

Glycogen Metabolism

**Clinical Chemistry Unit
Department of Pathology
College of Medicine, King Saud University**

Objectives:

By the end of this lecture, students should be familiar with:

- 1. The need to store carbohydrates in muscle**
- 2. The reason for carbohydrates to be stored as glycogen**
- 3. An overview of glycogen synthesis (Glycogenesis)**
- 4. An overview of glycogen breakdown (Glycogenolysis)**
- 5. Key elements in regulation of both Glycogenesis and Glycogenolysis**

Location & Functions of Glycogen

- **Location of glycogen in the body**

skeletal muscle & liver

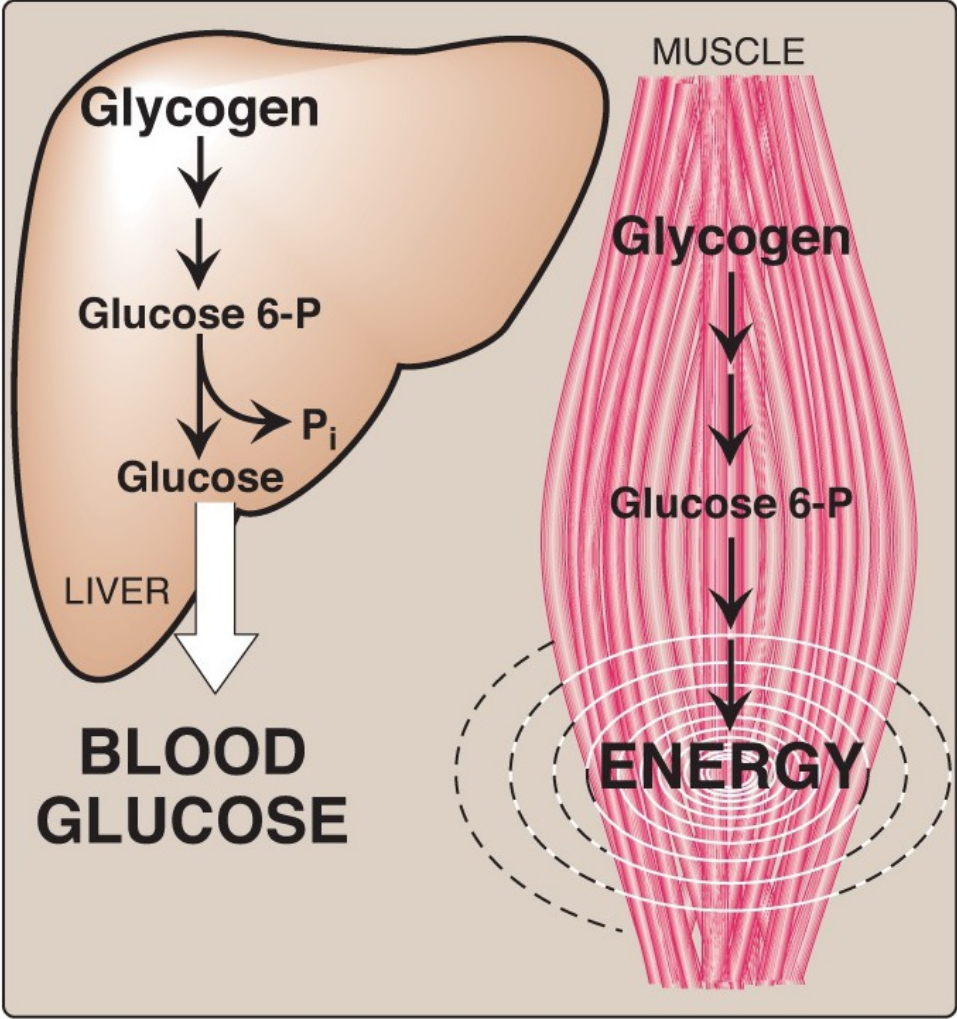
400 g in **muscles** (1-2% of resting muscles weight)

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

- **Functions of glycogen:**

Function of muscle glycogen: fuel reserve (ATP)
(during muscular exercise)

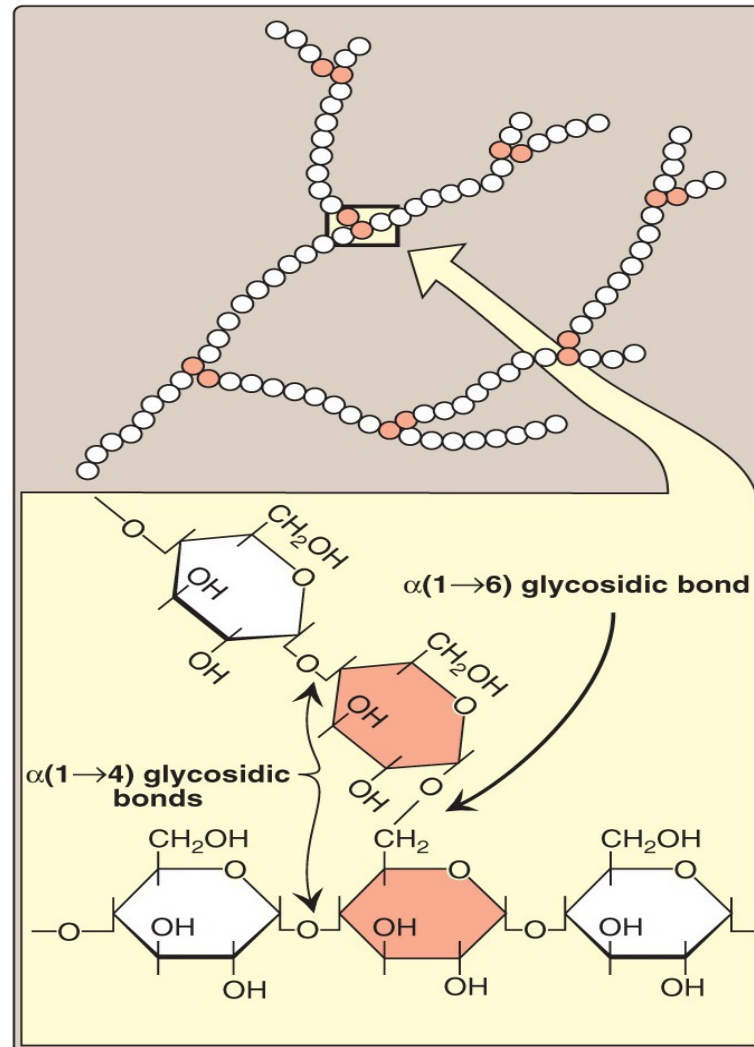
Function of liver glycogen: a source for blood glucose
(especially during early stages of fasting)



Structure of Glycogen

- Glycogen is a branched-chain homopolysaccharide made exclusively from α -D-glucose
- Glucose residues are bound by $\alpha(1 - 4)$ **glucosidic linkage**
- Branches (every 8-10 residue) are linked by $\alpha(1-6)$ **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



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

2- Initiation of synthesis:

Elongation of pre-existing glycogen fragment

OR

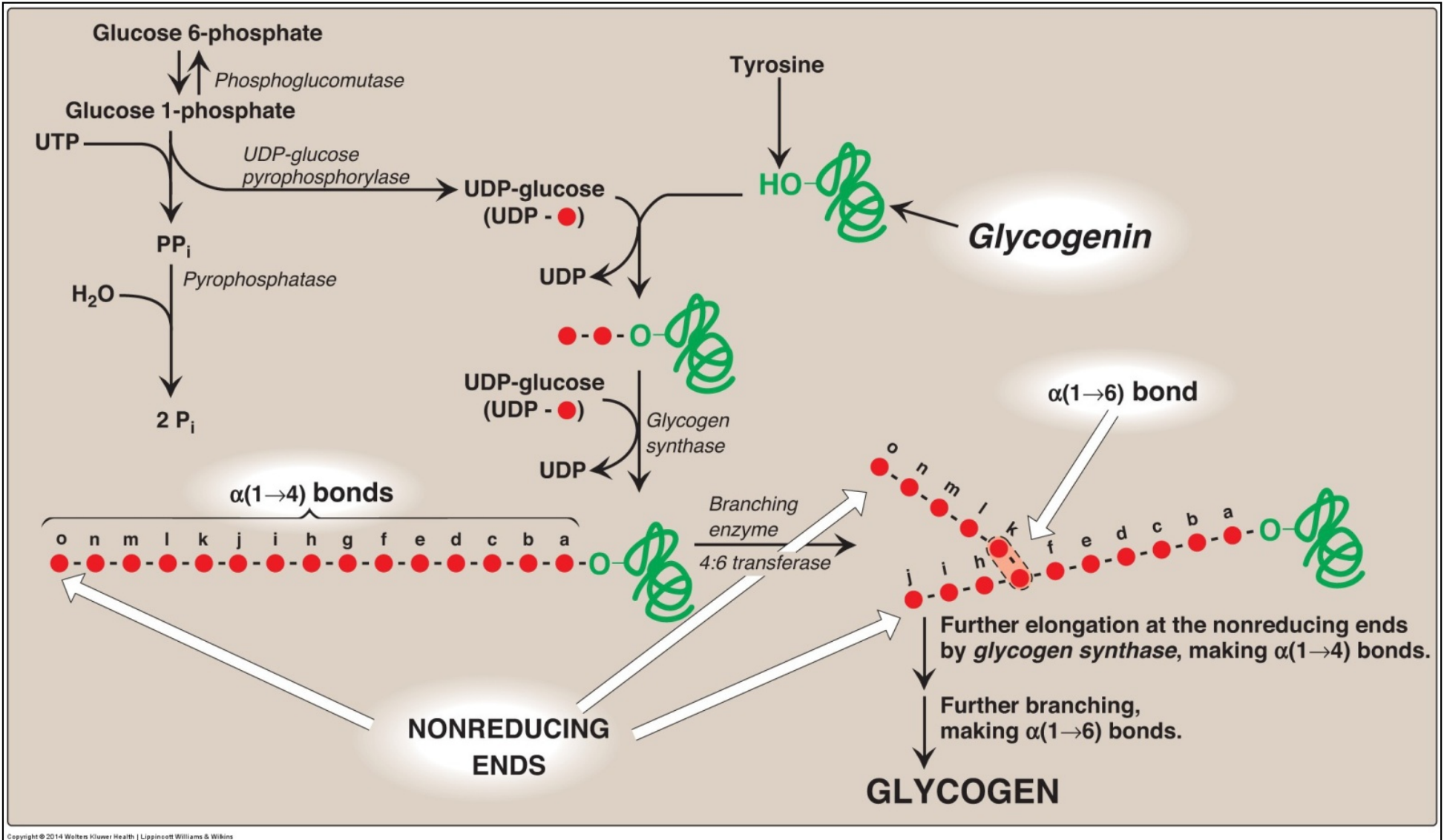
The use of glycogen primer (glycogenin)

3- ELONGATION: Glycogen synthase (for α 1-4 linkages)

Glycogen synthase cannot initiate synthesis but only elongates pre-existing glycogen fragment or glycogen primer (glycogenin)

4- BRANCHING: Branching enzyme (for α 1-6 linkages)

Synthesis of Glycogen



Glycogenolysis

(Breakdown of glycogen in skeletal muscles)

1- Shortening of glycogen chain: by glycogen phosphorylase

Cleaving of $\alpha(1-4)$ 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

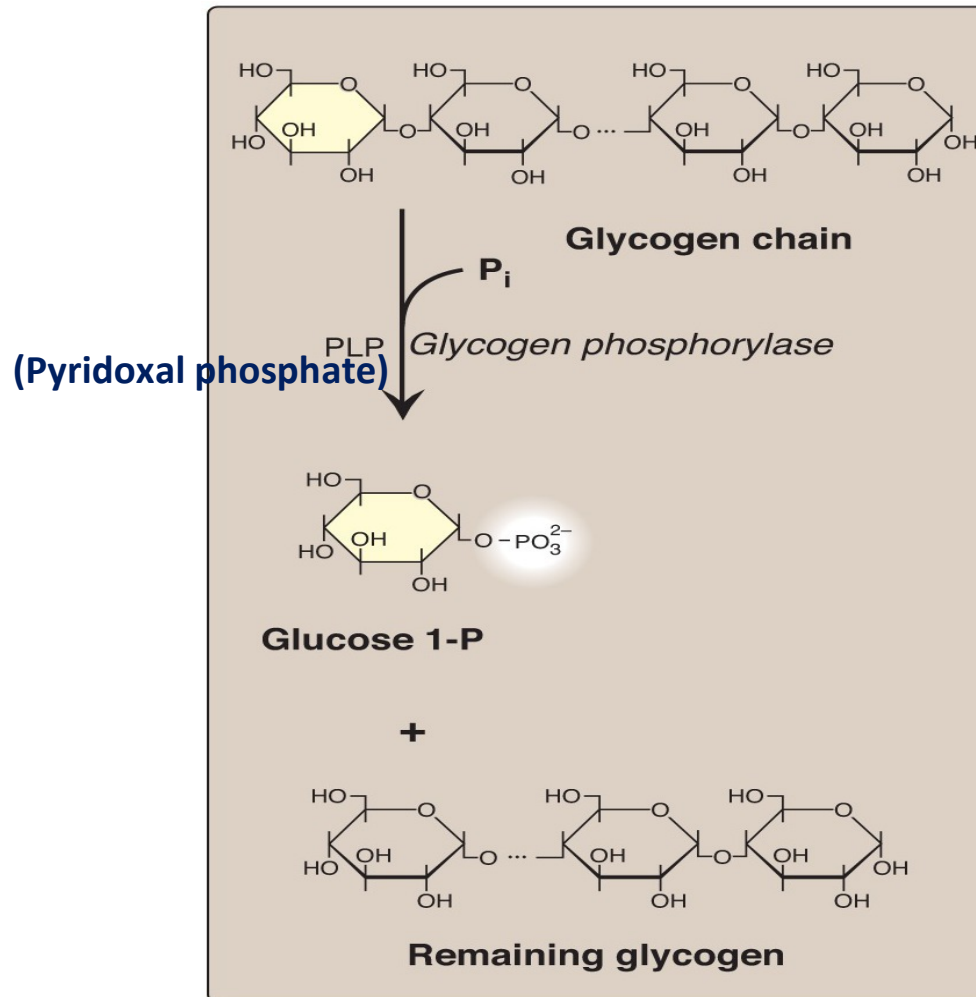
Cleaving of $\alpha(1-6)$ bonds of the glycogen chain producing **free glucose (few)**

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

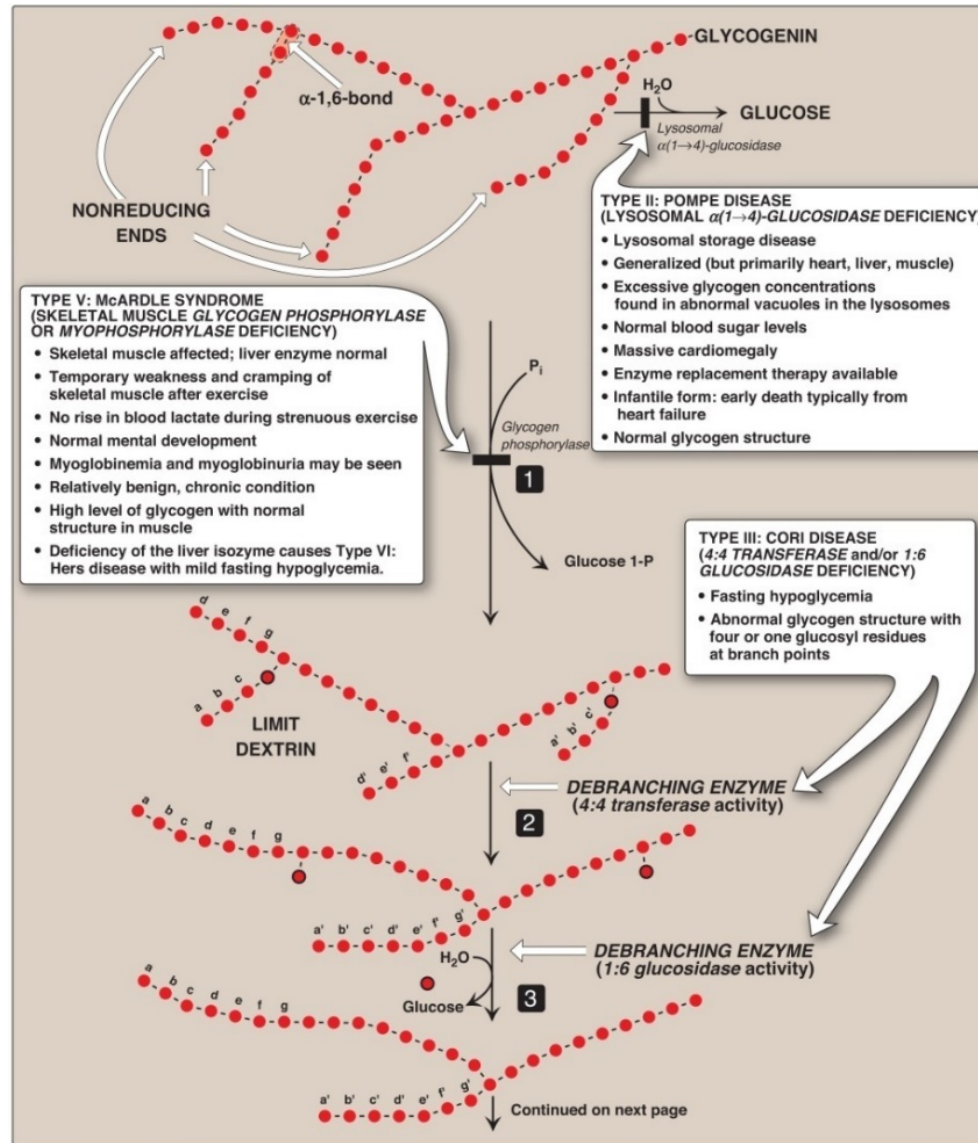
- G-6-P is **not** converted to free glucose

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

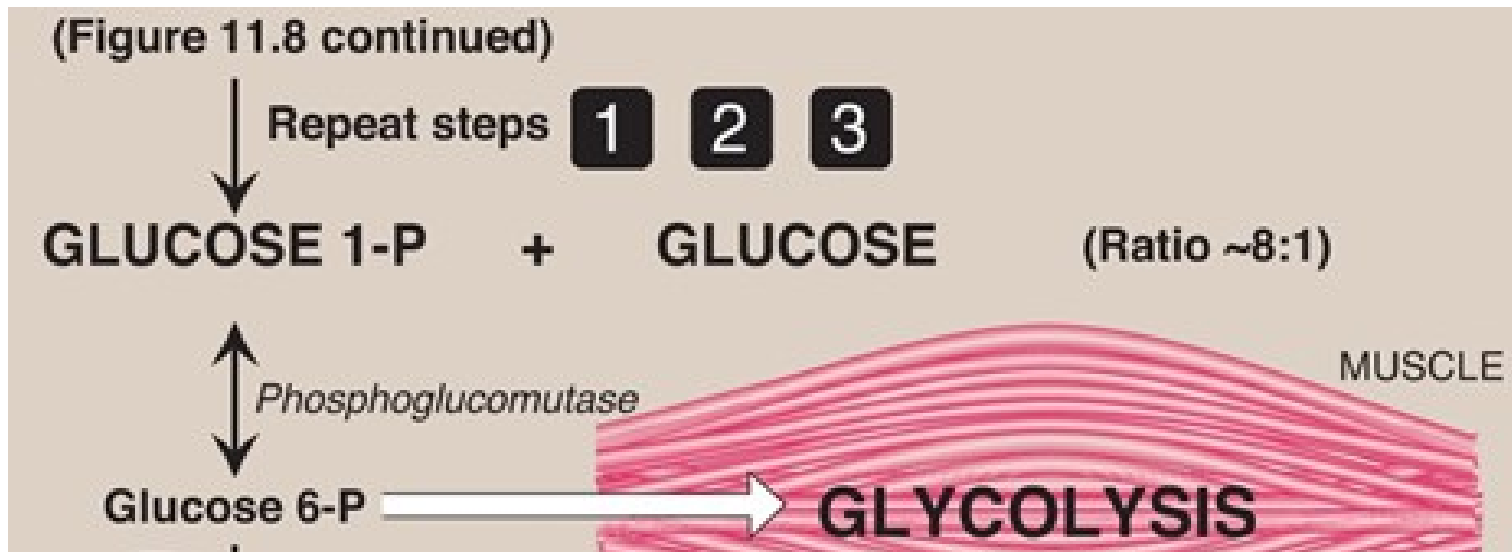
Glycogenolysis



Glycogenolysis



Glycogenolysis



Regulation of Glycogen Metabolism

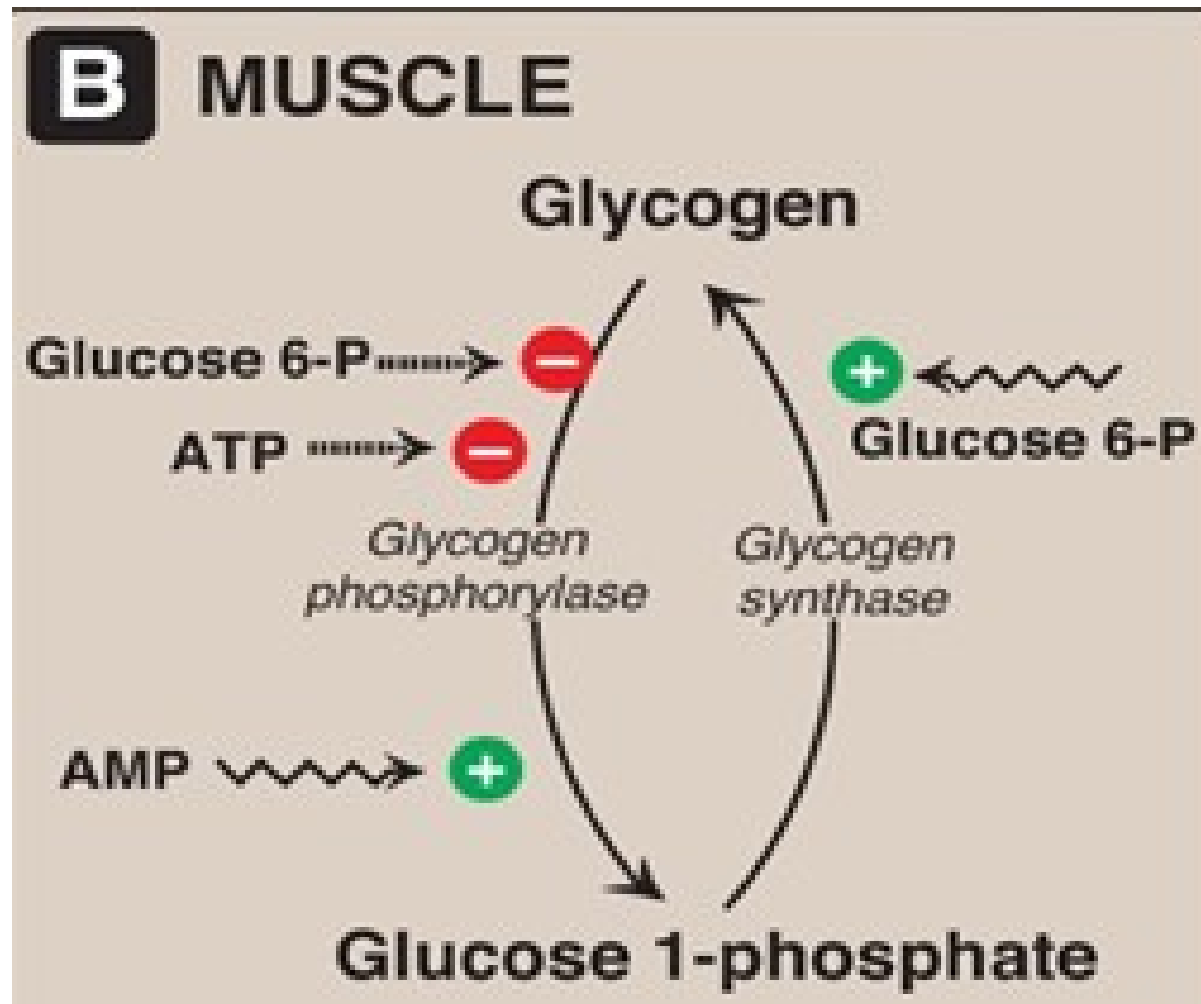
Synthesis & degradation of glycogen are tightly regulated

In Skeletal Muscles:

- Glycogen **degradation** occurs during **active exercise**
- Glycogen **synthesis** begins when the **muscle is at rest**
- Regulation occurs by 2 mechanisms:
 - 1- Allosteric regulation**
 - 2- Hormonal regulation
(Covalent modification)**

Regulation of Glycogen Metabolism

1. Allosteric Regulation

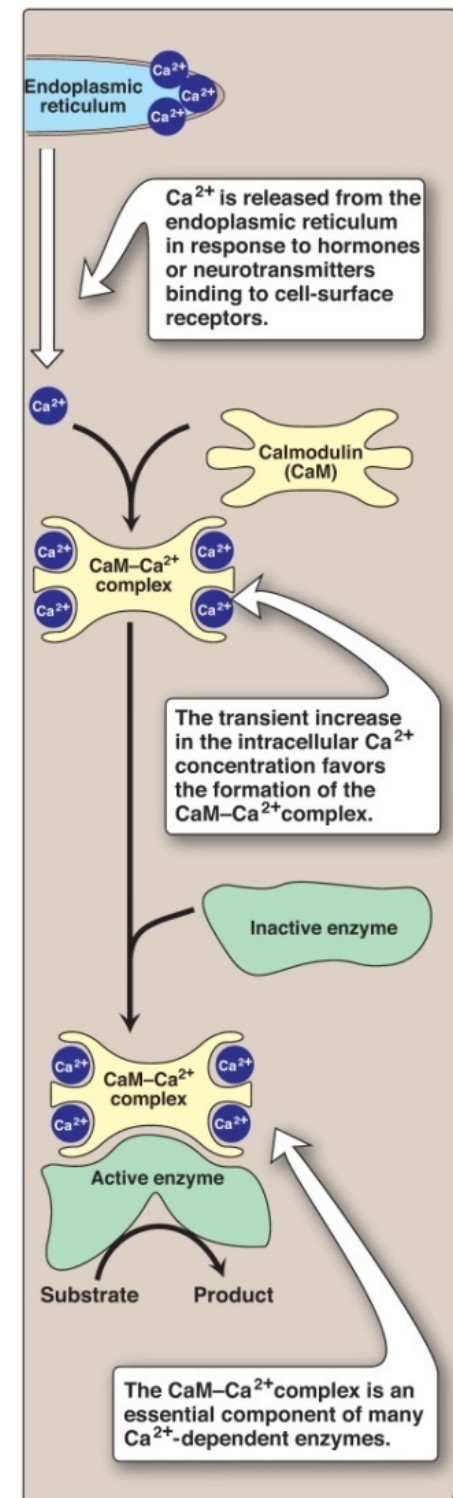


Regulation of Glycogen Metabolism

Increase of calcium during muscle contraction

Formation of Ca^{2+} -calmodulin complex

Activation of Ca^{2+} -dependent enzymes,
e.g., glycogen phosphorylase



Regulation of Glycogen Metabolism:

2. Hormonal Regulation by Epinephrine

Muscle contraction

Epinephrine release

Skeletal muscle: Epinephrine/receptor binding

Second messenger: cAMP

Response: Enzyme phosphorylation



Glycogen synthase
(Inactive form)



Glycogen phosphorylase
(Active form)

Inhibition of glycogenesis

Stimulation of glycogenolysis

Glycogen Storage Diseases (GSD)

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

They result in:

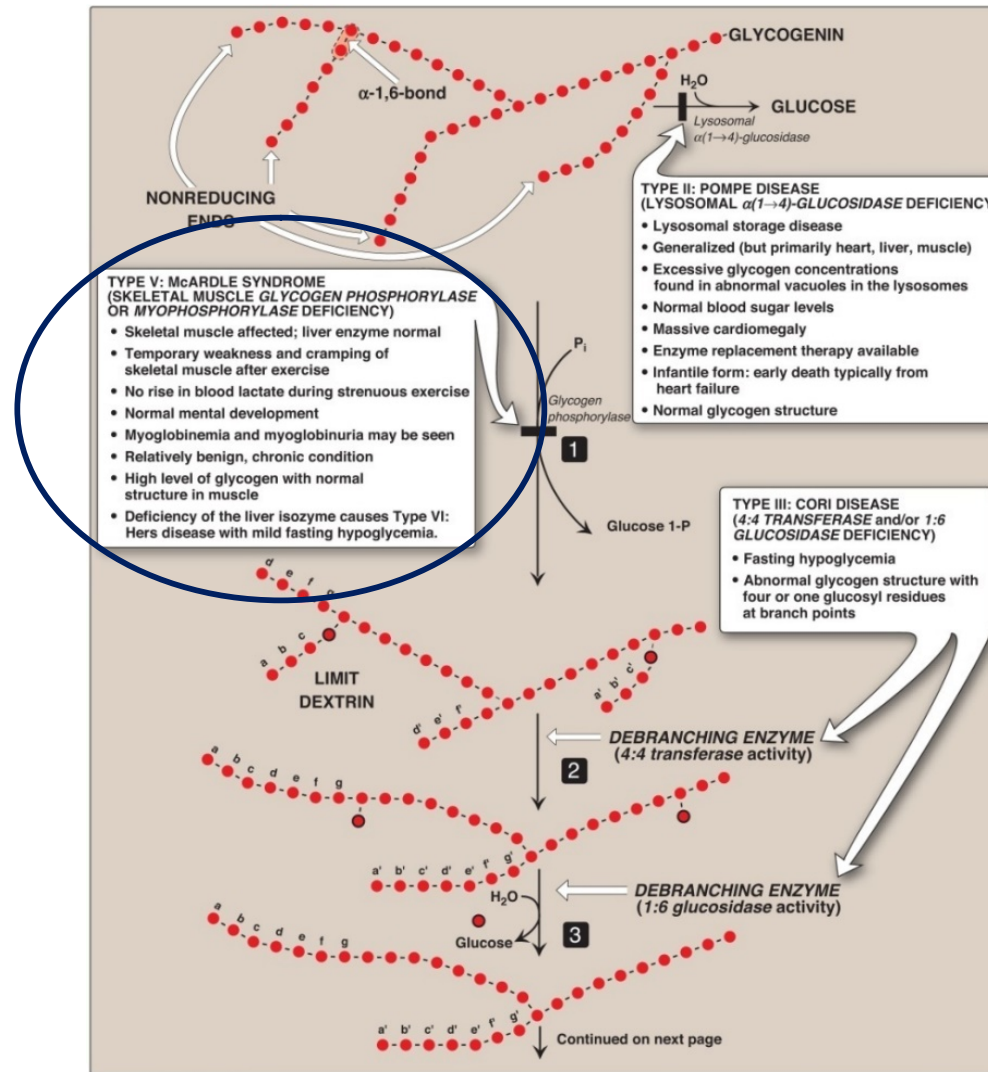
Formation of abnormal glycogen structure

OR

Excessive accumulation of normal glycogen in a specific tissue

Glycogen Storage Diseases

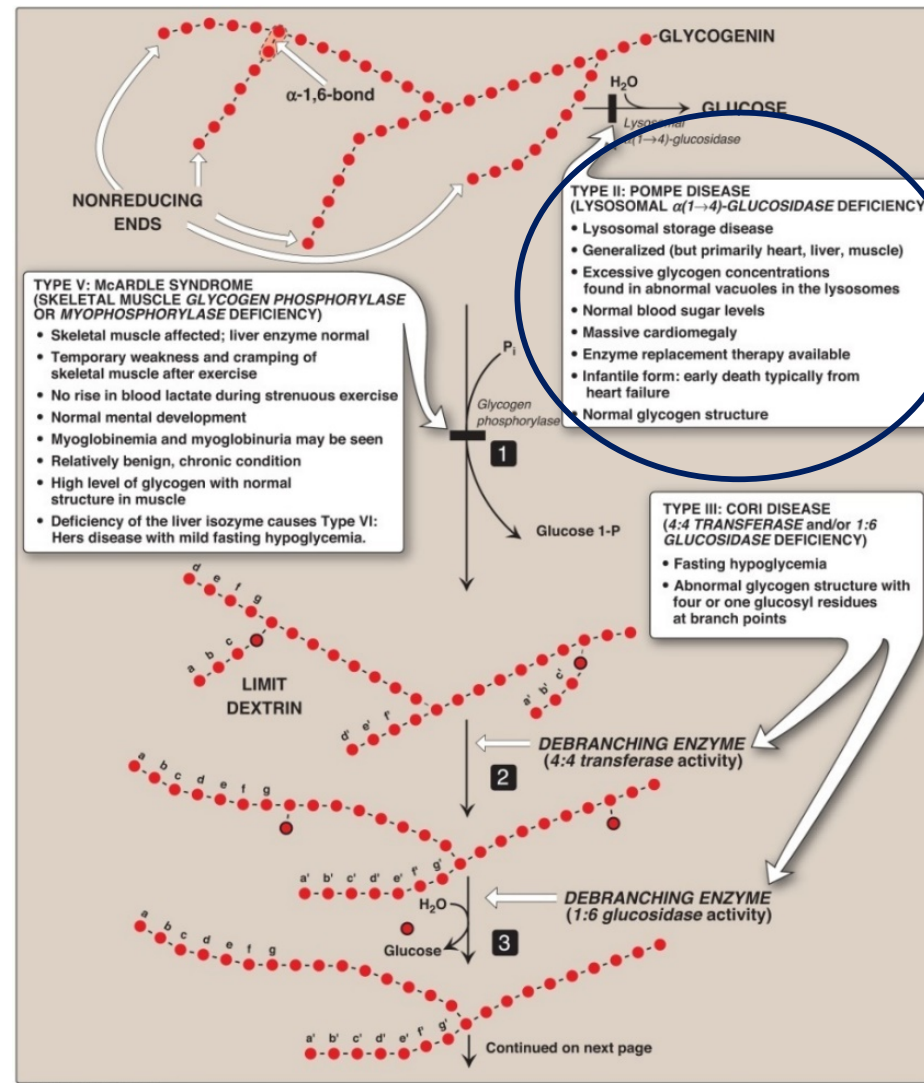
GSD Type V (McArdle Syndrome)



- Deficiency of skeletal muscle glycogen phosphorylase

Glycogen Storage Diseases

GSD Type II (POMPE DISEASE)



- Deficiency of Lysosomal $\alpha(1-4)$ glucosidase.

Reference

Lippincott's Illustrated Reviews Biochemistry: Unit II, Chapter 11, Pages 125 - 136.