- **pH:** Acidic pH in the proximal intestine increases solubility and absorption.
- **Compounds:** oxalates, phytates can reduce it


Lumen
Enterocytes
Blood
Calbindin
ATP
PMCA
[Ca] = 10⁻³M
CaT1
Ca
Ca
Ca
Ca
ADP
Transcellular absorption
[Ca] = 10⁻³M
Ca
Na
1,25(OH)2D3
VDR
Ca
Ca
Paracellular absorption
Ca
Fusion
Ca
Ca
Lysosome
Brush border


Thank
you