جامعة الملك سعود
King Saud University

"اللَّهُمَّ لا سَهْلَ إلاَّ ما جَعَلْتَهُ سَهْلاً، وأنْتَ تَجْعَلُ الحَزْنَ إذَا شِئْتَ سَهْلاً "

Biochemistry437

Biochemical Aspects of Proteins and Carbohydrates Digestion

Biochemistry Team 437

Color index:
Doctors slides
Doctor's notes
Extra information
Highlights

GNT block

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MED437
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Objectives:

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

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

EXTRA

Recall and Extra Explanation

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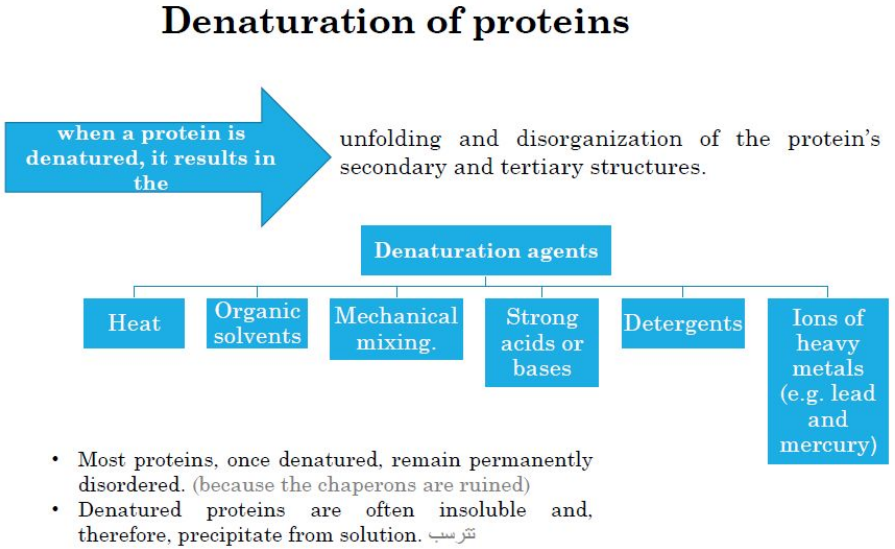
Proteins have different structures based on its complexity :

1. **Primary protein :**
   It's linear sequence of amino acids.
   Peptide bonds are not broken by conditions that denature the protein.

2. **Secondary protein :**
   It's regular arrangements of amino acids that are located near each other in linear sequence.

3. **Tertiary protein :**
   It is the three-dimensional (3D) structure of an entire structure of an entire polypeptide chain including side chains.

4. **Quaternary protein :**
   More complex.



Protein Digestion

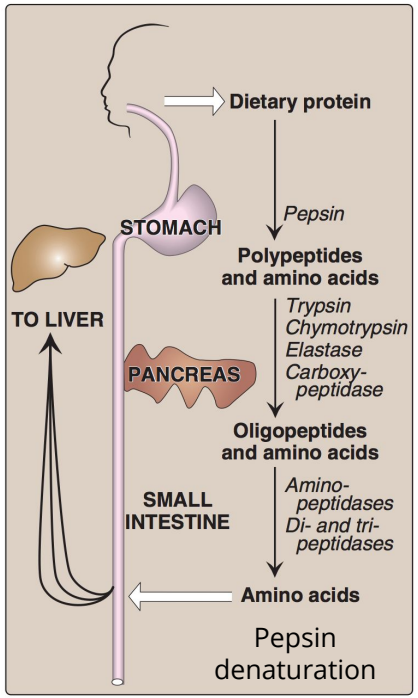
- Dietary proteins constitute 70-100 g/day.
- Proteins are generally too large to be absorbed by the intestine
- They must, therefore, be hydrolyzed to their constituent amino acids, which can be absorbed.

The Source of Proteolytic Enzymes Responsible for Degrading Dietary Proteins

1. The stomach
2. The pancreas (Pancreas release the enzymes which work in the duodenum)
3. The small intestine

Overview:
In the stomach:
- Proteins degraded by HCL
- Pepsin chops off amino acids {protease}

In the intestine:
- Pancreatic enzymes
- Intestinal enzymes
- Di-& Tripeptidase



Digestion of Proteins by Gastric Secretion

The gastric juice contains 2 components important for protein digestion:

1. Hydrochloric acid "HCL"
2. Pepsin

Digestion Agent	Description
Hydrochloric acid (strong acid)	• Kills some bacteria • Denatures proteins It's the main denaturation agent→ Denatured proteins are more susceptible to hydrolysis by proteases
Pepsin	• Acid-stable • Endopeptidase • Secreted as inactive zymogen* (pepsinogen) *enzyme that requires a biochemical modification to be active • Pepsinogen activated by : ○ Hydrochloric acid ○ Pepsin i.e. autocatalysis (it activates itself) • Protein digestion by stomach → polypeptides + few free amino acids

The proteins should be denatured then broken down (cut to small units "amino acids") to be ready to get absorbed.

*denaturation means return its origin structure back.
For ex. Tertiary protein to its primary structure by one of the denaturation agents.

Digestion of Proteins in Small Intestine

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a) Digestion by pancreatic enzymes.
b) Digestion by intestinal aminopeptidase.

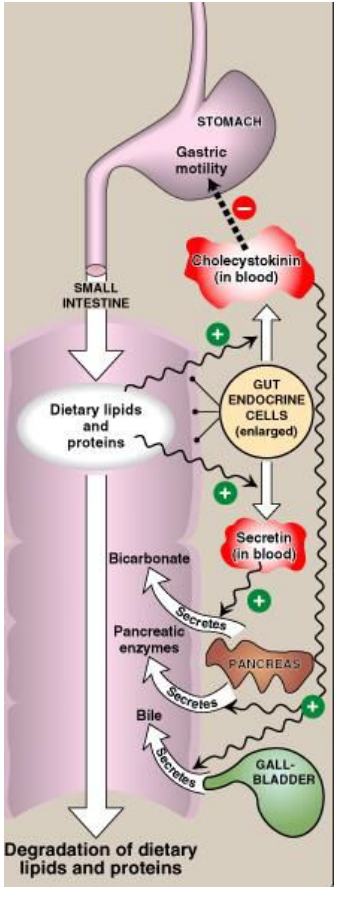
- The digestion in small intestine is hormonally controlled.
- Two small peptide hormones are released from cells of the upper part of small intestine:

Cholecystokinin (CCK):

- Secretion of pancreatic enzymes.
- Bile secretion.
- Slow release of gastric contents.

Secretin:

Release of watery solution rich in bicarbonate by pancreas.
to decrease the acidity of the chyme



Digestion of Proteins in Small Intestine

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The gut hormone	Stimulus for secretion	Effects
Cholecystokinin (CCK)	The presence of partially digested proteins (& lipids) in the upper small intestine	• Stimulates the release of pancreatic digestive enzymes • Stimulates the contraction of the gall bladder & release of bile • Decreases gastric motility slower release of gastric contents into the small intestine
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
  {trypsin , chymotrypsin, carboxypeptidase A&B and elastase}
- Each of these enzymes has different specificity for the cleavage sites
  they clave at a specific site “before or after a certain amino acid” ex. between lysine and serine only.
- 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) “autocatalysis”
- Enteropeptidase is an enzyme synthesized by, and present on the luminal surface of intestinal mucosal cells of the brush border membrane.

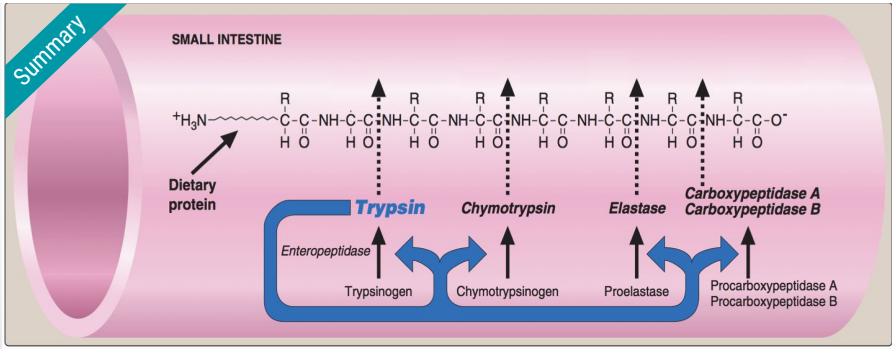
Enteropeptidase activate trypsinogen to become trypsin which in turn activates the rest of enzymes

We only need to know if it's exo or endo

Pancreatic Enzymes

Specific amino acid	Activating enzyme	Active enzyme	Zymogen
Arginine, lysine and a	1. Enteropeptidase 2. Trypsin	Trypsin **(endopeptidase)**	Trypsinogen
Tyrosine, tryptophan, methionine, leucine and phenylalanine	Trypsin	Chymotrypsin **(endopeptidase)**	Chymotrypsinogen
	Trypsin	Elastase **(endopeptidase)**	Proelastase
	Trypsin	Carboxypeptidase (A&B) **(exopeptidase)**	Procarboxypeptidases

Summary



Carboxypeptidases A&B : the amino acids are divided to 2 types A&B so every type has its own enzyme.

- Endopeptidase: cleaves the amino acids from the middle
- Exopeptidase: cleaves the amino acids from the end "C and N terminals"

Digestion of Proteins in Small Intestine

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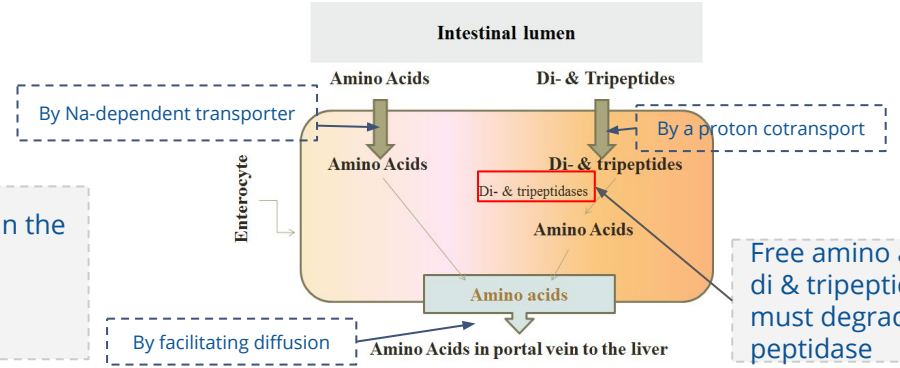
After being digested From the middle by pancreatic protease to smaller oligopeptides and some free amino acids, the intestinal aminopeptidase **"exopeptidase that works on the N terminals"** will start working.

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).

c) Absorption of digested proteins

- The free amino acids are transported to the inside of the enterocytes by NA dependant transporter.
- The the tri and di Peptides are transported by proton dependant pump, then **inside the enterocytes, they will be chopped off by tri and di peptidase that are present inside the enterocytes** to become free amino acids.
- All the free amino acids are transported by facilitated diffusion to the portal vein which carries them to the liver.



Recall:

- From the middle: trypsin,chymotrypsin,elastase
- From the N terminal: aminopeptidase
- From the c terminal: carboxypeptidase

Remember there are 2 enzymes in the luminal surface :
1- Enteropeptidase
2- Intestinal aminopeptidase

Free amino acid can diffuse directly to portal vein but di & tripeptidase they can enter enterocyte then they must degrade to free amino acid by Di- &Tri peptidase

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 because they are not absorbed in the intestine
- Clinically: there is **kidney stones formation**
- Oral hydration (drinking lots of water) is an important part of treatment (to prevent kidney stones formation)

- Cysteine: the amino acid
- Cystine: made from 2 cysteine residues
"the disease is related to this one"

- Cystine is transported along with Dibasic amino acids (amino acid containing 2 basic groups), these amino acids are: Ornithine, Arginine, Lysine
- In case of cystinuria, these 3 amino acids along with cystine are not absorbed
- The amino acids that are affected : Cystine, Ornithine, Lysine, Arginine
  • Mnemonic: COLA

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)

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- It is a disease of malabsorption resulting from immune-mediated damage to the villi of the small intestine in response to ingestion of gluten.
  The antibodies are against **gliadin,** a protein made of metabolism of gluten
- Gluten is a protein found in wheat, rye, and barley.
- Diagnosis >>> antigliadin antibodies

Recap of Protein Digestion:

1- Mechanical digestion
2- In stomach
- (HCL) will convert the protein to its primary structure (denaturation) and activates pepsinogen to pepsin
- Pepsin breaks down polypeptides to oligopeptides "smaller polypeptides"

3- In small intestine
- Enteropeptidase activates the trypsinogen to trypsin
- Trypsin activates the rest of the enzymes
- The final product is free amino acids "absorbed" and di & tripeptides "absorbed then broken down by its peptidase inside the enterocytes"

Diseases :
- **Of transport:** Cystinuria, defect in the transporter of COLA leads to renal stones, drinking water is really necessary
- **Of absorption:** Celiac, autoimmune disorder due to exposure of villi to gluten

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 mechanical + alpha amylase
  - The intestinal lumen
  - No digestion in the stomach due to high acidity

Dietary Carbohydrates

Mainly:

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

  Salivary α-amylase → Contain **α** (1→4) & **α** (1→6) bonds
  - Cellulose from plant origin → Contains β (1→4) bonds we can't digest but it helps in excretion
- **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

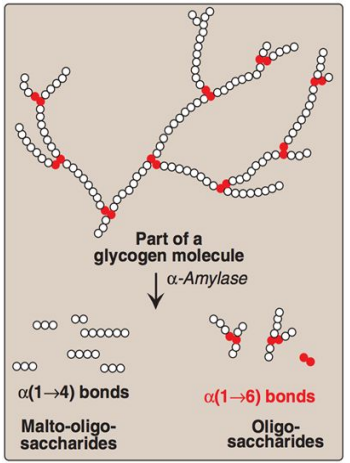
- **Isomaltase & α (1,6) glucosidase** (Intestinal).

  Substrate: Branch points of oligo- and disaccharides

Why pancreatic α -amylase target polys ?
Bc salivary α -amylase has short duration

Effects of α-amylase on Glycogen

Hydrolysis of	α(1,4) glycosidic bonds
Products	• Mixture of short oligosaccharides (both branched "dextrins" & unbranched) • Disaccharides: Maltose and isomaltose



Enzymes for Digestion of Dietary Carbohydrates

- **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

In the serum, we can find both salivary and pancreatic, but salivary is very low

- Normal level in serum: 25-125 U/L
- **The clinical significance of rising circulating levels of a-amylase activity:**
  - **Diagnosis of acute pancreatitis:**
    *(damage of pancreatic cells leads to 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

Multiple readings over different times can tell you about the progression of the disease

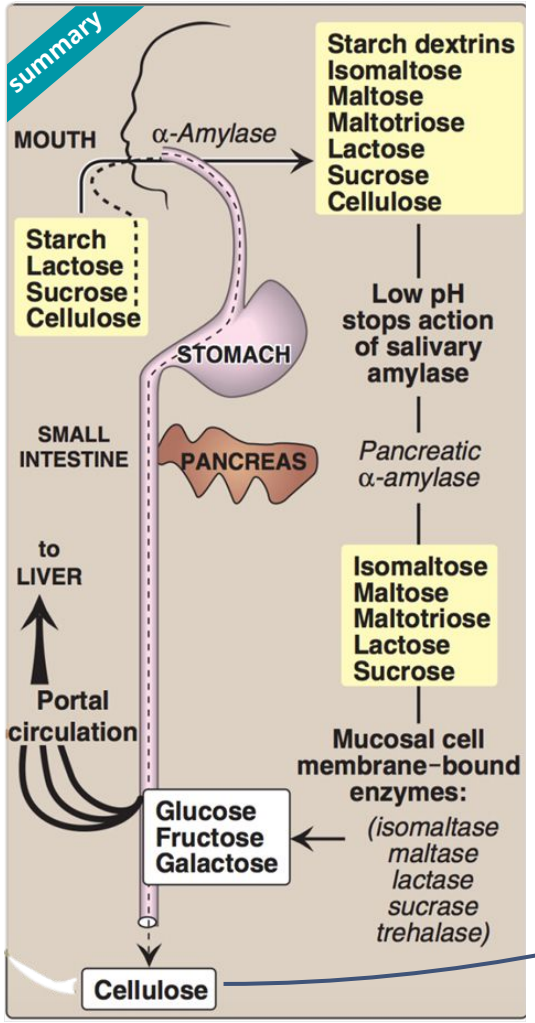
Final digestion of carbohydrates by intestinal enzymes in the small intestine

- **Enzymes:**
  - Disaccharidases
  - a(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

Substrate	Enzyme	Product
Isomaltose "α (1-6)"	Isomaltase	2 Glucose
Maltose " α(1-4)"	Maltase	2 Glucose
sucrose	Sucrase	Glucose & fructose
lactose	Lactase (β-galactosidase)	Glucose & galactose

Digestion of Carbohydrates



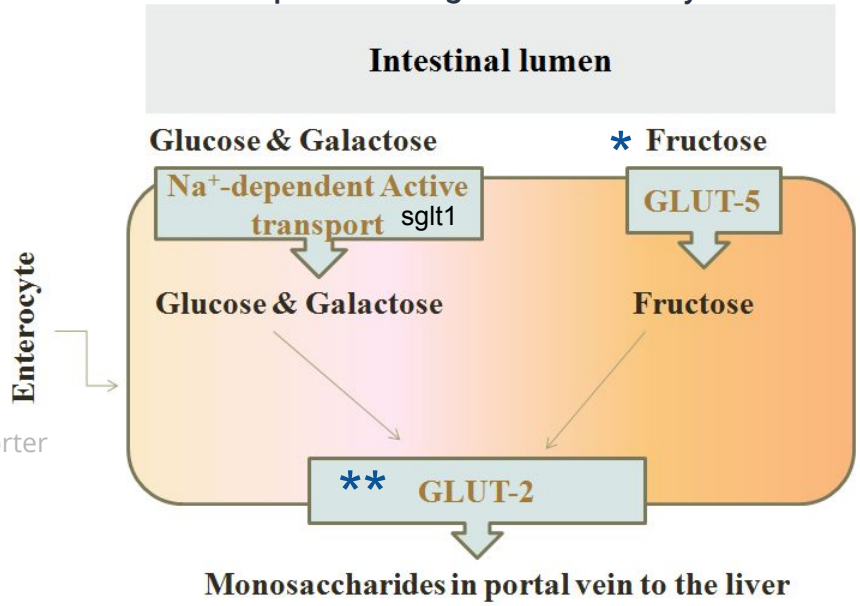
Dietary cellulose cannot be digested due to the absence of enzyme that can cleave β (1-4) bonds. It passes through the GIT largely intact. Despite that, it has several beneficial effects

Absorption of Monosaccharides by Intestinal Mucosal Cells

- **Location:**
  Duodenum & upper jejunum.
  Final step monosaccharides
- **Insulin:** is **NOT** required for the uptake of glucose by intestinal cells.
- **Different monosaccharides have different mechanisms of absorption:**
  - Facilitated diffusion (GLUT*-mediated)
  - Active transport (Energy-dependent): Cotransport with Na^+

*Glut: glucose transporter

Absorption of digested carbohydrates



*It's the only glucose transporter that does not carry glucose. it's specific for fructose.

** NOT insulin dependant

Abnormal Digestion of Disaccharides (e.g. of lactose)

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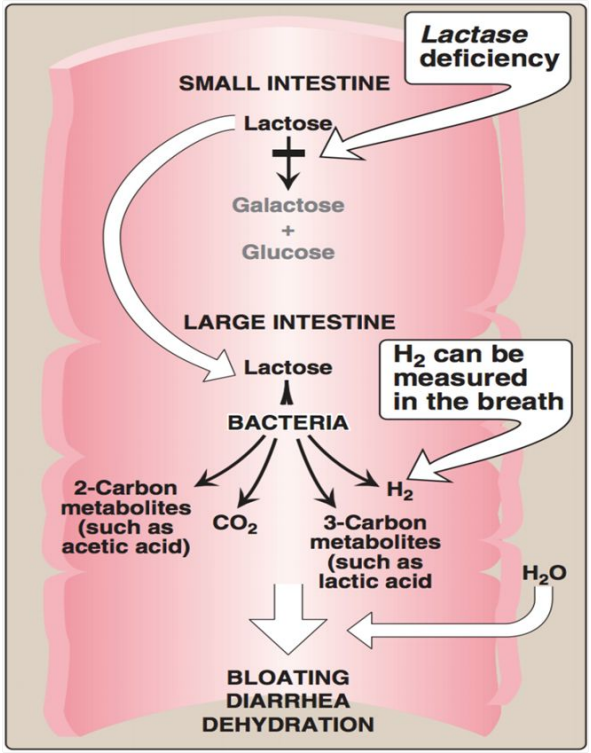
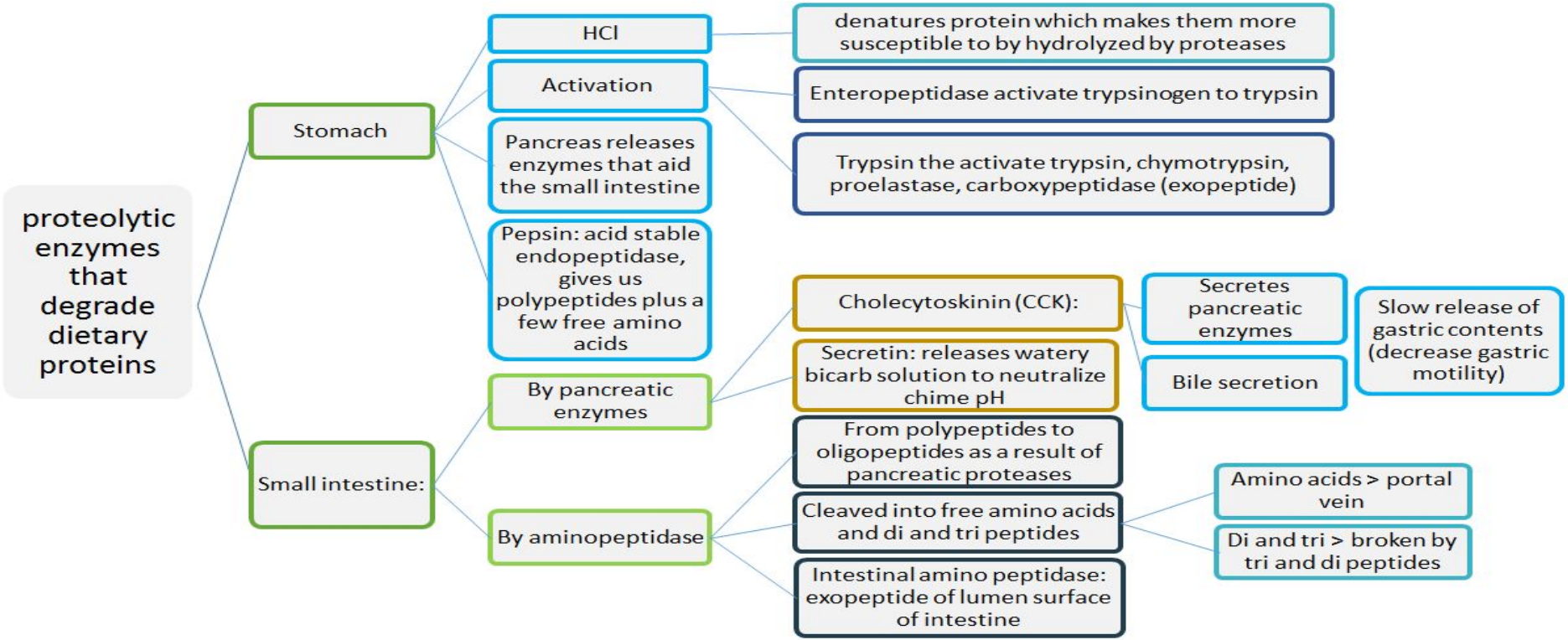
Lactose intolerance
(Lactase deficiency)

Lactase (β -galactosidase) deficiency → Undigested carbohydrate in large intestine → osmotic diarrhea.
Bc it pulls the water with it "osmotically active"

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

Bacterial fermentation also generates 2 Carbon compounds [acetic acid] & 3 Carbon compounds [lactic acid] → osmotically active → they pull water → osmotic diarrhea.




proteolytic enzymes that degrade dietary proteins
Stomach
HCl
denatures protein which makes them more susceptible to by hydrolyzed by proteases
Activation
Enteropeptidase activate trypsinogen to trypsin
Trypsin the activate trypsin, chymotrypsin, proelastase, carboxypeptidase (exopeptide)
Pancreas releases enzymes that aid the small intestine
Pepsin: acid stable endopeptidase, gives us polypeptides plus a few free amino acids
Small intestine:
By pancreatic enzymes
Cholecytoskinin (CCK):
Secretes pancreatic enzymes
Bile secretion
Slow release of gastric contents (decrease gastric motility)
Secretin: releases watery bicarb solution to neutralize chime pH
By aminopeptidase
From polypeptides to oligopeptides as a result of pancreatic proteases
Cleaved into free amino acids and di and tri peptides
Amino acids > portal vein
Di and tri > broken by tri and di peptides
Intestinal amino peptidase: exopeptide of lumen surface of intestine

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Diseases related to protein digestion		
Genetic errors of amino acid transport	**Abnormalities of protein digestion**	
Cystinuria	**Pancreatic insufficiency**	**Celiac disease**
• **Most common** genetic error of amino acid transport. • **Inherited**. • Affects the transport of **Cystine** and dibasic amino acids. • Affects **kidney and small intestine.** • Cystine appear in the urine. • **Kidney stones formation.** • Kidney stones formation treated by hydration.	• Such as in: chronic pancreatitis, cystic fibrosis, and removal of pancreas. • Leads to **Incomplete digestion and absorption of lipids** and proteins because of lack of pancreatic enzymes . • Which lead to **Abnormal appearance of lipids (steatorrhea)** & undigested proteins in feces.	It is a disease of **malabsorption** resulting from **immune-mediated damage to the villi of the small intestine** in response to ingestion of gluten.

Summary

Intestinal Disaccharides		
Enzyme	**Substrate**	**Product**
Isomaltase	Isomaltose	2 glucose
Maltase	Maltose	2 glucose
Sucrase	Sucrose	Glucose and fructose
Lactase	Lactose	Glucose and galactose

Absorption of monosaccharides:

- Occurs in duodenum and jejunum.
- No insulin required for reuptake of glucose by intestinal cells
- Two Mechanisms of absorption:
  - Facilitated diffusion (GLUT-mediated). such as in fructose.
  - Active transport (Energy-dependent): Co-transport with Na+. such as in glucose and galactose.

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.
- 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 a-amylase acts on dietary glycogen & starch in the mouth.
- Pancreatic a-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 & a(1,6) glucosidase.
- Dietary cellulose cannot be digested due to the absence of enzyme that can cleave b (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

MCQs:

Q1 : digestion of proteins by pancreatic enzymes result in : A-polypeptides B-fatty acid only C-Oligopeptides?
A- Polypeptides
B- Fatty acids only
C- Oligopeptides
D- None of the above

Q2 : Trypsin activates all pancreatic enzymes including it precursor ?
A- True
B- False

Q3 : Incomplete transport & digestion of Fat and Proteins is a sign of ?
A- Pancreatic Insufficiency
B- Stomach Insufficiency
C- Intestinal Insufficiency
D- Spleen Disease

Q4 : Carbohydrate can not be digested in ?
A- Mouth
B- Stomach
C- duodenum
D- None of them

Q5 : Which ONE of the following causes rising in α-Amylase levels ?
A- Peptic Ulcer
B- Acute Pancreatitis
C- Appendicitis
D- None of the above

Q6 : 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

1- C
2- A
3- A
4- D
5- B
6- C

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Team leaders

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Boys team

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