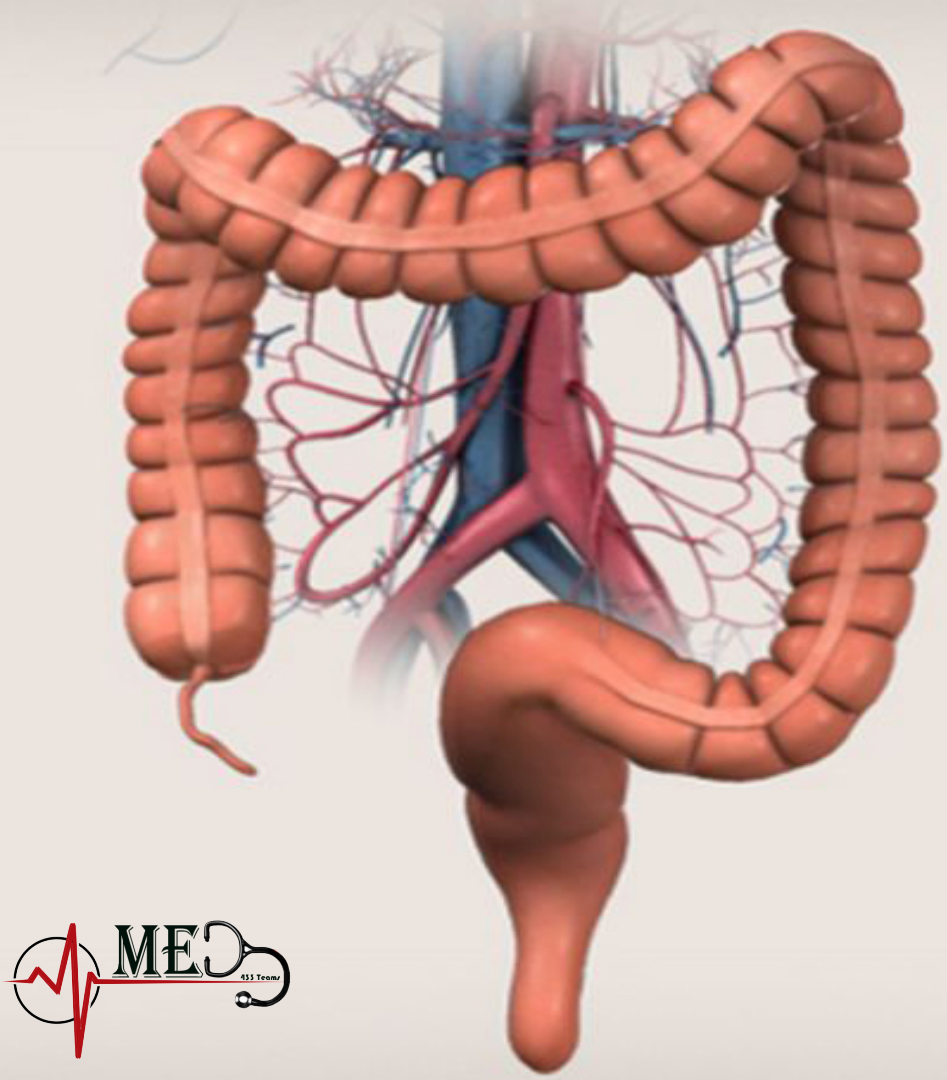

# L3,4
# Biochemical Aspects of Digestion of Lipids, Proteins, and Carbohydrates

## OBJECTIVES:

- Understand the process of digestion of dietary lipids, protein and carbohydrates including, the organs involved, the enzymes required, and the end products.
- Implement the basic science knowledge of the process of lipids, proteins,& carbohydrates digestion to understand the clinical manifestations of diseases that involve defective digestion &/or absorption.

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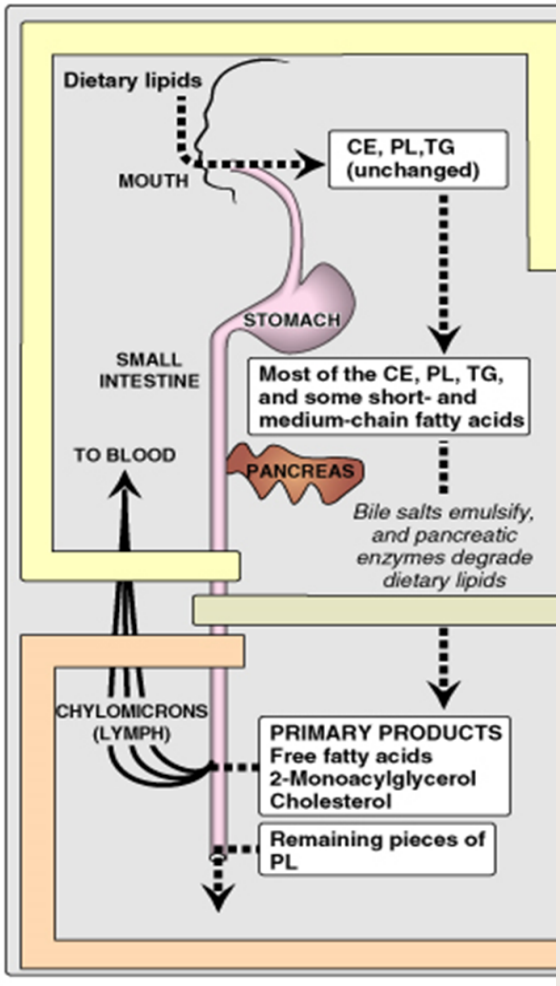
# Lipid Digestion

The main End Products of Lipid digestion are:
- 2-Monoacylglycerol
- Cholesterol
- Free fatty acids
- Glycerylphosphoryl base

Dietary lipids intake is ~81 g/day
Triacylglycerol (TAG) is ~ 90%,
and the remainder 10% includes:
Cholesterol , Cholesterylester
Phospholipids, Glycolipids
Free fatty acids

| **Lipid digestion**<br>Lipid digestion begins in the stomach | | | |
|---|---|---|---|
| **Site** | Stomach 30% | | Small Intestines 70% |
| **Enzymes** | Mouth:<br>Lingual lipase | Stomach:<br>Gastric lipase | Pancreatic enzymes<br>• Lipase & co-lipase<br>• Cholesterol esterase<br>• Phospholipase A2<br>• Lysophospholipase |




**Note**: Lingual & Gastric Lipases act only on short and medium chain fatty acids therefore, their effect on TAG has little significance in adults.
But important for digestion of milk fat in neonates and infants because Milk fat has short and medium chain fatty acids.

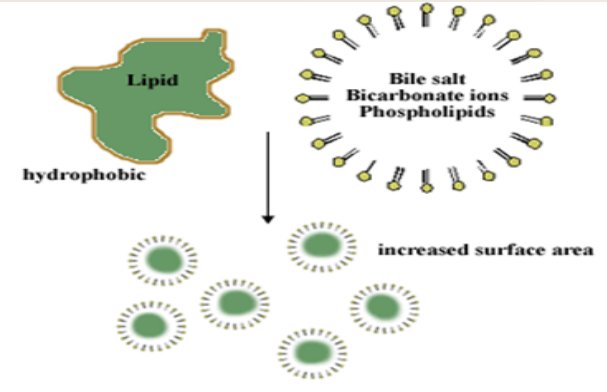
## Emulsification of dietary lipids

- The digestion of lipids is preceded by emulsification
  - it occurs in the Duodenum
- It increases the surface area of lipid droplets, therefore the digestive enzymes can effectively act on them

## Mechanisms of Emulsification:

1. Mechanical mixing by peristalsis[1]
2. Detergent effect of bile salt:
Bile salts interact with lipid particles and aqueous duodenal contents, stabilizing the particles as they become smaller, and preventing them from coalescing [2].

1: Waves of involuntary contraction passing along the walls of a hallow muscular structure and forcing content outward.
2: To grow together.




**Emulsification Example: (to understand)**

Say you have a glass of water, add oil, the oil will make a thin layer on top. If you start mixing vigorously you will see a lot of small droplets of oil. By mixing you increased the surface area of the oil.

The same happens with lipids when the surface area is increased then the enzymes are able to work on them.

## Pancreatic enzymes for Digestion of Lipids

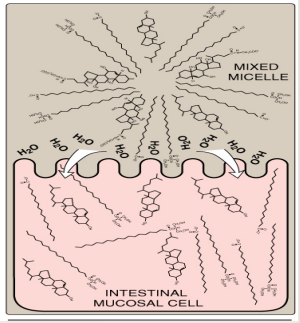
| Enzyme | Lipase and co-lipase | Cholesterol esterase | Phospholipase A2 | Lysophospholipase |
|---|---|---|---|---|
| Digests | Triacylglycerol (TAG) | Cholestryl ester | Phospholipids (PL) | |
| | TAG → (Lipase& co-lipase, $H_2O$) → Fatty acid + 2-Monoacylglycerol | Cholestryl ester → (Cholesterol esterase, $H_2O$) → Fatty acid + Cholesterol | Phospholipase → (Phospholipase A2, $H_2O$) → Fatty acid + Lysophospholipid | Lysophospholipid → (Lysophospholipase, $H_2O$) → Fatty acid + Glycerylphosphoryl base |
| | Pancreatic Lipase:<br>• Found in high concentration in pancreatic secretion (2-3% of total proteins)<br>• Inhibited by Orlistat, an anti-obesity drug | | | |

# Absorption & Re-synthesis of Lipids by Intestinal Mucosal Cells

## Absorption: (by Mixed micelles )

- They are disc-shaped clusters of amphipathic lipids (hydrophobic inside and hydrophilic outside)
- They include:

1. End products of lipid digestion
2. Bile salts
3. Fat-soluble vitamins.




Short- and medium-chain fatty acids do not require mixed micelle for absorption by intestinal cells because they are digested by lipases in the mouth and stomach.

## Re-synthesis:

1. Activation of long chain fatty acids into Acyl CoA.
2. Synthesis of:
   - TAG from Monoacylglycerol
   - Cholesterol ester from Cholesterol
   - PL from Glycerylphosphoryl Base

**Short and medium chain fatty acids are not converted into their CoA derivatives. Instead, they are released into portal circulation, carried by serum albumin.

# Assembly & Secretion of Chylomicrons by Intestinal Mucosal Cells

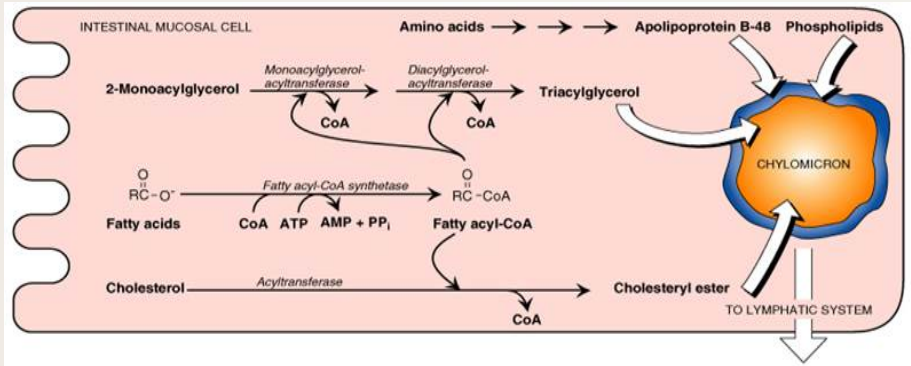
## Assembly of Chylomicrons:

The core of the Chylomicron has packaged TAG & Cholestryl esters as lipid droplets, surrounded by Apo B-48, Phospholipids and free Cholesterol.

## Secretion of Chylomicrons:

By exocytosis into lymphatic vessels around villi of small intestine (lacteals) then enter into systemic circulation.

Milky-appearance of serum after lipid-rich meal



# Protein Digestion

Sources of Proteolytic enzymes

Dietary proteins → 70-100 g/day
They are too large to be absorbed by the intestine, therefore they're hydrolyzed to **AA** to be absorbed.

## Stomach – By Gastric Secretions

Protein digestion into Polypeptides

1. Hydrochloric acid (HCL)
2. Pepsin
3. Renin

## Pancreas – By Pancreatic Secretion

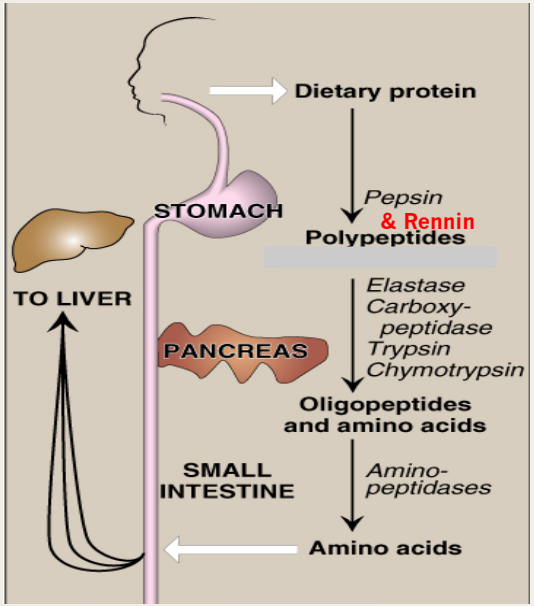
- The pancreatic secretion contains a group of pancreatic proteases.
- Each of these enzymes has different specificity for the cleavage sites
- These proteases are synthesized and secreted as inactive zymogens

## Small Intestine

Oligopeptides from Pancreatic proteases are cleaved into free amino acids and di-&tri-peptides by

**Intestinal Aminopeptidase**

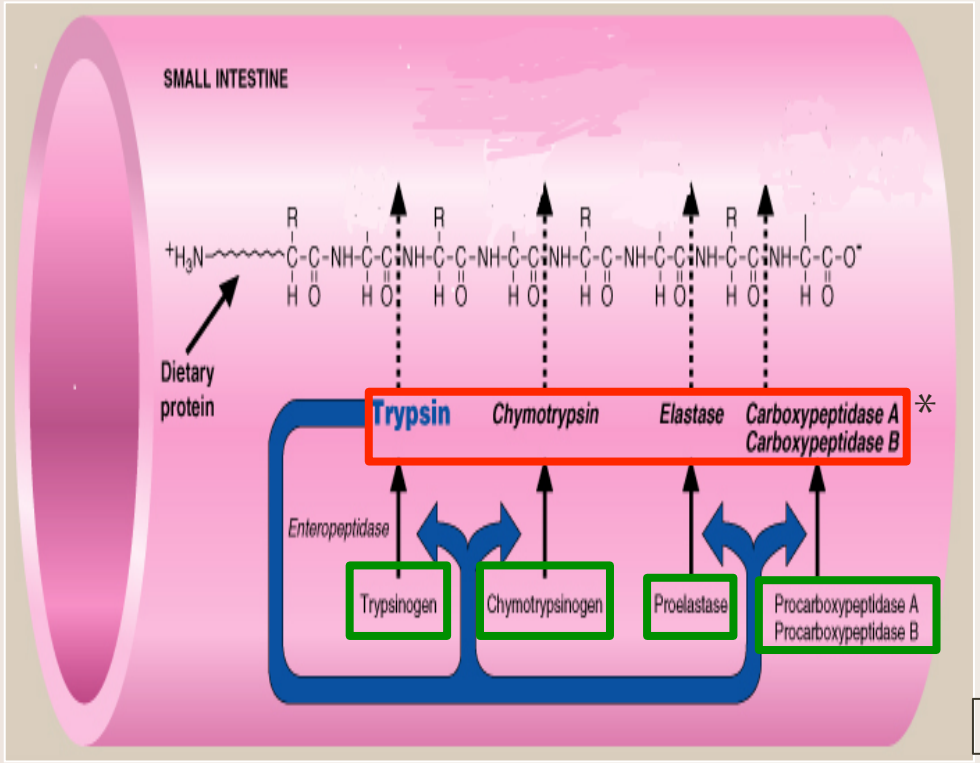
(Exopeptidase on the luminal surface of the Intestine)



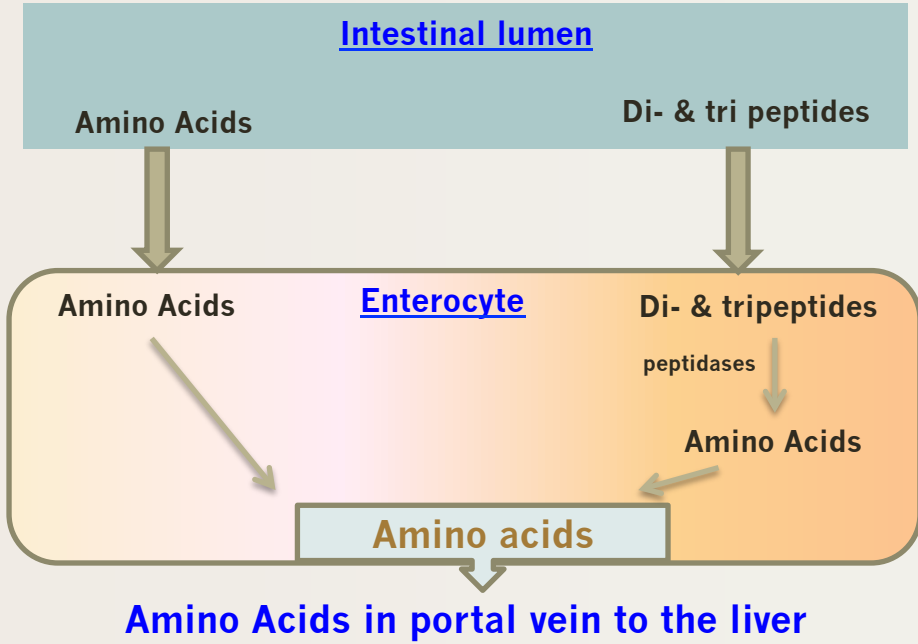

**AA:** Amino Acids

# Activation of Pancreatic enzymes

Enteropeptidase[3] converts Trypsinogen (inactive) into Trypsin (active).
Trypsin activates itself and all other Pancreatic Zymogen.




# Absorption of digested proteins




*Carboxypeptidases is an exopeptidases

3: is an enzyme synthesized by, and present on the luminal surface of intestinal mucosal cells (the brush border membrane)

# Carbohydrate Digestion

**Dietary carbohydrates:**

- **Polysaccharides**:
  1) Containing α (1,4) & α (1,6) bonds: Starch from plants & Glycogen from animals
  2) Contains β (1,4) bonds: Cellulose* from plants
- **Oligosaccharides**
- **Disaccharides:**
  1) Sucrose
  2) Lactose
  3) Maltose
- **Monosaccharides:** Little amounts

- Digestion is rapid.
- Generally completed by the time the gastric contents reach the junction of the Duodenum & Jejunum.
- No digestion occurs in the stomach because the high acidity inactivates the **Salivary α-amylase.**
- **Pancreatic α-amylase** continues the process of Starch & Glycogen digestion in Small Intestine.

Sites for digestion of dietary carbohydrates:

- The mouth
- The intestinal lumen

*: It can't be digested in humans due to the absence of enzyme that can cleave β (1,4) bonds.

| Enzymes for Digestion of Dietary Carbohydrates | | | |
|---|---|---|---|
| Enzyme | **α-amylase** | **Disaccharidases** | **Isomaltase & α(1,6) glucosidase** |
| Substrate | Polysaccharides | Disaccharides | Brach points of oligo- & di-saccharides |
| Type | Both Salivary & Pancreatic | Intestinal | Intestinal |

**1. α-Amylases**

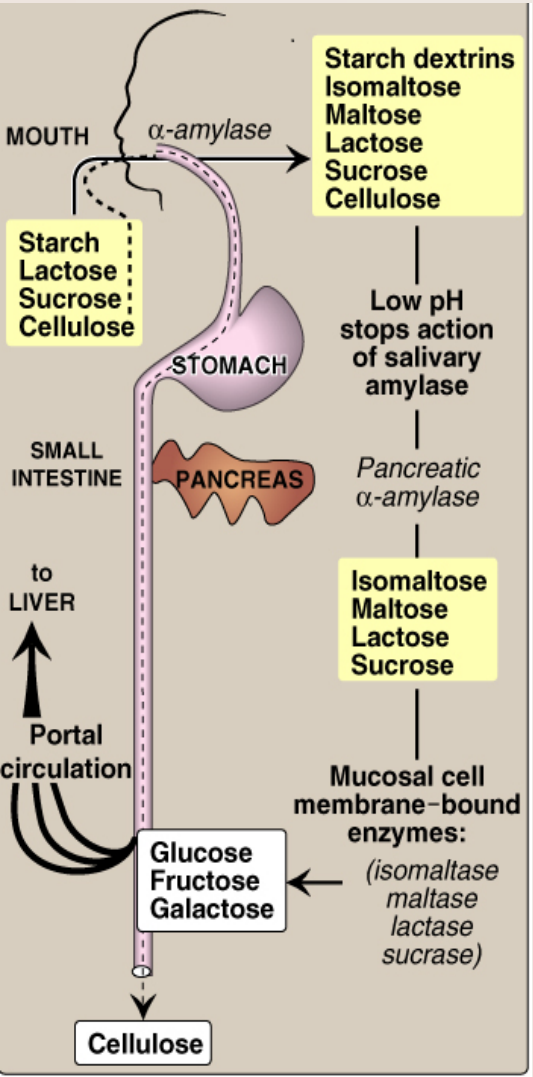
Normal level in serum → 25 -125 U/L
The clinical significance of rising circulating levels of α-amylase activity is a diagnosis of **Acute Pancreatitis**[4].

- Start to rise → Few hours
- Peak → 12 – 72 hours
- Returns to Normal → Few days

**2. Intestinal enzymes** are secreted by & remain associated with the luminal side of the brush border membranes of the intestinal mucosal cells in mucosal lining of the Jejunum.

| Intestinal Di-saccharidases<br>They are responsible for the final digestion of lipids | | | | |
|---|---|---|---|---|
| Enzyme | **Isomaltase** | **Maltase** | **Sucrase** | **Lactase (β-galactosidase)** |
| Substrate | Isomaltose | Maltose | Sucrose | Lactose |
| Product | 2 Glucose | 2 Glucose | Glucose & Fructose | Glucose & Galactose |

4: Damage of pancreatic cells which leads to release & activation of intracellular enzymes into the blood.
**You can find the effect of α- amylase on Glycogen in the previous lecture.**

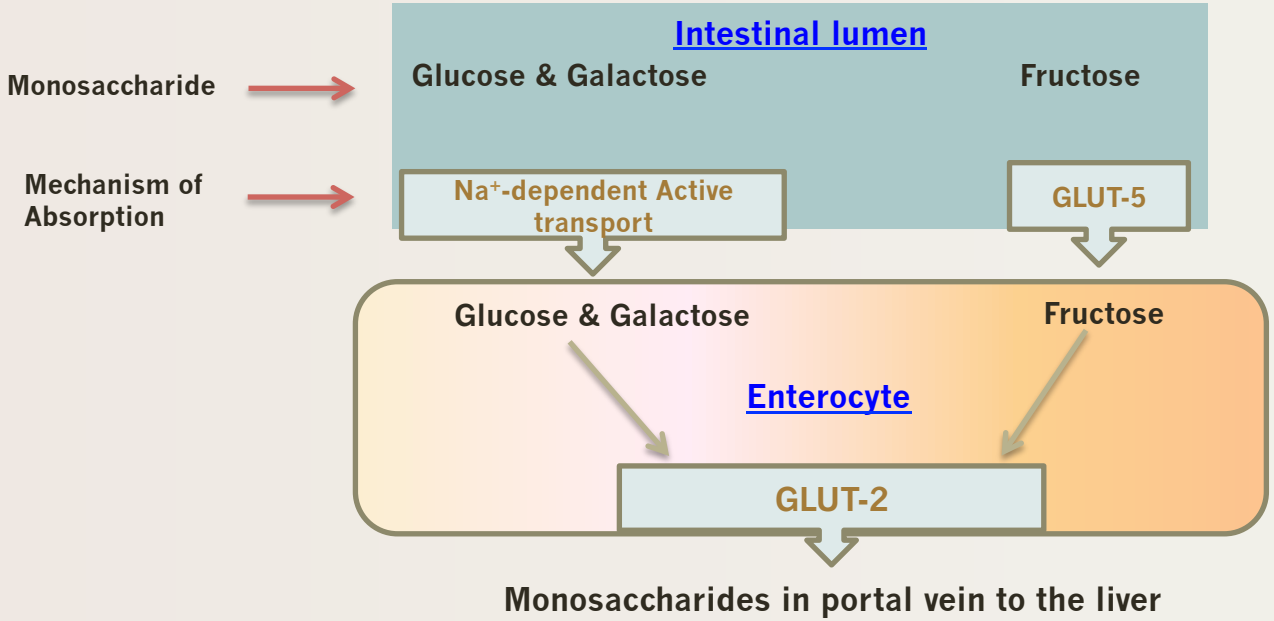



**Absorption of Monosaccharides** by Intestinal Mucosal Cells occurs in the Duodenum & upper Jejunum.

Different Monosaccharides have different mechanisms of absorption:

1. Facilitated diffusion (GLUT-mediated)
2. Active transport (Energy-dependent): Co-transport with Na+

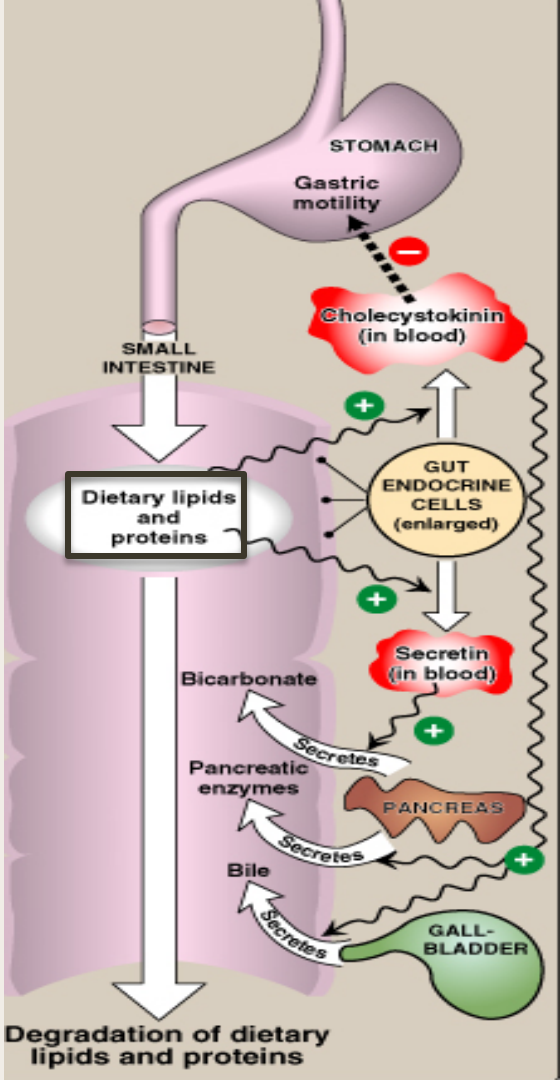
*Note: Insulin is not required for the uptake of glucose by intestinal cells*



# Hormonal control of digestion in small intestine

- The digestion in small intestine is hormonally controlled.
- Two small peptide hormones are released from cells of the upper part of small intestine:

| The Gut Hormone | Cholecystokinin (CCK) | Secretin |
|---|---|---|
| Stimulus of secretion | The presence of partially digested lipids & proteins in the **Upper Small Intestine.** | Low pH of the Chyme entering the Intestine. |
| Effects | • Stimulates the release of Pancreatic Enzymes.<br>• Stimulates the contraction of Gall Bladder & release of bile<br>• ↓ Gastric motility → slower release of gastric contents into Small Intestine. | Stimulates the Pancreas to release a watery solution high in HCO3 to neutralize the pH of the intestinal contents.( to reach the optimum pH for digestive activity by pancreatic enzymes) |



# Abnormalities in Lipid & protien Digestion/ Absorption

- Liver and Gall Bladder diseases
- Intestinal diseases (Intestinal resection- shortened bowl motion)
- Pancreatic insufficiency (Chronic pancreatitis, CF, surgical removal of the pancreas): There is incomplete digestion & absorption of fat & protein

→ Steatorrhea[5] & undigested proteins in the feces.

## Abnormal digestion of disaccharides:
## Lactose intolerance (Lactase deficiency)

- Lactase (β-galactosidase) deficiency leads to undigested carbohydrate in large intestine → Osmotic Diarrhea.
- Bacterial fermentation of the undigested compounds lead to accumulation of $CO_2$ & $H_2$ gases → Abdominal cramps, diarrhea, and distention (flatulence)

# Cystic Fibrosis

- Autosomal recessive disorder due to mutation of CFTR[6] gene.
- CFTR protein is a Cl channel on epithelium.
- It affects the lungs mainly, and also pancreas, liver, and intestines.
- Characterized by abnormal transport of Cl & Na across an epithelium, leading to thick, viscous secretions.
- Defects leads to decreased secretion of Cl and increased reabsorption of Na & H2O.
- In pancreas, decreased hydration results in thickened secretions which can't reach the intestine, causing Pancreatic insufficiency.

## Abnormality in protein digestion:
## Celiac Disease (Celiac sprue)

- It is a disease of malabsorption resulting from immune-mediated damage to the Small Intestine in response to ingestion of Gluten.
- Gluten is a protein found in wheat, rye, & barley.

5: The excretion of fat with the feces because of reduced absorption of fat by intestine.
6: Cystic Fibrosis Transmembrane Conductance Regulator gene.

# All the digestive enzymes in GI tract

| | Lipid | Protein | COH |
|---|---|---|---|
| Mouth | Lingual lipase | | Salivary $\alpha$-amylase |
| Stomach | • Gastric lipase | • Renin<br>• Pepsin | Low pH > No digestion for COH |
| Pancreas | • Lipase &co-lipase<br>• Cholestryl esterase<br>• Phospholipase $A_2$<br>• Lysphospholipase | • Trypsin<br>• Elastase<br>• Chymotrypsin<br>• Carboxypeptidase | • Pancreatic $\alpha$-amylase |
| Intestine | Short & medium-chain fatty acids are absorbed directly in intestine to portal circulation. Long-chains are resynthesized and secreted into systemic circulation | Di-peptidase | • Isomaltase<br>• maltase<br>• Sucrase<br>• Lactase |

1) Lipid digestion occurs in:
   A. Stomach
   B. Colon
   C. Small Intestine
   D. Both A & C
2) Which one of the following does not require Micelle for absorption?
   A. Long chain fatty acid
   B. Phospholipids
   C. Short & Medium chain fatty acids
   D. Cholesterol
3) Which one of the following is a characteristic of dietary lipids?
   A. Hydrophilic
   B. Hydrophobic
   C. Amphipathic
   D. None of the above
4) The first site where lipids are digested is:
   A. Stomach
   B. Colon
   C. Small Intestine
   D. None of the above
5) Where is TAG re-synthesized?
   A. Intestinal Basal Cells
   B. Intestinal Mucosal Cells
   C. Intestinal Wall
   D. Wall of the Stomach
6) Intestinal digestion of lipids is done by:
   A. Stomach Enzymes
   B. Intestinal Enzymes
   C. Pancreatic Enzymes
   D. Enzymes in Portal Circulation
7) Assembly & secretion of Chylomicrons into Lymphatic Lacteals & then into.....:
   A. Systemic circulation
   B. Stomach
   C. Portal circulation
   D. Colon
8) Which one of the following leads to incomplete absorption of fat & protein?
   A. Liver Disease
   B. Pancreatic insufficiency
   C. Intestinal Disease
   D. All of the above
9) Which one of the following enzymes is not essential for adults but important for infants:
   A. Cholesterol Estrase
   B. Phospholipase A2
   C. Gastric Lipase
   D. Lysophospholipase
10) The effect of Secretin is:
   A. Stimulates the release of pancreatic digestive enzymes.
   B. Stimulates the contraction of the gall bladder and release of bile.
   C. Decreases gastric motility.
   D. Stimulates the pancreas to neutralize the pH of the intestinal contents.

Answers: 1) D 2) C 3) B 4) A 5) B 6) C 7) A 8) D 9) C 10)D

11) The Gastric secretion for neonates & infants is:
   A. HCL
   B. Pepsin
   C. Renin
   D. None of the above

12) Pancreatic Enzymes will be secreted in:
   A. Stomach
   B. Intestines
   C. Pancreas
   D. None of the above

13) The low pH of Chyme Enzyme entering the Intestines will stimulate?
   A. Secretin
   B. Cholecystokinin
   C. Renin
   D. All of the above

14) Whish one of the following activates Trypsin?
   A. Gastric Enzyme
   B. Trypsin
   C. Enteropeptidease
   D. Both B & C

15) Trypsin converts Proelastase into ...:
   A. Trypsinogen
   B. Elastase
   C. Chymotrypsinogin
   D. Trypsin

16) Where is the dietary carbohydrate NOT digested?
   A. Stomach
   B. Mouth
   C. Intestine
   D. All of the above

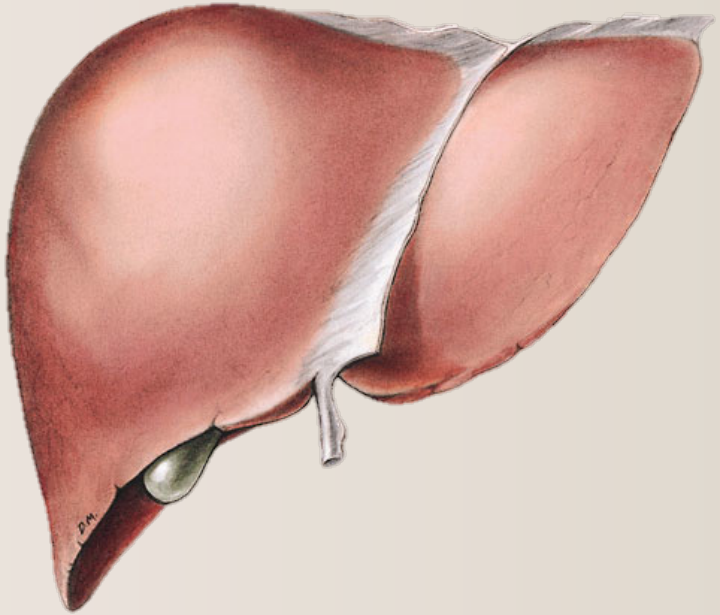
17) The rising in α-Amylase is due to :
   A. Peptic Ulcer
   B. Acute Pancreatitis
   C. Appendicitis
   D. None of the above

18) The product from action of isomaltase on intestinal disaccharides is:
   A. 2 Glucose
   B. 3 Glucose
   C. Glucose & Fructose
   D. Glucose & Galactose

19) Incomplete transport& digestion of Fat and Proteins is a sign of...:
   A. Pancreatic Insufficiency
   B. Stomach Insufficiency
   C. Intestinal Insufficiency
   D. Spleen Disease

20) The final digestion of carbohydrates occurs in..:
   A. Mucosal lining of Large Intestine
   B. Mucosal lining of Stomach
   C. Mucosal lining of Small Intestine
   D. None of the above

Answers: 11)C 12)B 13)A 14)D 15)B 16)A 17)B 18)A 19)A 20)C



# Thank You!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