Glycogen Metabolism

CLOSE YOUR EYES ,BREATH AND LET US START OUR EASY LECTURE

Objectives ..

- Why do we need to store carbohydrates in muscle? عشان نستخدمها وقت الحاجه
- Why carbohydrates are stored as glycogen?
- Overview of glycogen synthesis (Glycogenesis)
- Overview of glycogen breakdown (Glycogenolysis)
- Key elements in regulation of both Glycogenesis and Glycogenolysis

Location & Functions of Glycogen ..

هذه النسبة لكل عضله على حده ، وبما أن العضلات منتشرة في جميع انحاء الجسم نستنتج أن نسبة glycogenالمخزن في العضلات أكثر من الكبد

- **Location of glycogen in the body**

skeletal muscle & liver :

* 400 g in muscles (1-2% of resting muscles weight)

*100 g in liver (~ 10% of well-fed liver)

الـ contractive musclesتستخدم الـ Glycogenلذلك لا يمكننا حسابه !

Both (liver & muscles) are storege sites

- contaction في حاله ال ← في العضله يكون الجلايكوجين في كميه اقل بعد الاكل

- **Functions of glycogen:**

1-Function of muscle glycogen:
fuel reserve (ATP) => (during muscular exercise)

2- Function of liver glycogen:
a source for blood glucose => (especially during early stages of fasting) ⟶
مثل لما نكون نايمين

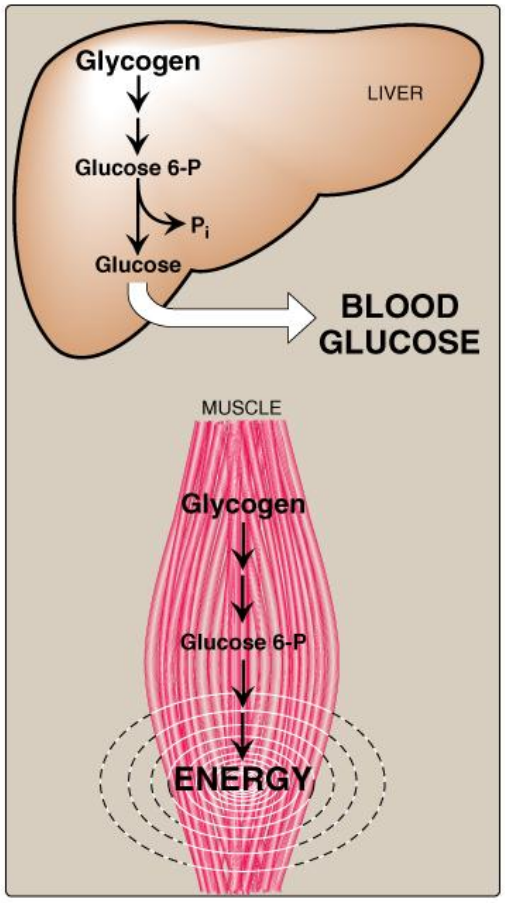
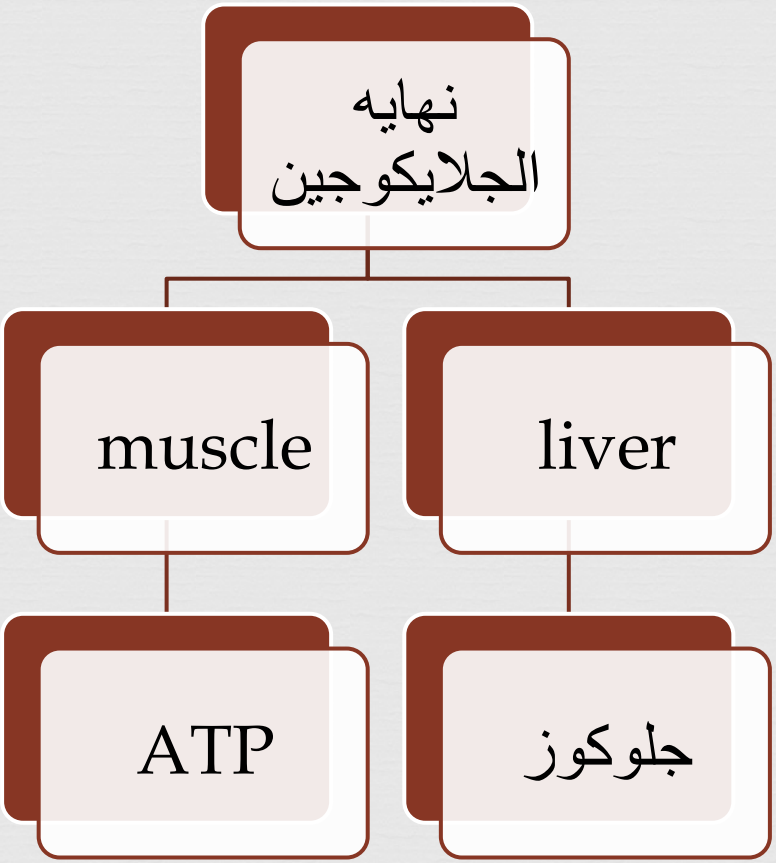
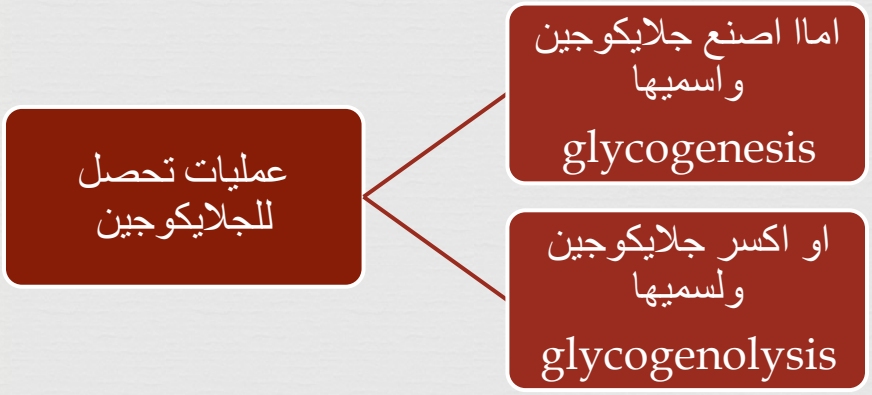


Figure 11.2
Functions of muscle and liver glycogen.

الانزيم .. Glucose 6-phosphatase
موجود في مكانين فقط ، هما الكبد والكلية ،
ويقوم بتحويل الـ glycogen إلى Glucose ..
وهذا الانزيم مفقود في العضلات ولذلك تجري
نفس هذه العملية في العضلات ولكن تقف عند
Glucose 6-P وبذلك تم توفير 1ATP خلال
هذه العملية في العضلات

*باختصار





هذول العمليتين للجلايكوجين بشكل كبير منظمات<

Structure of Glycogen ..

- Glycogen is a branched-chain homopolysaccharide made exclusively from **α- D-glucose**

*ذرة الكربون الأولى من الجلوكوز ترتبط بذرة الكربون رقم ٤ من الجلوكوز المقابل

- Glucose residues are bound by **α(1 - 4) glucosidic linkage**

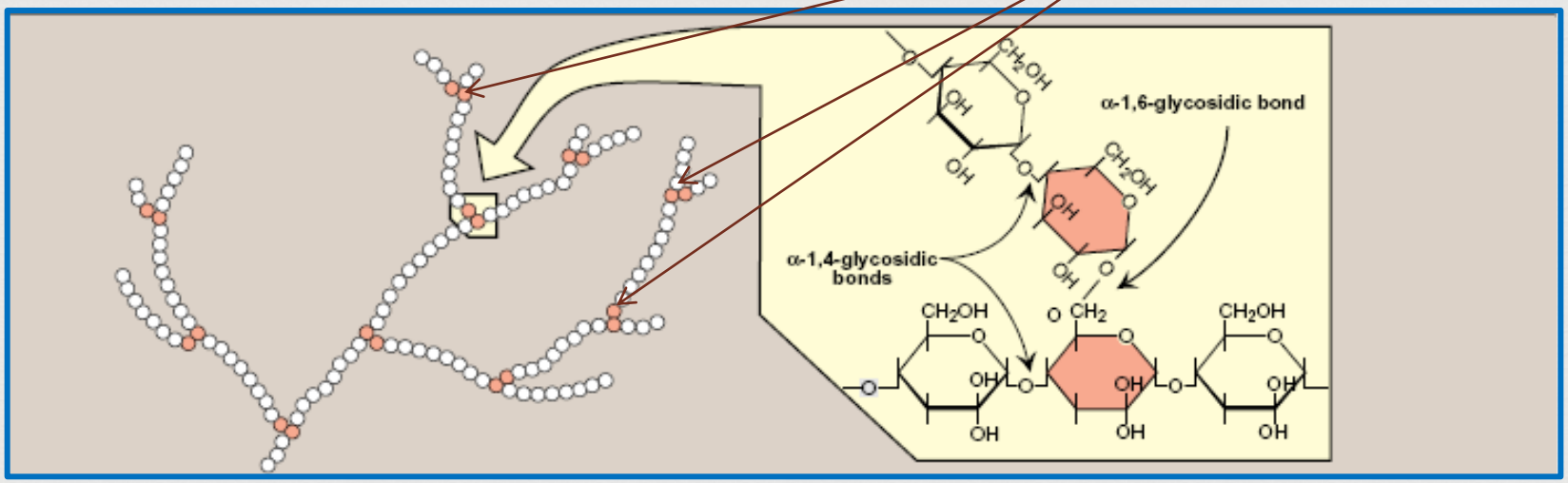
*ذرة الكربون الأولى من الجلوكوز ترتبط بذرة الكربون رقم ٦ من الجلوكوز المقابل

- Branches (every 8-10 residue) are linked **α(1-6) glucosidic linkage**

- Glycogen is present in the **cytoplasm** in the form of granules which contain most of the enzymes necessary for glycogen synthesis & degradation

Structure of Glycogen ..

تمثل الـBranches point التي وردت في السلايد السابق <= α(1-6) glucosidic linkage



باختصار

- خصائص الجلايكوجين :
- branched
- Polysaccharide
- Homopolysaccharide
- انه يتكون من جلوكوز مرتبطين مع بعض برابطه وهي
- **α glucosidic linkage**
- **كل (٨-١٠)وحدات جلوكوز يكون فيه تفرع**

Metabolism of Glycogen in Skeletal Muscle ..

- **Glycogenesis**:
  Synthesis of Glycogen from Glucose

- **Glycogenolysis**:
  Breakdown of Glycogen to Glucose-6-phosphate

GLYCOGENESIS
(Synthesis of Glycogen in Skeletal Muscles)

1- Building blocks: UDP-GLUCOSE

الجلوكوز لوحدة لا يستطيع أن يتحول إلى جلايكوجينيسس إلا إذا حصل له **activation** ويتم ذلك عن طريق إلتصاقه بالـUredines DiPhosphate

2- Initiation of synthesis:

Elongation of pre-existing glycogen fragment

OR A protein attached to glucose unite

The use of glycogen primer (glycogenin)

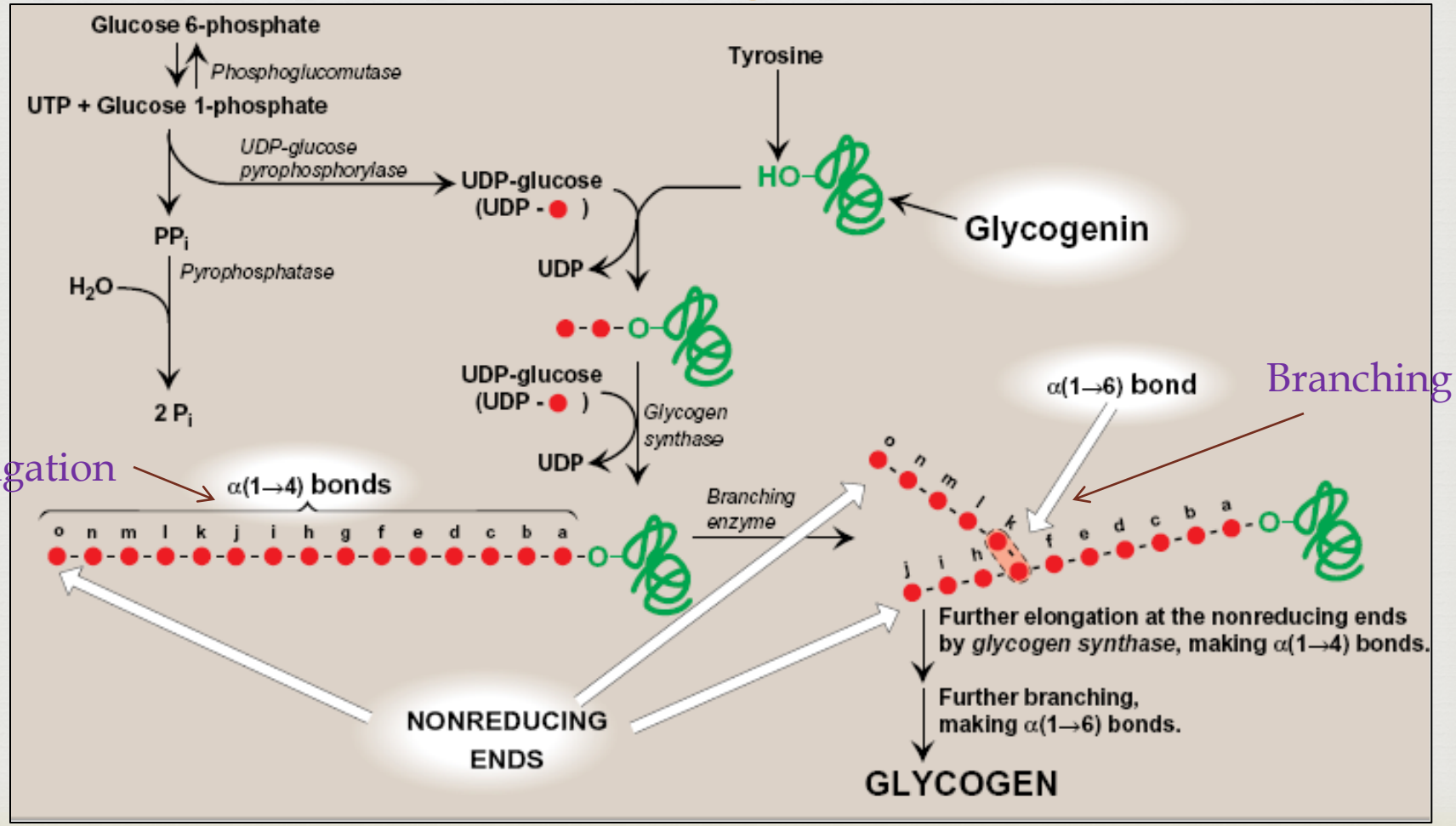
3- ELONGATION: Glycogen synthase (for α1-4 linkages)

Enzyme that can not initiate synthesis but it can only elongation pre-existing chain

4- BRANCHING: Branching enzyme (for α1-6 linkages)

Specific enzyme for formation of branch point

Synthesis of Glycogen ..



Glycogenolysis
(Breakdown of glycogen in skeletal muscles)

1- Shortening of glycogen chain: by glycogen phosphorylase

Cleaving of α(1-4) bonds of the glycogen chain producing glucose 1-phosphate

Glucose 1-phosphate is converted to => **glucose 6-phosphate** (by mutase enzyme)

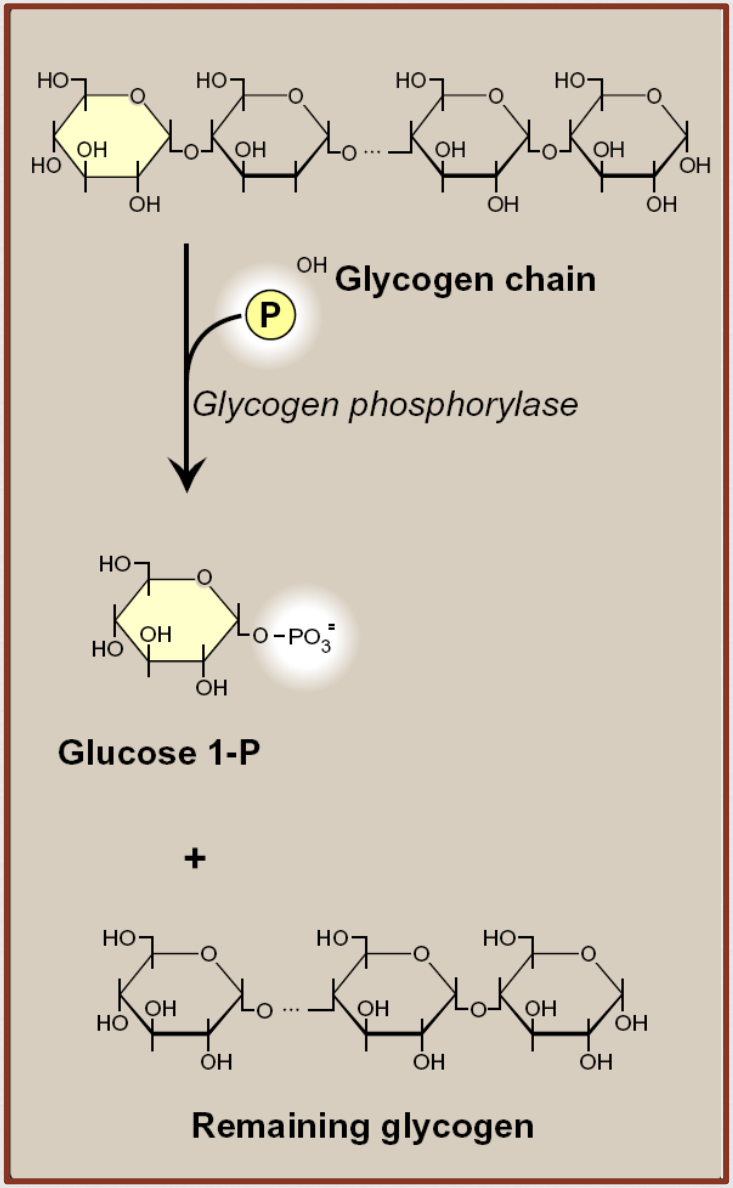
2- Removal of branches : by debranching enzymes

Cleaving of α(1-6) bonds of the glycogen chain producing **free glucose** **(few)**

3- Fate of glucose 6-phosphate (G-6-P) :

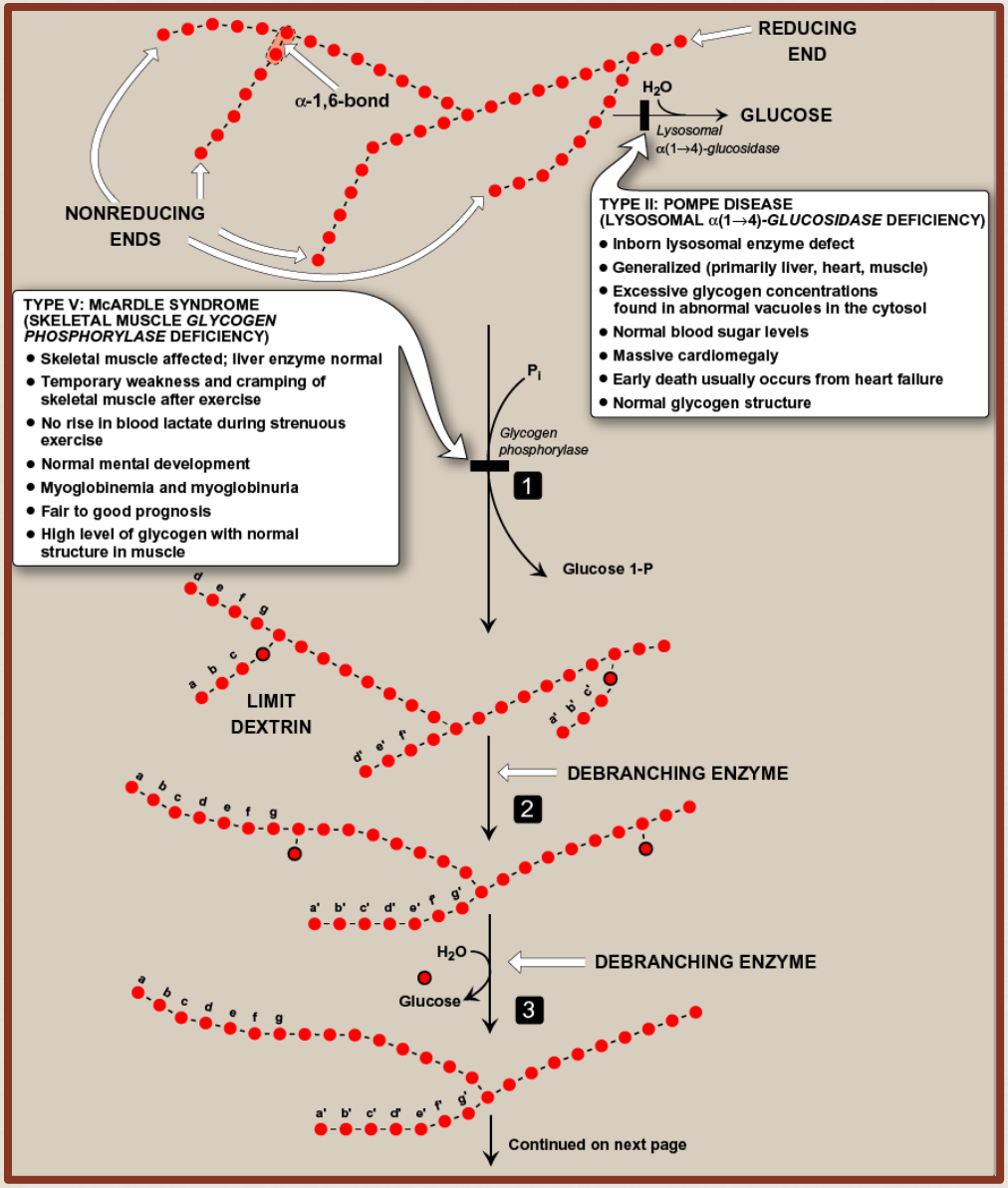
* G-6-P is **not** converted to free glucose

* It is used as a source of energy for skeletal muscles during muscular exercise (by anaerobic glycolysis starting from G-6-P step)



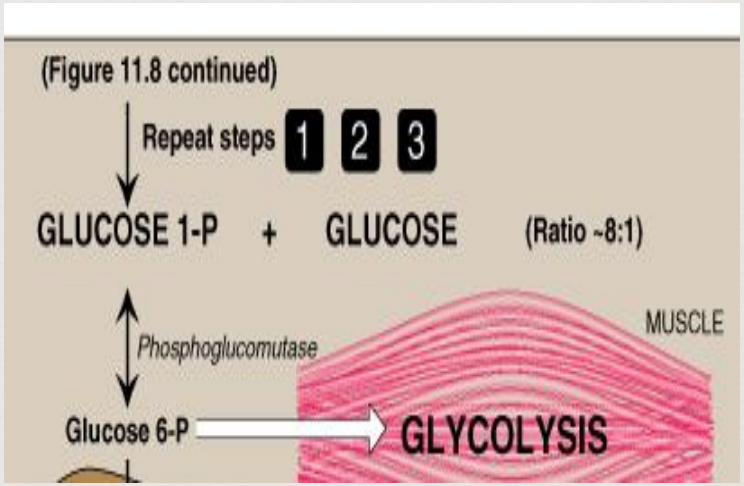
الانزيم اللي يكسر
الجلايكوجين الى
glucose 1-p
هو
glycogen
phosphorylase
ويساعد هذا الانزيم
co – enzyme
نسميه
Pyridoxal
phosphate

Glycogenolysis ..



Glycogenolysis ..

limit dextrin:
Molecule that limit the action of glycogen phosphorylase,,



شرح للسلايد السابق

في البدايه لما ابغى اكسر الجلايكوجين استخدم انزيم
Glycogen phosphorylase
هذا الانزيم يكسر الجلايكوجين الى
Glucose 1-p
ولكنه يوقف عمله عند ثلاث نقاط قبل التفرع ونسمي هذا المكان او بالاحرى الجزئ ب
Limit dextrin
وبعدها يبدا عمل الانزيم الثاني الذي هو مخصص للتفرع وهو
Debranching enzyme
هذا الانزيم يكسر باستخدام الهيدرولايسيس والناتج يكون جلوكوز

وبالتالي بعدها تكون النسبه بين الجلوكوز ,
glucose 1-p

Regulation of Glycogen Metabolism..

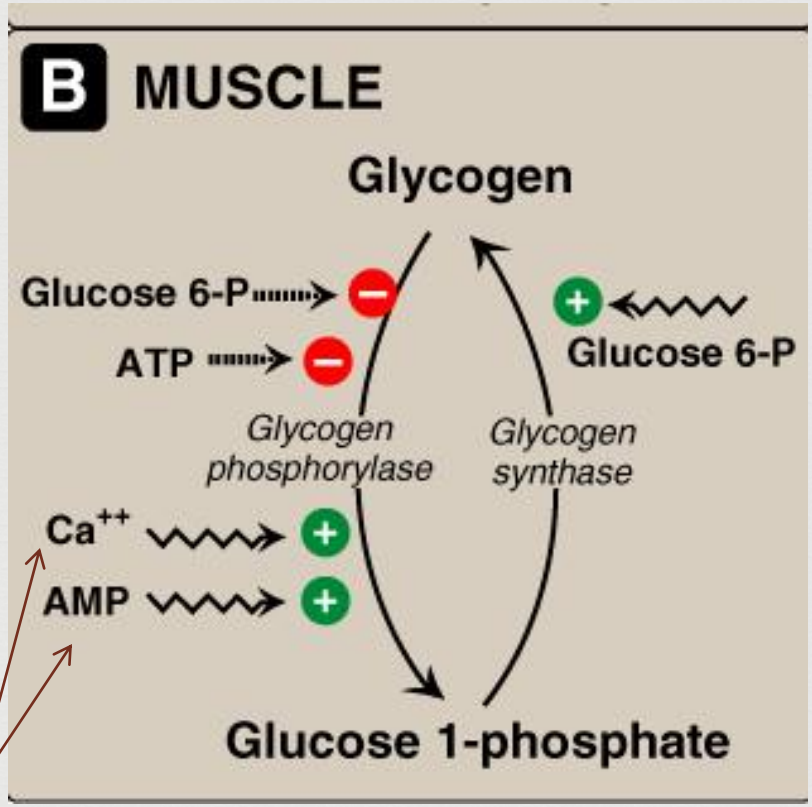
***Synthesis & degradation of glycogen are tightly regulated**

In Skeletal Muscles:

- Glycogen **degradation** occurs during **active exercise** During muscle contraction
- Glycogen **synthesis** begins when the **muscle is at rest**

- **Regulation occurs by 2 mechanisms:**
  1- Allosteric regulation

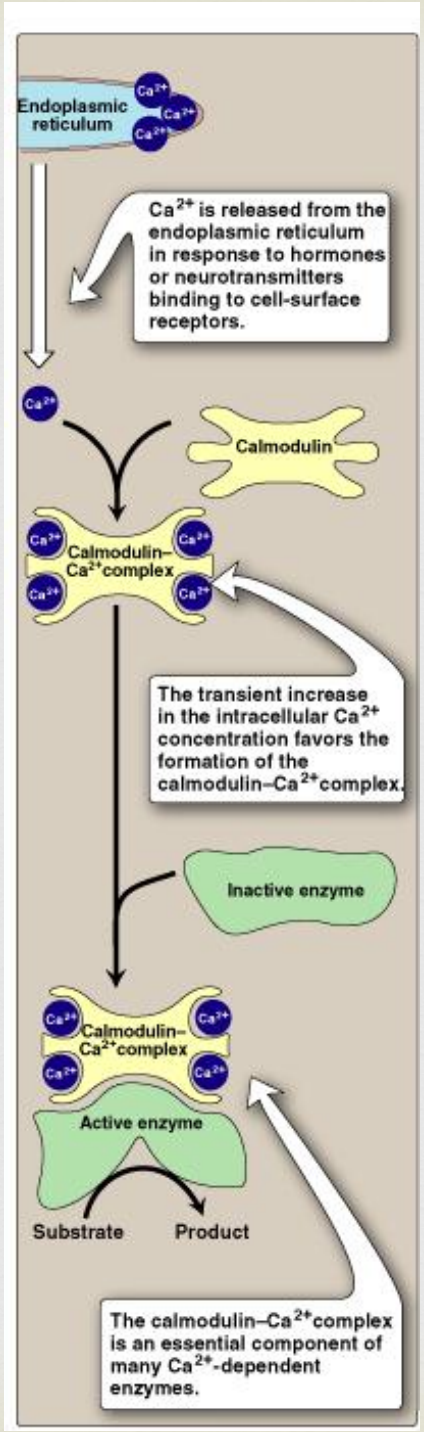
  2- Hormonal regulation (Covalent modification)



Important activators and Specific for the muscles

Regulation of Glycogen Metabolism :

1. Allosteric Regulation



Regulation of Glycogen Metabolism

طريقة عمل الكالسيوم ..

*Increase of calcium during muscle contraction.

*Formation of **Ca^{2+}** -calmodulin complex.

Calcium modulating protein

*Activation of **Ca^{2+}** -dependent enzymes,

e.g., glycogen phosphorylase.

Regulation of Glycogen Metabolism ..

2. Hormonal Regulation by Epinephrine :

***Muscle contraction**
***Epinephrine release**

Glucagon will not work on the muscles, because of it has not receptors.

Skeletal muscle => Epinephrin/receptor binding

Second messenger => cAMP

Response => Enzyme phosphorylation

Glycogen phosphorylase
(Active form)

Stimulation of glycogenolysis

Glycogen synthase
(Inactive form)

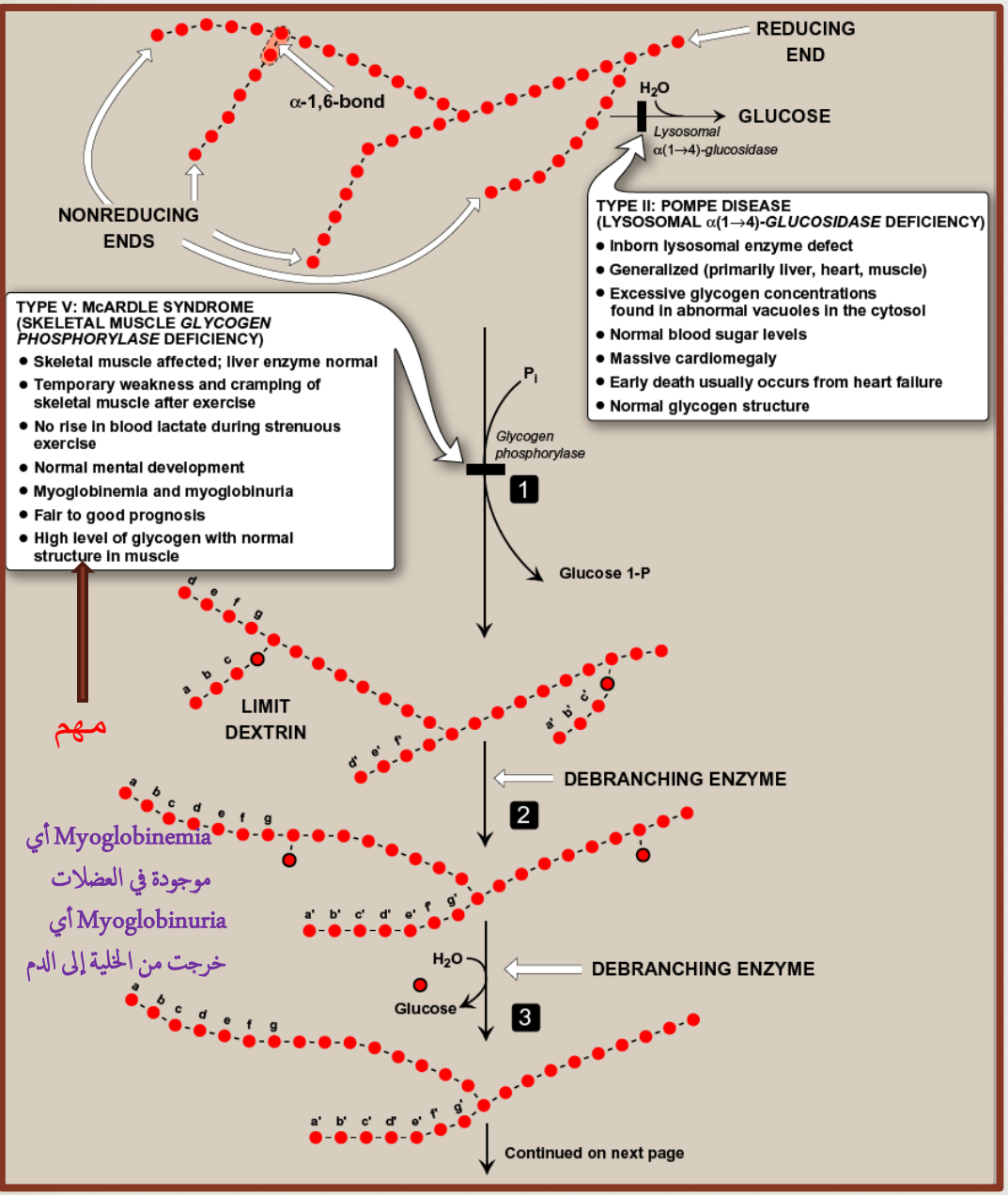
Inhibition of glycogenesis

Glycogen Storage Diseases..

- A group of genetic diseases that result from a defect in an enzyme required for glycogen synthesis or degradation

- They result in:

  - Formation of abnormal glycogen structure
  - **OR**
  - Excessive accumulation of normal glycogen in a specific tissue



Glycogen Storage Diseases .. (GSD)

- **GSD Type V (Mc Ardle Syndrome)**

Deficiency of skeletal muscle glycogen phosphorylase

Questions for review .. MCQs

1- The total amount of glycogen is stored in …….. ?

*Liver *Muscles

2-Removal of branches (By debranching enzyme) will cleavage ……. Of the glycogen chain.

* α(1-6) bonds * α(1-4) bonds

3-An important activators and specific for muscles are: Ca++ and ……..

*AMP * ADP

4- a lot of ca will ……glycogenolysis
*inhibit *stimulate

- a lot of Glucose 6-p will……. The Glycogen synthesis *inhibit *stimulate

- A lot of ATP will……glycogenesis

*inhibit *stimulate

Biochemistry Team

Good Luck ^_^