Biochemical Aspects of Digestion of Proteins and Carbohydrates

(GIT/Hematology Block)

Learning outcomes

By the end of this lecture, the student should be able to:

- Understand the overall process of dietary proteins' and carbohydrates' digestion, the organs involved, the enzymes required, and the end products.

- Implement the basic science knowledge of the process of proteins & carbohydrates digestion to understand the clinical manifestations of diseases that involve defective proteins' or carbohydrates' digestion &/or absorption.

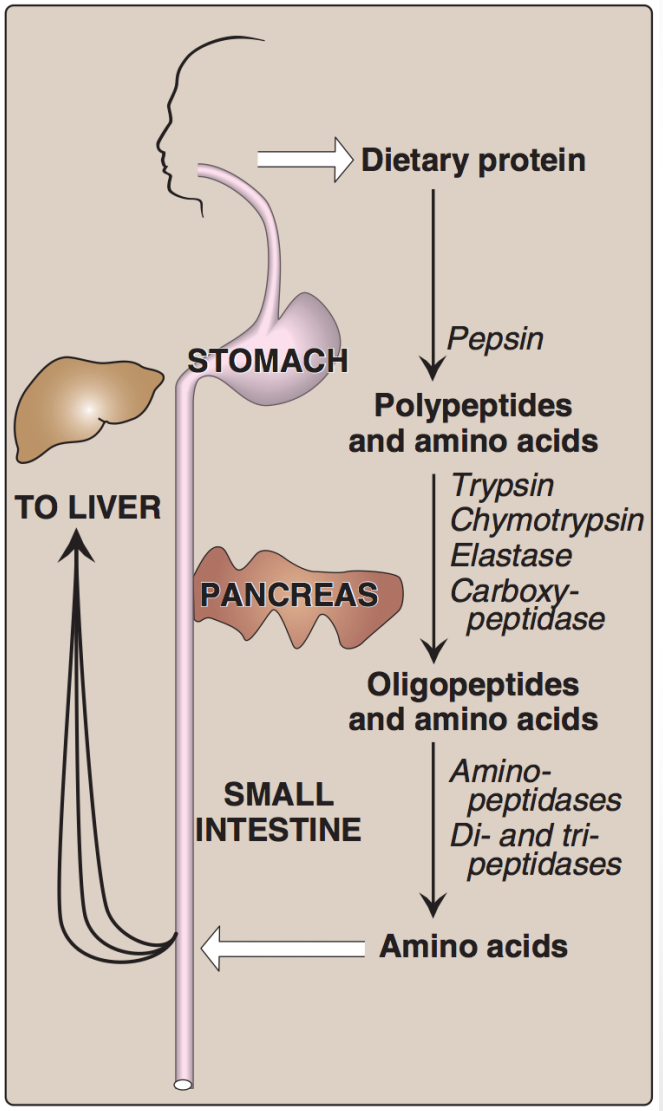
Biochemical Aspects of Digestion of Dietary Proteins

Protein Digestion

- Dietary proteins constitute 70-100 g/day.
- Proteins are generally too large to be absorbed by the intestine.
- They must, therefore, be hydrolyzed to their constituent amino acids, which can be absorbed.

The Source of Proteolytic Enzymes Responsible for Degrading Dietary Proteins

1. The stomach
2. The pancreas
3. The small intestine



1- Digestion of proteins by gastric secretion

- The gastric juice contains 2 components important for protein digestion:
    1. Hydrochloric acid.
    2. Pepsin.

Digesting agent	Description
Hydrochloric acid	1. kills some bacteria 2. Denatures proteins→ denatured proteins are more susceptible to hydrolysis by proteases.
Pepsin	• Acid-stable • Endopeptidase • Secreted as inactive zymogen (pepsinogen) • Pepsinogen is activated by: 1. hydrochloric acid 2. pepsin, i.e. autocatalysis • Protein digestion by stomach ➔Polypeptides + few free amino acids

2- Digestion of proteins in small intestine

a) digestion by pancreatic enzymes.

b) digestion by intestinal aminopeptidase.

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

1. **Cholecystokinin (CCK)**
2. **Secretin**

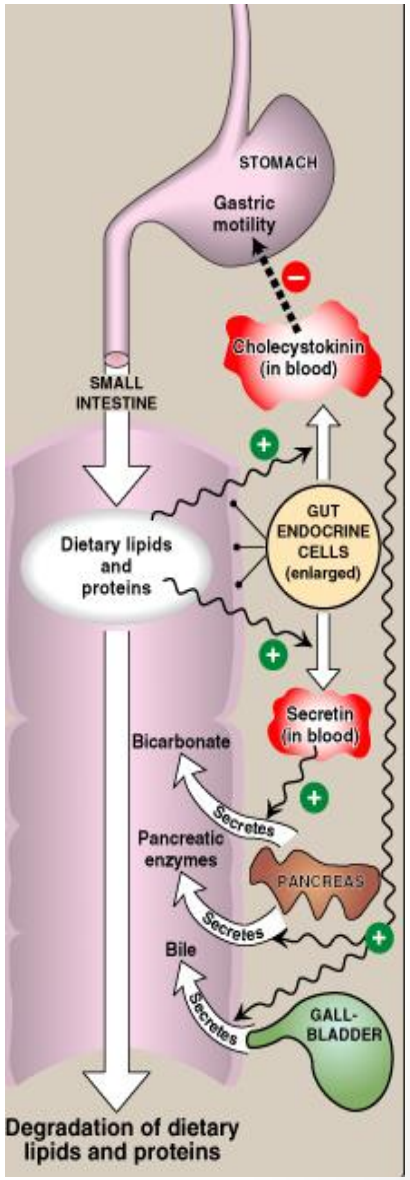
Hormonal control of digestion in small intestine:

Cholecystokinin (CCK):

1. Secretion of pancreatic enzymes.
2. Bile secretion.
3. Slow release of gastric contents.

Secretin:

Release of watery solution rich in bicarbonate by pancreas.



The gut hormones

The gut hormone	Stimulus for secretion	Effects
1- Cholecystokinin (CCK)	The presence of partially digested proteins (& lipids) in the upper small intestine	1. Stimulates the release of pancreatic digestive enzymes 2. Stimulates the contraction of the gall bladder & release of bile 3. Decreases gastric motility → slower release of gastric contents into the small intestine

The gut hormones: *continued…*

The gut hormone	Stimulus for secretion	Effects
2- Secretin	Low pH of the chyme entering the intestine	Stimulates the pancreas to release a watery solution rich in bicarbonate to neutralize the pH of the intestinal contents (to reach the optimum pH for digestive activity by pancreatic enzymes)

Pancreatic enzymes for digestion of proteins

- 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

Activation of pancreatic enzymes

- **Enteropeptidase:** It converts trypsinogen to trypsin

Trypsin then activates all the other pancreatic zymogens (including itself)

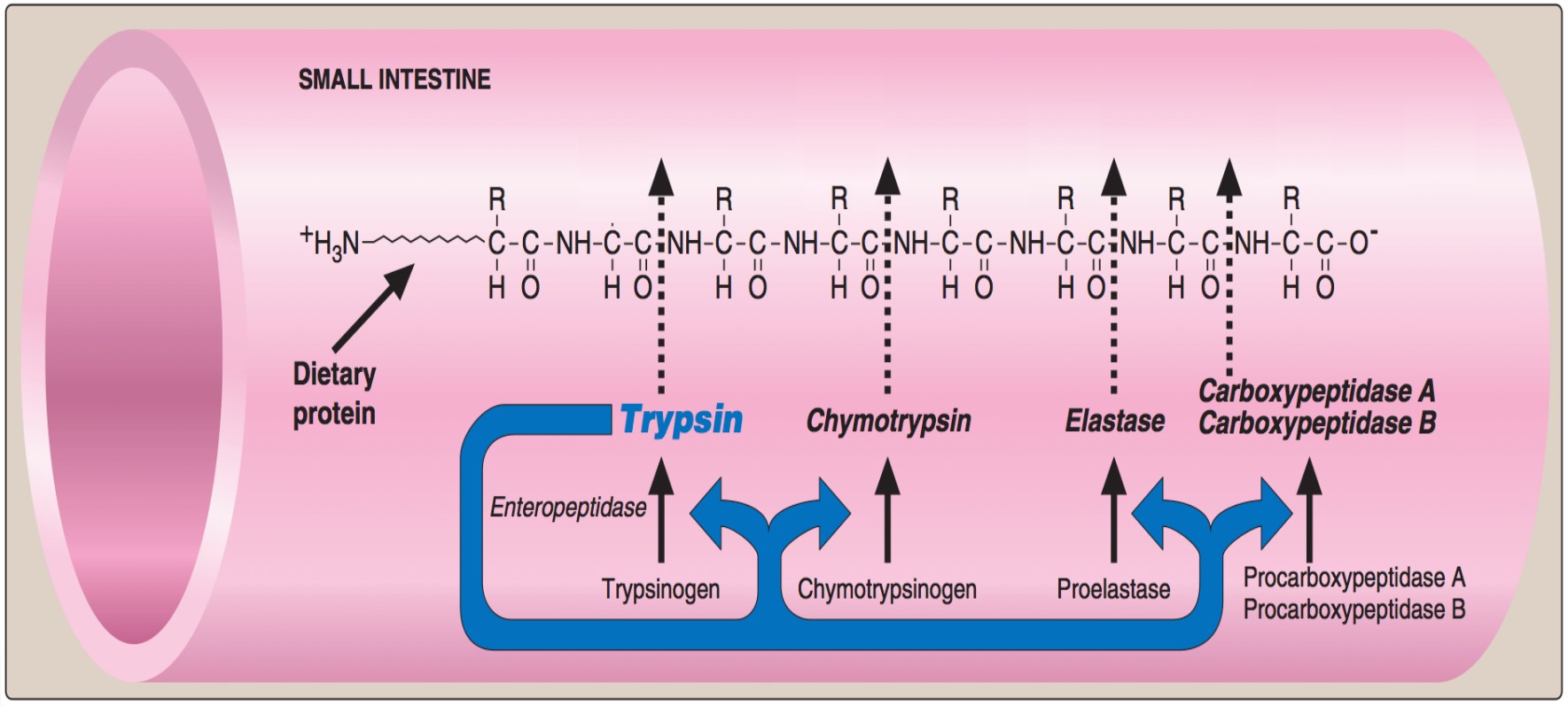
- *Enteropeptidase is an enzyme synthesized by, and present on the luminal surface of intestinal mucosal cells of the brush border membrane.*

Pancreatic enzymes: *continued …*

Zymogen	Active enzyme	Activating enzyme
Trypsinogen	Trypsin (endopeptidase)	1- Enteropeptidase 2- Trypsin (autocatalysis)
Chymotrypsinogen	Chymotrypsin (endopeptidase)	Trypsin
Proelastase	Elastase (endopeptidase)	Trypsin
Procarboxypeptidases	Carboxypeptidases (exopeptidases)	Trypsin

Activation of pancreatic enzymes:

continued …



2- Digestion of proteins in small intestine: *continued …*

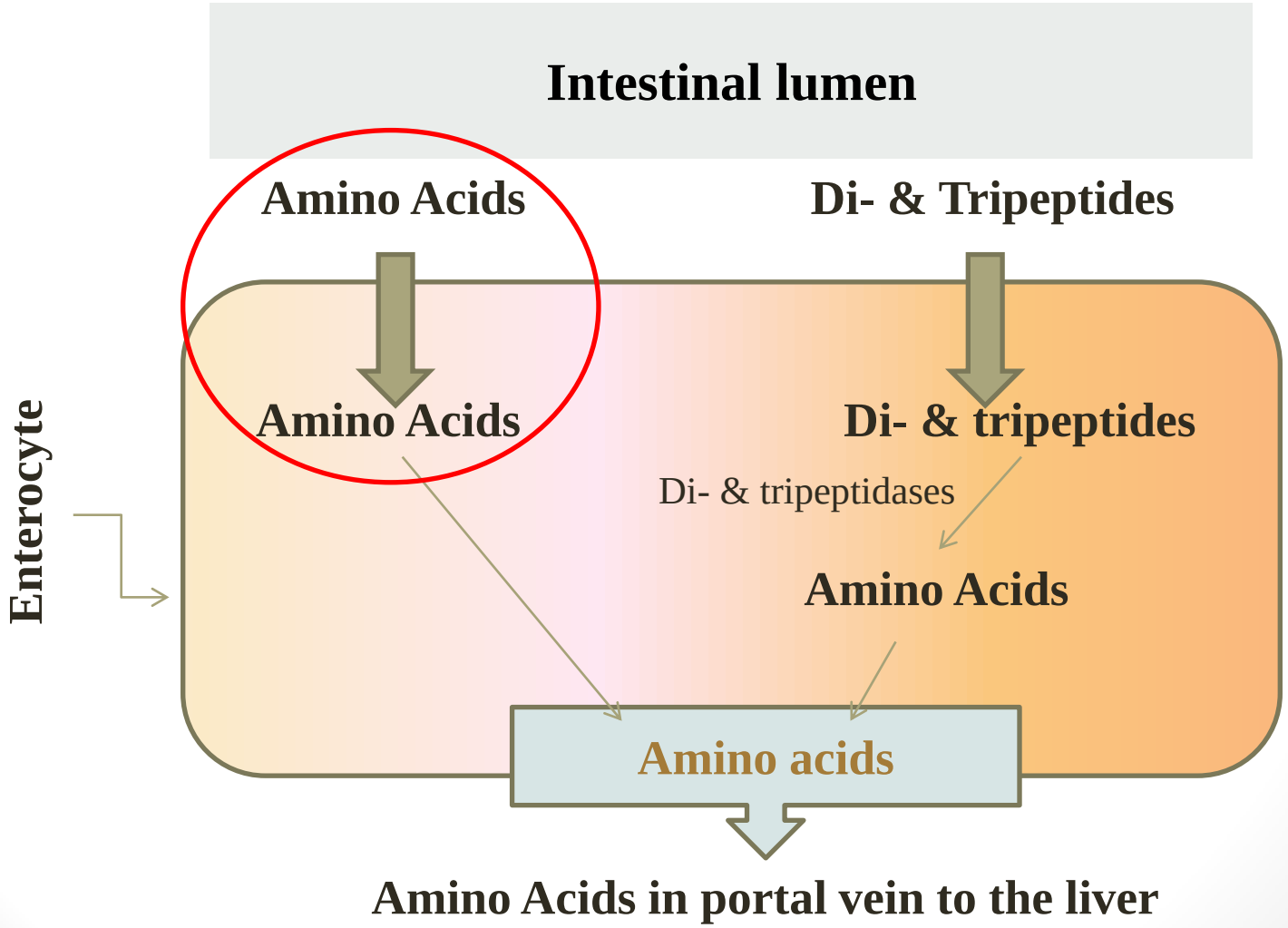
b) digestion by intestinal aminopeptidase.

Oligopeptides that result from the action of pancreatic proteases are cleaved into free amino acids and smaller peptides (di- & tri-peptides) by

intestinal aminopeptidase

(an exopeptidase on the luminal surface of the intestine)

Absorption of digested proteins



Genetic Errors in Amino Acids Transport

- Cystinuria is one of the most common genetic error of amino acid transport
- It is an example of inherited disorder in the transport of certain amino acids
- It affects the transport of Cystine and dibasic amino acids
- The organs affected are the small intestine and the kidney
- Cystine and dibasic amino acids appear in the urine
- Clinically: there is kidney stones formation
- Oral hydration (drinking lots of water) is an important part of treatment (to prevent kidney stones formation)

Abnormalities of protein digestion

Pancreatic insufficiency, e.g., chronic pancreatitis, cystic fibrosis, surgical removal of the pancreas

↓

incomplete digestion & absorption of lipids & proteins

↓

abnormal appearance of lipids (steatorrhea) & undigested proteins in the feces

Celiac Disease (Celiac sprue)

- It is a disease of malabsorption resulting from immune-mediated damage to the villi of the small intestine in response to ingestion of gluten.

- Gluten is a protein found in wheat, rye, and barley.

Biochemical Aspects of Digestion of Dietary Carbohydrates

Carbohydrates digestion

- **Carbohydrates digestion is rapid:**

  Generally completed by the time the gastric contents reach the junction of the duodenum & jejunum.

- **Sites for digestion of dietary carbohydrates:**
  - The mouth
  - The intestinal lumen

Dietary Carbohydrates

- **Mainly:**
  - **Polysaccharides:**
    - Starch from plant origin
    - Glycogen from animal origin

    } Contain α (1→4) & α (1→6) bonds
    - Cellulose from plant origin ⟶ Contains β (1→4) bonds
  - **Oligosaccharides**
  - **Disaccharides:**
    - Sucrose
    - Lactose
    - Maltose
  - **Monosaccharides:** Little amounts

Enzymes for Digestion of Dietary Carbohydrates

- **α-amylase** (Both salivary & pancreatic).

  Substrate: Polysaccharides

- **Disaccharidases** (Intestinal).

  Substrate: Disaccharides

- **Isomaltase & α(1,6) glucosidase** (Intestinal).

  Substrate: Branch points of oligo- and di-saccharides

Effects of α-amylase on Glycogen

- **Hydrolysis of:**

  α(1,4) glycosidic bonds

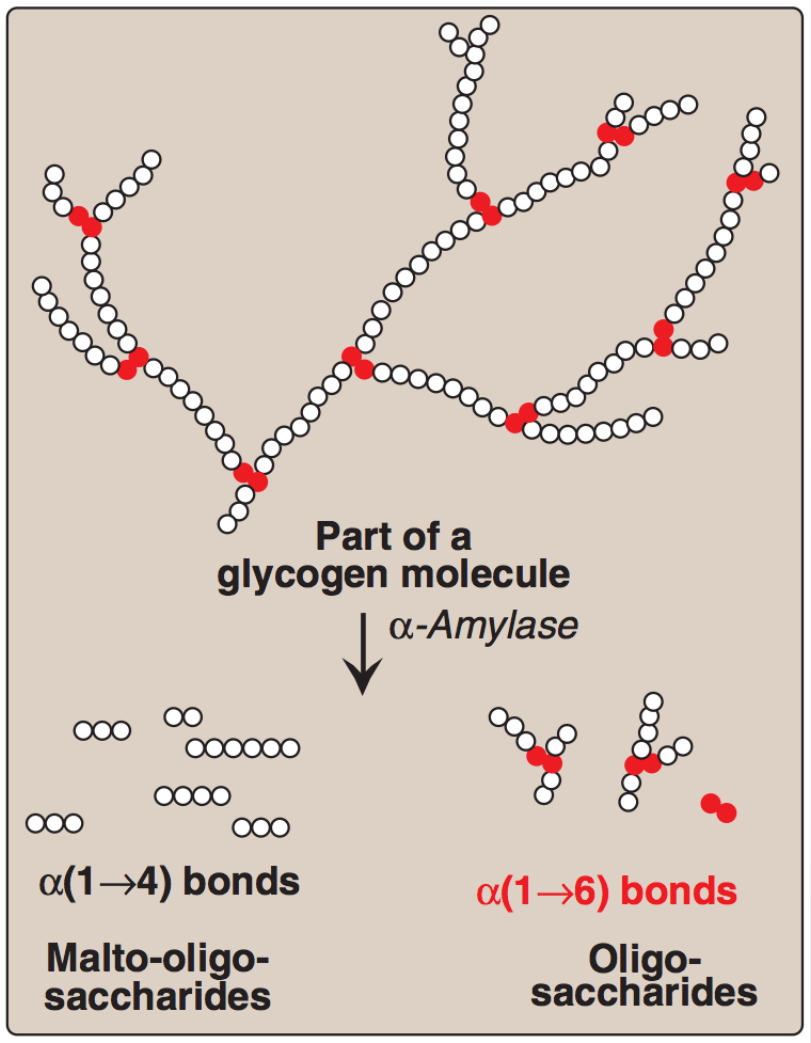
- **Products:**

  - Mixture of short oligosaccharides

    (both branched & unbranched)

  - Disaccharides:

    Maltose and isomaltose



Enzymes for Digestion of Dietary Carbohydrates: continued …

- **No dietary carbohydrate digestion occurs in the stomach** *(the high acidity of the stomach inactivates the salivary α–amylase)***.**

- **Pancreatic α–amylase continues the process of starch & glycogen digestion in the small intestine.**

  (Secreted by pancreas and works in small intestine)

Serum level of α-amylases

- **Normal level in serum:** 25 -125 U/L

- **The clinical significance of rising circulating levels of α-amylase activity:**

  - **Diagnosis of acute pancreatitis:**

    (damage of pancreatic cells ➔ release & activation of the intracellular enzymes into the blood)

    - Its level starts to rise within few hours.
    - Reaches a peak within 12- 72 hours.
    - Then returns to normal within few days.

Final digestion of carbohydrates by intestinal enzymes in the small intestine

- **Enzymes:**
  - Disaccharidases
  - α(1,6) Glucosidase (for branched oligosaccharides)
- **Source:**

  Secreted by & remain associated with the luminal side of the brush border membranes of the intestinal mucosal cells

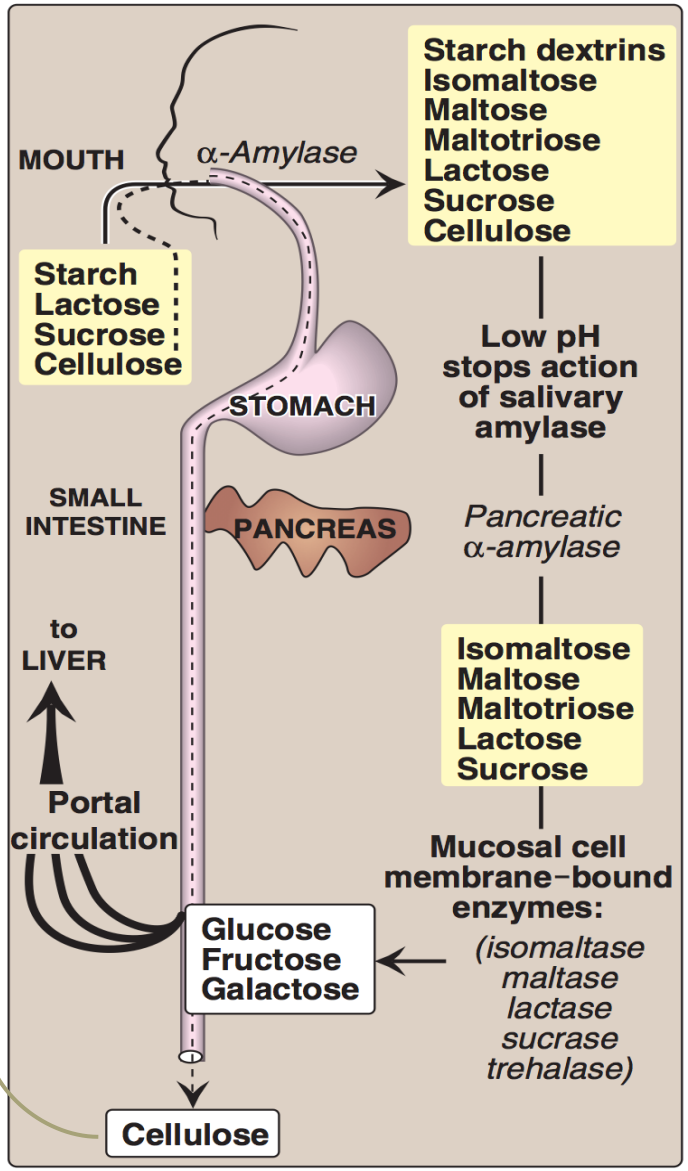
- **Location of their action:** the mucosal lining of the jejunum.

Intestinal disaccharidases

Enzyme	Substrate	Product
Isomaltase	isomaltose	2 Glucose
Maltase	maltose	2 Glucose
Sucrase	sucrose	Glucose & fructose
Lactase (β-galactosidase)	lactose	Glucose & galactose

Digestion of Carbohydrates

Dietary cellulose cannot be digested due to the absence of enzyme that can cleave β (1-4) bonds. It passes through the GIT largely intact. Despite that, it has several beneficial effects.

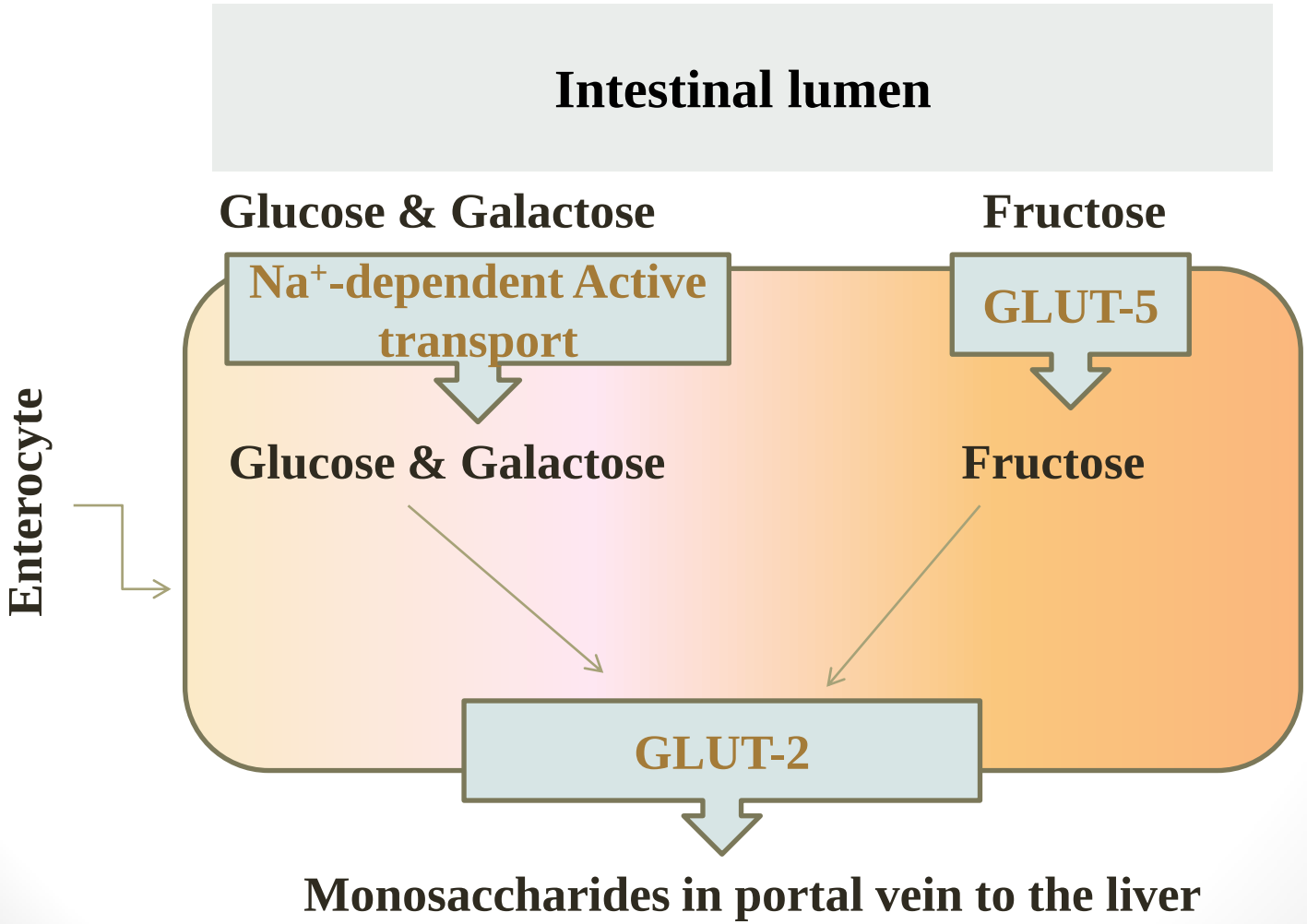


Absorption of Monosaccharaides by Intestinal Mucosal Cells

- **Location:** Duodenum & upper jejunum.
- **Insulin:** is **NOT** required for the uptake of glucose by intestinal cells.
- **Different monosaccharides have different mechanisms of absorption:**

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

Absorption of digested carbohydrates

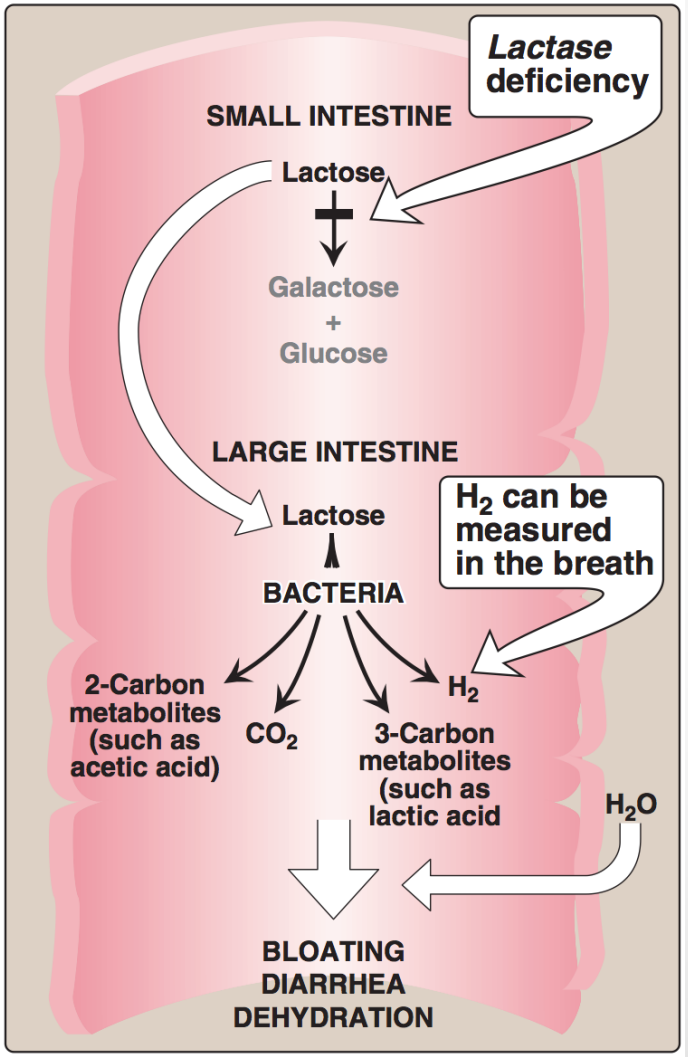


Abnormal digestion of disaccharides (e.g. of lactose)

Lactose intolerance (Lactase deficiency)

Lactase (β-galactosidase) deficiency → Undigested carbohydrate in large intestine → osmotic diarrhea.

Bacterial fermentation of the undigested compounds in the large intestine → CO_2, H_2 gas → abdominal cramps, diarrhea & distension (flatulence)



Take Home Messages Digestion of Dietary proteins

- Proteolytic enzymes responsible for digestion of dietary proteins are produced by the stomach, the pancreas & the small intestine.
- The digestion of proteins in the stomach is the result of the action of HCl and pepsin.
- Pancreatic proteases are, like pepsin, synthesized and secreted as inactive zymogens.

Take Home Messages Digestion of Dietary proteins

- The intestinal digestion of proteins occurs in the small intestine's lumen, on the luminal surface of the small intestine, and is completed intracellularly to produce free amino acids.

- In pancreatic insufficiency, the digestion and absorption of fat & protein is incomplete → steatorrhea & appearance of undigested proteins in the feces.

Take Home Messages
Digestion of Dietary carbohydrates

- Salivary α-amylase acts on dietary glycogen & starch in the mouth.
- Pancreatic α-amylase continues the process of polysaccharide digestion in small intestine.
- The final digestive processes of carbohydrates into monosaccharides occur at the mucosal lining of the small intestine by disaccharidases & α(1,6) glucosidase.

Take Home Messages
Digestion of Dietary carbohydrates

- Dietary cellulose cannot be digested due to the absence of enzyme that can cleave β (1-4) bonds, so it passes through the GIT largely intact. Despite that, it has several beneficial effects.

- Absorption of the monosaccharides requires specific transporters (GLUTs).

- Lactose intolerance is due to deficiency of lactase enzyme and causes abdominal cramps, diarrhea & flatulence

Reference

Lippincott's Illustrated reviews: Biochemistry 6th edition – chapters 7 and 19.