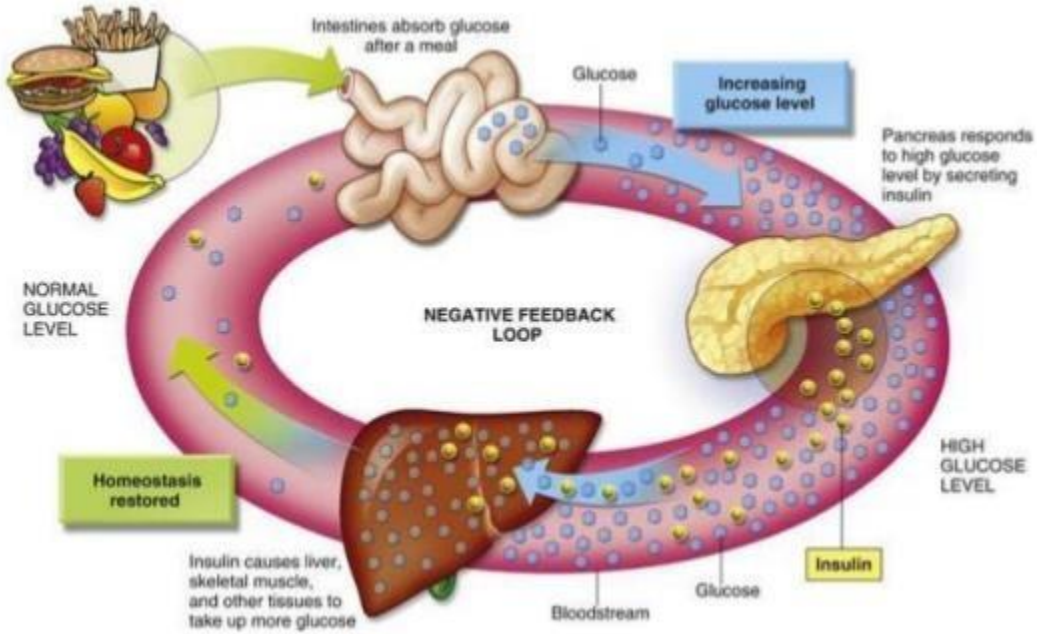


Carbohydrates Metabolism

Dr. Diala Abu-Hassan

Review of Carbohydrates

Digestion and absorption of carbohydrates

Suggested Readings:

1: Lippincott's Illustrated reviews: Biochemistry

2: Marks' Basic Medical Biochemistry

Metabolism differ from Digestion.

Digestion :- Something about GI system, How the food molecule will be degraded into smaller (absorber) Molecules → (إلي ممكن يمتصه الجسم) كيف يمتصه؟ → passage of these molecule into intestinal lumen through intestinal cells to the portal circulation.

- while Metabolism :- what happen to these molecules inside the cells (بغض النظر من وين اجوا الـ Molecules)

→ سواء من Diet أو other Sources.

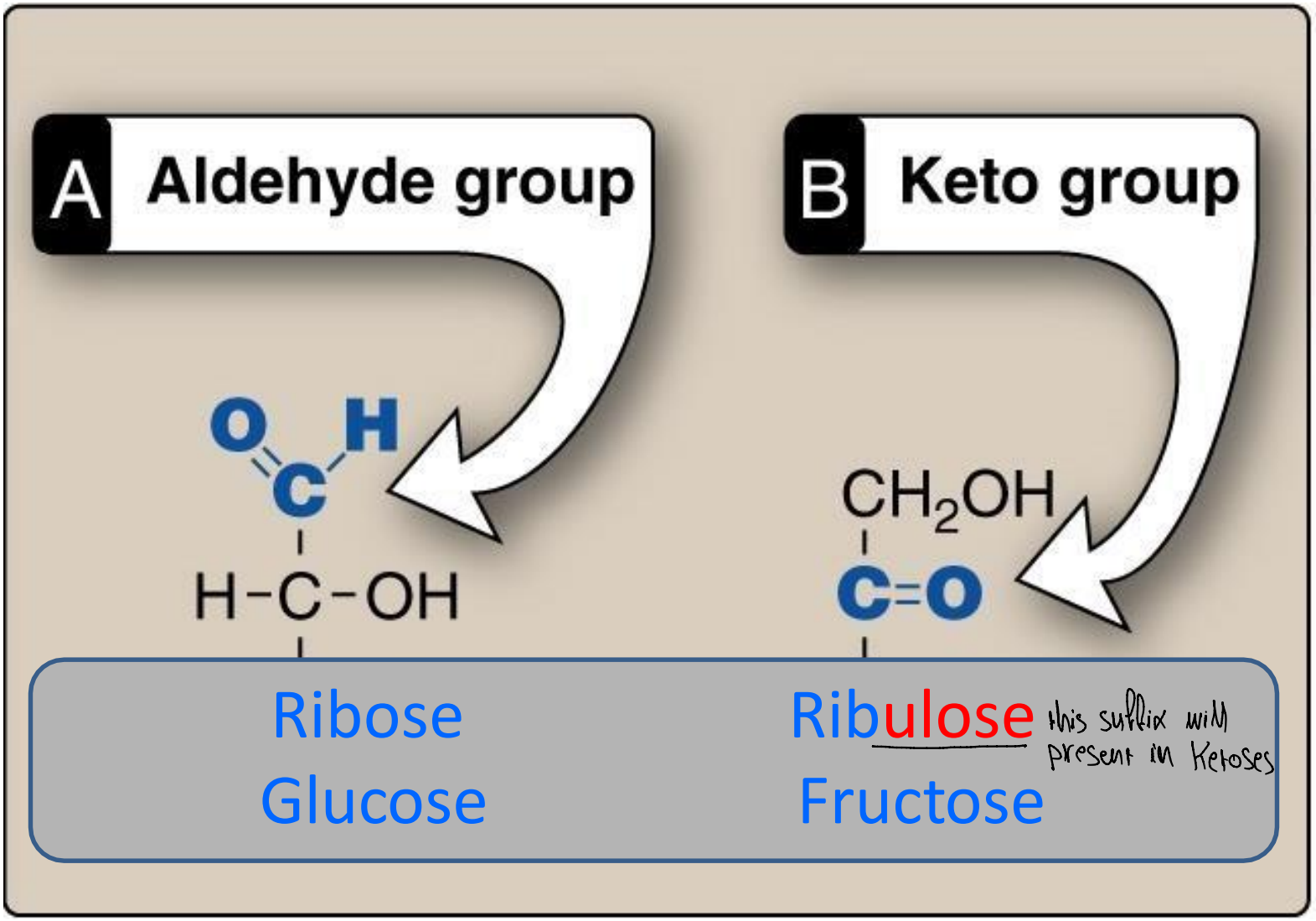
- The definition of carbohydrate :- They are Poly hydroxy Keton or Aldehyde
- Most of Suger are Aldoses.
- The simplest Aldehyde has a Chiral Center while the simplest Keton hasn't

So we don't have Steroisomer for Dihydroxyaceton (DHAP)

Carbohydrates Metabolism Topics

- Utilization of Glucose → Energy
- Non-Carbohydrates → Glucose
- Storage of Glucose → Glycogen
- Release of Glucose from Glycogen
- Reducing Power NADPH >> GSH
- Glucuronic acid >> Drug metabolism
- Interconversion of sugars

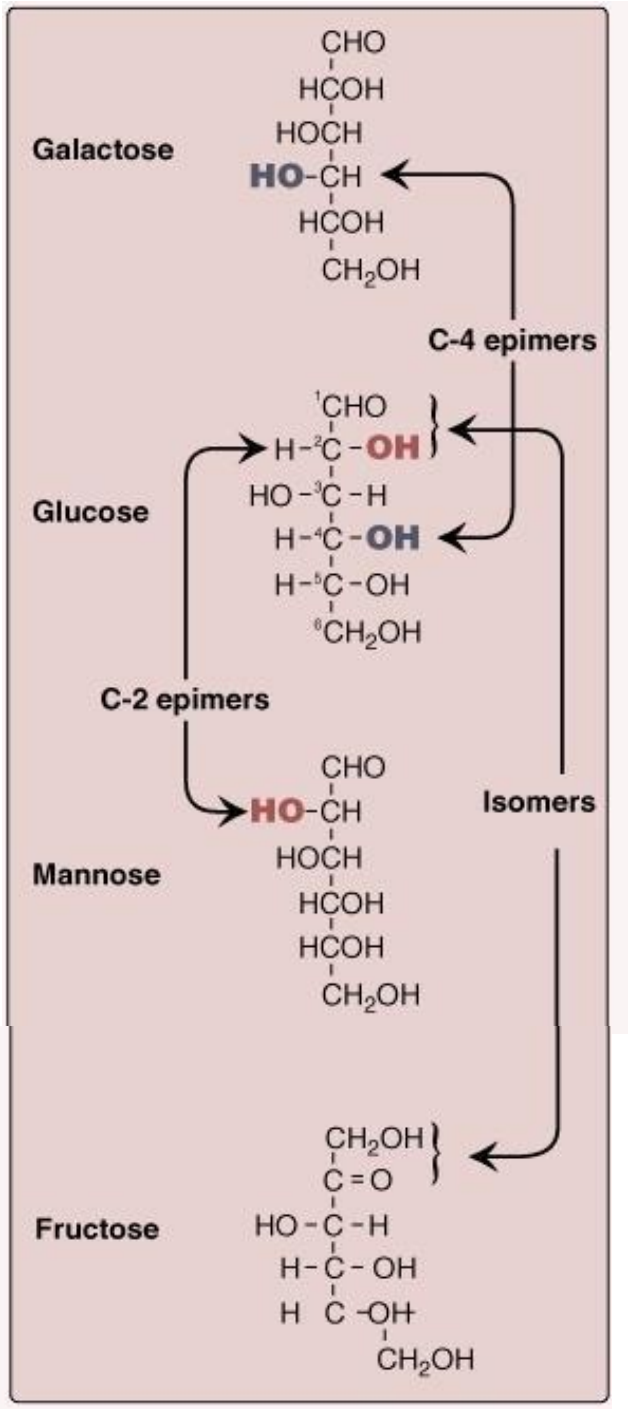
Sugars are either aldoses or ketoses



Examples of monosaccharides found in human

- موجودة الأكثر إما Pentoses or hexoses

Generic names		Examples
3 carbons:	trioses	Glyceraldehyde
4 carbons:	tetroses	Erythrose
5 carbons:	pentoses	Ribose
6 carbons:	hexoses	Glucose
7 carbons:	heptoses	Sedoheptulose
9 carbons:	nonoses	Neuraminic acid



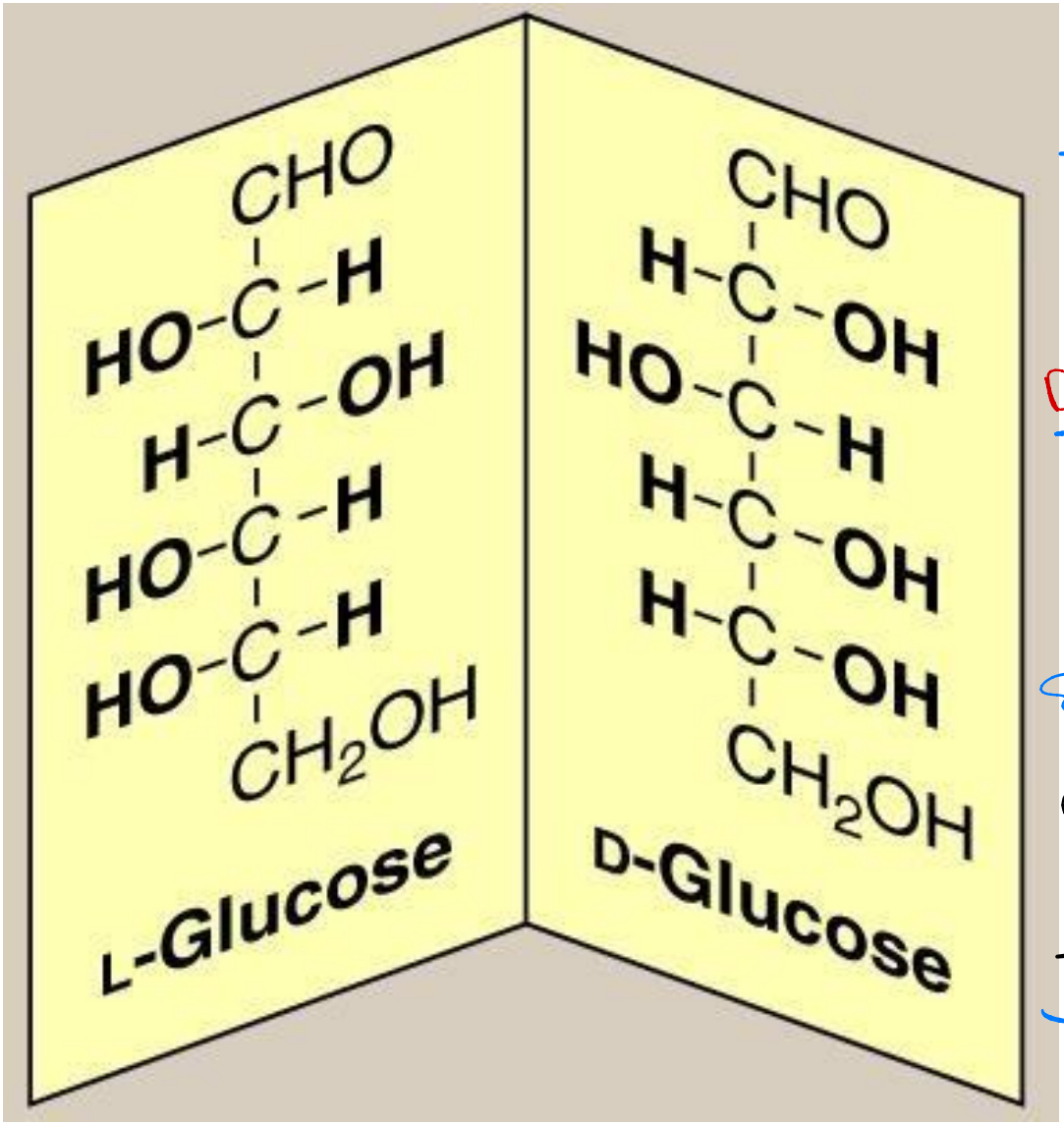
Sugars have Isomers

Epimers are isomers:

Changing the orientation of one hydroxyl group will produce a different sugar

Glucose and Fructose are isomers

Enantiomers



- The predomenant isomer in our cells is D-Sugar.

- اللي كيس:-

- في حالة enantiomers بظل السكر نفس الاسم بس بيبلش مرة D ومرة L

- في حالة Diasteriomers بتغير الاسم مثل:- glucose Vs. mannose.

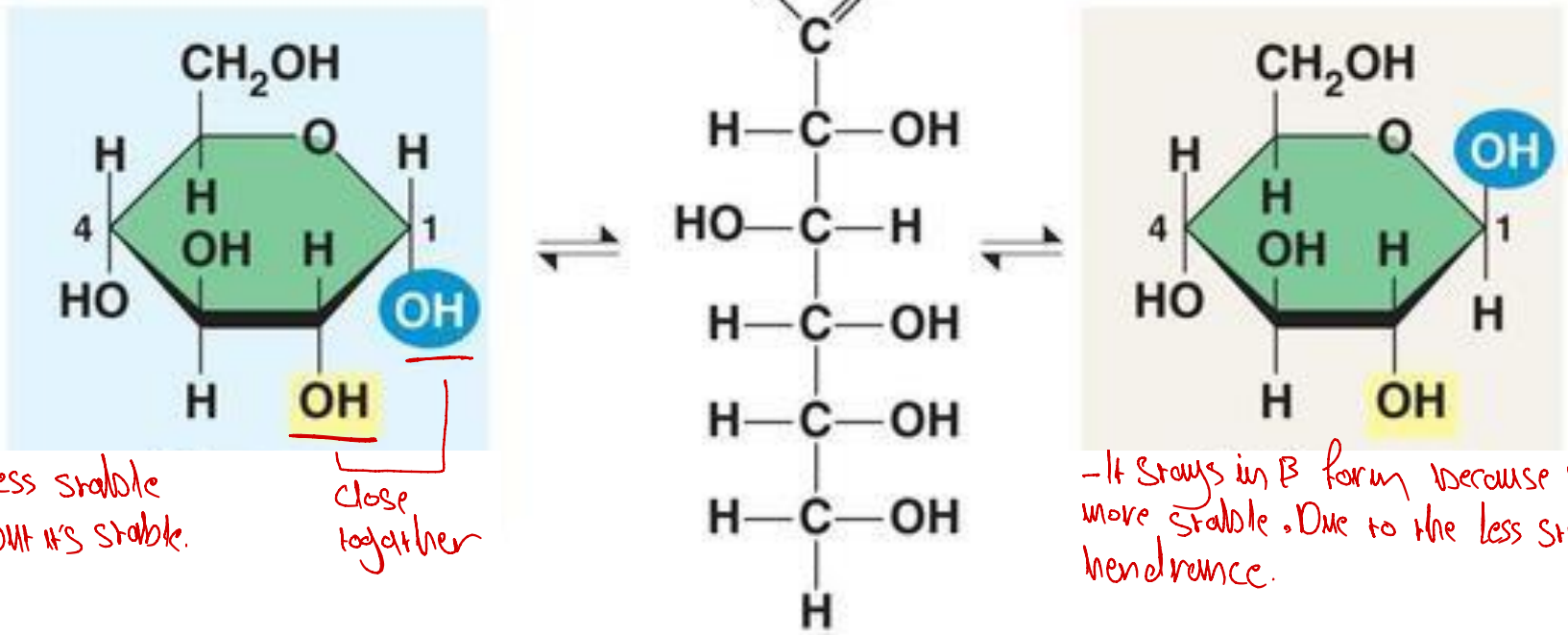
- في حال ما انعكس اتجاه كل الـ OH، مجرد كذا، وهي انعكسوا بسمي العلاقة Diasteriomer

- في عنا نوع منه بكون اسمه epimers لما يتغير اتجاه OH وحدة (يعني بس Chiral center وحدة بس عليها تغير)

- مثال عليها العلاقة بين glucose Vs. galactose.

Alpha and Beta Sugars (Anomers)

-Here the OH oriented in two form : ① below the ring which called ∝
② above the ring which called β



-∝ just less stable than β, but it's stable.

close together

-It stays in β form because it is more stable. Due to the less steric hendrance.

α-D-Gluco-pyranose | D-Glucose | β-D-Gluco-pyranose

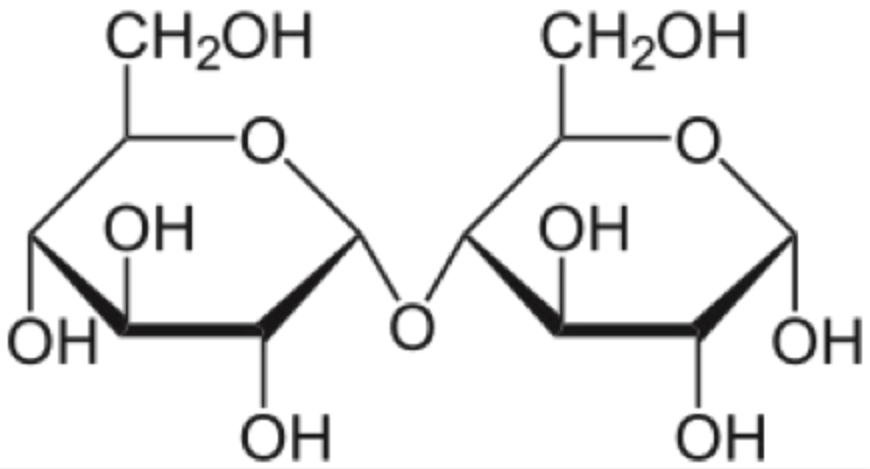
*Sugers they are ring structure more than linear because of the reaction between OH group and Carbonyl group

*The ring structure more stable.

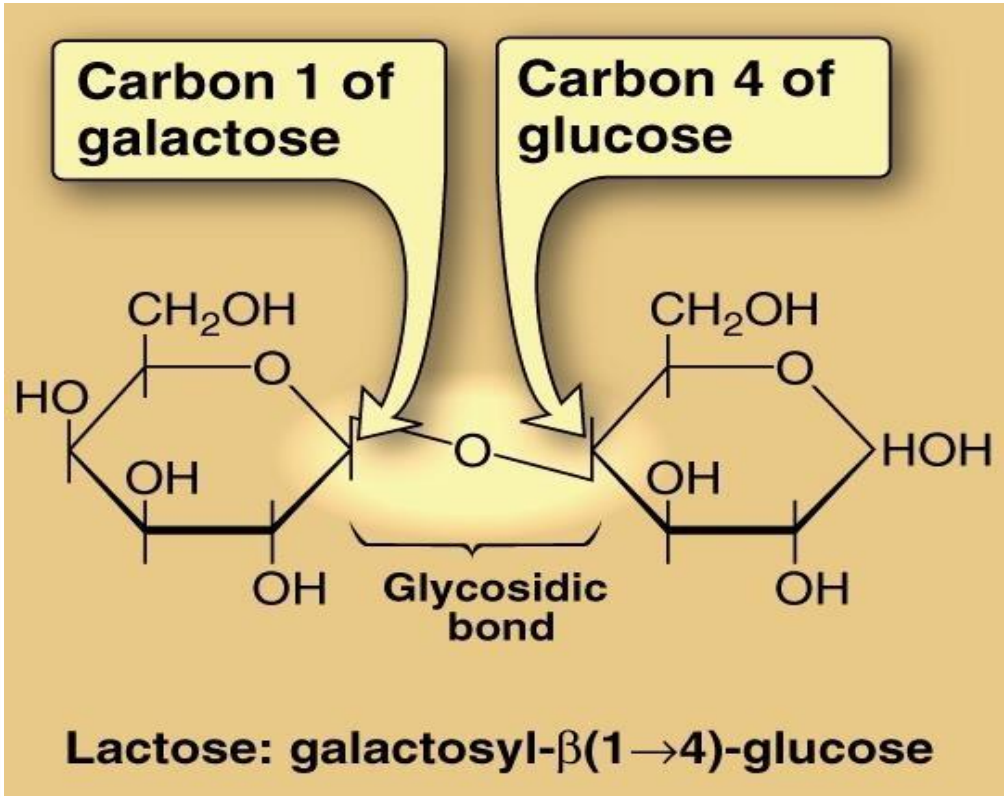
https://mysciencesquad.weebly.com/ib-hl-23a1--s1-cellulose--starch-v-glycogen.html

Disaccharides

Sugars made of two monosaccharide units joined by a glycosidic bond

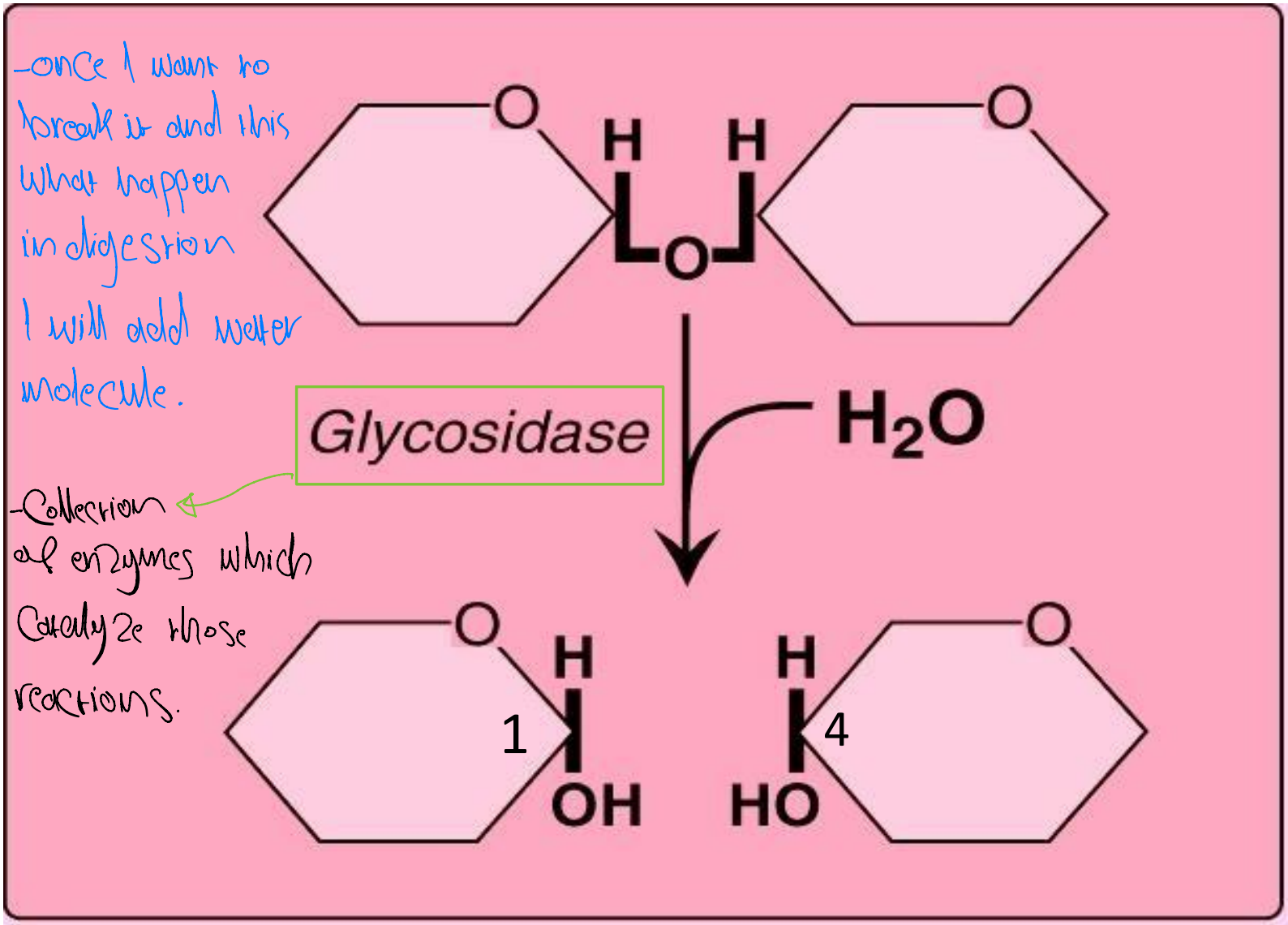


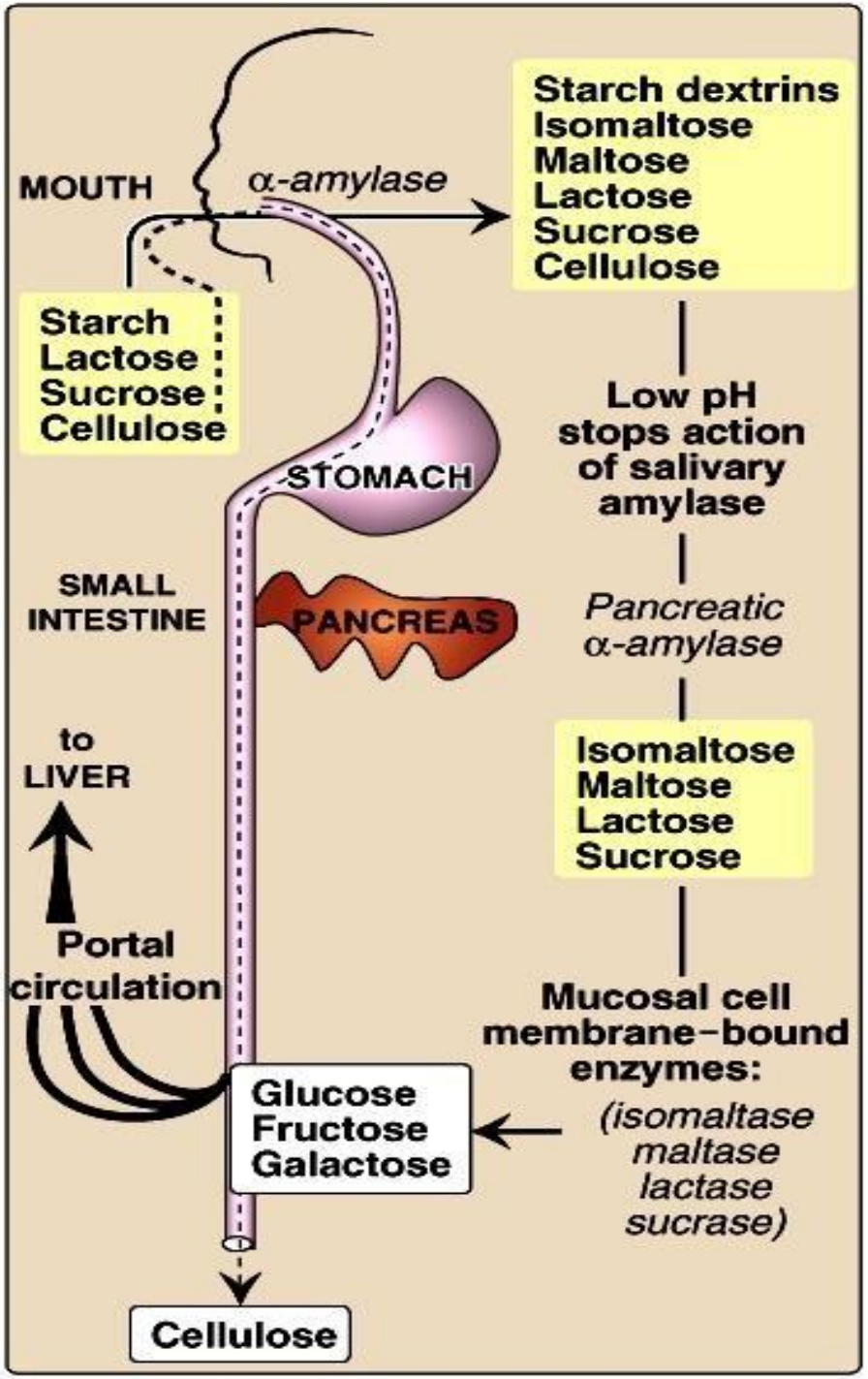
Maltose: a disaccharide made from two glucose units (α 1-4 linkage)



- Homo disaccharide which has the same monosaccharides residue

Glycosidic bond is cleaved by glycosidase enzyme





Digestion of Carbohydrates

How does digestion occure for Carbs ? اول شي تخيل انك أكلت (مثلاً مهلبية

- The sugers enter into oral cavity where we have α-amylase that act on α 1-4 linkage between glucose residue ⟶ Maltose and starch وهاي الرابطة في، But this enzyme ⟶ بشتغل بس ع starch

- This enzyme is an endoglycosidase which act on the inside linkage and break it down randomly which usually result in Disacharides production (sometime monosacharides).

في الصورة بالسلايد اللي بعده انشوف نواتج أول عملية بالهضم (مش ممكن يطلع انواع سكر معنا).

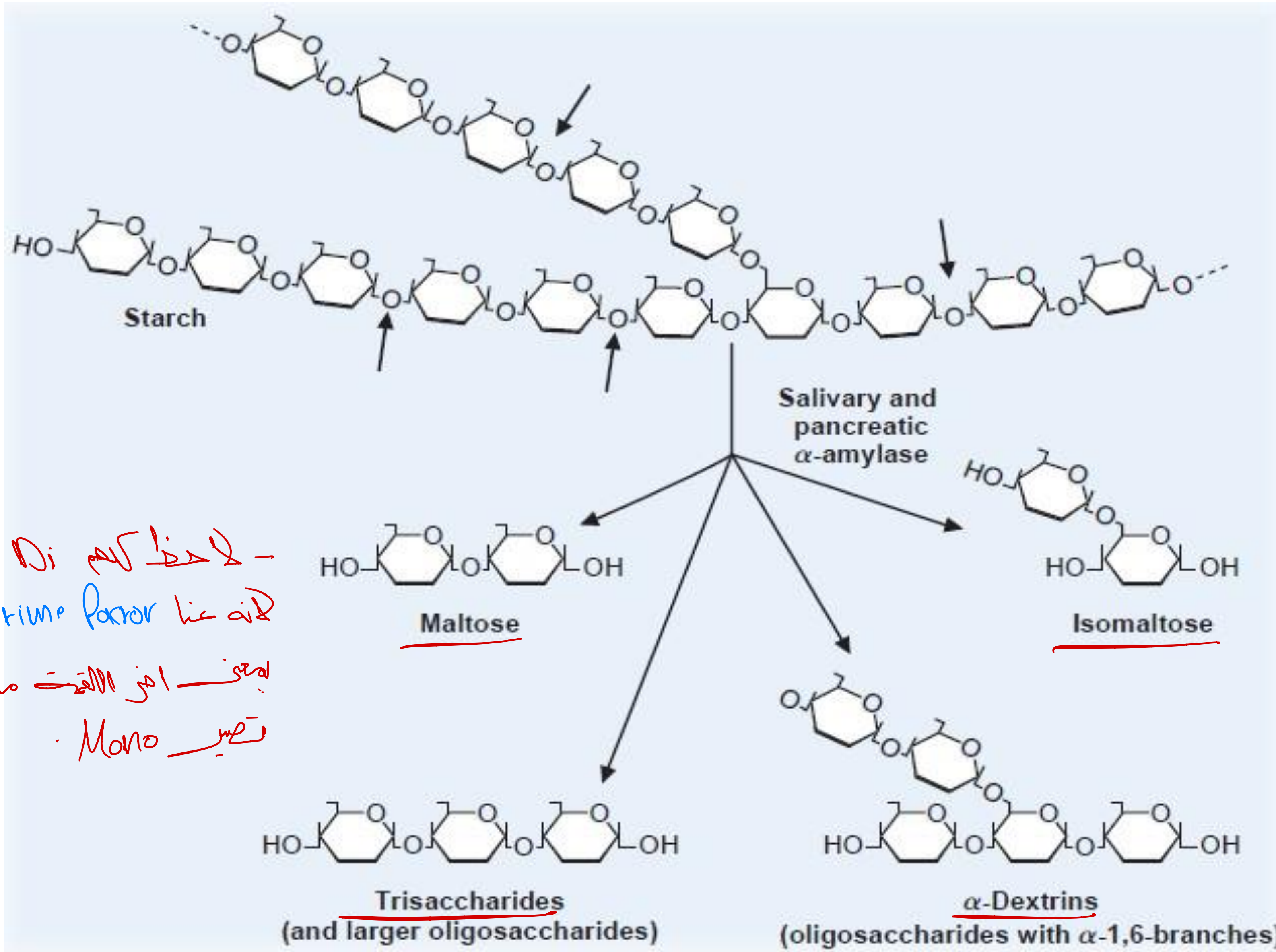
- The second step is ⟹ after we break down this starch. the mixture of sugers will move to the stomach (The acidic environment where the pepsine enzyme there) but pepsine is a hydrolyze enzyme for proteins Not carbs ! So no thing happen to carb in stomach.

- The 3rd step ⟹ They move to the Duodenum (where the pancreatic secreations are released) pancareatic acid is a mixture of enzymes (amylase, lipase, protease) amylase digest starch.

- The resulting disacharides will move deeper to small intistin where they incounter the intistinal mucosal enzymes. هدول موجودين بنفس ال intistin مش جايين من pancreas

في الهم جدول بيجي بالسلايدات .

Starch Digestion



- لاحظ كلهم Di مش Mono
لأنه عنا time factor
يعني أمر اللقمة ما بتلحق
تصير Mono.

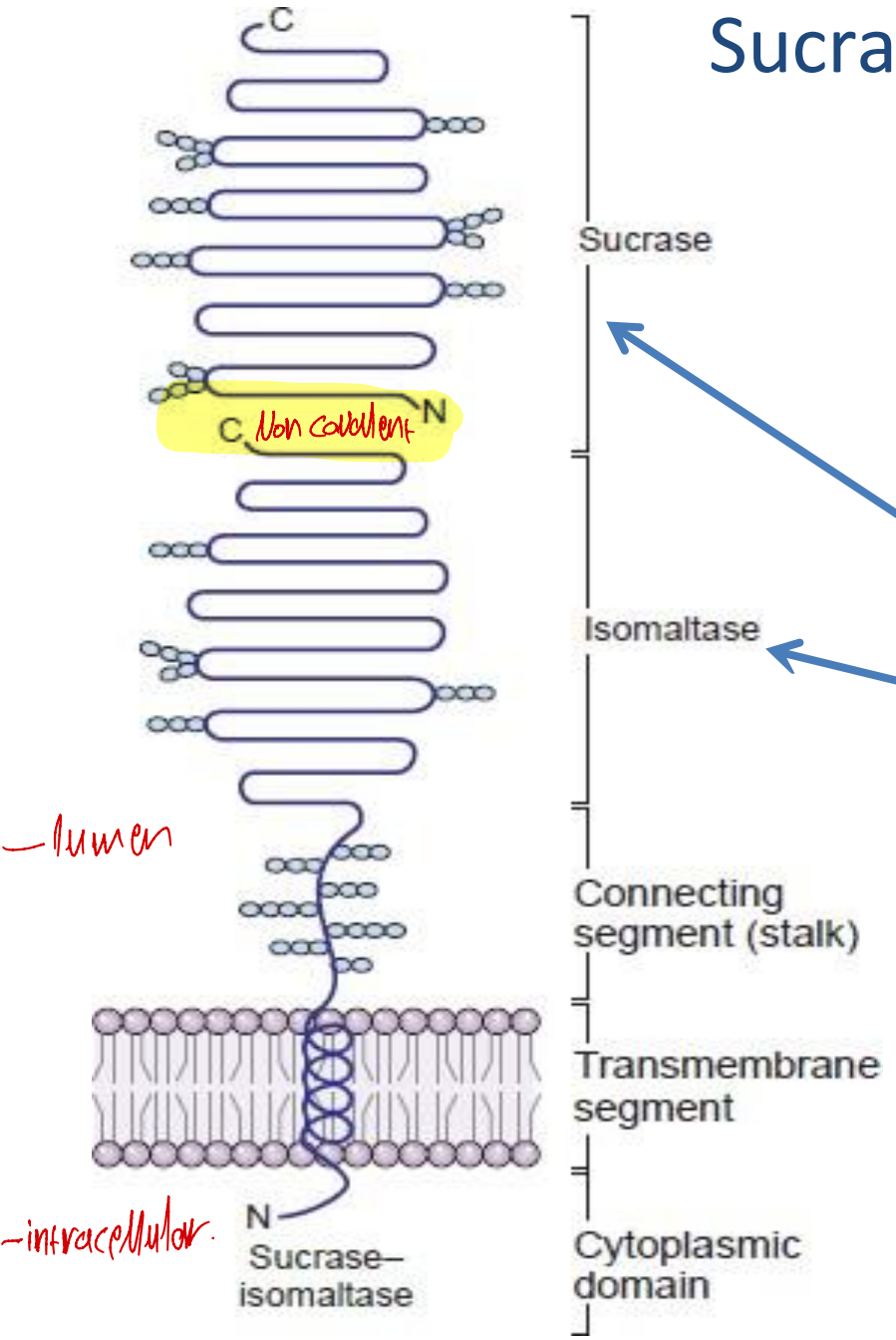
affinity of binding to its receptors.

Mucosal cell membrane-bound enzymes

ENZYME	Bond Cleaved	Substrates
Isomaltase	α 1→6 between glucose and glucose	Isomaltose
Maltase	α 1→4 between glucose and glucose	Maltose
Sucrase	α 1→2 between glucose and fructose	Sucrose
Lactase	β 1→4 between glucose and galactose	Lactose
Trehalase	α 1→1 between glucose and glucose	Trehalose
Exoglycosidase	α 1→4	Glucoamylose

- Trehalose : Disaccharide that is made of two glucose and the linkage is (α 1-1) between 2 anomerics
- has protective role in body.

Sucrase-isomaltase complex and Glucoamylase



* Sucrase + isomaltase
  Single protein → complex of two associated subunits
  -Sucrase-maltase
  - Isomaltase-maltase
  Together 80% of the maltase activity

*Maltase + exoglycosidase (glucoamylase): no split

Sucrase and isomaltase are incoded by one gene So it is one poly peptide chain

سب !! هاد الـ poly peptide منطقة منها تشتغل لـ Sucrase ومنطقة لـ isomaltase

- This polypeptide chain is going to be inserted into the membrane of the intestinal cells where very smalle part of it intracellular and the majority is extracellular in the lumen part (where the residue of sugers found).

- Both part of this enzyme have a maltase activity ⇝ يعني تشتغلوا كمان ع الـ Maltose

- They are encoded by the same gene, they are single polypeptide chain that is get glycosalyted as a posttranslation modification + it get cleaved posttranslationally

- لاحظوا بالسلايد الي فوق عند الهايلايت الأصفر صار عنا N-terminus جديدة وعنا كمان C-termenus بس !!

شو بصير بـ sucrase، هل راح تنبت بالـ lumen ؟ - لا طبعًا (ممنوع حد تنايت عنا ☺)

- It stays connected to the same protein to the same complex by non-Covalent interactions. ⇝ covalent شو ممكن تكون اهميتها ؟ - بتعطيها flixibility بالحركة أكثر مما لو كانت

- وفي عنا واحد ثاني اسمه Maltase exoglycosidase complex نفس قصة الي فوق بس اللهم ما بصير فيه cleavage

Lujain

Sucrase-isomaltase complex

FIG. 27.5. The major portion of the sucrase–isomaltase complex, containing the catalytic sites, protrudes from the absorptive cells into the lumen of the intestine. Other domains of the protein form a connecting segment (stalk) and an anchoring segment that extends through the membrane into the cell. The complex is synthesized as a single polypeptide chain that is split into its two enzyme subunits extracellularly. Each subunit is a domain with a catalytic site (distinct sucrase–maltase and isomaltase–maltase sites). In spite of their maltase activity, these catalytic sites are often called just *sucrase* and *isomaltase*.

Clinical Hint: Abnormal Degradation of disaccharides

1. Sucrase-isomaltase deficiency:

يعني يكون بالوضع الطبيعي ... او العكس تماماً.

all or non

بشكل عام دائماً لما تشكوا بـ mutation ما توخذوها انها all or non

عادي في mutations ممكن تأثر ع 80% من عمل الجين وبعضها ع 20% وهكذا.

- Causes:
  - Genetics
  - Variety of intestinal diseases
  - Malnutrition
  - Injury of mucosa i.e by drugs
  - Severe diarrhea

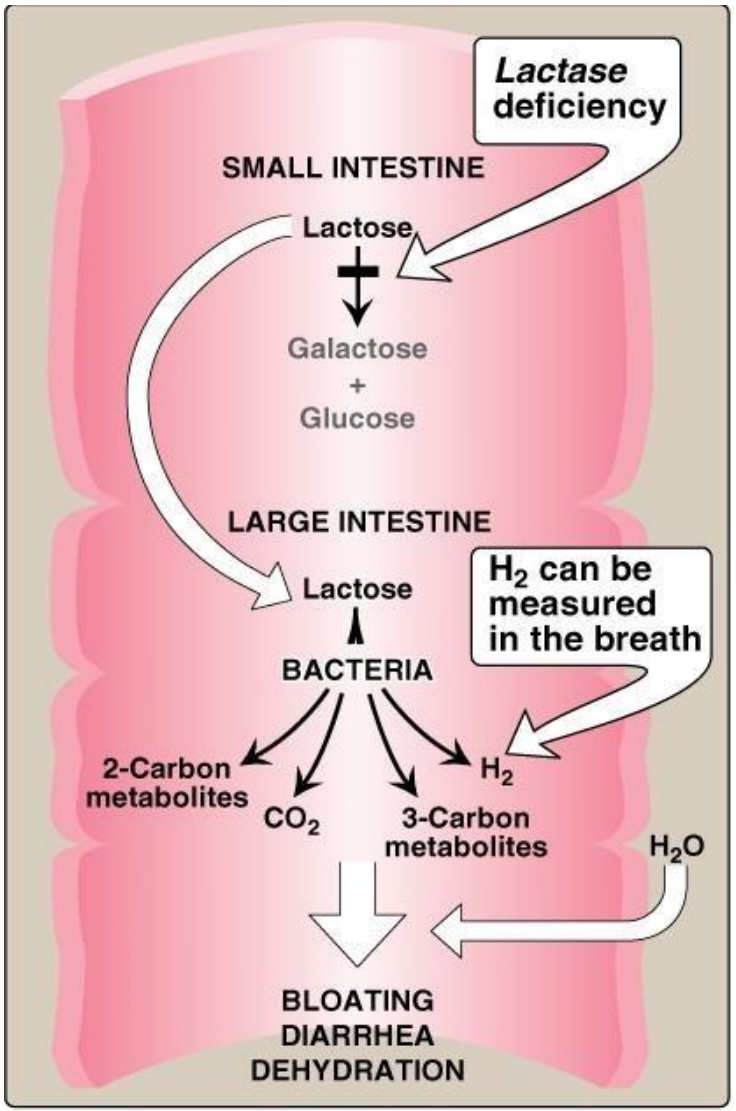
→ بأثر ع all enzyme

يعني مش بس هضم الكارب يتأثر

Clinical Hint: Abnormal Degradation of disaccharides

2. Lactase deficiency: ½ world's population

Lactose intolerence



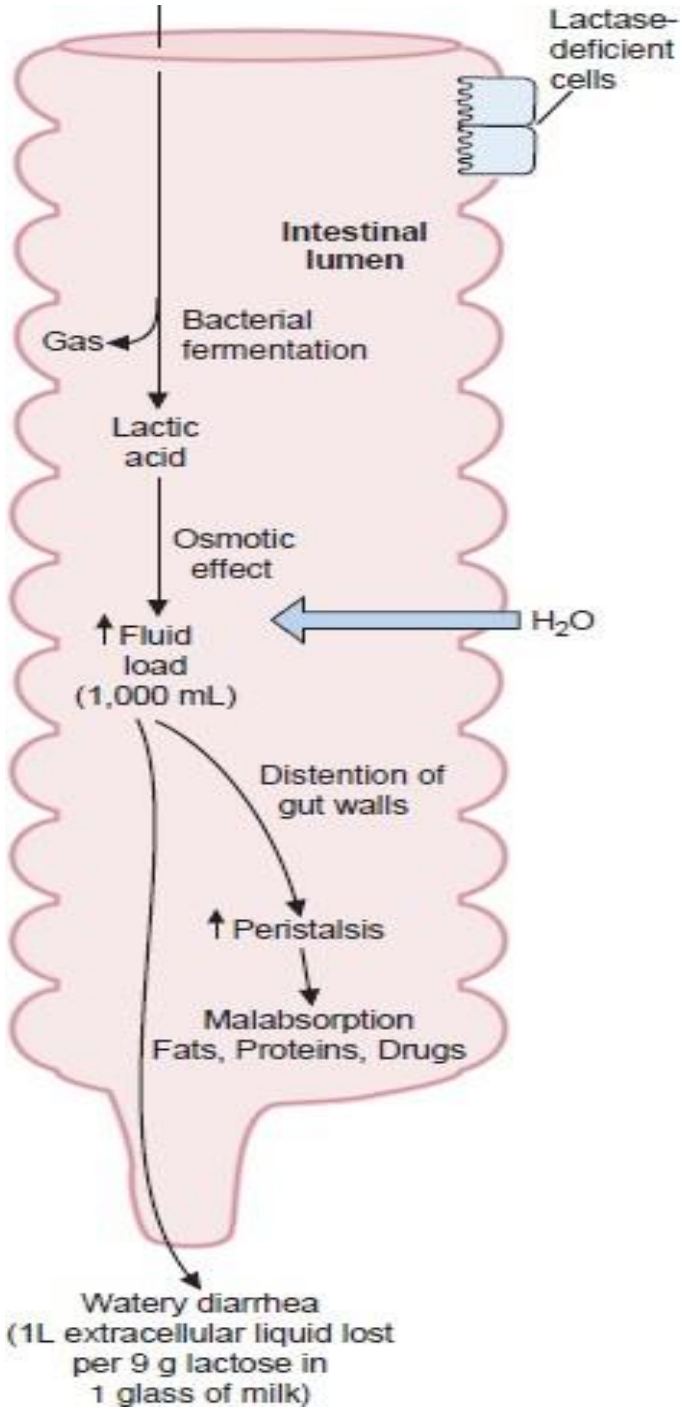
Lactase reached maximal activity @ 1 month of age

Declines ----- >> adult level at 5 to 7 year of age

10 % of infant level

— normally the infant rely mainly on milk

1 cup of milk (9 grams of lactose) → loss of 1 liter of extracellular fluid — The osmoric pressure will increase due to drain more H_2O from cells and interstetium fluid to the lumen. (cause diarrhea)



Lactase deficiency

- because of lack of this enzyme lactase.

bacteria will use lactose in its metabolism and produce gases (methan, CO_2).

→ Movement of sugar from the lumen to intestinal cells to portal circulation.

Absorption of Sugars

— Here we need sugar to be Monosaccharides.

Polar molecules can not diffuse

A: Na^+-independent facilitated diffusion transport

- No need of energy
- They need carriers.
- Down the gradient.

GLUT 1-----GLUT 14

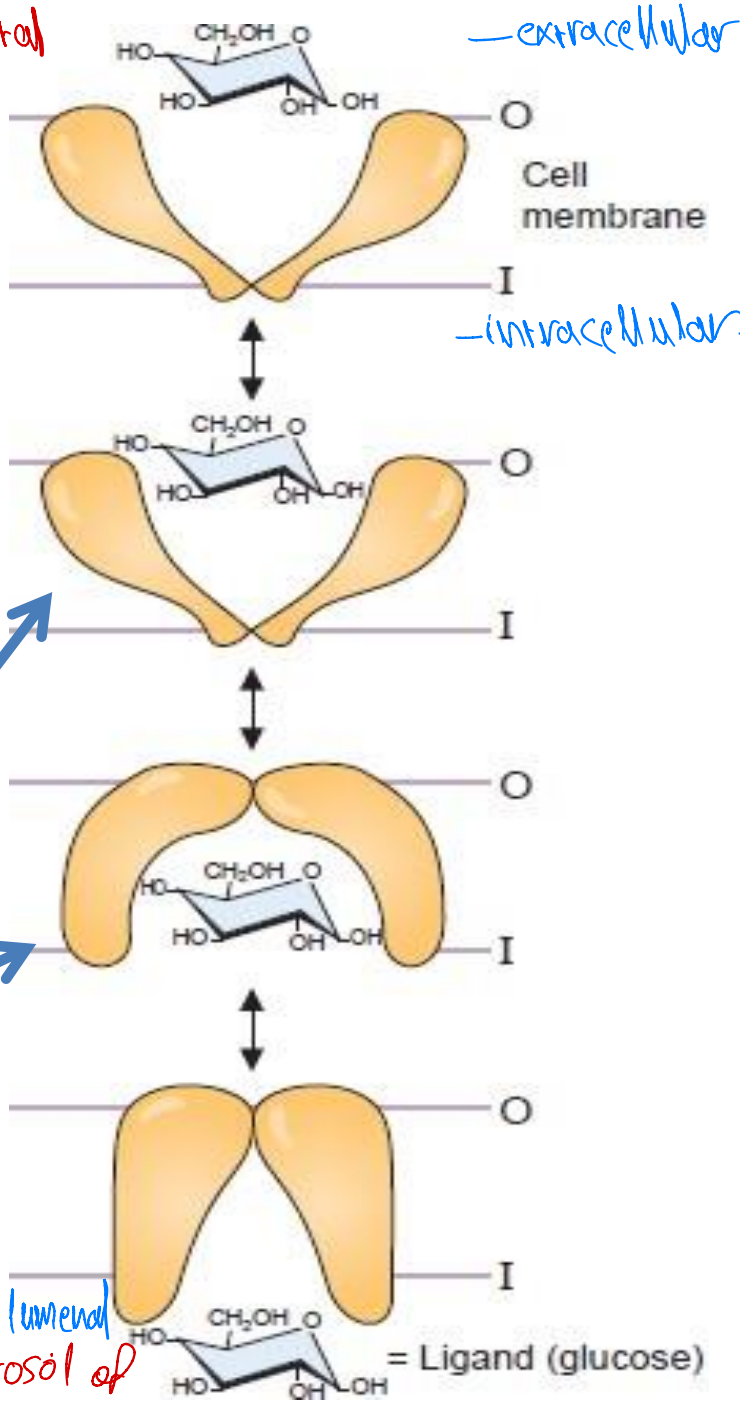
— Glucose transporter

Glu جزيئات.

Glc. Movement follows concentration gradient

This type of transporter have:

Two conformational states



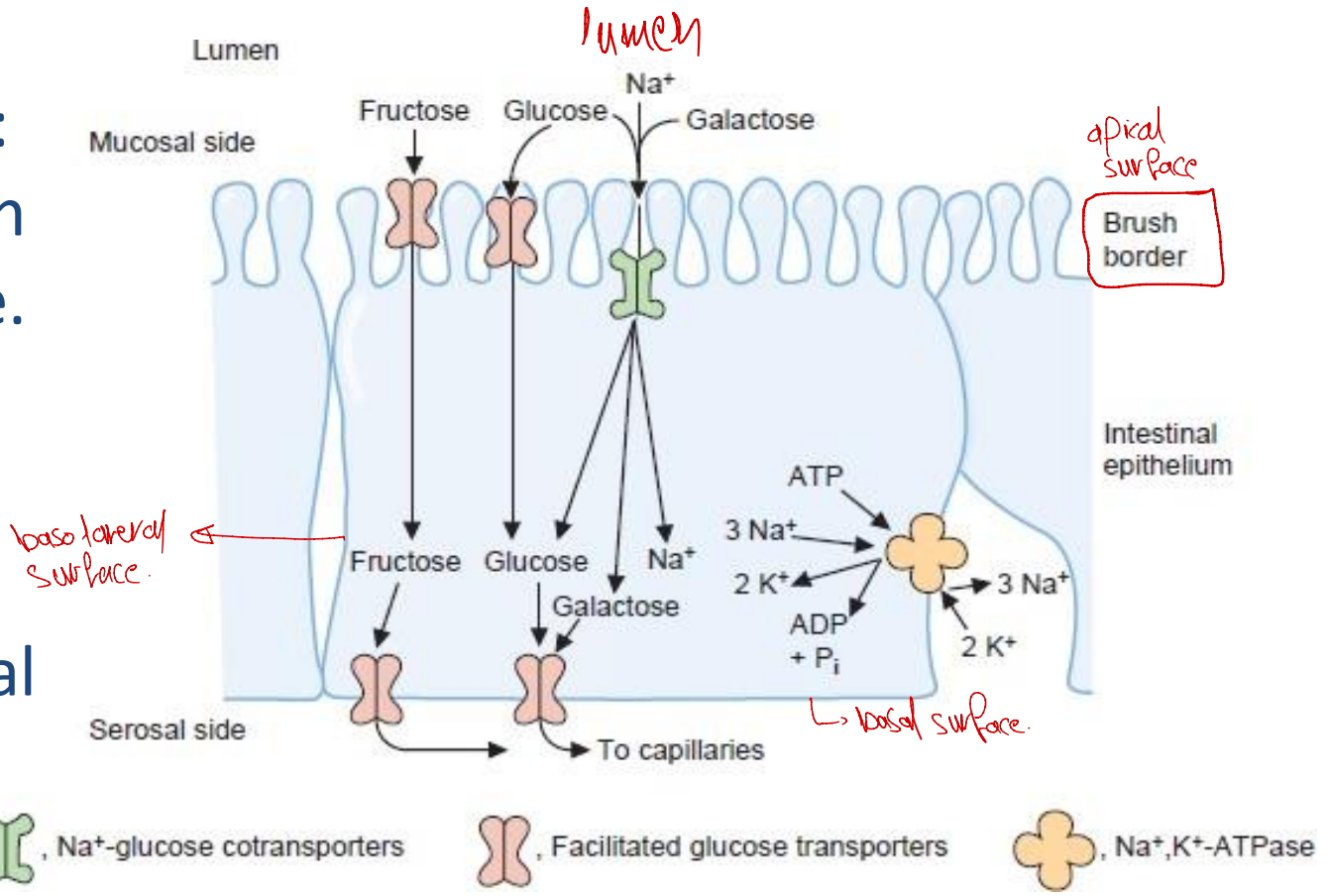
— Ok, the molecules which found in the lumen will bind to the 1st conformation, once bound they going to induce conformational changes that closes the lumenal side and open intracellular side result in release them into cytosol of small intestinal cells.

Na^+ monosaccharide cotranspoerter system (SGLT)

- Against concentration gradient (requires energy).

* Small intestine: Active uptake from lumen of intestine.

* Kidney: reabsorption of glucose in proximal tubule.



- For glucose and galactose absorption

The sugars Continuos to movement from lumen to intracellular space by Gluts but in some point the concentration of sugen inside will be more out side which result in stopping the role of those Gluts, However the SGLT will help to continue this process by depend on the Na^+ movement inside to move (تاكي) suger inside the cell. بمعنى آخر راح يستغلوا دخول Na^+ لمصلحتهم ويهربوا suger عكس تركيزهم.

But the movement of Na^+ inside cell will result in accumulation of positive charge intracellular.

ومشان احافظ ع اتزان الخلية بحتاج اطلع هدول الـ Na^+.

- The sodium-potassium pump which found on basolateral surface will exit Na^+
- This pump require energy and that is why we need ATP on this type of transport.

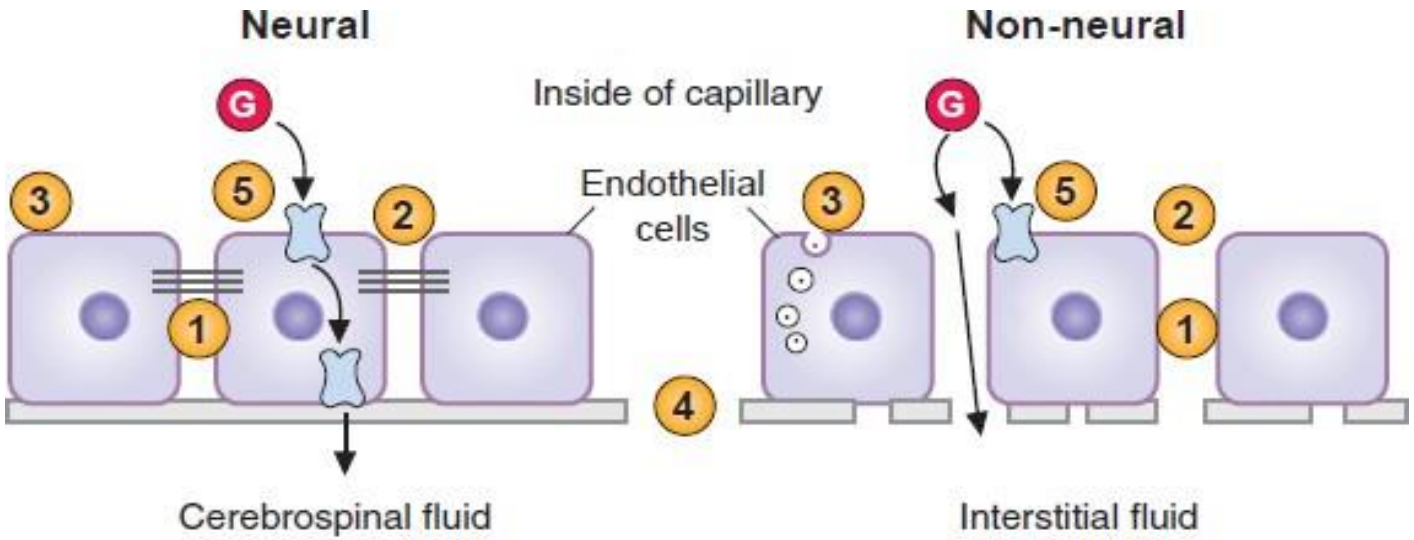
- There is no SGLT in basolateral surface but it contain Gluts.
- In kidney we have SGLT, During the formation of urine and still we have fluid in the tubules to reabsorbtion and excretion, one of the molecule that reabsorbed is suger. يعني بالعادي المفروض ما يكون فيه سكر في البول في الوضع الطبيعي، علمًا انه مرضى السكري عندهم سكر.

*All Gluts are bidirectional → gradient حسب ال gradient يعني بقدروا يدخلوا ويطلعوا الجزيئات *

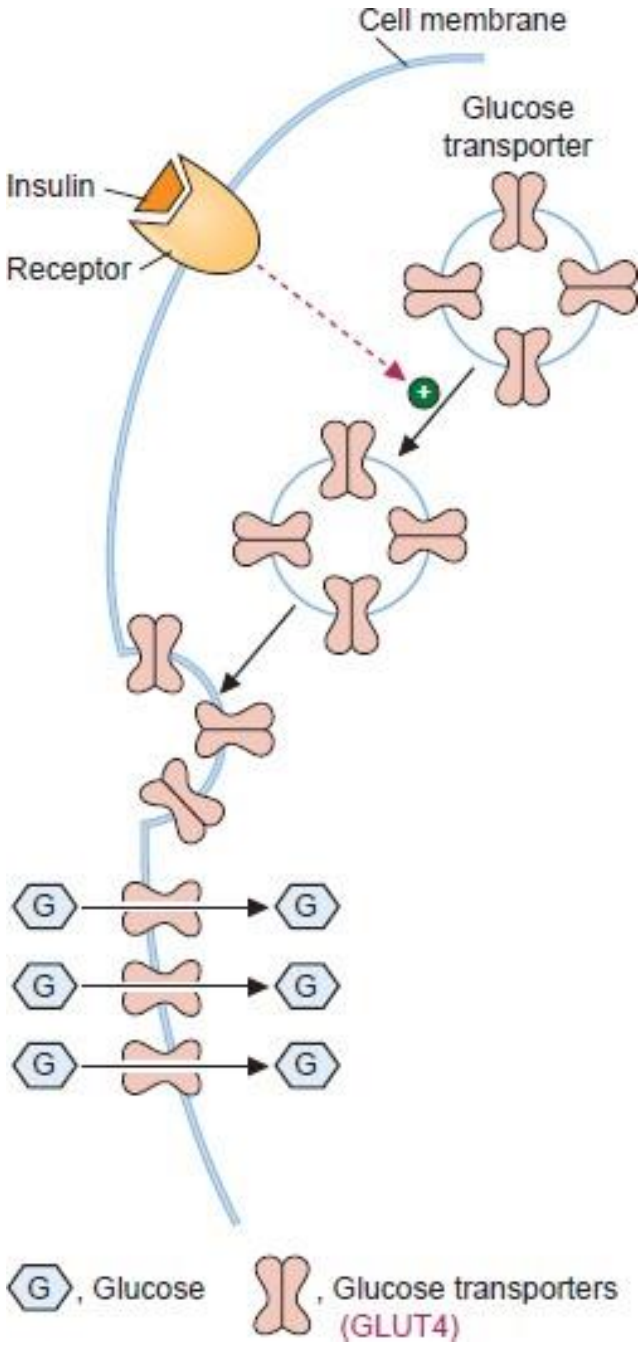
Table 27.5 Properties of the GLUT 1 to GLUT 5 Isoforms of the Glucose Transport Proteins

Transporter	*Tissue Distribution*	*Comments*
GLUT 1 Barriers → [illegible]	Human erythrocyte Blood–brain barrier Blood–retinal barrier Blood–placental barrier Blood–testis barrier	Expressed in cell types with barrier functions; a high-affinity glucose transport system
GLUT 2 Non specific type of transporter Glucose, galactose and fructose	Liver Kidney Pancreatic β-cell Serosal surface of intestinal mucosa cells	A high-capacity, low-affinity transporter ← يدخل كثير اشياء بدون ما يميز بينهم في دائما الد كثرة (الشغال النظيف) [illegible]. May be used as the glucose sensor in the pancreas (Basolateral surface)
GLUT 3	Brain (neurons)	Major transporter in the central nervous system, a high-affinity system
GLUT 4 (hormons)	Adipose tissue Skeletal muscle Heart muscle	Insulin-sensitive transporter. In the presence of insulin, the number of GLUT 4 transporters increases on the cell surface; a high-affinity system
GLUT 5 Fructose Some cell depend on fructose to get energy as sperm.	Intestinal epithelium Spermatozoa	This is actually a fructose transporter Na independent جميع Gluts موجودين in the plasma membrane باستثناء Glut7
GLUT 7	Glucogenic tissues	at endoplasmic reticulum membrane

Glucose transport in neural vs. non-neural cells



	Neural	Non-neural
1	Tight junctions between endothelial cells	No tight junctions
2	Narrow intercellular space	Sometimes wide intercellular gaps
3	Lack of pinocytosis	Pinocytosis
4	Continuous basement membrane	Discontinuous basement membrane
5	Glucose transporters in both membranes	Glucose can diffuse between cells and into interstitial fluid

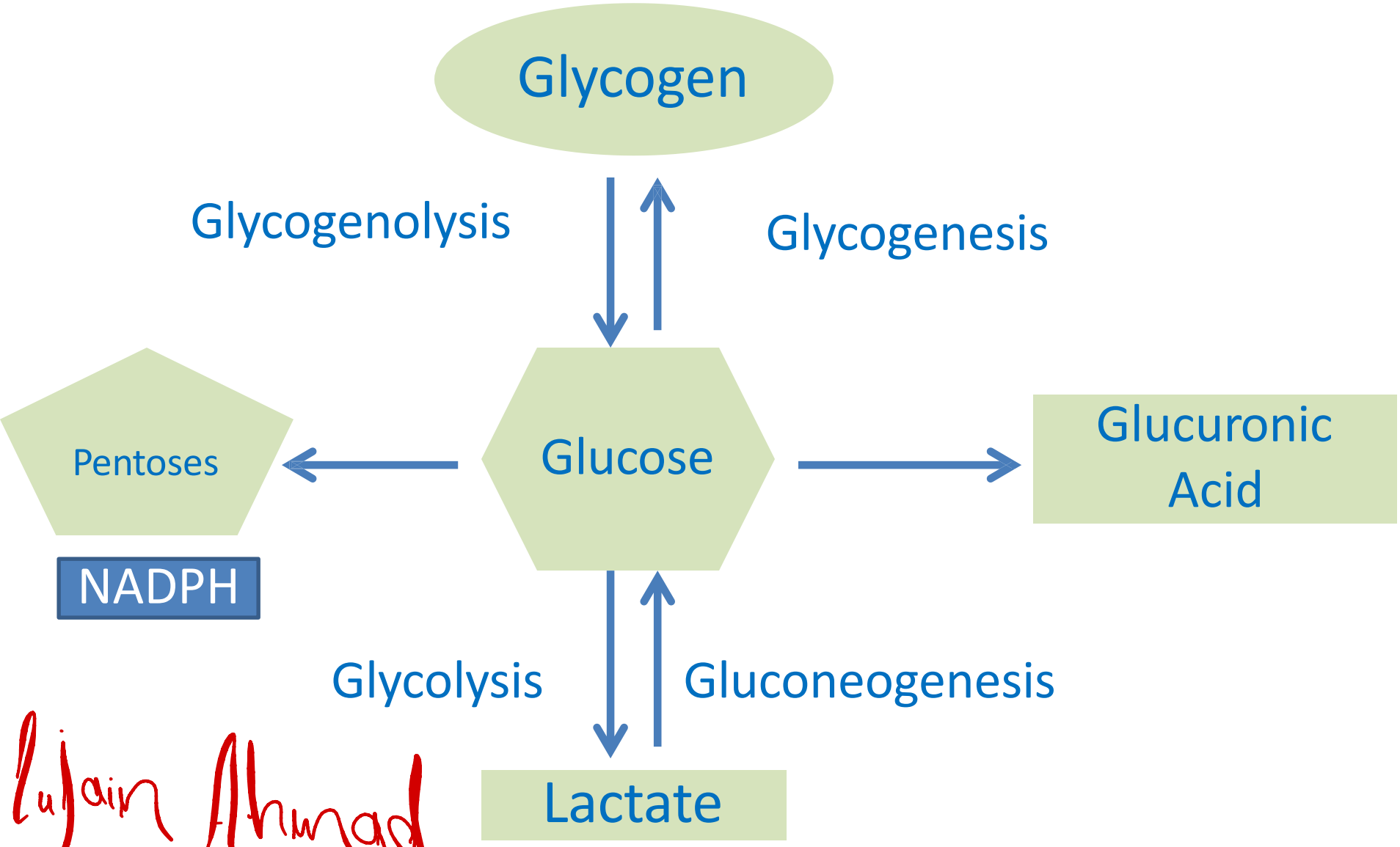


Insulin stimulates transport of glucose into muscle and adipose tissues

-Insulin is going to bind on its receptors on the target cells (receptor tyrosine kinase) activation. وبعدين

and then activate so many proteins which lead to response in cell that affect the Metabolism and activate transcriptional factors which move to the nucleus and bind to a certain sequence to activate the target gene which is Glut 4

An overview of glucose metabolism



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