GIS 7

PHYSIOLOGY

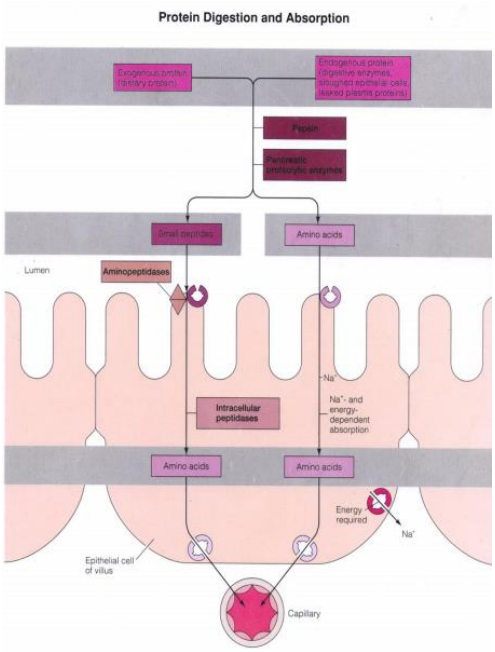
Done by: Adnan M. AL-Kababji

Scientific Correction: Emad Abu Ahmad

Gramatical Correction: Ibrahim N. Dbaybo

Doctor: Mohammad AL-Katatbeh

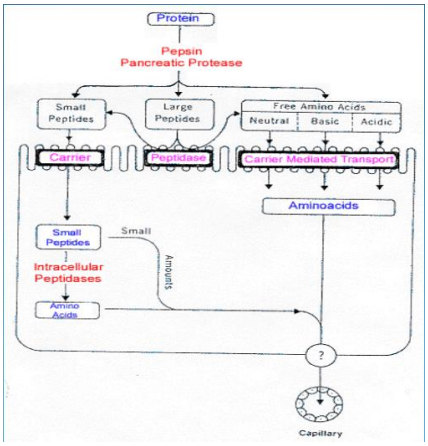
❖ Digestion of proteins



- ✓ The process of protein digestion **starts at the level of stomach,** by the activity of pepsin.
- ✓ The optimum activity of pepsin is at acidic environment, when the is **PH 2-3**. As soon as the emptying of stomach content have taken place, the activity of pepsin decreases due to the alkaline environment.
- ✓ Other enzymes that are needed in the process of these proteins are :-
  - **Trypsin and chemotrypsin** (endopeptidases)
  - **Carboxypeptidases** (exopeptidases)
- ✓ By the activity of these enzymes, the net products are **amino acids and small peptides**.
- ✓ Protein digestion will continue at the brush border of small intestine by the activity of **aminopeptidase**, which will yield **smaller peptides and more amino acids**.
- ✓ The final digestion process of these small peptides takes place after absorption, **inside the absorptive cells,** by the activity of **intracellular peptidases,** which will result in the production of amino acids.
- ✓ **After this process, the protein will be totally broken down into amino acids.**

- There is also aminopeptidases at the brush border, which will lead to shortening of the small peptides .

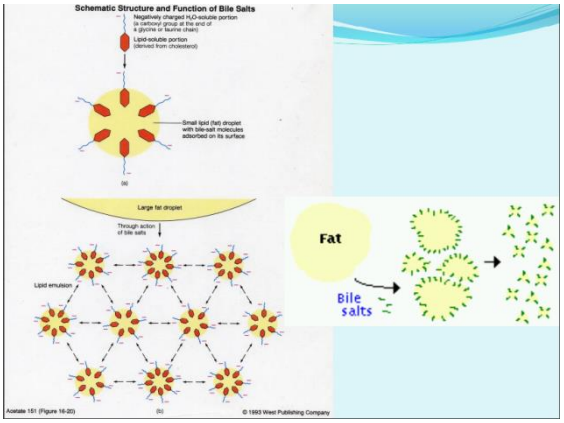
❖ Protein absorption



- ✓ Unlike carbohydrates small peptides like **di-peptides, tri-peptides, and tetra-peptides** are transported into the enterocytes by a sodium dependent carrier mediated transport system (secondary active co-transport).
- ✓ We also have membrane bound carriers at the lumen side for amino acids absorption, which are divided into 2 categories, according to their dependence on sodium.

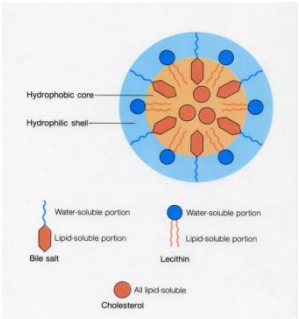
- **Sodium dependent carriers**:-
  - For neutral amino acids
  - For proline and hydroxyproline
  - For phenylalanine and methionine
- **Sodium independent carriers**:-
  - For basic and neutral amino acids

❖ Lipid digestion and absorption

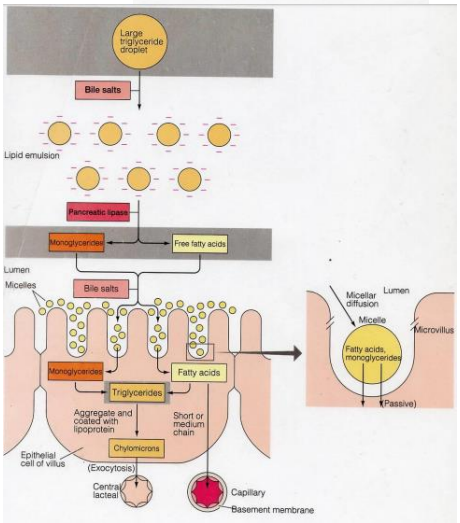


- ✓ There is **little or no** digestion or absorption of fat in the **stomach**.
- ✓ Most of lipids are been absorbed at the level of small **intestine**.
- ✓ By the activity of **bile salts** in the duodenum, large fat droplets are emulsified into small droplets (0.5-1 micron).
- ✓ Without bile salts, lipids in chyme will form large droplets which **cannot be absorbed**. Meanwhile in the presence of bile salts, lipids are emulsified into micelles.
- ✓ Bile salts are **amphipathic molecules,** so they have both hydrophilic and lipophilic parts. The hydrophilic part will be oriented to the aqueous part and lipophilic part will be oriented to the fat media in these droplets.
- ✓ This process is important in the digestion and absorption of lipids, by which it **increases the surface area** (the sum of small droplets surface areas is much larger than the large fat droplets) **for the action of enzymes**.

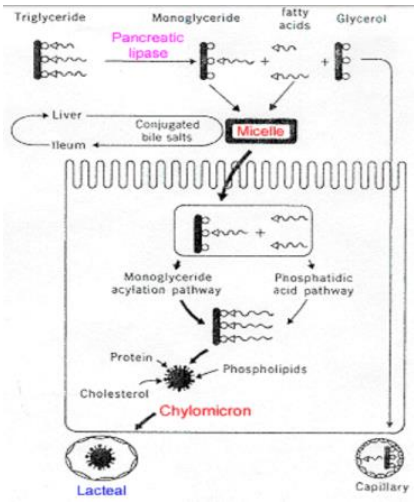
Structure of micelles



- Have **hydrophilic shell and hydrophobic core**.
- Hydrophilic parts of bile salts and lipids will be oriented towards hydrophilic shell.
- Hydrophobic parts of bile salts and lipids will orient towards hydrophobic core.



- ✓ The enzymes that work on digestion of lipids are **hydro-soluble**, so they cannot act on lipids while they are in the core of the large droplet.
- ✓ At the level of **oil water interface** (boundary between hydrophilic shell and hydrophobic core) the action of these enzymes on triglycerides takes place.
- The product of this reaction is :-
  - **Free Fatty Acids + monoglycerides** , which will be absorbed from the lumen towards the absorptive cells.
- ✓ These products are **liposoluble** so they can cross the luminal membrane by **simple diffusion**.



- ✓ Once they are inside the cell the will combine and **reform triglycerides**.
- ✓ Triglycerides (80-90%) + cholesterol (3%) + phospholipids (10%) + B- lipoprotein (5%) are combined to form **chylomicrons** (60-750 nm diameter) which will be expelled by exocytosis from the **basolateral membrane** towards **interstitial fluid**.
- ✓ The process of absorption of small molecules (Free Fatty Acids + monoglycerides) is **much easier** than the absorption of triglycerides. This is why we digest them in the lumen and reform them inside the cells.
- ✓ Chylomicrons are removed away from villi by **lymphatic circulation** (central lacteals) which enters the circulation at the **thoracic duct**.
- ✓ Any pathological condition result in decreasing the process of digestion and/or absorption will lead to increase fat content in the stool (whitish or yellowish in color), that's called **steatorrhea**.

❖ Absorption of water and electrolytes :-

- **Absorption of sodium, chloride, and water:**
- ✓ At the **basolateral membrane**, we have **active transport of sodium** by the activity of **sodium/potassium pump**. These pumps transport sodium **from inside the cell, towers interstitial fluid**, keeping the contraction gradient of sodium between the lumen and inside the cell. This gradient is important for co-transport mechanisms (glucose, fructose, small peptides, amino acids).
- ✓ Once we have transported sodium towards interstitial fluid we created a **potential across the absorptive cell**, **between the lumen and interstitial fluid**(trans-cellular potential), **with small positive towards interstitial fluid**.
- ✓ This trans-cellular potential **attracts negatively charged particles** towards absorptive cells, and we have plenty of **chloride** ion in the lumen. **The absorption of chloride is derived by the potential that is mediated by the absorption sodium**.
- ✓ Once we have absorbed sodium and chloride we have **increased the osmotic pressure at the interstitial fluid**. **This will lead to an increase in the osmosis of water from the lumen towards interstitial fluid**.
- **For the absorption of potassium**
- ✓ Potassium is transported across the membrane **according to the electrochemical equilibrium**. This means that Potassium is **absorbed passively in small intestine**, **and secreted in the colon in exchange with sodium**.

- **Transport of calcium**

✓ Calcium is **transported actively** by a special mechanism. It binds to a protein at the brush border membrane (may be a carrier).

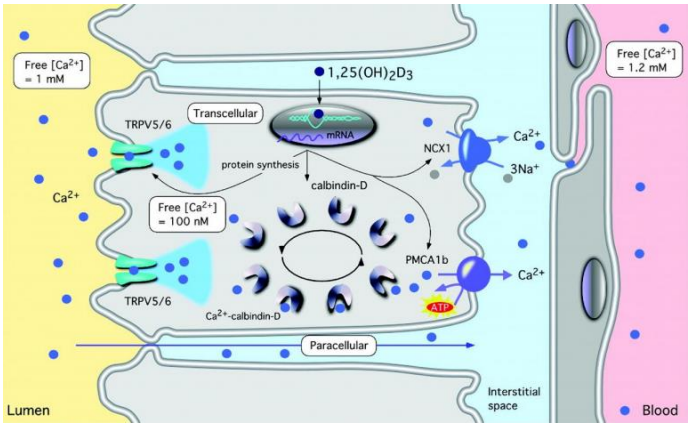
✓ Enterocytes form a protein molecule to which we can have calcium binding, called **calbindin**.

✓ Calbindin transports **calcium across the absorptive cell**.

✓ At the **basolateral membrane** we have pumps that pump calcium towards interstitial fluid actively.

✓ Calcium absorption can be **increased by vitamin D and parathyroid hormone**, **by increasing the expression of calbindin inside the absorptive cells**.

✓ Once we have **increased the expression of calbindin**, we will have much **lower concentration of free calcium inside the absorptive cell**, and this will **ensure the movement of more calcium ions towards the absorptive cells.**



- **Iron absorption**

✓ First of all, iron is transported in the **ferrous form**(Fe++) rather than the **ferric form** (Fe+++).

✓ Iron absorption is affected by the presence of some factors :-

- **Vitamin C** and **acidic PH enhance the absorption of iron** (by reducing the ferric iron to ferrous iron).
- **Phosphates**, **oxalates**, **phytic acid** (found in cereals) and **pancreatic juice** (alkaline media) **inhibit iron absorption** (by oxidation of ferrous iron to ferric iron).

✓ The detailed mechanisms of iron absorption are still **unsettled**.

✓ Some believe that there is an **active transport at the luminal membrane**. Another theory for iron transport is by secreting a globular protein from the epithelial cells, known as **apoferritin** (most acceptable theory).

✓ Apoferritin is **released first into the lumen of the small intestine**. It then **binds to iron to form ferritin molecule**.

✓ At the luminal membrane, there are **receptors of the ferritin molecules**, and by the binding of ferritin to their receptors, we activate the process of **endocytosis**.

- ✓ **So the process of iron absorption is a receptor mediated endocytosis.**
- ✓ After absorption, iron will **remains at the level of absorptive cell**, and it will be **transported towards body fluid if there is a need for iron**.
- ✓ **In case there is no need for iron, it will remain in the absorptive cells** (mucosal block).
- ✓ **Mucosal block** :- blocking the absorption of iron at the level of absorptive cells.
- ✓ Inside the body iron is transported by another protein called **transferrin**. When all these proteins are loaded with iron, this means that there is no need for iron to be moved from the absorptive cells towards interstitial fluid.
- ✓ If there's an increase in the concentration of un-loaded transferrin, this indicates that there's a need for iron, so iron will moved from absorptive cells, towards interstitial fluid.
- ✓ Iron absorption and storage inside the absorptive cells **can be lost** by the process of **desquamation** of interstitial cells, which occurs every 3-4 days.

❖ Vitamin absorption

- ✓ Most vitamin are absorbed **at the upper part of the small intestine**, but **some are absorbed in the lower part of the small intestine** (e.g. vitamin B12).
- Water soluble vitamins are **absorbed passively** expect **vitamin C**, **vitamin B1** and **vitamin B12**.
- ✓ For the absorption of **vitamin B12,** we need **intrinsic factor,** which is released form the **oxyntic cells of the stomach**.
- Lipid soluble vitamins (vitamins A,D,E,K)
- ✓ **Are absorbed by the same way as lipids**.
- ✓ So first, they are **solubilized in micelles,** then **transported across the luminal membrane** of the absorptive cells by **simple diffusion**, then **incorporated in chylomicrons**, finally, they are **taken by lymphatic circulation**.

- Any medical condition that results in **maldigestion** and/or **malabsorption of lipids** may results in **decreased absorption of one or more of these vitamins**. This will cause a **medical condition related to the deficiency of one or more of these vitamins**.

- Some notes from the handout :-
  - ✓ Resource of proteins are food, mucus, enzymes, and desquamated cells.
  - ✓ Protein digestion in stomach is little, because the pepsin and HCl cannot attack the interior of food mass.
  - ✓ Bile salts are amphipathic molecules having both hydrophilic and hydrophobic portions. The sterol nucleus is hydrophobic. The hydroxyl groups, peptide linkage and the amino acid conjugate are hydrophilic. The conjugated bile acids are more hydrophilic. The more hydroxyl groups they have ⟹ more hydrophilic.
  - ✓ Pancreatic lipase and co-lipase can act on the water/oil interface to hydrolyze the 1st and 3rd ester linkages of the triglyceride between glycerol and fatty acids. The result of this digestion is :- two free fatty acids and a 2-monoglyceride.
  - ✓ In the terminal ileum, bile salts are absorbed actively.
  - ✓ The effect of aldosterone:
    a hormone secreted by adrenal glands after dehydration. This hormone increases Na+ absorption by enhancing the enzymes and transport mechanisms of Na+. This hormone is important mainly in the colon.
  - ✓ Places where electrolyte's absorption mostly occurs :-
    - Sodium ⟹ duodenum.
    - Chloride ⟹ upper part of the small intestine (duodenum and jejunum).
    - Iron ⟹ upper part of the small intestine (duodenum and the adjacent jejunum).

Best of luck