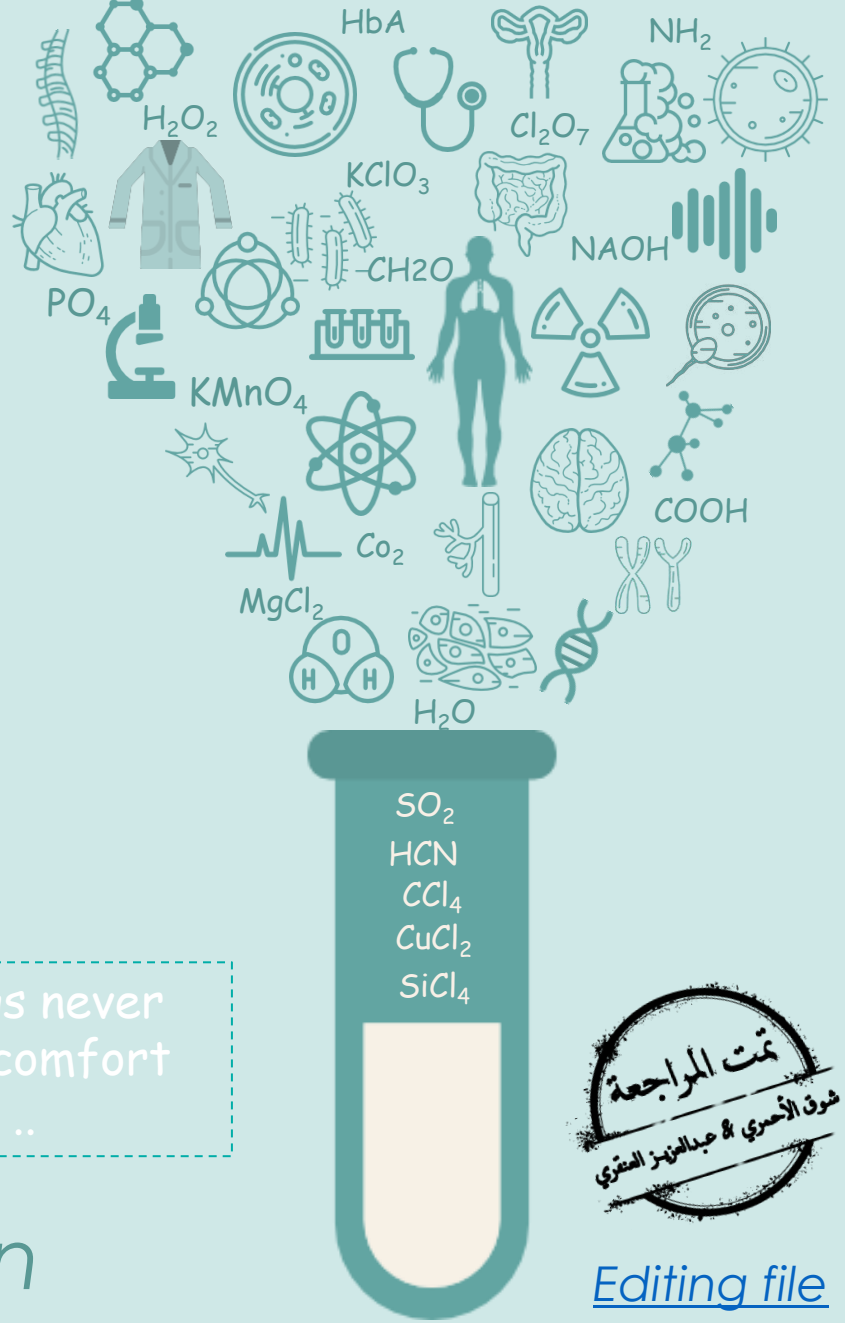


Important Doctors slides

Extra Information **Doctors notes**

Biochemistry

Biochemical aspects of the digestion of Protein and carbohydrates

Great things never came from comfort zones ..

تحت المراجعة
شوق الأحمري & عبدالعزيز العنقري

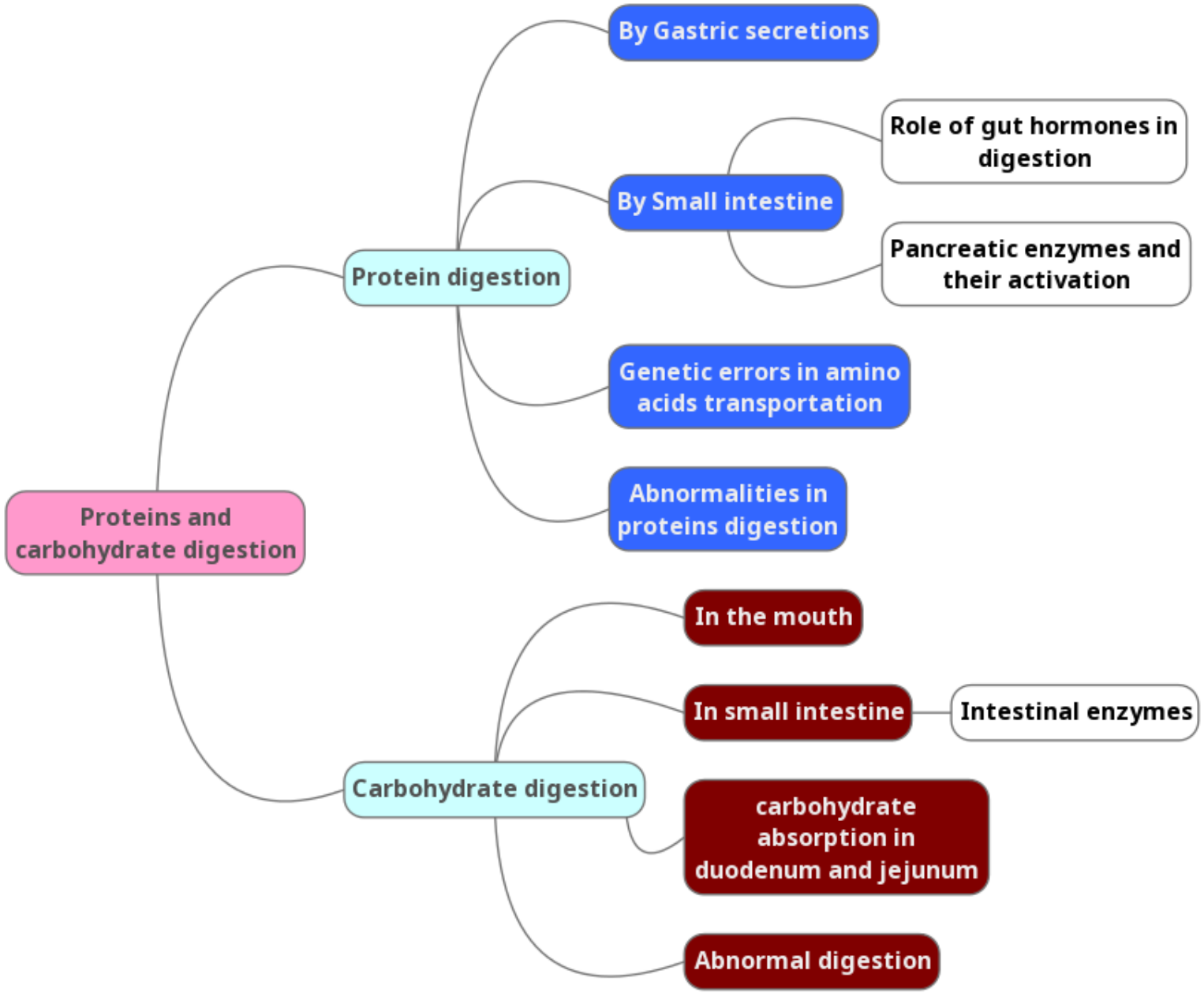
[Editing file]

OBJECTIVES

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

- Understand the overall digestion process of dietary proteins and carbohydrates
- To understand the clinical manifestations of diseases that involve defective proteins or carbohydrates digestion and/or absorption.

Key principles

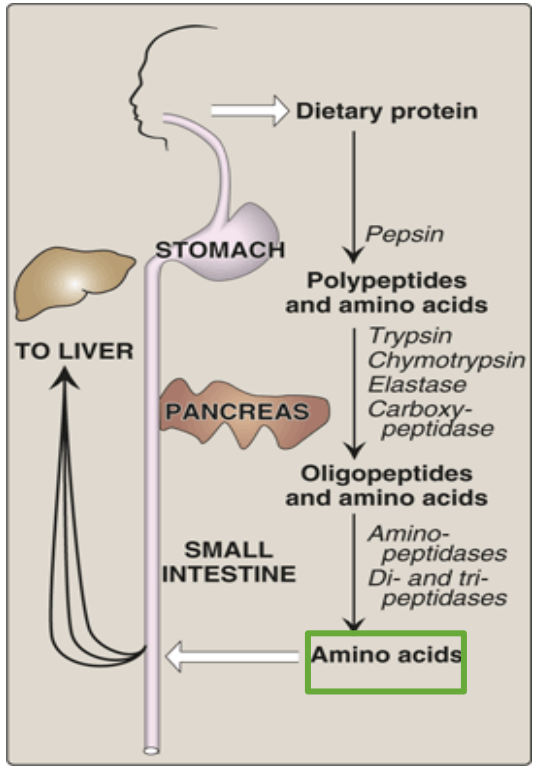


Protein digestion:

- 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

- The stomach
- The pancreas
- The small intestine



In the mouth protein undergoes only physical cutting and mixing with saliva but no digestion occur in the mouth. Then it goes to the stomach as a bolus.

- When proteins are denatured, enzymes can act on it easily because of increased surface area
- Pepsin and HCL helps in protein denaturation

Only amino acids and di and tri peptides can be absorbed

In adults, absorption of protein occur only to be used in renewing cells, otherwise protein levels are constant.

1) Digestion of proteins by gastric secretion(stomach):

The gastric juice contains two components important for protein digestion:

1) Hydrochloric acid (HCL). 2) Pepsin in the form of pepsinogen .

Autocatalysis*: one of the reactions products e.g. (pepsin), acts as a catalyst for the reaction (in activating pepsinogen)

Digesting agent	Description
1-Hydrochloric acid (A strong acid)	1. kills some bacteria, which is not a part of digestion of proteins. 2. Denatures proteins : denatured proteins are more susceptible to hydrolysis by proteases. protease is any enzyme that performs proteolysis; protein catabolism byhydrolysis of peptide bonds • Strong alkaline media can also denature protein
2-Pepsin	• Acid-stable • Endopeptidase (internal protein enzyme) • Cuts the band which is present in the middle of the peptide • Secreted as inactive zymogen (pepsinogen) • Pepsinogen is activated by: 1) Hydrochloric acid OR 2) Pepsin, i.e. autocatalysis (self-destruction) • Protein digestion by stomach end product is (Polypeptides + few free amino acids)

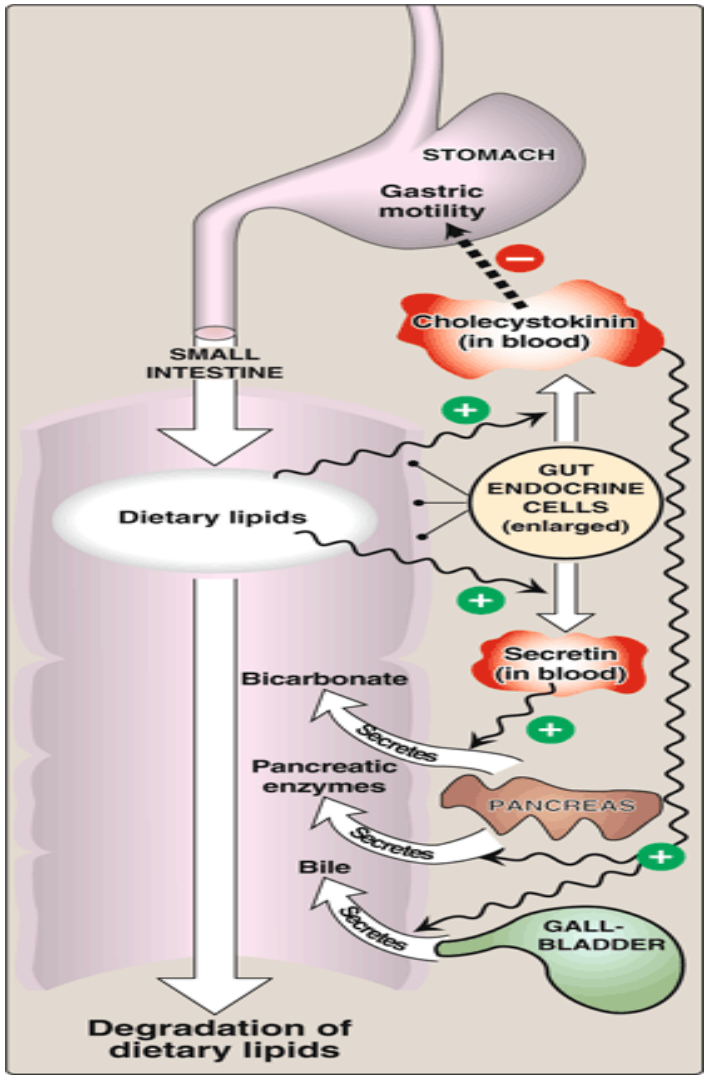
2) Digestion of proteins in small intestine:

A-Digestion by pancreatic enzymes. CCK الي راح تفرز من خلال هرمون

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:		
Hormone:	Cholecystokinin (CCK)	Secretin
Functions:	Secretion of pancreatic enzymes.	Release of watery solution rich in bicarbonate by pancreas
	Bile secretion.	-
	Slow release of gastric contents. (similar to rennin), decreases motility.	-



The gut hormones:

ممكن بعضكم يسال عن الفرق في الكلام الي هنا والسلايد الي قبلها هو نفس الشي اللهم زيادة في التفصيل.

The gut hormones	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 gall bladder & 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)

2) Digestion of proteins in small intestine

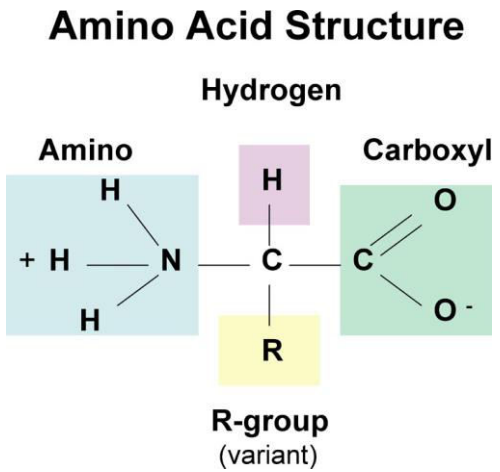
A. Digestion by pancreatic enzymes:

- 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

*In proteins, we have two terminals:
1)N-terminals: containing amino acids.
2)C-terminals: containing carboxyl group.
Carboxypeptidases break the C-terminals

Pancreatic enzymes:

Zymogen	Active enzyme	Activating enzyme
Trypsinogen	Trypsin (endopeptidase)	1) Enteropeptidase 2) Trypsin (autocatalysis)
Chymotrypsinogen	Chymotrypsin (endopeptidase)	Trypsin
Proelastase	Elastase (endopeptidase)	Trypsin
Procarboxypeptidases	Carboxypeptidases (exopeptidases)* Two types A & B	Trypsin

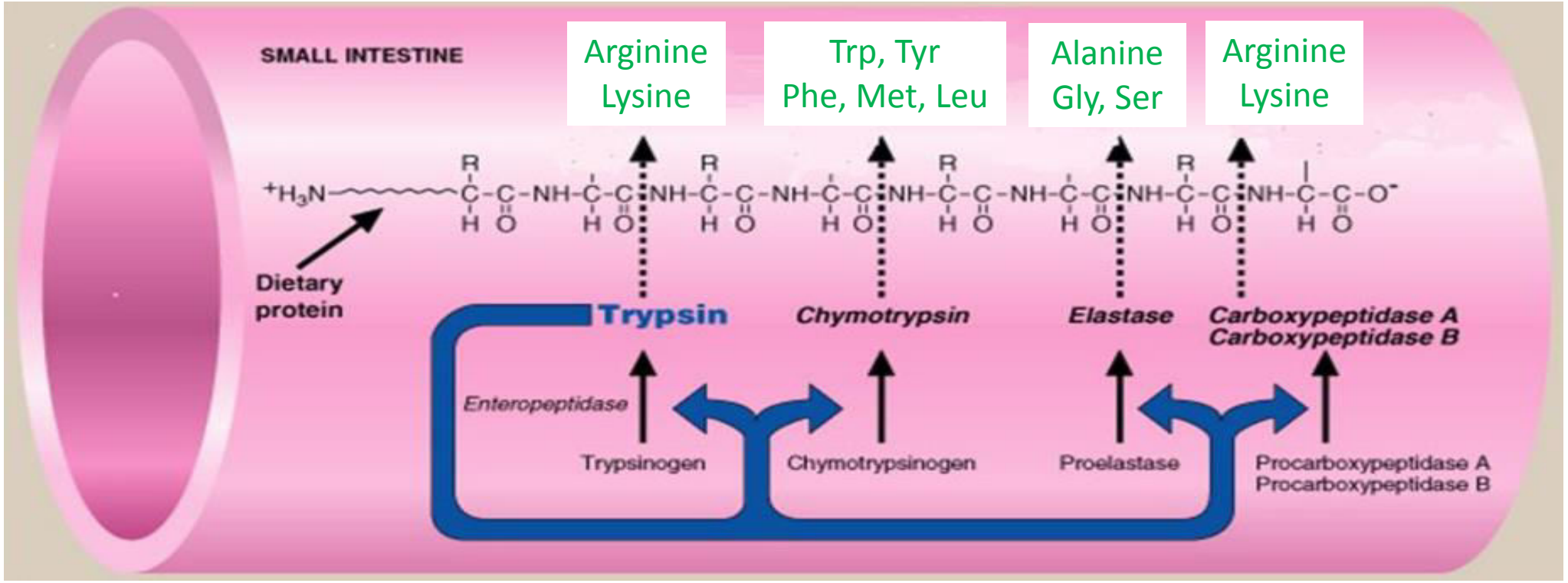


the structure of proteins

Activation of pancreatic enzymes

- Enteropeptidase is an enzyme synthesized by, and present on the luminal surface of intestinal mucosal cells of the brush border membrane,
- It Converts trypsinogen to trypsin (the conversion is initiated by this enzyme)
- Trypsin then activates all the other pancreatic zymogens (including itself)

Trypsin starts a cascade because it can activate all other pancreatic enzymes. Every protease is specific for different active site, polypeptides are their substrates and their products are oligopeptides and amino acids.



*Trp : Tryptophan , Tyr : Tyrosine , Phe : Phenylalanine , Met : Methionine , Leu : Leucine , Gly : Glycine , Ser : Serine

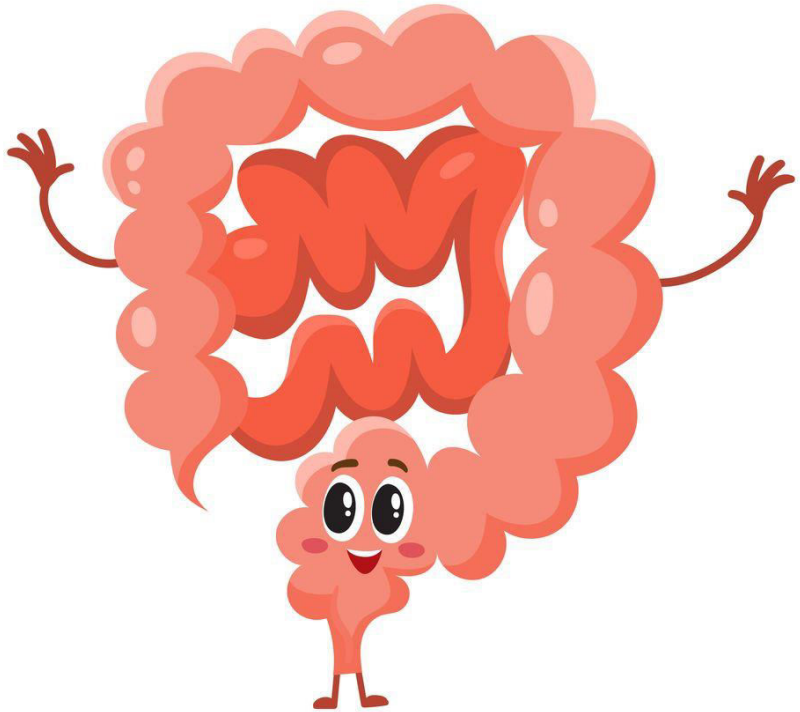
2) Digestion of proteins in small intestine

B. Digestion by intestinal aminopeptidase, which break the N-terminals of proteins > giving a lot of amino acids.

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

intestinal aminopeptidase

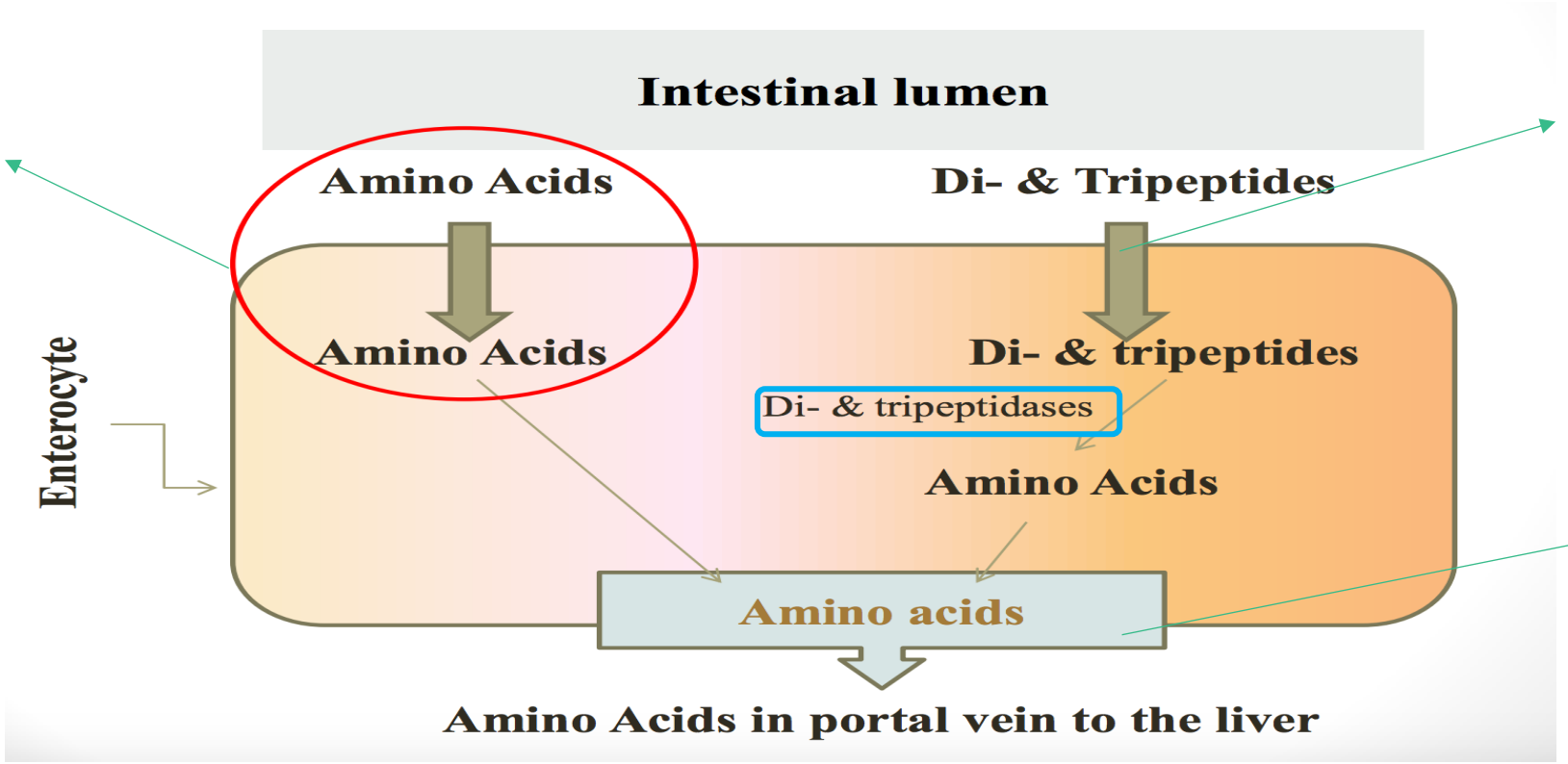
(an exopeptidase on the luminal surface of the intestine)



Absorption of digested proteins:

By sodium dependent transporter

They are formed by enterocyte and present inside it and also in brush boarder membrane in the luminal surface



By proton co-transporter

Released into blood by facilitated diffusion.

Genetic errors in amino acid transport:

Cystinuria	
About the disease:	is one of the most common genetic error of amino acid transport
Example of:	inherited disorder in the transport of certain amino acids
Affects:	the transport of Cystine and dibasic amino acids
Organs affected:	small intestine and the kidney
Clinically:	Cystine and dibasic amino acids appear in the urine
	there is kidney stones formation because they're not absorbed
Treatment:	Oral hydration (drinking lots of water) is an important part of treatment (to prevent kidney stones formation)

- Cystine = Amino acid
- Cysteine = 2 cystine (Di-peptide)

Dibasic amino acids : Have two replaceable H atoms (or two amino groups) and they are:

- Ornithine.
- Arginine.
- Lysine.

So the this 3 dibasic amino acids and the cystine are not reabsorbed.

COLA is a mnemonic can help to remember the 4 of them.

Abnormalities of protein digestion

Pancreatic insufficiency
(chronic pancreatitis, cystic fibrosis, and removal of pancreas)

→ Incomplete digestion and absorption of lipids and proteins because of lack of pancreatic enzymes .

→ Abnormal appearance of lipids (steatorrhea) & undigested proteins in 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.

Diagnosis is made by looking for anti-gliadin antibodies levels

Auto immune disease , gluten is metabolized to gliadin which will be attacked by anti-gliadin antibodies which will lead to inflammation, damage to enterocytes and malabsorption.
Symptoms are frequent diarrhea, abdominal pain, decrease in weight.

Carbohydrates digestion:

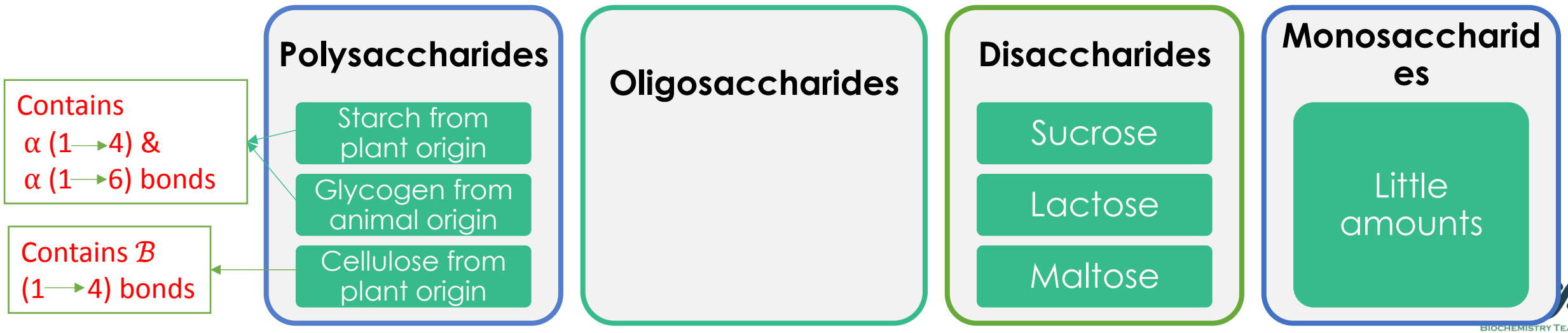
- Carbohydrates digestion is rapid:
- Generally completed by the time the gastric contents reach the junction of the duodenum & jejunum.
- Sites for digestion of dietary carbohydrates:

1. Mouth
2. Intestinal lumen

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

- $\mathcal{B}$ (1 , 4) can not be digested in human because we don't have enzymes for it
- Sucrose = Glucose & fructose
- Lactose = Glucose & galactose
- Maltose = two glucose units

Dietary carbohydrates



Enzymes for digestion of dietary carbohydrates:

Enzyme	Type of enzyme	Substrate
α-amylase	Salivary and pancreatic*	Polysaccharides
Disaccharidase	Intestinal	Disaccharides
Isomaltase=	Intestinal	Branch points of oligo- and di-saccharides
α (1,6) glucosidase		

- 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)

*Most of the digestion is due to pancreatic α-amylase because food doesn't stay in the mouth for a long time.

Serum level of α-amylase:

Normal level in serum: 25 -125 U/L (unit per liter)

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

It is usually coming from the pancreas to the serum

Diagnosis of acute pancreatitis:

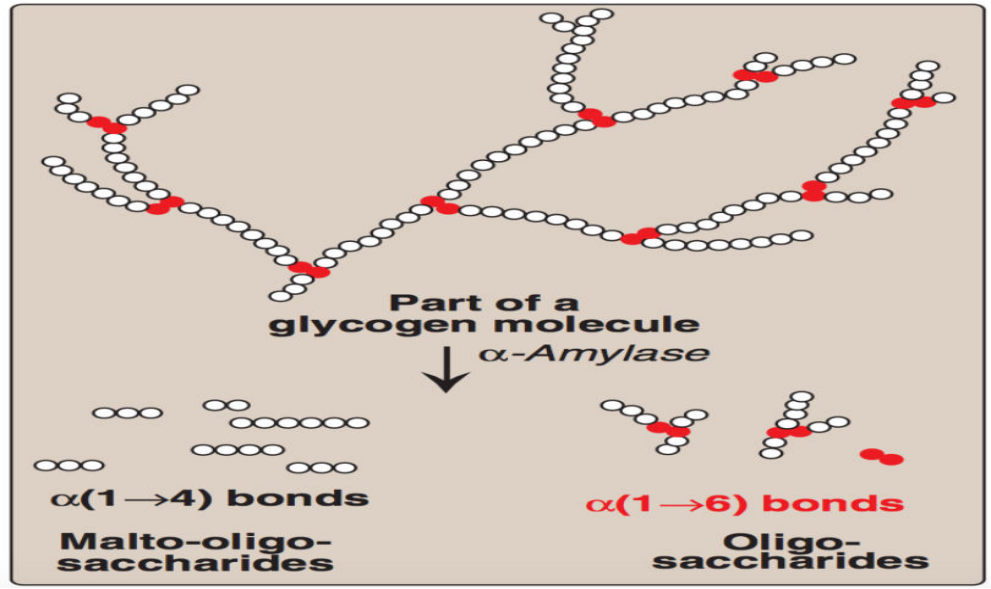
(damage of pancreatic cells : release & activation of the intracellular enzymes into the blood)

- Its level starts to rise within few hours.
- Reaches a peak within 12- 72 hours.
- Then returns to normal within few days, usually 5 days.

- α-amylase is not specific for pancreatitis so there is another enzyme (pancreatic lipase) when it also elevated we can confirm the diagnosis
- So if you make measurement after a week you won't find elevated levels of α-amylase, but lipase is much more specific when it is elevated it will be maintained for 8 days, then returns gradually to its normal levels within 14 days.

Effects of α-amylase on glycogen:

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



After every 8 to 10 amino acids we have a branch point

Final digestion of carbohydrates by intestinal enzymes in small intestine:

Enzymes	Source	Location of their action
• Disaccharidases • α (1,6) Glucosidase (for branched oligosaccharides)	Secreted by & remain associated with the luminal side of the brush border membranes of the intestinal mucosal cells	the mucosal lining of the jejunum.

Intestinal disaccharides:

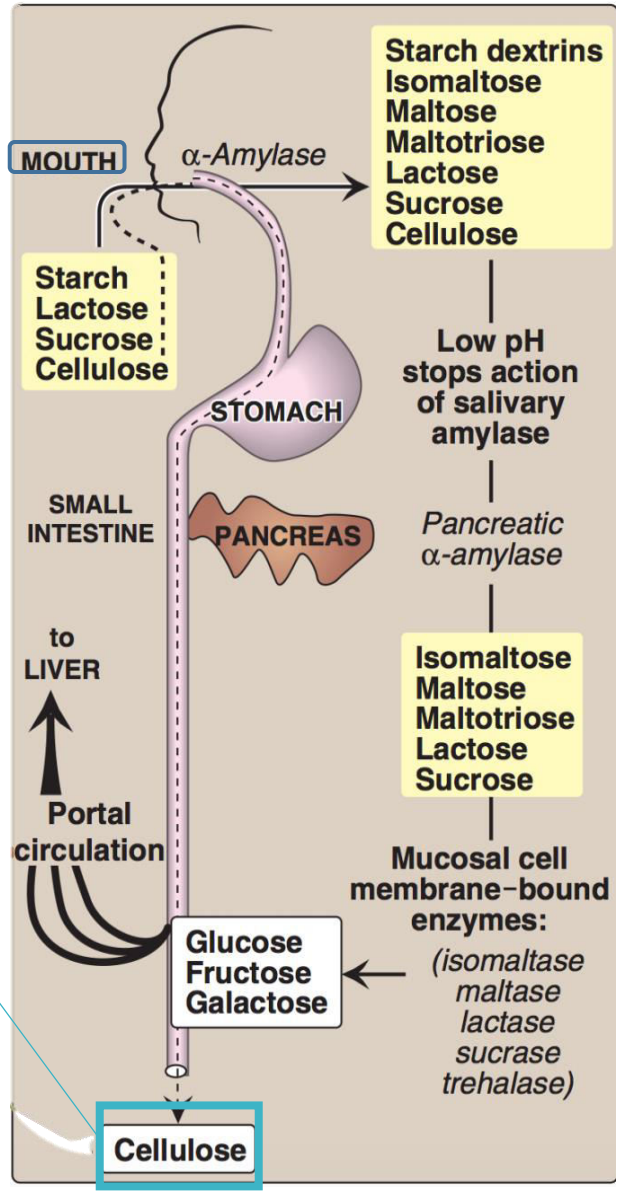
Enzymes	Substrate	Product
Isomaltase	Isomaltose	Two glucose
Maltase	Maltose	Two glucose
Sucrase	Sucrose	Glucose + Fructose
Lactase (α-galactosidase)	Lactose	Glucose + Galactose

Digestion of carbohydrates:

- Dietary cellulose *cannot be digested* due to the absence of enzyme that can cleave $\mathcal{B}$ (1-4) bonds.

  It passes through the GIT largely intact.
- Despite that, it has several beneficial* effects.
- *It Increases motility and treat constipation

Maltotriose = 3 glucose molecules connected together by alpha (1,4) bond

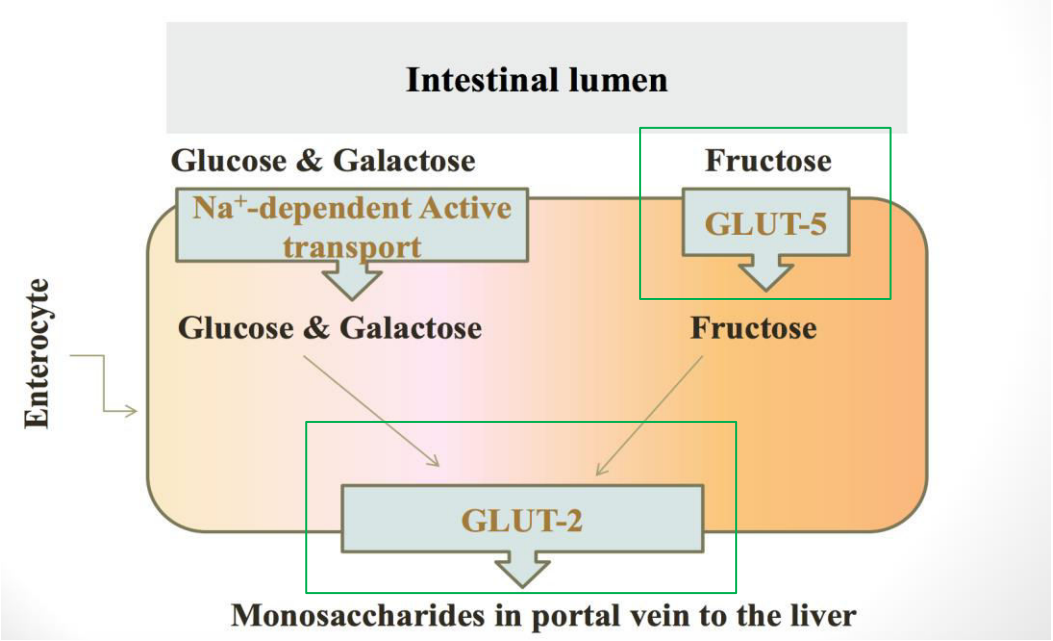


Absorption of monosaccharides by intestinal mucosal cells

- 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) Sodium independent
2) Active transport (Energy-dependent): Co-transport with Na^+ Sodium dependent

Absorption of digested carbohydrates



GLUT : Transports all monosaccharaides into the blood stream
Fructose enters the enterocytes by GLUT-5

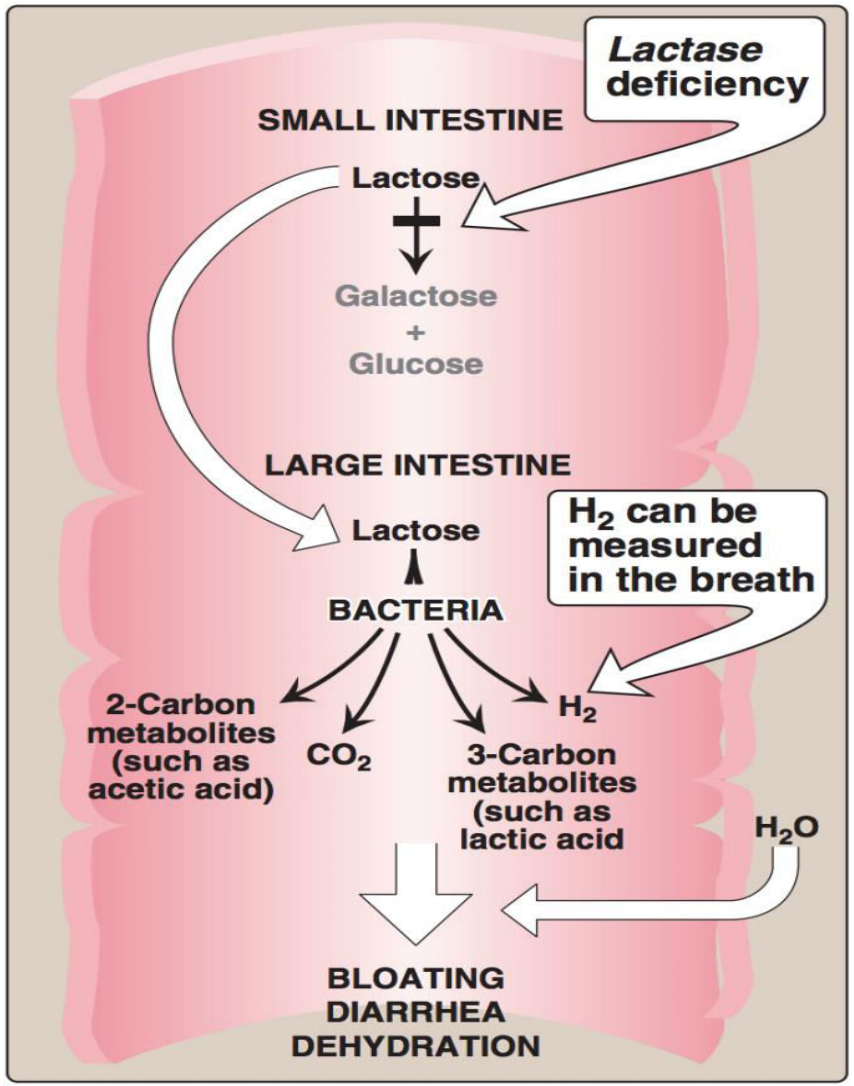
Abnormal digestion of disaccharides (e.g: lactose)

- **Lactose intolerance (Lactase deficiency)**

- Lactase (ℬ-galactosidase) deficiency → Undigested carbohydrate in large intestine → osmotic diarrhea.
- Bacterial fermentation of the undigested compounds in the large intestine → CO2 , H2 gas → abdominal cramps, diarrhea & distension (flatulence)

Lactose intolerance is common in adults

There are bacteria present in the large intestine, and the water reabsorbed to make the feces solid, people who have indigested carbohydrates in large intestine it is osmotically active and it will hold on to the water so these people develop diarrhea



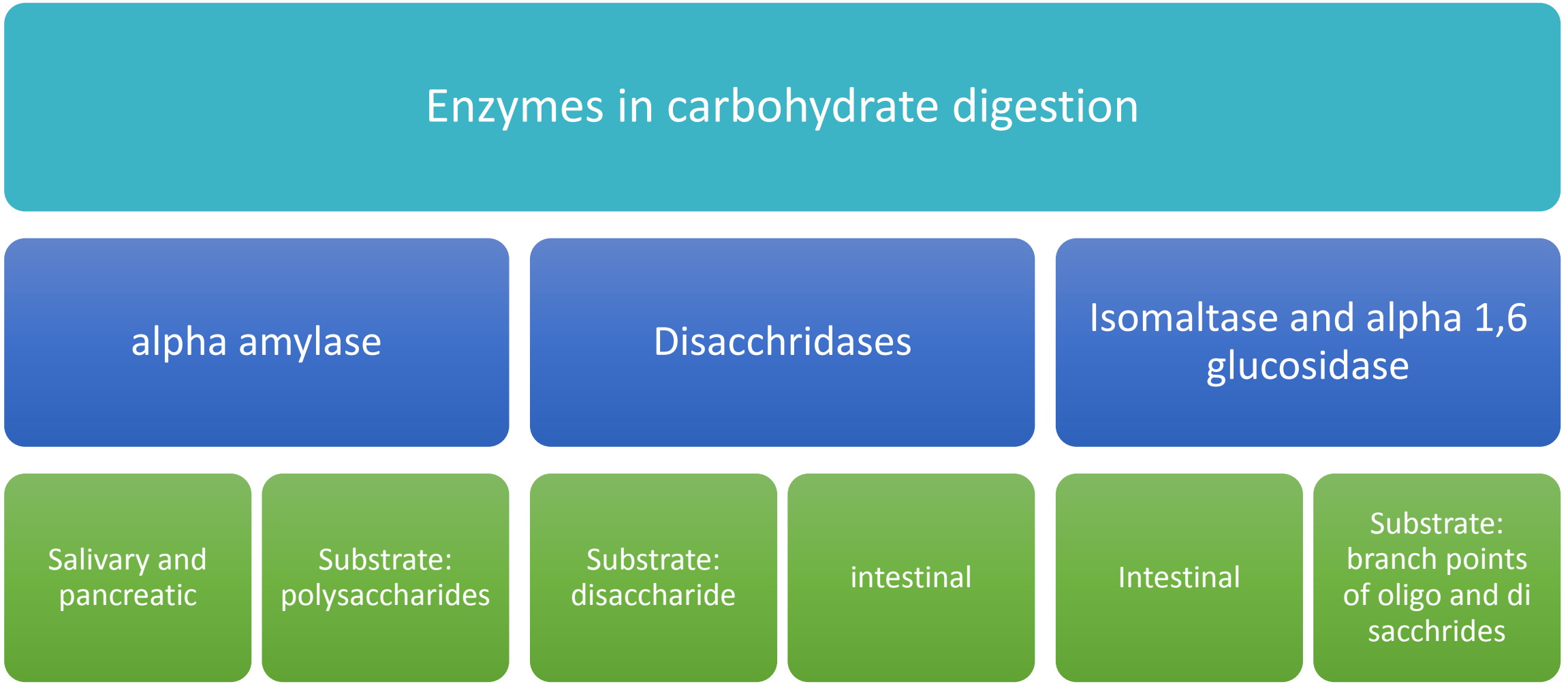
Take Home Messages -Digestion of Dietary proteins:

- ✓ 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.

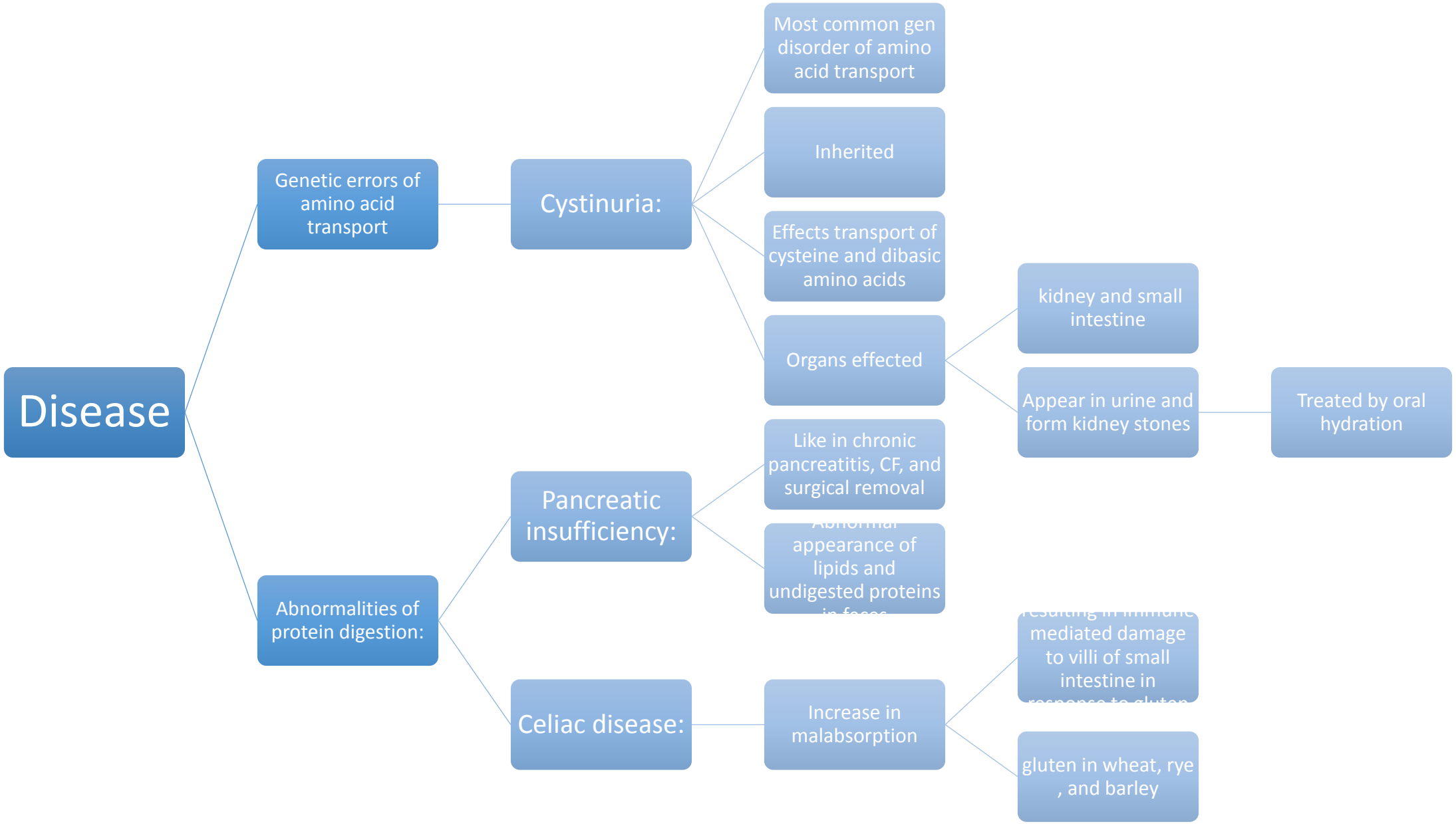
Take Home Messages -Digestion of Dietary carbohydrates:

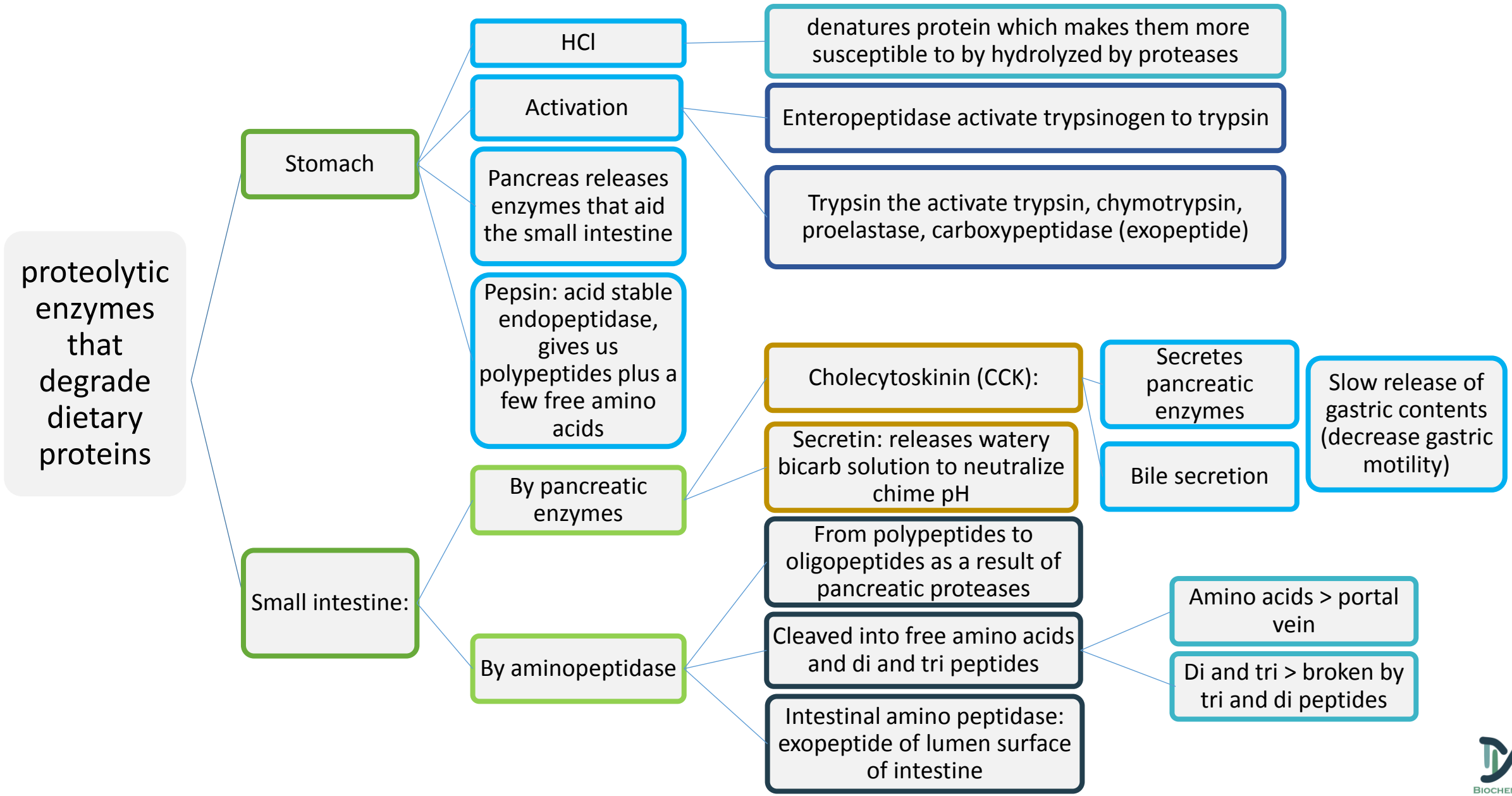
- ✓ Salivary α-amylase acts on dietary glycogen & starch in the mouth.
- ✓ Pancreatic α-amylase continues the process of polysaccharide digestion in small intestine.
- ✓ The final digestive processes of carbohydrates into monosaccharides occur at the mucosal lining of the small intestine by disaccharidases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

Summary


Enzymes in carbohydrate digestion
alpha amylase
Disacchridases
Isomaltase and alpha 1,6 glucosidase
Salivary and pancreatic
Substrate: polysaccharides
Substrate: disaccharide
intestinal
Intestinal
Substrate: branch points of oligo and di sacchrides

Summary


Disease
Genetic errors of amino acid transport
Cystinuria:
Most common gen disorder of amino acid transport
Inherited
Effects transport of cysteine and dibasic amino acids
Organs effected
kidney and small intestine
Appear in urine and form kidney stones
Treated by oral hydration
Abnormalities of protein digestion:
Pancreatic insufficiency:
Like in chronic pancreatitis, CF, and surgical removal
appearance of lipids and undigested proteins
Celiac disease:
Increase in malabsorption
mediated damage to villi of small intestine in
gluten in wheat, rye , and barley



Summary

Intestinal Disaccharides			Absorption of monosaccharides
Enzyme	Substrate	Product	Location: Duodenum and jejunum
isomaltase	isomaltose	2 glucose	No insulin required for reuptake of glucose by intestinal cells
maltase	maltose	2 glucose	Mechanisms of absorption:
sucrase	sucrose	Glucose and fructose	GLUT- facilitated
Lactase	lactose	Glucose and galactose	Active – Na co-transport

QUIZ

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

QUIZ

Q7 : The absorption of monosaccharides occurs in ?

Duodenum & upper jejunum.

Q8 : Mention two hormones that control the digestion of proteins in small intestine?

1. Cholecystokinin (CCK)
2. Secretin

Q9 : Name three disorders that will result in Proteins malabsorption ?

1.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.

2.Pancreatic insufficiency
incomplete digestion & absorption of lipids & proteins
abnormal appearance of lipids (steatorrhea)

3. Cystinuria
Inherited disorder - affect the transport of cystine + dibasic Amino Acid which will appear in the urine. - the organ affected is small intestine and kidney. - Kidney stone formation-Oral hydration .

Suggestions and recommendations

1) C 2) A 3) A 4) B 5) B 6) C

TEAM LEADERS

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Rania Alessa

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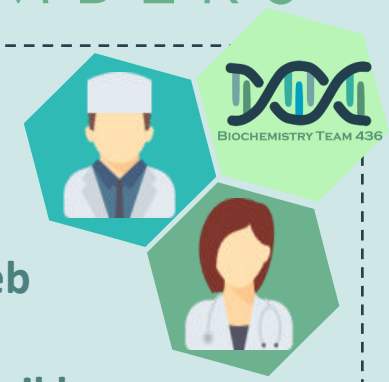

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Heba Alnasser

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THANK YOU

FOR CHECKING OUR WORK

PLEASE CONTACT US IF YOU HAVE ANY ISSUE

- Lippincott's Illusrated Reviews Biochemistry 6th E

Review the notes

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