L4:

Biochemical aspects of digestion of proteins and carbohydrates

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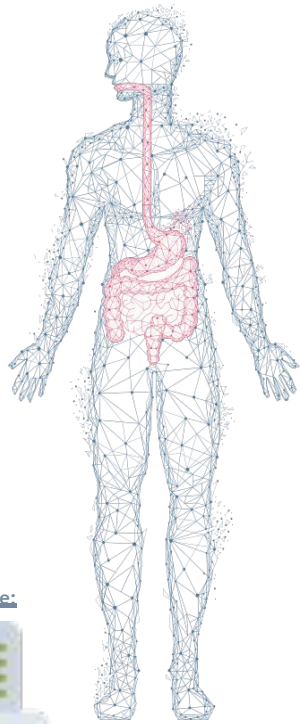

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Objectives:

- 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.

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Ninja Nerd

Ninja Nerd

Biochemical Aspects of Digestion of Dietary Proteins

Protein digestion :

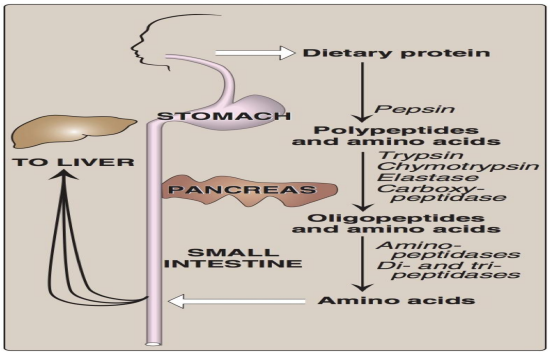
Dietary proteins constitute 70-100 g/day

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

- Stomach
- Pancreas
- small intestine



Digestion of protein in gastric secretion:

The gastric juice contain 2 component important for protein digestion:

Digesting agent	Description ⚠ Important
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

Digestion of proteins in small intestine :

1- digestion by pancreatic enzymes. (requires enteropeptidase)

2-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

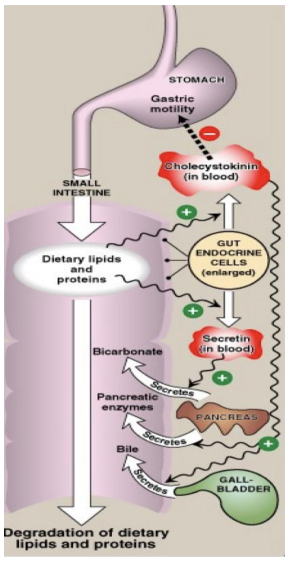
Hormonal control of digestion in small intestine:

Cholecystokinin (CCK)

-Secretion of pancreatic enzymes.
-Bile secretion.
-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
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 gallbladder & release of bile. 3. 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

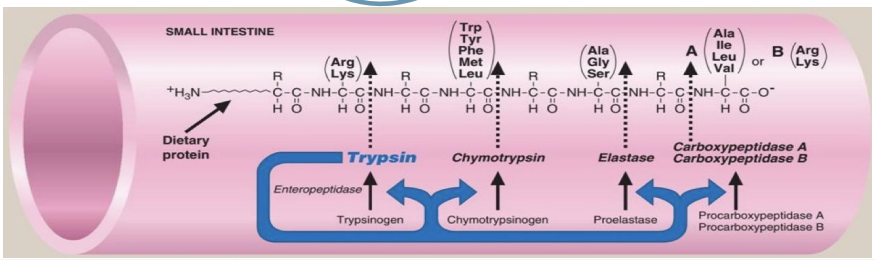
-The pancreatic secretion contains a group of pancreatic proteases.
- Each of these enzymes has different specificity for the cleavage sites.
-These proteases are synthesized and secreted as inactive zymogens.

Activation of pancreatic enzymes

Enteropeptidase 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.



Nothing is important in pic

Important

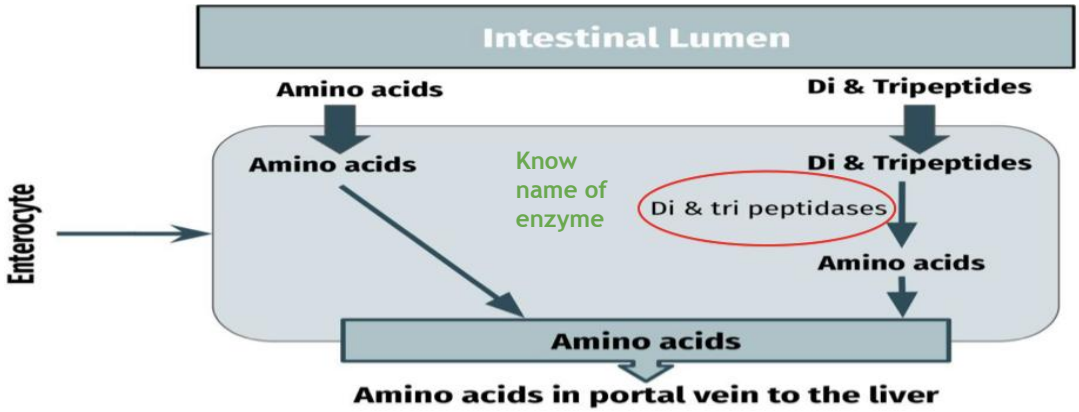
Zymogen	Active enzyme		Activating enzyme
Trypsinogen	Trypsin	**Endopeptidase** Break peptide bonds within the molecule.	1- Enteropeptidase 2- Trypsin (autocatalysis)
Chymotrypsinogen	Chymotrypsin		Trypsin
Proelastase	Elastase		Trypsin
Procarboxypeptidases	Carboxypeptidases	**Exopeptidases** Break peptide bonds from end-pieces of terminal amino acids	Trypsin

Digestion of proteins in small intestine

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)

Example of

inherited disorder in the transport of certain amino acids

Organs affected

are the small intestine and the kidney

Management

Oral hydration (drinking lots of water) is an important part of treatment (to prevent kidney stones formation)

01 02 03 04 05 06

About the disease

Cystinuria is one of the most common genetic error of amino acid transport

Affects

transport of Cystine and dibasic amino acids

Clinically

Cystine and dibasic amino acids appear in the urine, kidney stones formation

COLA or COAL
mnemonic for dibasic a.a -> Cystine, Ornithine, Lysine, Arginine
Female Dr. its important to know all affected a.a

Cysteine: is a sulfur-containing amino acid.
Cystine: is formed from two cysteine molecules joined together

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)

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

Celiac disease is a hereditary disorder caused by sensitivity to the gliadin fraction of gluten, a protein found in wheat; similar proteins are present in rye and barley. In a genetically susceptible person, gluten-sensitive T cells are activated when gluten-derived peptide epitopes are presented. The inflammatory response causes characteristic mucosal villous atrophy in the small bowel.

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

The antibodies are against gliadin, a protein made of metabolism of gluten

Biochemical aspects of digestion of dietary carbohydrate

Carbohydrates Digestion: Rapid digestion because it starts in the mouth (physical chewing and alpha amylase enzyme) No carbs digestion in the stomach (due to high acidity)

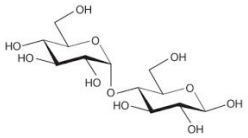
Carbohydrates digestion is rapid: Generally completed by the time the gastric contents reach the junction of the duodenum & jejunum. After neutralization of pH by secretin, the chyme now is in the intestines with more neutral pH and more enzymes are ready to start to work, this happens in the duodenum and upper jejunum

Sites for digestion of dietary carbohydrates:

- The mouth
- The intestinal lumen

It starts here

Dietary Carbohydrates Mainly:

Monosaccharide	Disaccharides	Oligosaccharides	Polysaccharides
Little amounts Dietary food contains little amounts of monosaccharides because it's expensive in the food industry	• Sucrose • Lactose • Maltose	 The structure is Extra	• **Glycogen** from **animal** origin **Contain** α(1-4) & α (1-6) bonds • **Starch** from **plant** origin • **Cellulose** from **plant** origin β **(1-4) bond**

Enzymes for Digestion of Dietary Carbohydrates

Cellulose is not absorbed by the body because there is no enzyme that cleaves its bond β(1-4)

Important

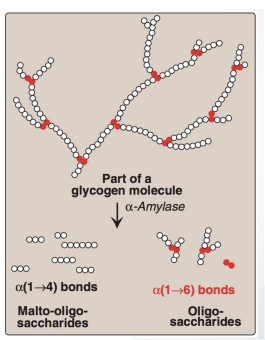
Enzymes

- **α-amylase** — **-location:** Both salivary & pancreatic. **-Substrate:** Polysaccharides
- **Disaccharidases** — **-location:** Intestinal **-Substrate:** Disaccharides
- **Isomaltase & α(1,6) glucosidase** — **-location:** Intestinal **-Substrate:** Branch points of oligo- and di-saccharides

Effects of α-amylase on Glycogen

Hydrolysis of: α(1,4) glycosidic bonds → **Productes: -Mixture of short oligosaccharides (both branched & unbranched) -Disaccharides: Maltose and isomaltose**

- **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

very important for OSPE

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

Location of their action:

The mucosal lining of the **jejunum**

1 **Enzymes:**

1- Disaccharidases

2- α(1,6) Glucosidase (for branched oligosaccharides)

2 **Source:**

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

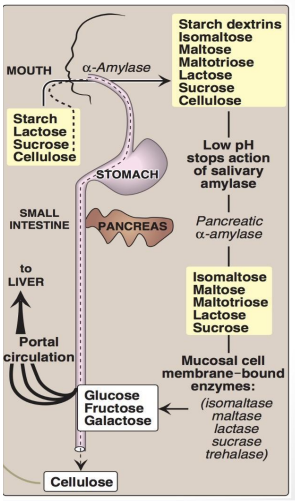
Table is important

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 Monosaccharides by Intestinal Mucosal Cells

Location: Duodenum & upper jejunum.

Insulin: is **NOT** required for the uptake of glucose by intestinal cells.

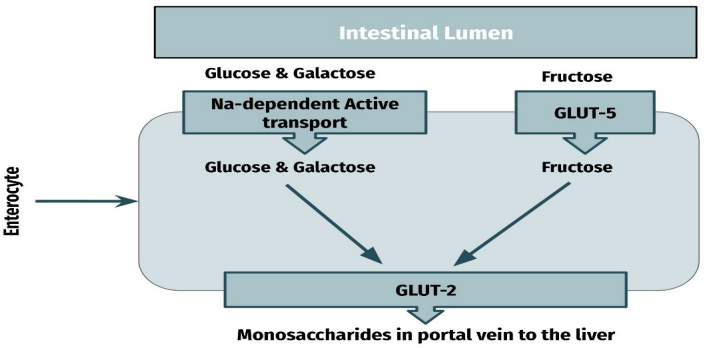
Different monosaccharides have different mechanisms of absorption:

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

Absorption of digested carbohydrates

-Fructose is carried to enterocytes by GLUT5
-Glucose and Galactose are carried by SGLT1 and SGLT2
They are carried from enterocytes to live by GLUT2

Click here for the original picture



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

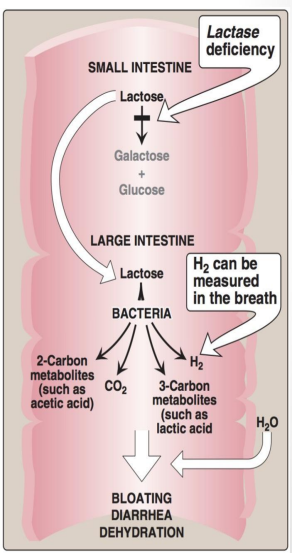
In people who have lactose intolerance due to deficiency of Lactase, the GIT Normal flora utilizes lactose and causes the symptoms of intolerance like increase co2, diarrhea, distention, etc,

Lactose intolerance (Lactase deficiency)

Acetic acid & lactic acid are osmotically active → pulling water to intestinal lumen

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)



Summary

	Protein Digestion	Carbohydrates Digestion
Site	• The stomach • The pancreas • The small intestine	• The mouth • The intestinal lumen
secretions	**Gastric secretions:** • HCL • Pepsin. Pepsinogen is activated by: • hydrochloric acid • pepsin, i.e. autocatalysis **Intestinal digestion:** • pancreatic enzymes (inactive zymogens) • Intestinal aminopeptidase	• α-amylase • Disaccharidases • Isomaltase & a(1,6) glucosidase
Activation of pancreatic enzymes	1. Enteropeptidase Converts trypsinogen to trypsin. 2. Trypsin then activates all the other pancreatic zymogens (including itself): a. Chymotrypsin (endopeptidase) b. Elastase (endopeptidase) c. Carboxypeptidases (exopeptidases)	**α-amylase:** Normal level in serum: 25 -125 U/L significance: **Diagnosis of acute pancreatitis**
Hormonal control of digestion in small intestine	• Cholecystokinin (CCK) • Secretin	**Absorption of monosaccharides:** 1. Facilitated diffusion (GLUT-mediate 2. Active transport (Energy-depender Co-transport with Na
Abnormallties	1. **Cystinuria** : Genetic errors in Cystine and dibasic amino acids transport. 2. **celiac disease** : immune mediated damage to the villi of the small intestine in response to ingestion of gluten.	Lactose intolerance

Take home messages

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

Quiz

MCQs

Q1: Humans can't absorb cellulose due to absence of?
A- cellulose a-(1,4) glycosidase
B- cellulose b-(1,6) glycosidase
C- cellulose b-(1,4) glycosidase
D- cellulose a-(1,6) glycosidase

Q2: which hormonal release of watery solution rich in bicarbonate by pancreas?
A- CCK
B- secretin
C- gastrin
D- pepsin

Q3: which enzymes convert trypsinogen to trypsin?
A- trypsin
B- elastase
C- carboxypeptidase
D- pepsin

Q4: which one is a site for carbohydrates digestion?
A- stomach
B- pancreas
C- small intestine
D- mouth & intestinal lumen

Q5: one of the following is normal of serum level of a-amylases?
A- 24
B- 30
C- 129
D- 13

Q6: An 7 month old infant developed diarrhea and abdominal distention after breastfeeding , which of the following enzymes is deficient in this case ?
A- lactase
B- sucrase
C- maltase
D- amylase

Q1:C | Q2:B | Q3:A | Q4:D | Q5:B | Q6:A

SAQ

Q1: Mention The source of proteolytic enzymes?

1- stomach
2- pancreas
3- intestine

Q2: What are some of the effects of Cholecystokinin (CCK)?

1. Stimulates the release of pancreatic digestive enzymes
2. Stimulates the contraction of the gallbladder & release of bile (bile is used for lipids)
3. Decreases gastric motility → slower release of gastric contents into the small intestine (to give more time for the digestion)

Q3: what amino acids transport is effected in cystinuria?

Cystine, Ornithine, Lysine, Arginine “COLA or COAL”

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