

# Glycogen Metabolism

By

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# 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**

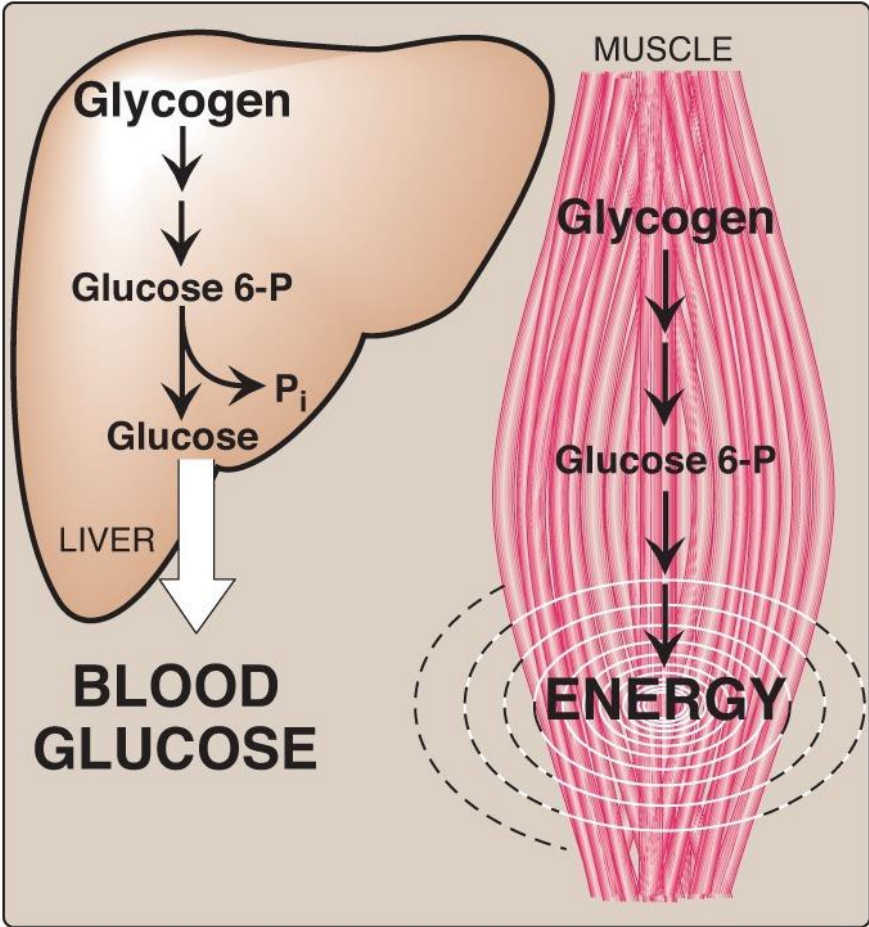
400 g in **muscles** (1-2% of resting muscles weight)

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

- **Functions of glycogen:**

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

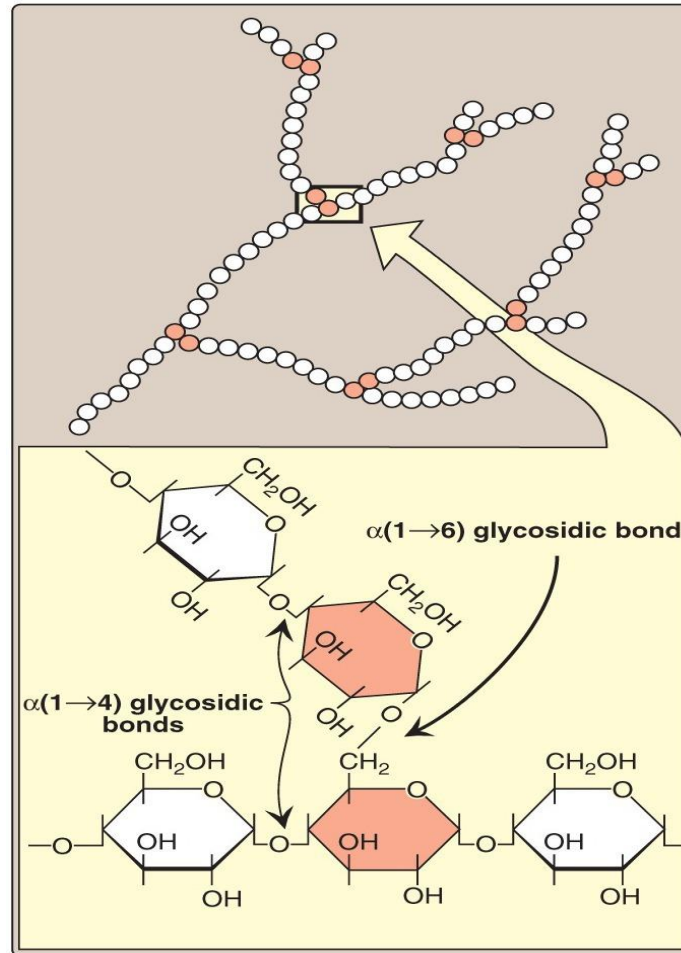
**Function of liver glycogen:** a source for blood glucose  
(especially during early stages of fasting)



# Structure of Glycogen

- Glycogen is a branched-chain homopolysaccharide made exclusively from  $\alpha$ -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)**

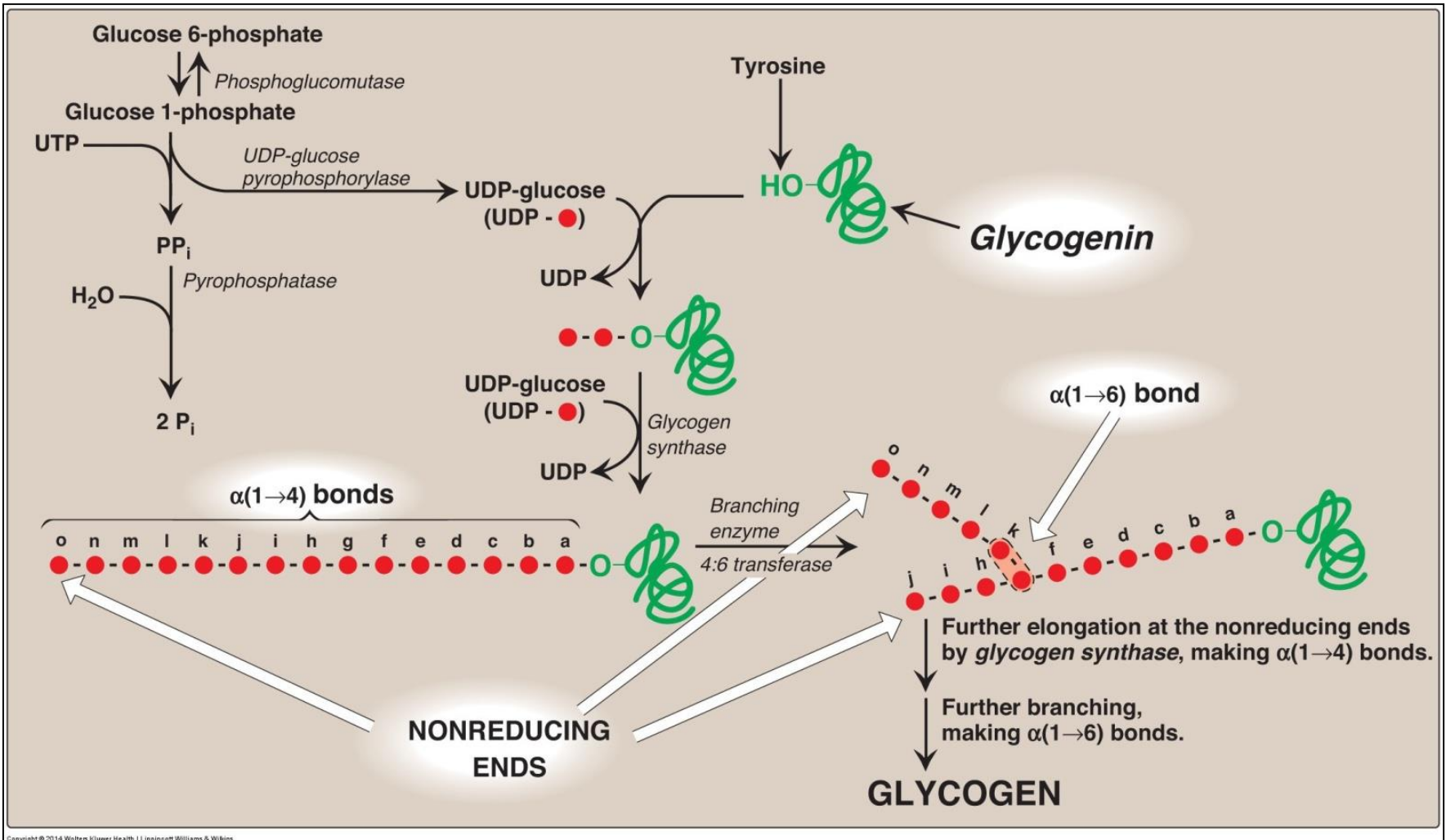
**3- ELONGATION: Glycogen synthase** (for  $\alpha$ 1-4 linkages)

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

**4- BRANCHING: Branching enzyme** (for  $\alpha$ 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)

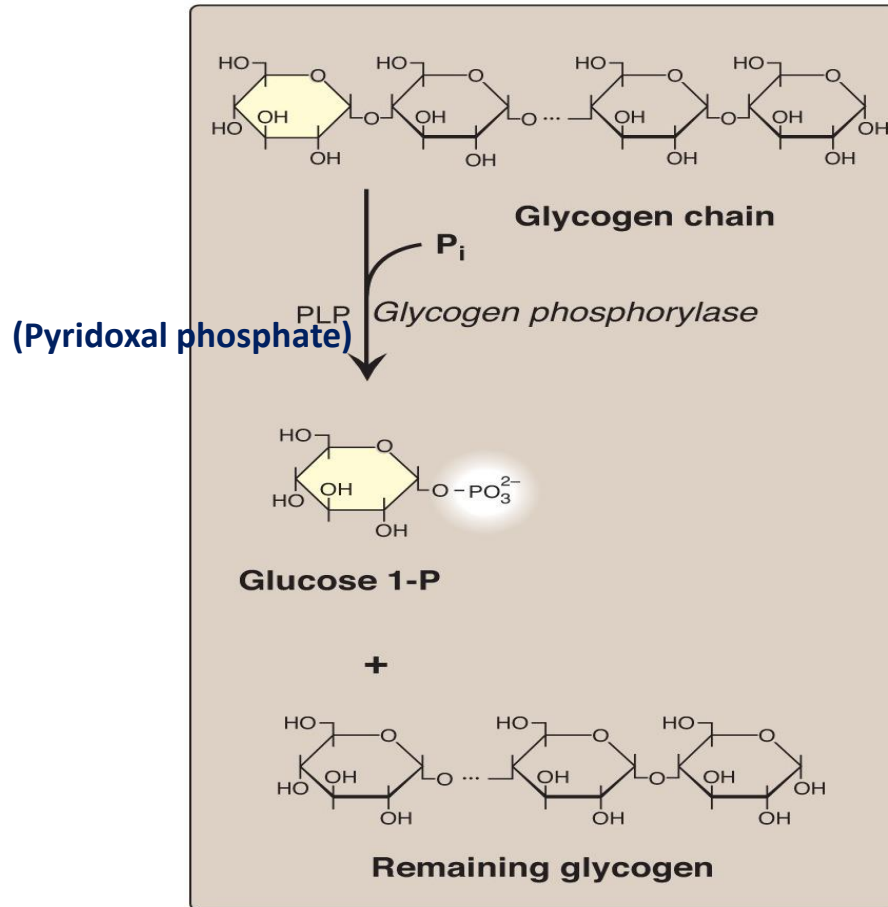
## 2- Removal of branches : by debranching enzymes

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

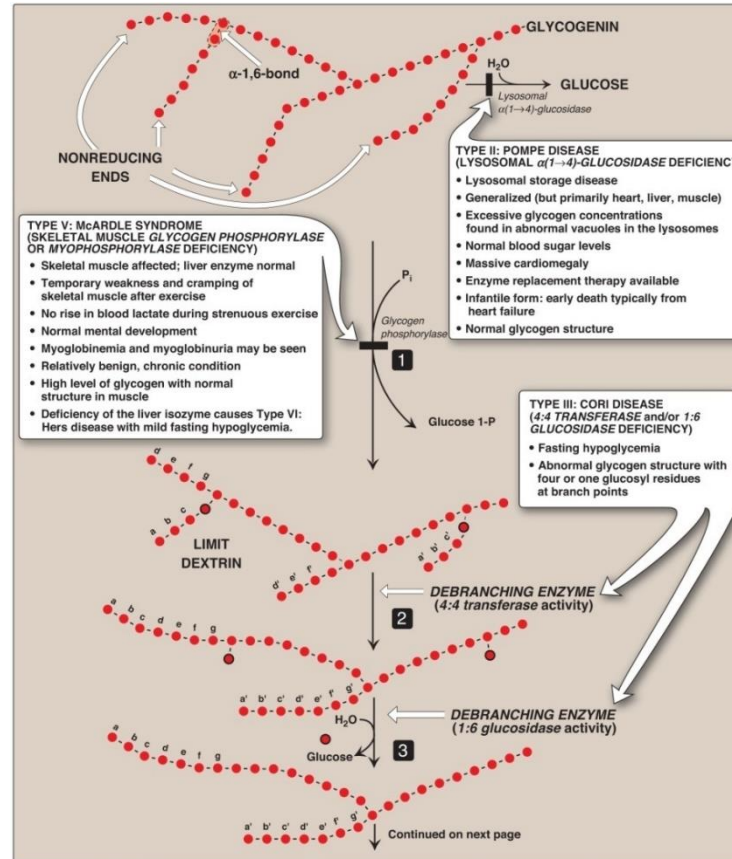
## 3- Fate of glucose 6-phosphate (G-6-P):

- 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)

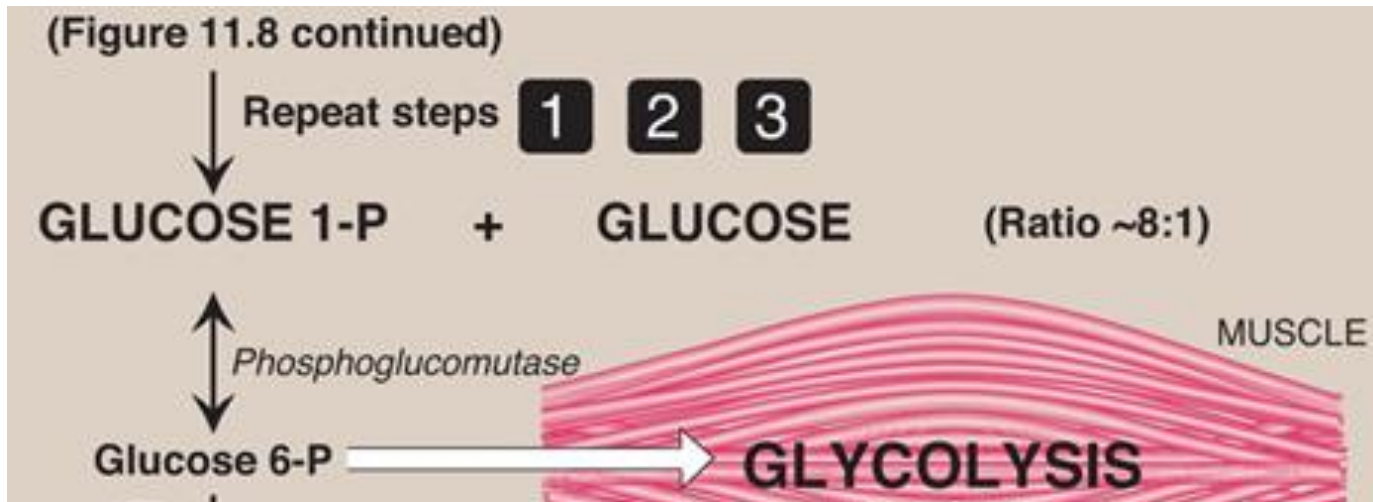
# Glycogenolysis



# Glycogenolysis



# Glycogenolysis



# Regulation of Glycogen Metabolism

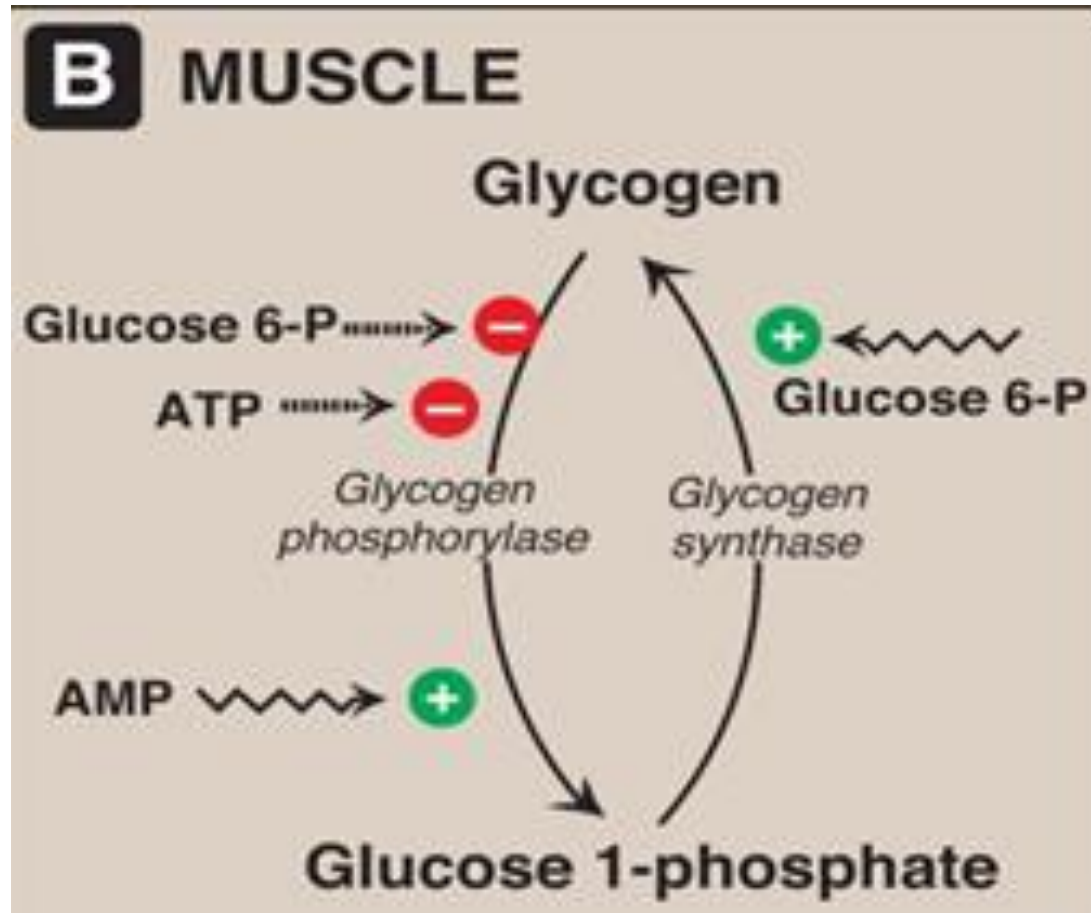
**Synthesis & degradation of glycogen are tightly regulated**

## **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

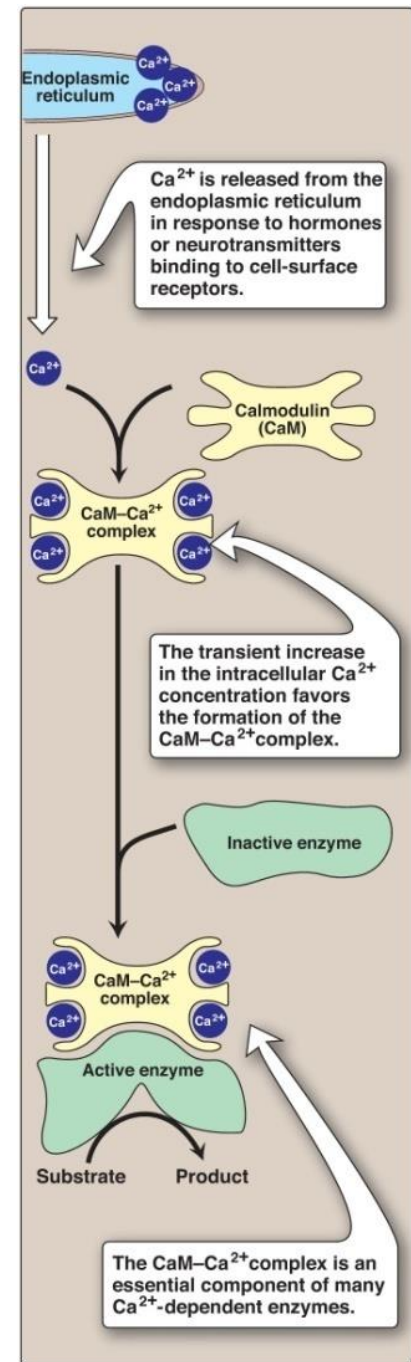


# Regulation of Glycogen Metabolism

Increase of calcium during muscle contraction

Formation of  $\text{Ca}^{2+}$  -calmodulin complex

Activation of  $\text{Ca}^{2+}$  -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:

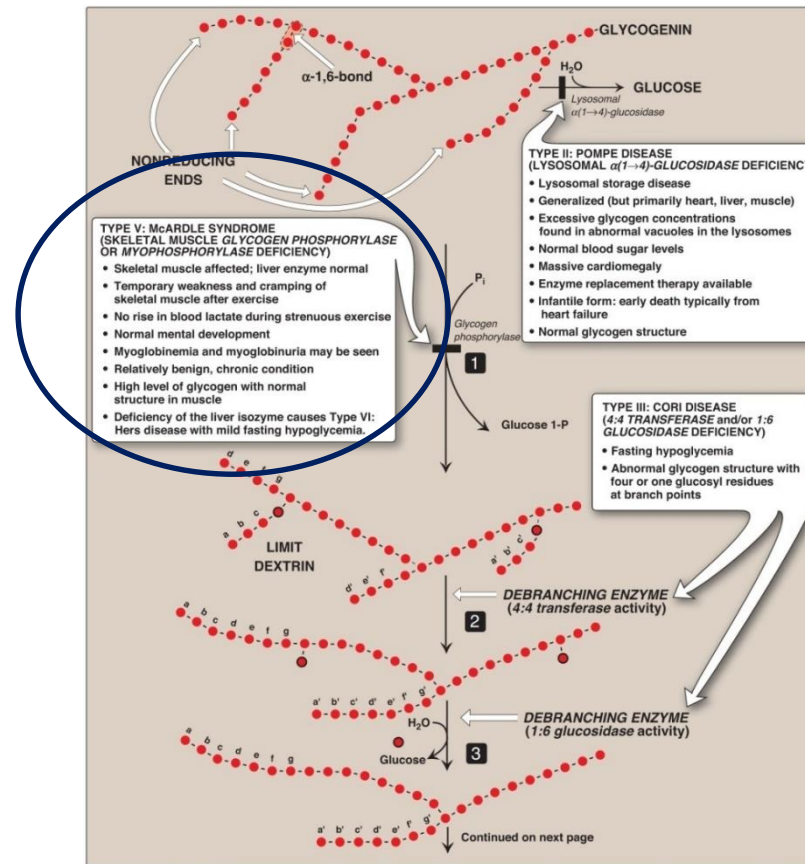
Formation of abnormal glycogen structure

OR

Excessive accumulation of normal glycogen in a specific tissue

# Glycogen Storage Diseases

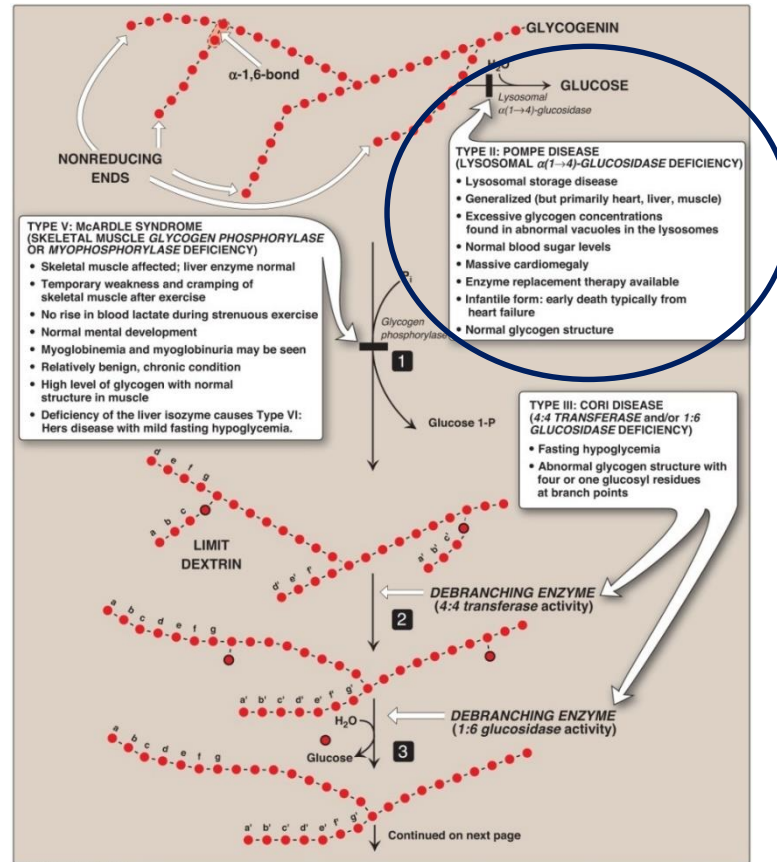
## GSD Type V (Mc Ardle Syndrome)



- Deficiency of skeletal muscle glycogen phosphorylase

# Glycogen Storage Diseases

## GSD Type II (POMPE DISEASE)



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

**THANK YOU 😊**