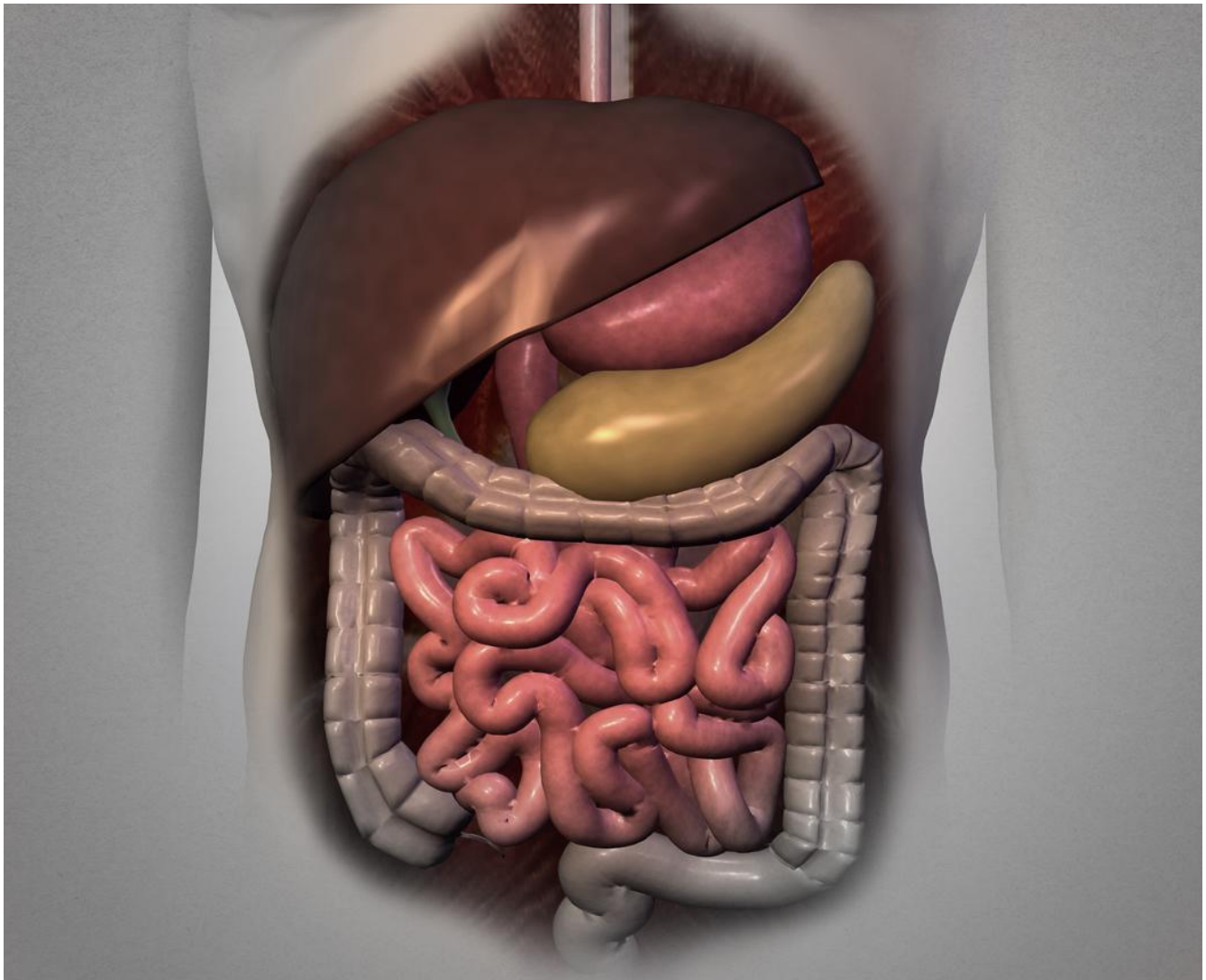

GIT Block

Physiology Team 431

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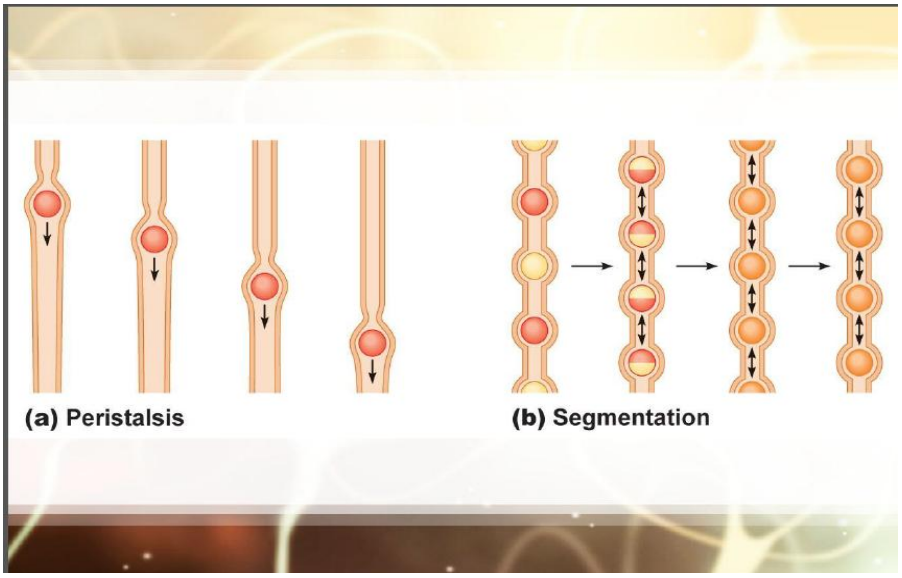
Motility in the Small Intestine

The movements of the small intestine can be divided into:

- Segmenting (Mixing) contractions.
- Propulsive contractions (Peristalsis).
- Migrating motor complex.
- Antiperistalsis.
- Peristaltic rush.

1) Mixing Contractions (Segmentation Contractions): (mentioned in the first lecture)

- ❖ When a portion of small intestine becomes distended, the segmentation contraction is activated by enteric nervous system (ENS) at regular intervals to divide the intestine (loop of small intestine) into spaced segments which last for fraction of min, and have the appearance of a chain of sausages.
- ❖ As the segmentation contractions disappear (relaxes), a new set often begins at points between the previous ones. (Arranged such that the parts that were contracted become relaxed).
- ❖ The segmentation contractions become weak when the excitatory activity of ENS is blocked by the drug atropine.
- ❖ It depends on myenteric plexus, and inhibited by anticholinergic (atropine).
- ❖ The significance of segmentation contractions:
  - •Blend different juices with the chyme.
  - •Bring products of digestion in contact with absorptive surfaces. (Bringing chyme closer to the mucosa to get absorbed).



2) Propulsive Movements or Peristalsis movement: (was mentioned in the first)

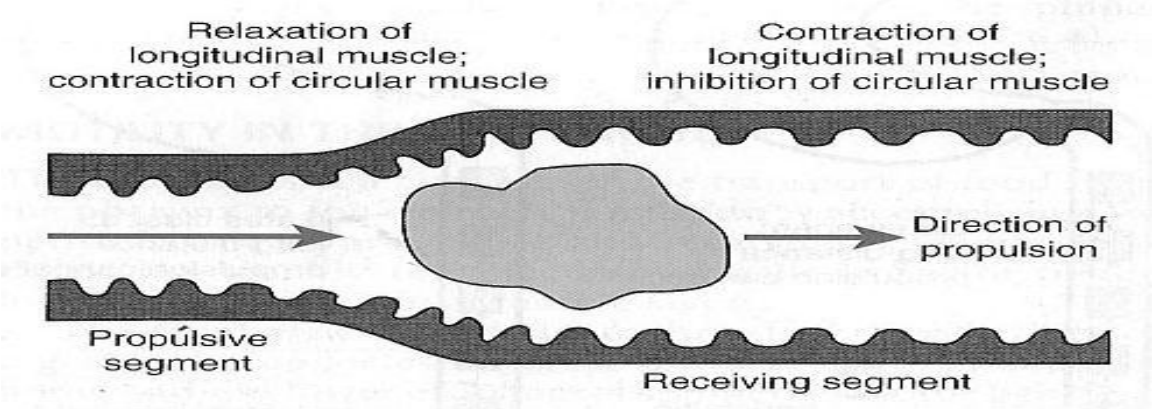
- ❖ Propulsive movements can occur in any part of the small intestine, at a velocity of 0.5 to 2.0 cm/sec.
- ❖ Usually stimulated by distension and travels in an oral-caudal direction.
- ❖ They are faster in the proximal intestine and slower in the terminal intestine. More develop in the duodenum and proximal part of jejunum, and decreases in the ileum. (Because once we reach the terminal ileum we need enough time to get the materials back via different transport mechanisms, to give them time to get back to the portal circulation).

- ❖ They normally are very weak after traveling only 3 to 5 centimeters,
- ❖ The net movement along the small intestine normally averages only 1 cm/min → this means 3 to 5 hours are required for passage of chyme from the pylorus to the ileocecal valve.
- ❖ Organizes propulsion of material over variable distances within the intestinal lumen
- ❖ Myenteric plexus is important for these movements
- ❖ It can be blocked by the drug atropine
- ❖ Mechanism of propulsive movements:
  - Receiving segment: contraction (longitudinal M.), relaxation (circular M.)
  - Propulsive segment: contraction (circular M.), relaxation (longitudinal M.)

N.B
Circular muscles contract → constricting passageway and pushing chyme forward
Longitudinal muscles contract → shortening passageway ahead of chyme
So we can say Peristalsis movement consists of:

- Travelling wave of contraction above the bolus duo to contraction of circular M. and relaxation of longitudinal M.

- Preceded by relaxation at the bolus site and below by contraction of longitudinal M. and relaxation of circular M.



3) Migrating Motor complex (MMC):

- ❖ It is bursts of depolarization accompanied by peristaltic contraction.
- ❖ Begins in empty stomach during interdigestive period(When the digestion and absorption of nutrients are completed, 2-3 hours after a meal)
- ❖ Then travels a long whole length of small intestine to reach ileocaecal valve after 1.5-2 h. where it disappears. A new wave of MMC starts.
- ❖ The activity of MMC terminates as soon as food is ingested.
- ❖ The function of MMC is to propel any remnants in stomach & small intestine into colon during the interdigestive period.

4) Antiperistalsis:

- ❖ In the opposite direction occurs between stomach and duodenum (chyme return to stomach) to allow more time for neutralization of chyme and between ileum and caecum to allow time for absorption.

Neutralization: The interaction between an acid and a base that produces a solution that is neither acidic nor basic.

Chyme: The thick semifluid mass of partly digested food that is passed from the stomach to the duodenum.

5) Peristaltic rush:

- ❖ Powerful rapid peristalsis due to intense irritation of intestinal mucosa as in infectious diarrhea.

(Irritation of general mucosa by pathogenic organism initiates rapid peristalsis propagates along the entire loop of small intestine to get rid of the harmful substance).

- ❖ It is initiated mainly by extrinsic nervous reflexes (vaso vagal reflex) to brain stem and back to gut.
- ❖ It sweeps the contents of intestine into the colon and thereby relieving the small intestine of irritative chyme or excessive distension.

Movement of the villi

- The villous movements consists of fast shortening and slow lengthening as well as side to side movements.
- Villous contractions are initiated by local nervous reflexes in response to chyme in small intestine. (Chyme come in contact with the lining of the villi initiates this contraction).
- They are stimulated by villikinin hormone released by intestinal mucosa when it comes in contact with digestive products.
- They facilitate absorption and lymph flow from central lacteals into lymphatic system. (Suction of fluid from lumen into the villi to help in absorption and in lymph flow).

Control of intestinal motility

1- Neural factors:

- Vagal excitation (parasympathetic) increases intestinal and villous movements.
- Sympathetic excitation decreases intestinal and villous movements.

Gastroileal reflex: is initiated in the stomach by gastric distension. Impulses are conducted through myenteric plexus (motor plexus) to initiate a fast peristaltic wave (effect) passing to the ileum. The ileocaecal valve relaxes allowing chyme to pass into cecum. This reflex is mediated by vagus nerve.

2- Hormonal factors:

Gastrin, CCK(Cholecystokinin), insulin and serotonin	Stimulate intestinal motility
Gastrin and CCK	relax ileocaecal sphincter
Motilin(secreted from duodenum)	Stimulates intestinal motility and regulate MMC.
Secretin and glucagons	Inhibits intestinal motility and contract ileocaecal sphincter.
*** Villikinin**	Stimulates movement of the villi.

Secretions of the small intestine

1) Secretion of Mucus by Brunner's Glands in the Duodenum:

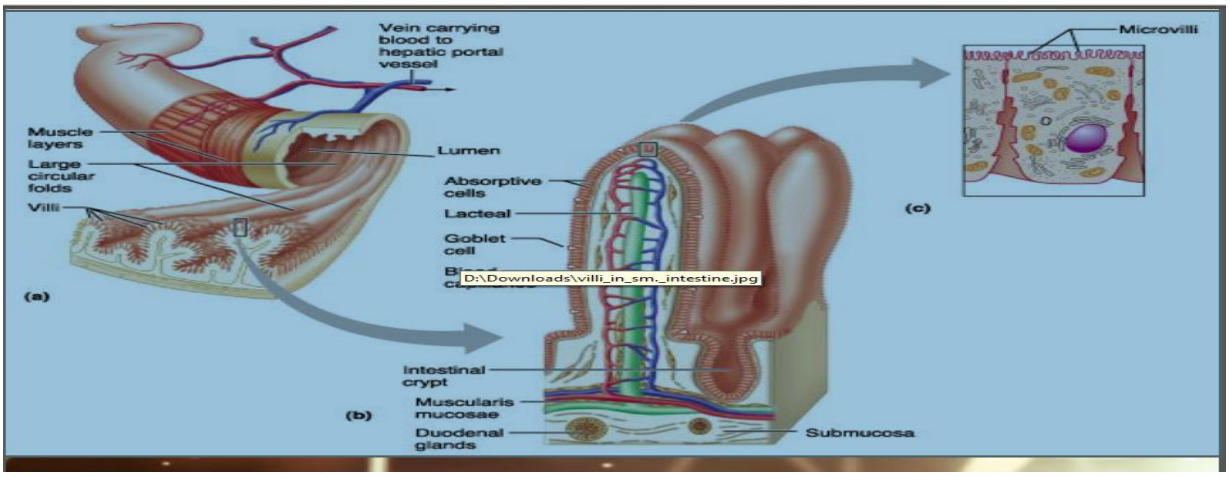
- ❖ Brunner's glands are located in the wall of the first few centimeters of the duodenum.
- ❖ They secrete large amounts of alkaline mucus, which contains a large amount of bicarbonate ions.
- ❖ Stimulated by: (1) irritating stimuli on the duodenal mucosa (contact of the chyme with the mucosa). (2) Vagal stimulation, (3) secretin.
- ❖ Inhibited by sympathetic stimulation.
- ❖ Mucus protects the mucosa.

2) Secretion of intestinal juices (Succus Entericus) by the Crypts of Lieberkuhn:

- ❖ Crypts of Lieberkühn are small pits which lie between intestinal villi.
- ❖ The surfaces of both the crypts and the villi are covered by an epithelium composed of 2 types of cells:

(1) Goblet cells secrete mucus.

(2) Enterocytes (digestive and absorptive cells). Secrete large quantities of H2O and electrolytes. Reabsorb H2O, electrolytes & end products of digestion.



Succus Entericus

- ❖ Is intestinal secretion secreted from intestinal crypts
- ❖ Volume: 1800 ml/day. (2L/day)
- ❖ PH: 7.5-8(Alkaline). It participates in the neutralization of acid chyme delivered from stomach.

> Importance of neutralization: (1) to provide the optimal PH for the action of the enzymes.
> (2) Protection of intestinal glands.

- ❖ Composition: water and solutes 0.6 % organic (enzymes), 1 % inorganic substance.
- ❖ Most of the enzymes are found either in the brush border or in the cytoplasm of the enterocytes (can digest intracellular). The enzymes that are actually secreted into the lumen are enteropeptidase and amylase.

Digestive Enzymes in the Small Intestinal Secretion

The enterocytes of the mucosa contain digestive enzymes that digest food into their end products. These enzymes are the following:

1. Aminopeptidases, Oligopeptidases, Intracellular di and tripeptidases for splitting small peptides into amino acids.
2. Four enzymes: sucrase, maltase, isomaltase, and lactase—for splitting disaccharides into monosaccharides.
3. Small amounts of intestinal lipase (weaker than pancreatic lipase) for splitting neutral fats into glycerol and fatty acids.
4. Nucleotidases for splitting nucleotides (DNA, RNA) into purine and pyrimidine bases, phosphoric acid and pentose sugar.

- Aminopeptidases act on amino acid terminal of the peptide chain to release free amino acid.
- Oligopeptidases act on short peptide chain to release AA.
- Di and tripeptidases act on di and tripeptides to release amino acid.

- Sucrase act on sucrose (candy)
- Maltase act on maltose
- Isomaltase act in isomaltoes
- Lactase acts on lactose (milk).

Control of Intestinal Secretions:

1. Brunner's gland secretion is stimulated by secretin (increases secretions and decreases motility), tactile and vagal stimulation (Ach).
2. Intestinal juice secretion is stimulated by:
   a. Distension, tactile and vagal stimulation.
   b. Hormones as gastrin, secretin, CCK, glucagons, enterocrinin.
   Sympathetic stimulation exerts an inhibitory effect.

Tactile: the chyme is in contact with intestinal mucosa.

- Gastrin: increases motility and secretions.
- Enterocrinin released from intestinal mucosa. It increases intestinal secretions.

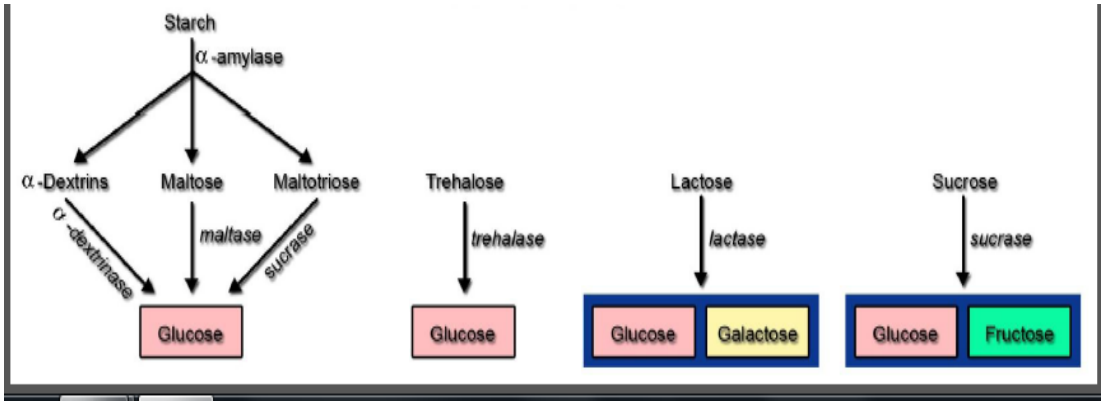
Digestion in the Small Intestine

1) Digestion of Carbohydrates:

- **Starts in the mouth and stomach:**
  - ❖ The ptyalin (an a-amylase) enzyme in saliva hydrolyzes starch into the disaccharide maltose and other small polymers of glucose.
  - ❖ The starch digestion sometimes continues in the body and fundus of the stomach for as long as 1 hour before the food becomes mixed with the stomach secretions. (When the HCl penetrates the chyme, the PH drops and the action stops).
- **In the small intestine:**
  - ❖ Digestion by Pancreatic Amylase (more powerful than salivary amylase). (Pancreatic amylase is physiologically important because food stay in the small intestine longer duration).
  - ❖ Pancreatic secretion has a-amylase that is almost identical in its function with the a-amylase of saliva but is several times as powerful. Therefore, within 15 to 30 minutes after the chyme empties from the stomach into the duodenum and mixes with pancreatic juice, virtually all the carbohydrates will have become digested.
  - ❖ The carbohydrates are almost totally converted into maltose and/or other very small glucose polymers before passing beyond the duodenum or upper jejunum.

Hydrolysis of Disaccharides by Intestinal Enzymes :

- ❖ The enterocytes lining the villi of the small intestine contain four enzymes lactase, sucrase, maltase, and a-dextrinase (disaccharidases), which are capable of splitting the disaccharides lactose, sucrose, and maltose, plus other small glucose polymers, into their constituent monosaccharides.
- ❖ These enzymes are located in the enterocytes covering the intestinal microvilli brush border, so that the disaccharides are digested as they come in contact with these enterocytes.
  - Pentose is digested from DNA and RNA.
  - Maltase splits maltose into 2 glucose
  - Sucrase splits sucrose into glucose + fructose.
  - Lactase splits lactose into glucose and galactose.

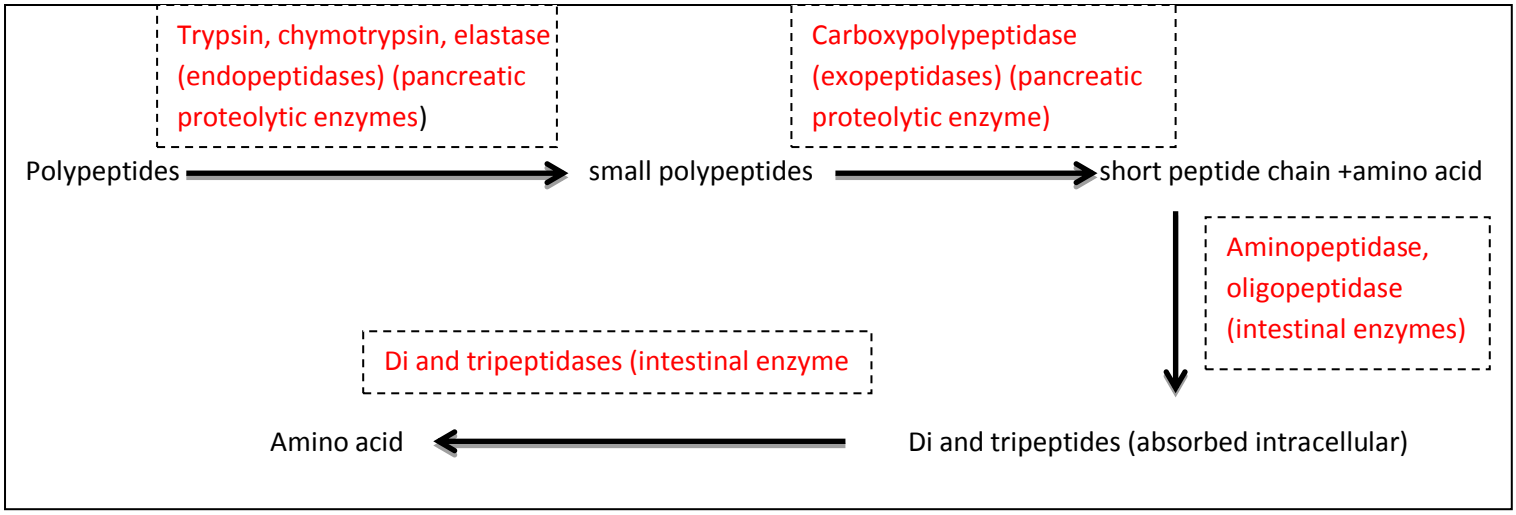


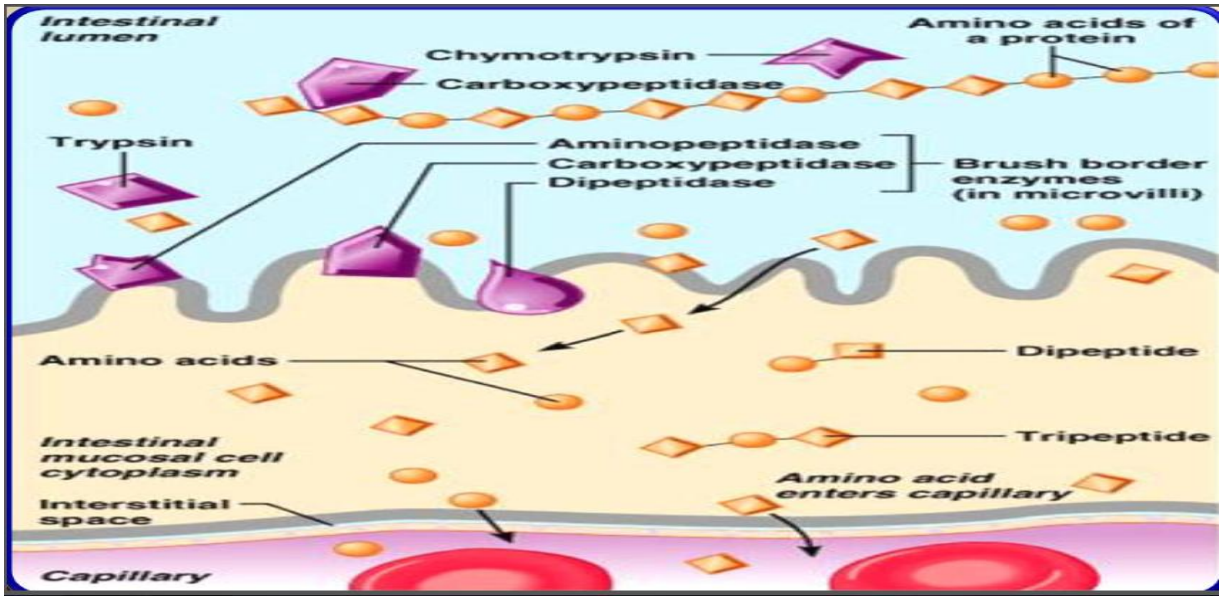
2) Digestion of Proteins:

- **Starts in the stomach:**
  - ❖ Pepsin is the important peptic enzyme of the stomach; it's secreted in inactive form.
  - ❖ It is activated by HCl which then causes autoactivation of the rest of pepsin. (Active at a pH=2.0 - 3.0 (acidic) and is inactive at a pH above about 5.0).
  - ❖ One of the important features of pepsin digestion is its ability to digest the protein collagen (elastic fibers).
  - ❖ Collagen is a major constituent of the intercellular connective tissue of meats; therefore, for the digestive enzymes of the digestive tract to penetrate meats and digest the other meat proteins, it is first necessary that the collagen fibers be digested.
  - ❖ Pepsin only initiates the process of protein digestion, usually providing only 10 to 20 per cent of the total protein digestion.

- **Digestion by Pancreatic Secretions:**
  - ❖ Most protein digestion occurs in the duodenum and jejunum (small intestine) by pancreatic and intestinal proteolytic enzymes.
  - ❖ Both trypsin and chymotrypsin split protein molecules into small polypeptides; carboxypolypeptidase then cleaves individual AA from the carboxyl ends of the polypeptides.
  - ❖ Proelastase is converted into elastase, which then digests elastin fibers that partially hold meats together.
  - ❖ Only a small percentage of the proteins are digested all the way to their constituent AA by the pancreatic juices.

❖ Most remain as dipeptides and tripeptides to be digested by Peptidases in the Enterocytes mainly in the duodenum and jejunum.





Fat:

1- Are water insoluble (do not dissolve in the digestive juice of small intestine).
2- Have high attractive force between their molecules (they form fat globule).

3) Digestion of Fats:

- **In the small intestine :**
  - ❖ Less than 10 % of triglycerides are digested in the stomach by lingual and gastric lipase (weak).
  - ❖ All fat digestion occurs in the small intestine by mainly pancreatic lipase (most powerful lipolytic enzyme) in addition to intestinal lipase.
  - ❖ Bile acids help fat digestion in process called emulsification of fat, by formation of micelles.

Formation of Micelles:

- ❖ Each bile salt molecule is composed of a sterol nucleus (fat-soluble end) (hydrophobic) and a polar group (water-soluble end) (hydrophilic). So that they are amphipathic molecules (contain polar and nonpolar portions).
- ❖ Micelles are small spherical, cylindrical globules 3 to 6 nm in diameter composed of 20 to 40 molecules of bile salts (bile salts aggregate that the hydrophobic part is in the center and the hydrophilic part is on the outer surface).
- ❖ The polar parts are (-) charged, they allow the entire micelle globule to dissolve in the water of the digestive fluids.
- ❖ Fat soluble substance (fatty acid, fat soluble vitamins, cholesterol, phospholipids) are found in the interior (center) of the micelle.

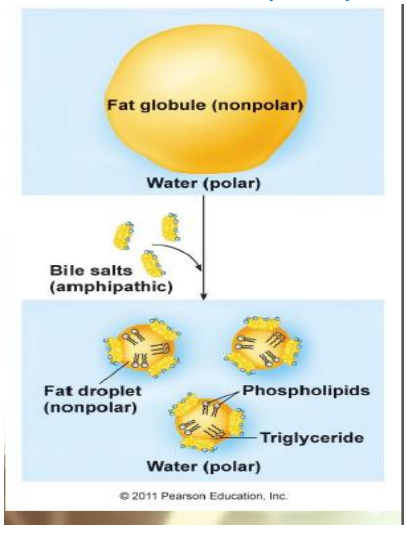
Role of Bile Salts to Accelerate Fat Digestion:

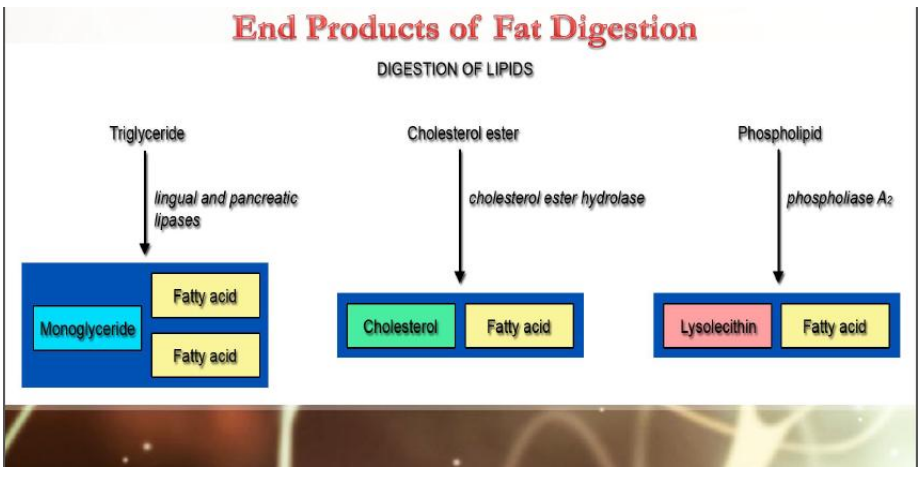
(By Emulsification of Fat)

- ❖ The major function of the bile salts and lecithin in the bile is to make the fat globules readily fragmentable with the water in the small bowel.
- ❖ Bile salts break the fat globules into very small sizes, so that the water-soluble digestive enzymes can act on the globule surfaces. (Increases the surface area upon which the lipolytic enzyme act on).

Digestion by Pancreatic Lipase: (mainly)

- ❖ The most important enzyme for digestion of the triglycerides is pancreatic lipase.
  - Triglyceride digested into monoglyceride and 2 fatty acids.
  - Cholesterol ester digested into cholesterol and fatty acid.
  - Phospholipid digested into lysophospholipid and fatty acid.





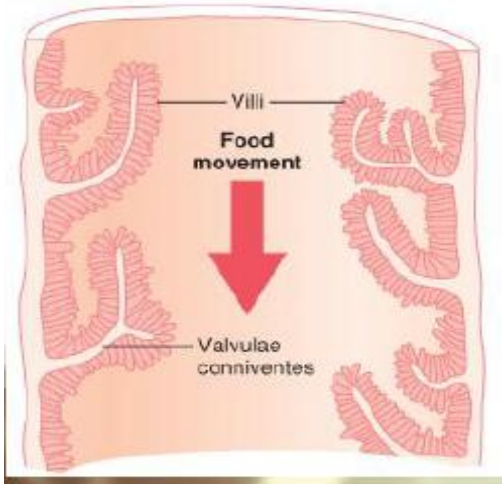
Basic principles of Gastrointestinal Absorption

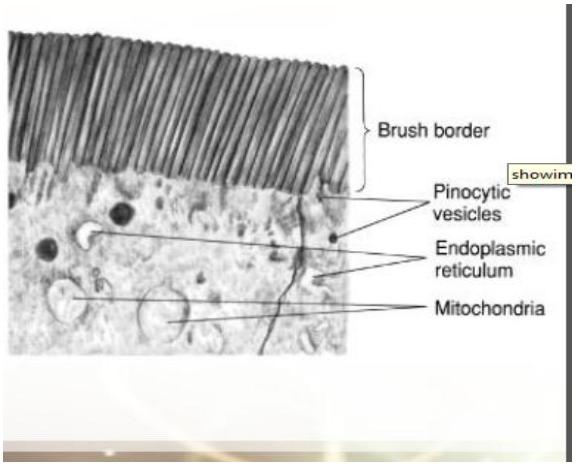
Absorptive Surface of the Small Intestinal Mucosa Villi:

(The small intestine is the main site of absorption of nutrients.)

- ❖ The absorptive surface of the small intestinal mucosa, showing many folds called valvulae conniventes. They increase the surface area of the absorptive mucosa about threefold.
- ❖ They are well developed in the duodenum and jejunum.
- ❖ The presence of villi on the mucosal surface enhances the total absorptive area another 10-fold.

- The epithelial cell on each villus is characterized by a brush border (consisting of as many as 1000 microvilli) protruding into the intestinal chyme (increases the surface area another 20-fold).





1) Absorption of Carbohydrates:

❖ All the carbohydrates in the food are absorbed in the form of monosaccharides (glucose, galactose, fructose, and pentose); only a small fraction is absorbed as disaccharides.

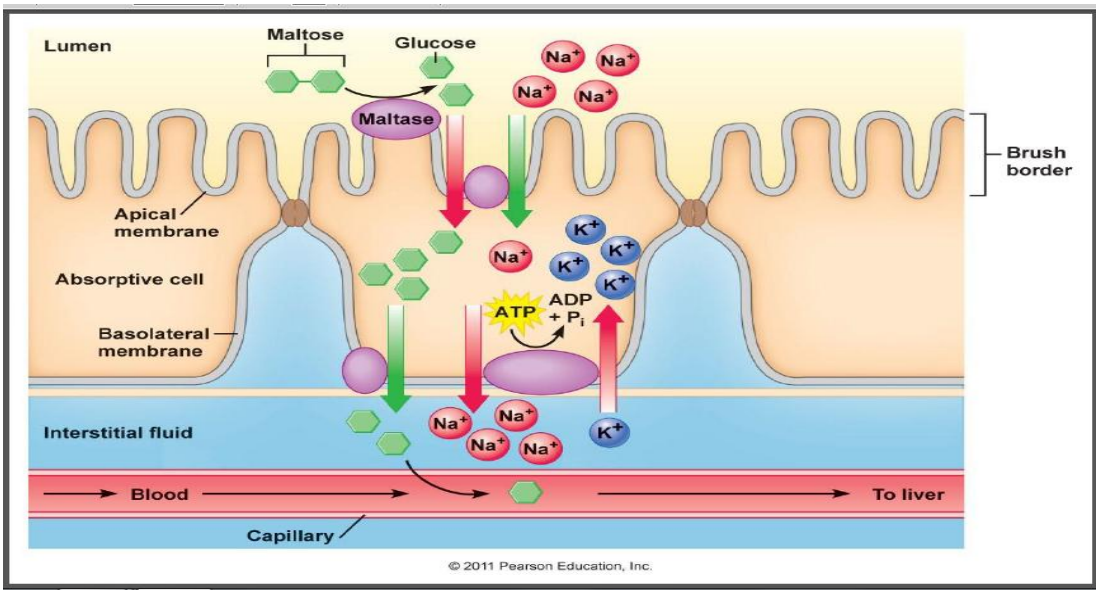
✓ **Glucose and galactose** absorption occurs in a cotransport mode with active transport of Na+ (2ry active transport) across the brush border i.e. 2ry to the action of Na+-K+ ATPase.).

1) At the basal border (toward circulation), active transport of Na+ by Na/K pump (pumping Na+ outside and K inside). (Glucose drives its energy from active transport of Na+ (concentration gradient)).
2) Concentration of Na+ decreases compared to those in the lumen.
3) This will cause passive diffusion of Na+ utilizing carrier, at the same time the carrier transport glucose from the brush border against concentration gradient (2ry active transport).
4) Glucose drives its energy indirectly from Na+ concentration gradient resulted from active transport of Na+.
5) Glucose is further transported by facilitated diffusion (need another carrier) across the basolateral membrane.
6) Then it's transported to the portal circulation (blood) to the liver.

- In diarrhea cases they give the patient glucose solution with salt (NaCl), because Na+ facilitates glucose absorption.

✓ **Fructose** is independent on Na+ but it transports in luminal membrane via facilitated diffusion (with concentration gradient) (needs carrier).

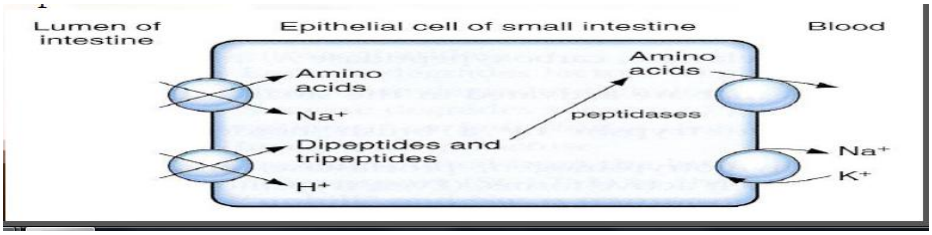
✓ **Pentose** is transported by passive diffusion. (It has slowest rate of absorption because there is no use of enzymes, carrier and energy).



2) Absorption of proteins:

Proteins are absorbed in the form of dipeptides, tripeptides, and a few free amino acids (2 isomers of AA).

- **D- AA** is transported by passive diffusion.
- **L- AA** is transported by 2ry active transport. (Same as glucose and galactose).
- **Di and tripeptides** cross the brush border by active transport protein carrier. They are hydrolyzed by brush border and cytoplasmic oligopeptidases.
- **AA leaves** the cell at the basolateral membrane by facilitated transport into the portal circulation to blood.

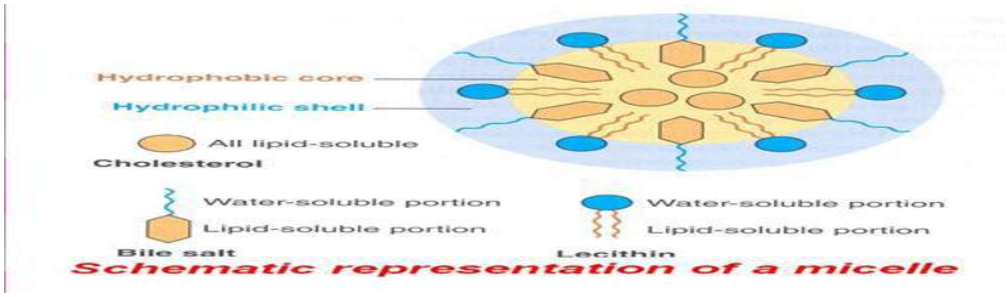


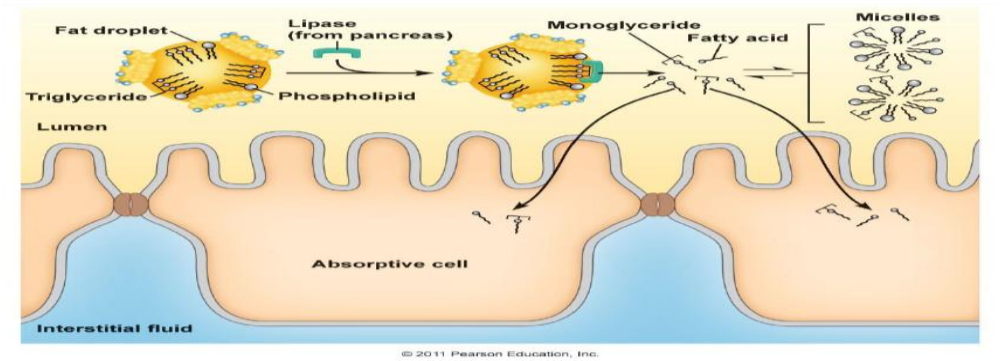
3) Absorption of Fats:

- Fats cannot pass the unstirred thin layer of water that covers the mucosa of small intestine (enterocytes) into the brush border because they are water insoluble.
- Micelles act as a carrier to help them pass.

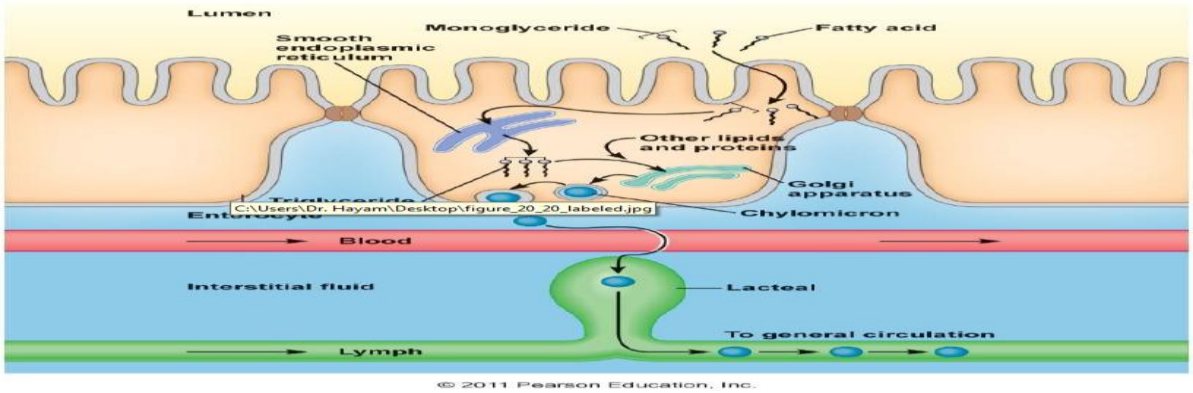
- In the presence of an abundance of bile micelles, about 97 per cent of the fat is absorbed; in the absence of the bile micelles, only 40 to 50 per cent can be absorbed.

- The micelles act as a transport medium to carry the monoglycerides and free fatty acids to the brush borders of the intestinal epithelial cells.(it covers the fat soluble substances).





Absorption occur by the help of micelle and once it enters the unstirred water layer and makes contact with brush border of enterocytes, the fatty acid, monoglyceride and cholesterol defuse passively (because the cell membrane is lipid bilayer) into the cytoplasm of enterocytes, and the micelle returns back to carry another fat soluble substances.



- In the enterocytes inside the smooth endoplasmic reticulum, Triglycerides are reformed again (from fatty acid, monoglyceride) and aggregate into globules along with the absorbed cholesterol and phospholipids. B-lipoprotein coat part of the surface of each globule to form chylomicrons. It diffuses to side of the cell and is excreted by exocytosis into the central lacteal of villi, to lymph, then to thoracic duct (general circulation to liver). (Short chain FA is absorbed directly into capillary blood of the villi to portal blood as they are more water soluble but all long chain fatty acid are absorbed first in the lymph).

4) Absorption of Vitamins:

a. Fat-soluble vitamins (A, D, E, & K) are incorporated into micelles and absorbed along with other lipids (Same mechanism of fatty acid and monoglyceride).
b. Most water-soluble vitamins (C, B1, B2, B6, and folic acid) are absorbed by Na-dependent cotransport mechanisms. (2ry)
c. Vitamin B12 is absorbed in the ileum and requires intrinsic factor

- Gastrectomy results in the loss of parietal cells and loss of intrinsic factor → pernicious anemia.

Absorption and secretion of electrolytes and water

❖ Electrolytes and H2O may cross intestinal epithelial cells by either cellular or paracellular route (brush border or tight junctions between cells).
❖ The permeability of the tight junctions varies with the type of epithelium
  - A tight epithelium is in the colon.
  - Leaky epithelia are the small intestine and gallbladder.

5) Absorption of Na+ :

Na moves into the intestinal cells by the following mechanisms:

a) Passive diffusion. (No energy, no carrier).
b) Na+-glucose, Na+-galactose or Na+-amino acid co-transport.
c) Na+-Cl- exchange.
d) Na+-H+ exchange.

❖ The next step in the transport process is osmosis of water into the paracellular spaces because a large osmotic gradient has been created by the elevated concentration of ions (Na+ diffusion) in the paracellular space.

❖ Aldosterone Greatly Enhances Na+ Absorption:
This effect of aldosterone is especially important in the colon because it allows virtually no loss of NaCl and water. (In cases of diarrhea).

- Water moves freely in and out of the lumen of small intestine depending on the osmotic pressure of its contents.

6) Absorption of Cl- :

Cl- absorption accompanies Na+ absorption by the following mechanisms:

1) Passive diffusion.
2) Na+-Cl- cotransport.
3) Cl--HCO3- exchange.

7) Absorption and secretion of K+ :

❖ K+ is absorbed in the small intestine by passive diffusion from brush border.
❖ K+ secretion through the basolateral border in the lumen of colon (by active transport mechanism Na+/ K+ pump). Stimulated by aldosterone.
❖ Excessive loss of K+ in diarrheal fluids causes hypokalemia.

Secretion of bicarbonate ions in the ileum:

❖ Secreted by epithelial cells on the surfaces of the villi in the ileum and large intestine have a special capability of secreting HCO3- in exchange for absorption of Cl-.
❖ This is important because it provides alkaline HCO3- that neutralizes acid products formed by bacteria in the large intestine. (Colon).

8) Ca++ Absorption by Enterocytes: depends on formation of Ca binding protein in the intestinal mucosal cells.

❖ ↓ plasma Ca

↓

↑ Parathyroid hormone (important in intestinal absorption of Ca)

↓

25-hydroxy-vitamin D3

↓ (Kidney)

1, 25 dihydroxy-vitamin D3

↓

Stimulates synthesis of Ca-binding protein and Ca-ATPase in enterocytes.

Hormonal control of absorption and secretion:

- Glucocorticoid = ⇧ absorption of H2O & ions (Small & large intestine)
- Somatostatin = ⇧ H2O & ions absorption (Ileum & colon)
- Epinephrine = ⇧ NaCl absorption (ileum)
- Aldosterone = ⇧ synthesis of Na channel (Colon)

(Help active transport of Na+).

- Catecholamines = ⇩ intestinal secretion

Questions

1) A 24 year-old male graduate student participates in a clinical research study on intestinal motility. Peristalsis of the small intestine

A- Mixes the food bolus

B- Is coordinated by the central nervous system

C- Involves contraction of the smooth muscle behind the food bolus and relaxation of the smooth muscle in front of the food bolus

D- Involves relaxation smooth muscle simultaneously throughout the small intestine

2) Emulsification of dietary lipids is brought by:

A- Secretin

B- Cholecystokinin

C- Bile salts

D- Pepsin

Answers:

1) C.
2) C.