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DIGESTION and ABSORPTION:

Digestion process occurs by the activity of enzymes that catalyze carbohydrates, lipids and proteins.

Absorption occurs by specialized epithelial cells.

General considerations:

- No absorption in esophagus, little in the stomach and vast majority of absorption occurs in small intestine. The small intestine has specialized structures to increase the absorptive capacity by increasing the absorptive surface area of the mucosa.

- Most nutrients are absorbed before reaching the ileum.
- Colon is responsible for final removal of electrolytes and water.

Intestinal specialization:

- Presence of mucosal folds (*Folds of Kerckring* or Circular Folds) increases the surface area three folds.
- Mucosa also has other structures called *villi* which increase surface area 10 more folds.
- The lumenal surface of the epithelial cells has *micrvilli*, which increase surface area 20 folds.

The net increase in the surface area is about 600 folds.

Villus:

This specialized structure has:

- Capillary network which removes the absorbed nutrients very quickly. This process maintains a concentration gradient between lumen and blood in capillaries.
- Lymphatic network of lacteals removes lipids and maintains gradient for lipid absorption.

* Other structures that help in absorption and digestion:

- Enteric innervation (mainly the submucosal plexus): provides mechanism to regulate secretion of secretory cells and blood flow to intestinal mucosa.
- Smooth muscle cells of the muscularis mucosa which allow villi to wave in lumen and folds to move, which permit more spreading of chyme over the absorptive area.
- Brush border enzymes (At luminal membrane of absorptive cells):
 - At the surface of microvilli, cells are equipped with enzymes which help in the final digestion of carbohydrates and proteins.

DIGESTION and ABSORPTION OF CARBOHYDRATES:

Forms of ingested carbohydrates:

- Mostly carbohydrates are ingested as starch (a polymer of glucose linked by *alpha 1-4* and *alpha 1-6* linkages at branches).
- Lesser amounts are ingested as sucrose (fructose and glucose) and lactose (glucose and galactose).
- Cellulose is a glucose polymer of 1-4 beta linkage. This is not digestible by enzymes of gut.

Digestion of carbohydrates:

The process of carbohydrate digestion begins in oral cavity.
Enzymes that involved in carbohydrate digestion and their activities are:

- **Ptyalin:** Salivary *alpha-amylase* that begins process of digestion in oral cavity.
This enzyme converts starches → smaller polymers of glucose and α limit dextrans. (larger molecules containing branch points).

The optimum activity of this enzyme is at neutral pH and is inactive at acidic pH. Therefore it is inactivated in stomach. The digestion continues in the stomach in the center of the food mass only which are not exposed to the acid and where the pH is still above 4.

- **Pancreatic amylase:** digests 50-80% of starch. Alpha amylase that can attack the alpha 1,4 linkage.
The result of this digestion is maltose (2 glucose molecules), maltotriose (3 glucose molecules), and alpha limit dextrins (structure containing ramified glucose polymer).

- **Brush border enzymes:** responsible for final hydrolysis of glucose polymers and disaccharides into monosaccharides.

4 enzymes are found at this site (brush border):

Lactase split lactose \rightarrow glucose + galactose

Sucrase split sucrose \rightarrow fructose + glucose.

Maltase split maltose and other glucose polymers \rightarrow Glucose.

α -Dextrinase attack at alpha 1,6 linkage in α - limit dextrins.

The final digestion of carbohydrate is glucose, fructose, galactose.

Absorption of carbohydrates:

1. Glucose:

* Absorption of glucose is taking place with the help of Na^+ linked carrier at the membrane of the epithelial cells.

- Binding of both Na^+ and glucose to a specialized carrier will result in transport of Na^+ and glucose into the cell.
- Then Na^+ is pumped out at basolateral membrane. And glucose is removed at the basolateral membrane by a facilitated diffusion into the capillaries of the villus.

The whole process depends on the pumping of Na^+ out of the enterocyte (epithelial cell). The process is a **secondary active co-transport**.

* Absorption with solvent drag through the tight junction.

Increased glucose concentration in chyme can result in increased absorption. This results in increased osmotic pressure in the paracellular space and consequently, increased fluid flow through the tight junction which carries anything dissolved in

fluids also. It could be important when glucose concentration is very high in chyme.

2. Galactose: uses the same mechanism as glucose (Na^+ linked carrier).
3. Fructose: enters by facilitated diffusion by using different type of carrier than Glucose/Galactose. The carrier is not linked to Na^+ . At the basal membrane it diffuses passively.

DIGESTION and ABSORPTION of PROTEINS:

Protein is a polymer of amino acids (aa) linked together by peptide bonds. About 60 grams of proteins are digested and absorbed by the gut per day.

This protein is derived from food, mucus, enzymes, and desquamated cells.

Protein digestion:

- **Proteolytic enzyme in the stomach:** Protein digestion in stomach is little, because the pepsin and HCl can not attack the interior of food mass. The food is in semisolid mass and the exterior of mass only can be exposed to the enzymes. The digestive enzyme in the stomach is *pepsin*.

Pepsin enzyme has an optimum activity at the pH 2-3. It is inactivated at a pH more than 5 in the small intestine. The activity of this enzyme results in hydrolysis of about 20% of proteins that enter the stomach by converting these large peptides of proteins into peptones and smaller polypeptides.

- **Proteolytic enzymes of the pancreas:**

Include: Endopeptidases (*trypsin* and *chymotrypsin*).

Exopeptidases: (*carboxypeptidases* and *aminopeptidases*)

These enzymes continue to hydrolyze protein by converting it to small peptides and amino acids.

- **Brush border (peptidases):** Located at the luminal membrane and convert small peptides into oligopeptides (di-, tri-, and tetra-peptides) and amino acids.

- Peptidases inside the cytosol of the enterocytes continue the hydrolysis of di-, and tri-, peptides after they have been transported inside the enterocyte and converting these small peptides into amino acids.

Protein absorption:

1. Small peptides: Di- and Tri-peptides are transported into the enterocyte by a carrier mediated transport system. This mode of transport is a secondary active co-transport which depends upon the activity of Na^+ pump to maintain a chemical gradient for Na^+ across the luminal membrane.

2. Amino acids:

Transported by a membrane bound carriers:

* Na^+ dependent carriers: 3 different carriers:

1. For neutral amino acids.
2. Proline and hydroxyproline.
3. Phenylalanine and methionine.

* Na^+ independent carriers: for basic and neutral aminoacids.

DIGESTION and ABSORPTION of LIPIDS:

Bile is required for fat digestion and absorption:

- Bile is secreted by liver to act in the lumen of intestine. It *solubilizes lipids and aids in their digestion*. 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. In aqueous environment, bile salts form *micelles* by the orientation of hydrophobic portion toward the center and the hydrophilic portion toward the periphery. In this way, lipid and non water-soluble molecules are *dissolved in the center of the micelle*.

Digestion of lipid:

Dietary lipid: fat is ingested mostly as triglycerides. Less as phospholipids and sterol.

In stomach: little or no digestion or absorption of fat in the stomach is taking place. No bile salts are present in the stomach to emulsify fat. Lipids tend to separate from the aqueous portion of the meal and tend to empty at slower rate than the rest of the meal.

In intestine:

- Most of lipid digestion appears in the intestine. As lipid enters in the duodenum it is emulsified into small droplets (0.5-1 micron) which are stabilized by bile salts. Once emulsified, 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.
- The free fatty acids (FFA), the 2-monoglyceride, phospholipids, cholesterol, and bile salts remain combined together in micelles (5nm diameter).
- When the micelles are in contact with the gut wall, FFA, monoglyceride, phospholipid, cholesterol diffuse out of the micelles across the brush border into the epithelial cell.

Note: in contrast to carbohydrate and proteins there are NO brush border enzymes for lipid digestion and there is NO carrier system at the luminal membrane for the transport of lipids. Transport appears as simple diffusion.

- Once micelles are empty they are loaded again and shuttle more lipids to the enterocytes. This process is repeated several times as the meal moves along the intestine.
- In the terminal ileum, bile salts are absorbed actively.

Absorption of lipids:

- Absorption across the luminal membrane of the intestinal epithelial cell is by *passive diffusion*.
- Once inside the epithelium,
FFA + monoglycerides reform *Triglycerides* again. (this process need ATP and Co-A).

Triglycerides (80-90%) + cholesterol (3%) + phospholipids (10%) + B- lipoprotein (5%) are combined together to form *chylomicrons* (60-750nm diameter).

- The chylomicrons are expelled from the epithelial cells by exocytosis. It diffuses through the extracellular space and is removed from the villus by lacteals (the terminal lymphatic vessel) and lymphatic circulation. Then enters the circulation at the thoracic duct.
- Some glycerol molecules which are not esterified into triglyceride and short chain fatty acids pass directly through the epithelial cells and removed from the villus by diffusion into blood capillaries.

ABSORPTION of WATER and ELECTROLYTES:

Water:

- Water absorption is driven by Na^+ absorption. Active transport of Na^+ at the basolateral membrane causes water to flow in through epithelial cells and through the tight junctions between the cells.
- Rapid removal of water through capillaries keeps the gradient intact.

Electrolytes:

- *Na⁺: Absorbed actively in the small intestine and colon.
- Diffusion is passive at the luminal membrane and active at basolateral membrane.
- Rapid removal of Na⁺ is critical to maintaining gradient.
- There is co-transport system with amino acids and monosaccharides.
- The absorption is greatest in duodenum and decreases caudad.

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.

In this way it conserves water and Na⁺ from loss with feces mainly when there is a need for Na⁺ and water in dehydration.

*Cl⁻:

- Absorbed mainly in the upper part of the small intestine (duodenum and jejunum). Cl⁻ moves in passive diffusion when an electrical gradient is established by the absorption of Na⁺.

*K⁺: absorbed passively in small intestine.

- In colon usually secreted in exchange for Na⁺.

Absorption of Ca⁺⁺:

- Ca⁺⁺ is actively absorbed throughout intestine.
- It binds to a protein at the brush border membrane (may be a carrier).
- Once Ca⁺⁺ is inside it binds to a cytosolic Ca⁺⁺ binding protein called *calbindin* Which transports Ca⁺⁺ across the cell.
- Ca⁺⁺ is pumped out at the basolateral membrane by an active process.
- Ca⁺⁺ absorption is increased by vitamin D and parathyroid hormone.

Absorption of Fe^{++} :

absorption is mainly in the upper part of the small intestine (duodenum and the adjacent jejunum).

- Iron absorption is promoted by acidic pH in the stomach and vitamin C.
- Fe^{++} (ferrous iron) is much more soluble than Fe^{+++} (ferric iron).

The effect of vitamin C in enhancing iron absorption is by reducing the ferric iron to ferrous iron.

Phosphates, oxalates, phytic acid (found in cereals) and pancreatic juice inhibit iron absorption.

- The detailed mechanisms of iron absorption are still unsettled. Some believe that there is an active transport at the luminal membrane. Other theory for iron transport is by secreting a globular protein from the epithelial cells known as apoferritin. This protein binds to $Fe^{++} \rightarrow$ ferritin. This complex of protein and iron is transported into the cell by receptor mediated endocytosis.
- Then iron stored in the epithelial cell in the form of ferritin, then transported into the blood where it binds transferrin as needed.
- If NOT needed, iron is lost when cells are desquamated. This mechanism prevents excess iron from entering the blood and causing toxic effects. This process is known as Mucosal Block.

Absorption of vitamins:

Most vitamins are absorbed in the upper part of the small intestine, but vitamin B12 is absorbed in the ileum.

1. Water soluble vitamins: water soluble vitamins are absorbed passively except Vit. C, Vit. B1, and Vit. B12.

Absorption of vit. B12 requires the ***intrinsic factor*** secreted by the oxyntic cells of the stomach.

2. Lipid soluble vitamins (Vit. A, D, E, K):

Follow the same route as lipids. They are solubilized in micelles and chylomicrons.