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

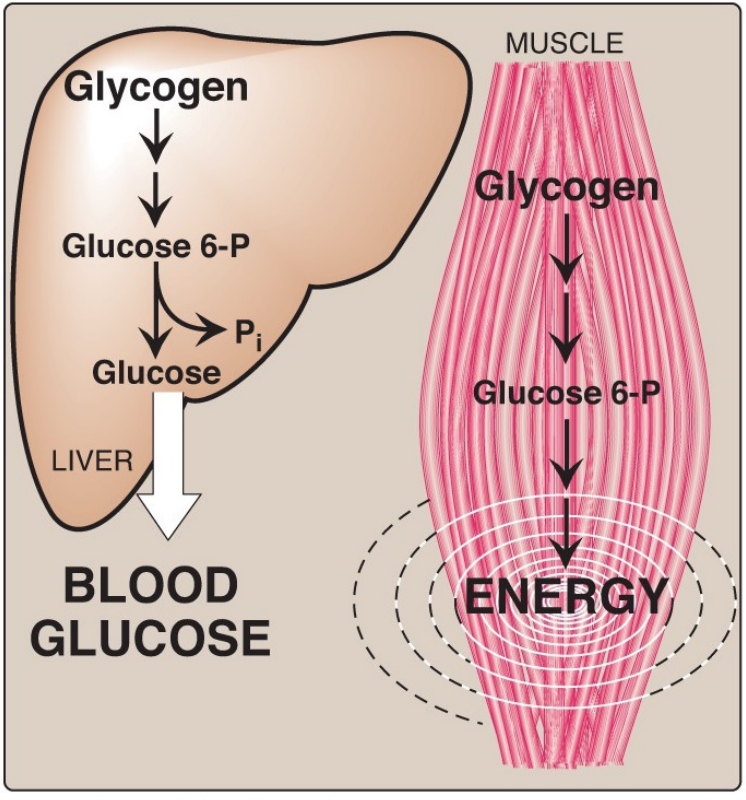
  400 g in muscles (1-2% of resting muscles weight)

  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)



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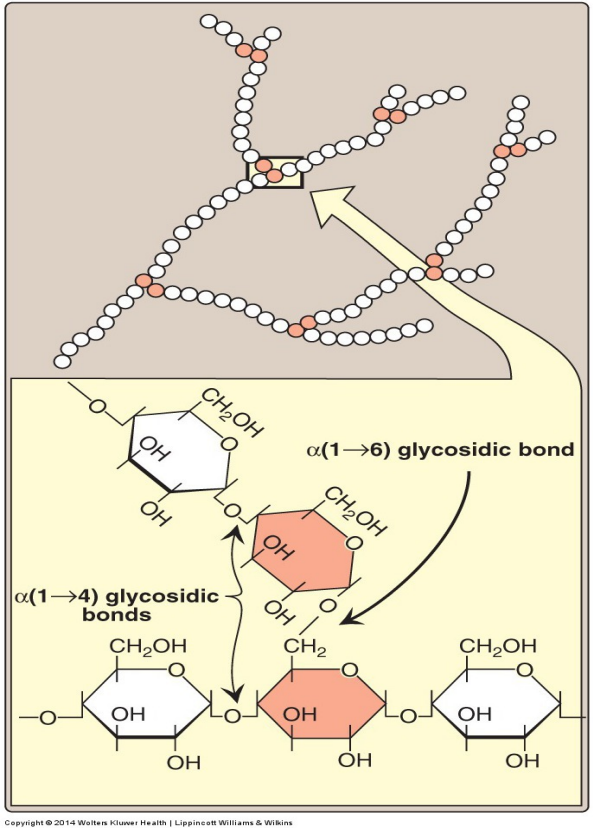
Structure of Glycogen

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



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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

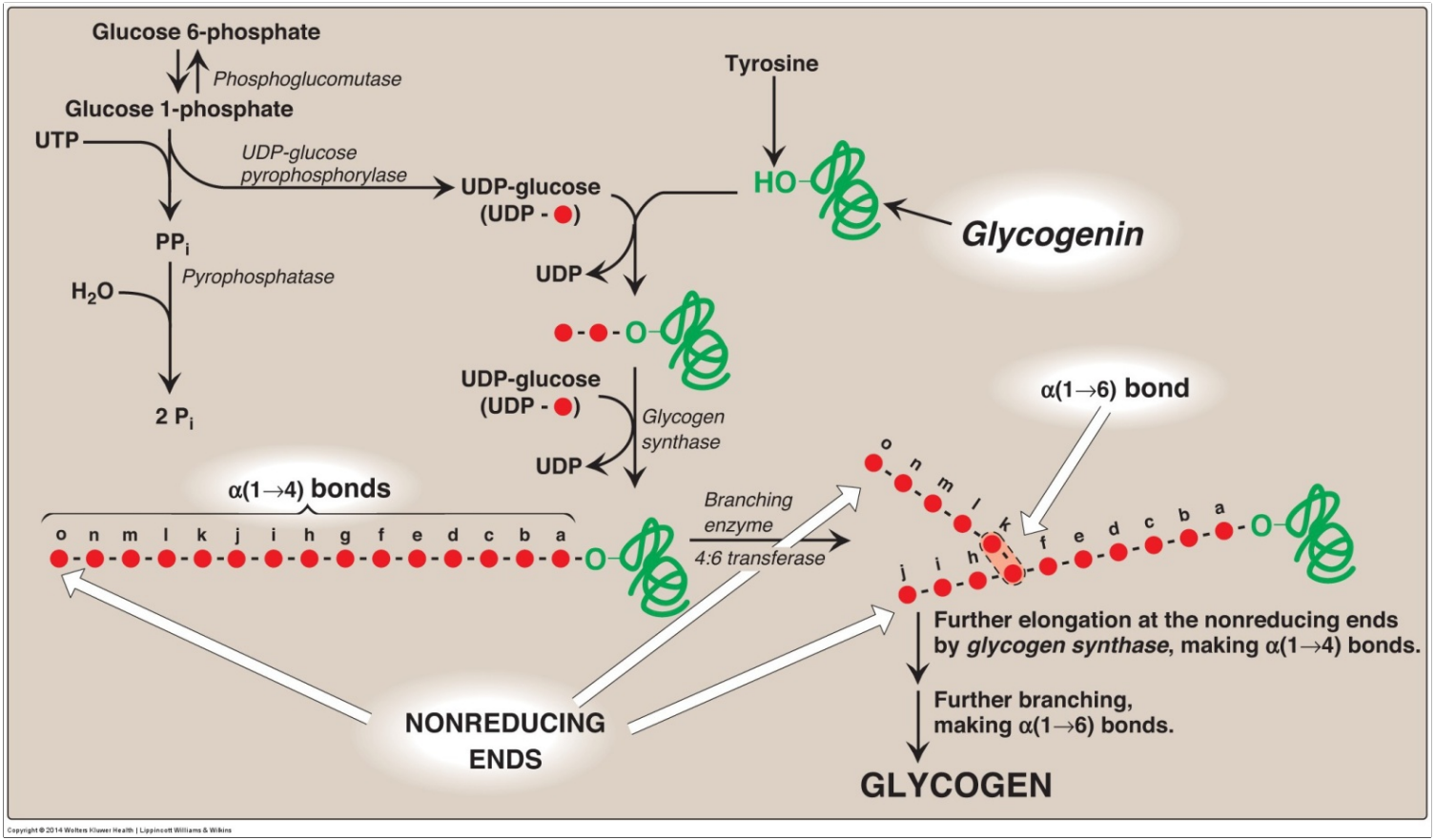
The use of glycogen primer (glycogenin)

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

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

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

Synthesis of Glycogen



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Glycogenolysis

(Breakdown of glycogen in skeletal muscles)

1- Shortening of glycogen chain: by glycogen phosphorylase

Cleaving of a(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

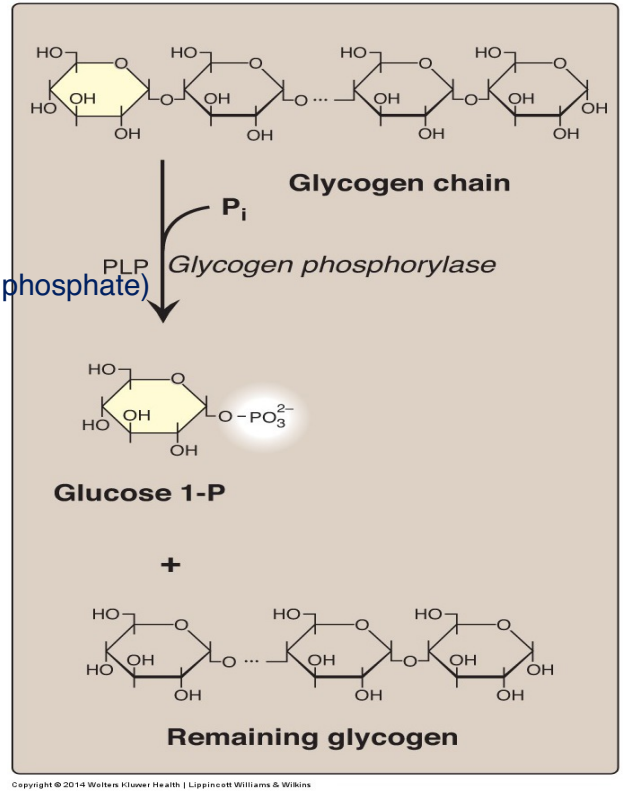
Cleaving of a(1-6) bonds of the glycogen chain producing free glucose (few)

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



(Pyridoxal phosphate)

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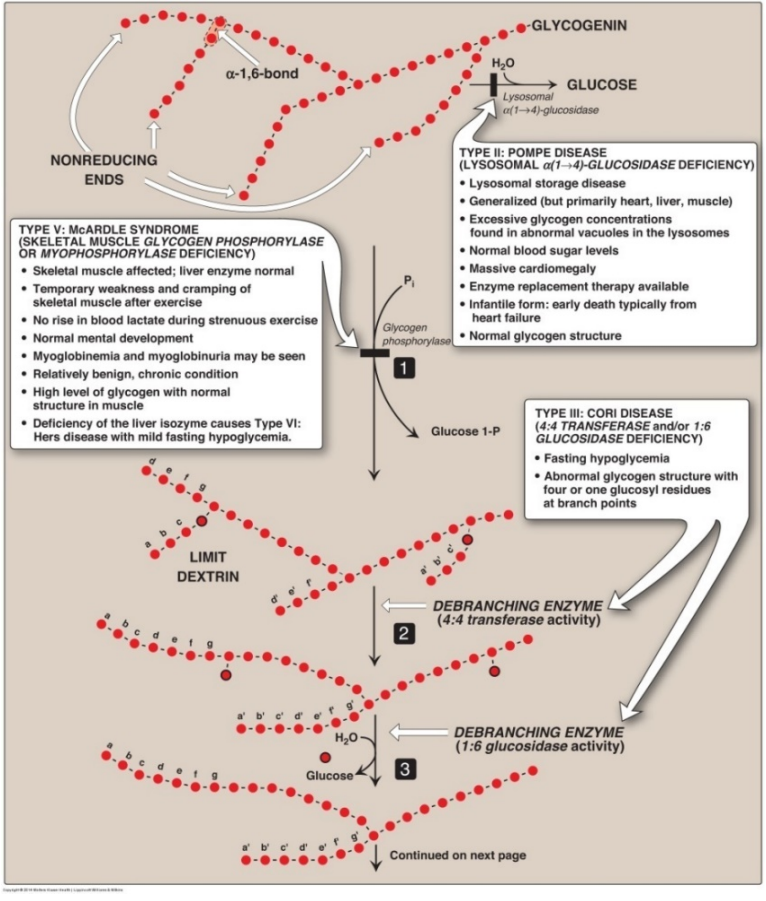
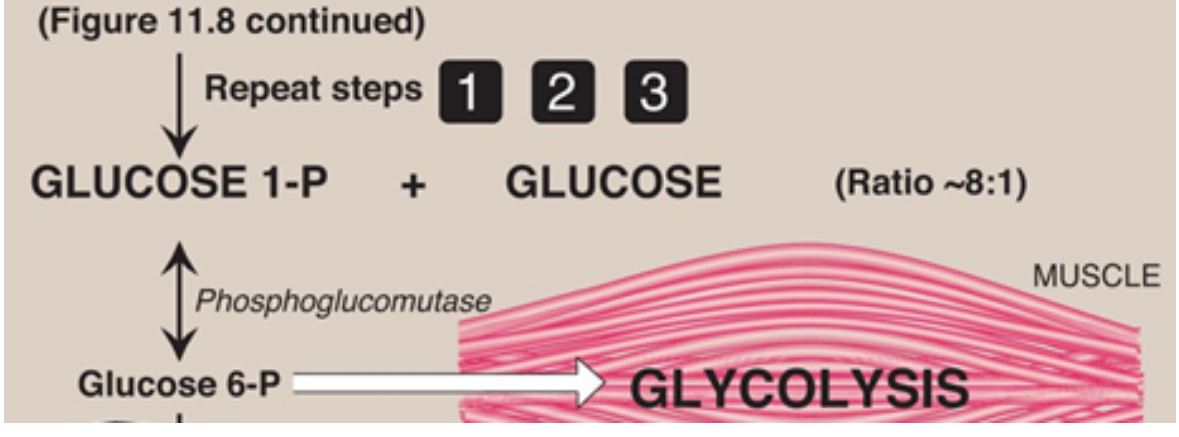
Glycogenolysis



Glycogenolysis



Regulation of Glycogen Metabolism

Synthesis & degradation of glycogen are tightly regulated

In Skeletal Muscles:

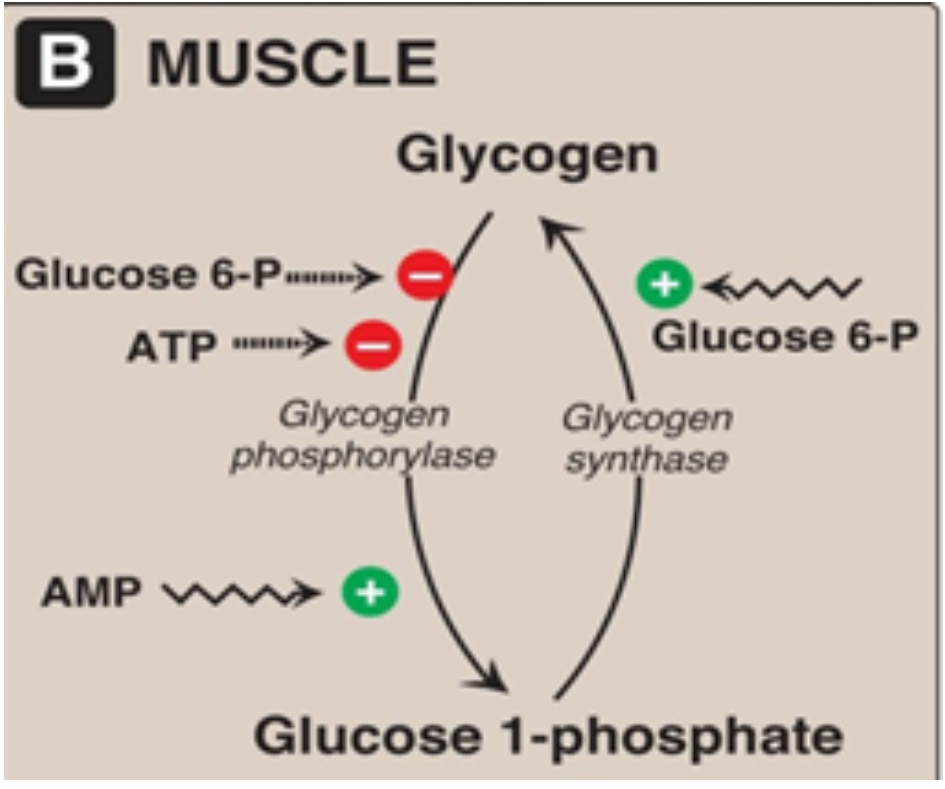
- Glycogen degradation occurs during active exercise
- Glycogen synthesis begins when the muscle is at rest

- Regulation occurs by 2 mechanisms:

1- Allosteric regulation

2- Hormonal regulation (Covalent modification)

Regulation of Glycogen Metabolism
1. Allosteric Regulation

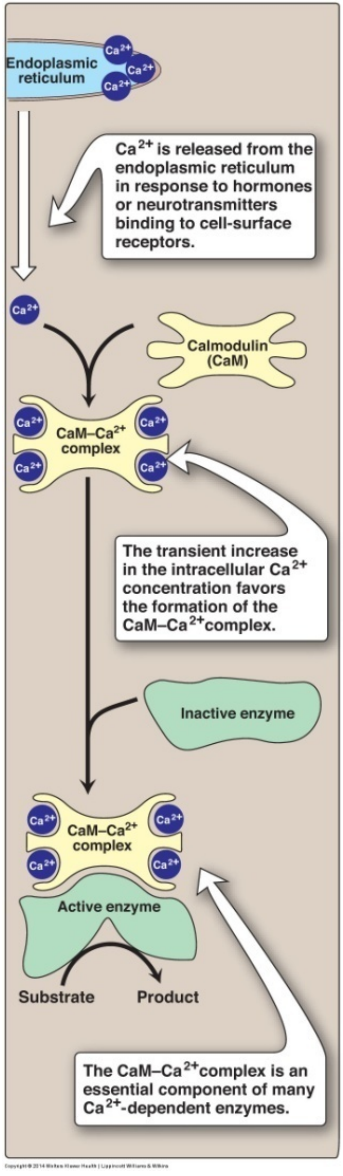


Regulation of Glycogen Metabolism

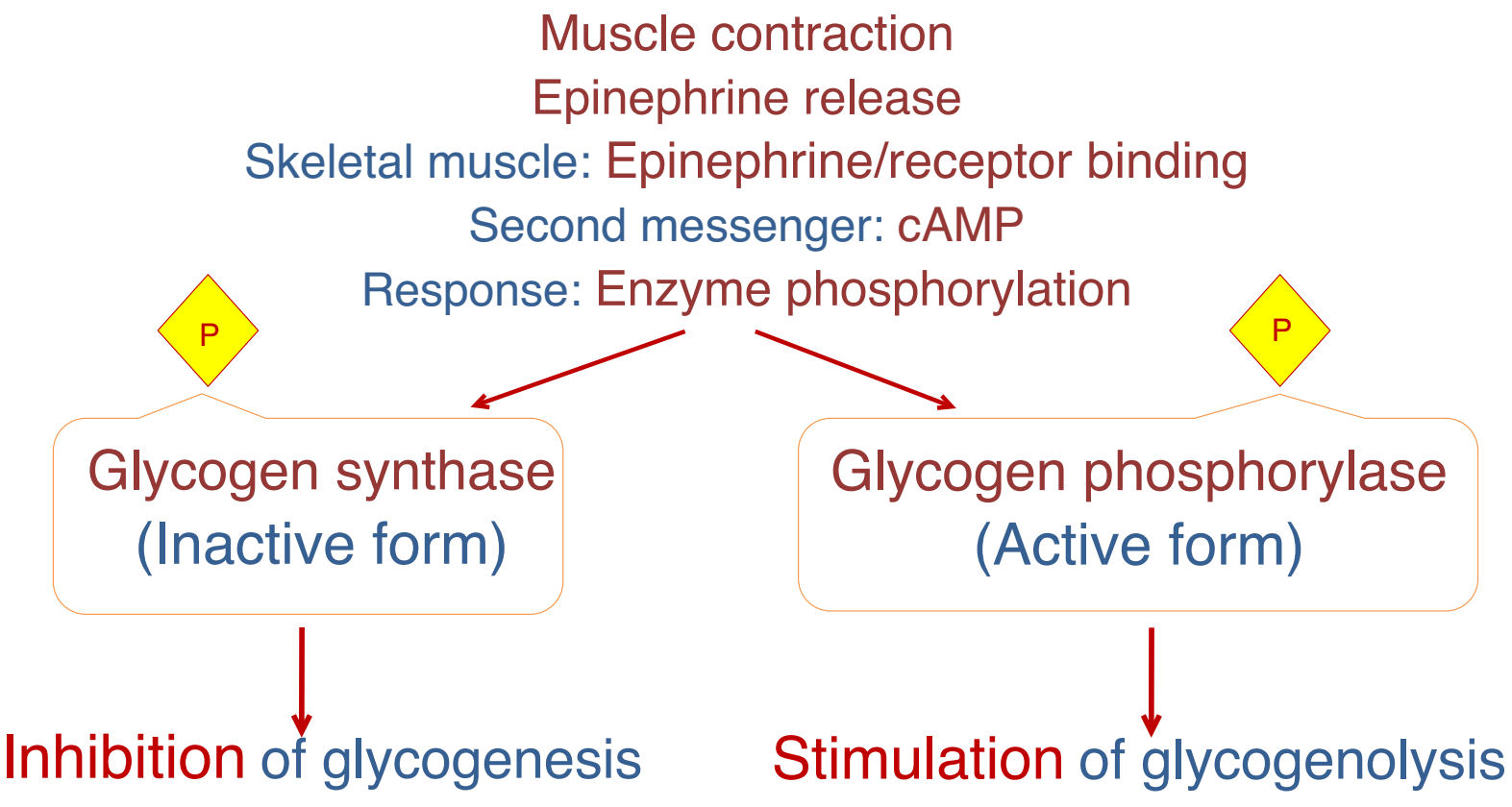
Increase of calcium during muscle contraction

Formation of Ca2+ -calmodulin complex

Activation of Ca2+ -dependent enzymes, e.g., glycogen phosphorylase



Regulation of Glycogen Metabolism: 2. Hormonal Regulation by Epinephrine



Glycogen Storage Diseases (GSD)

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

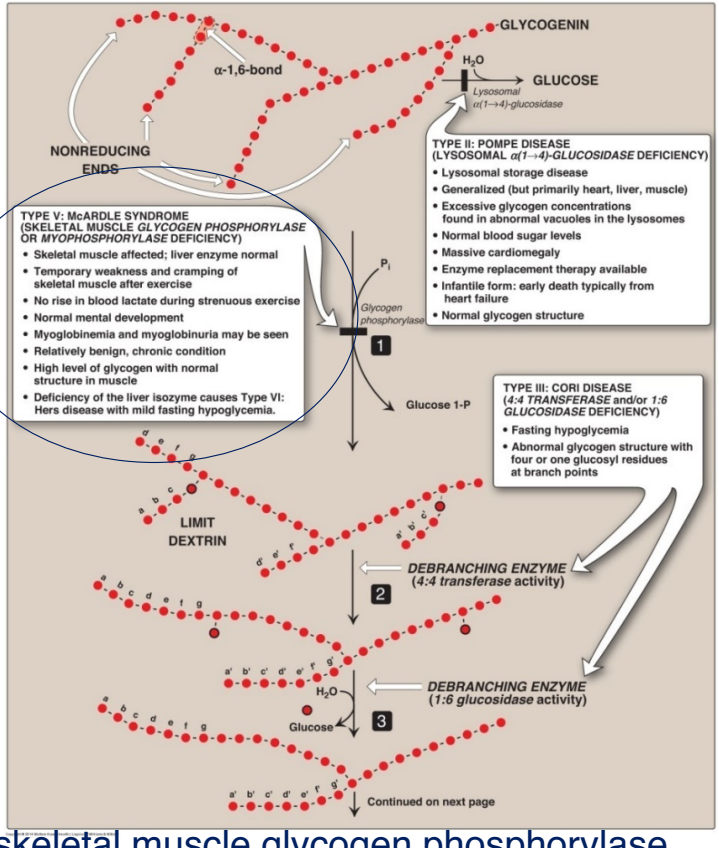
They result in:

Formation of abnormal glycogen structure

OR

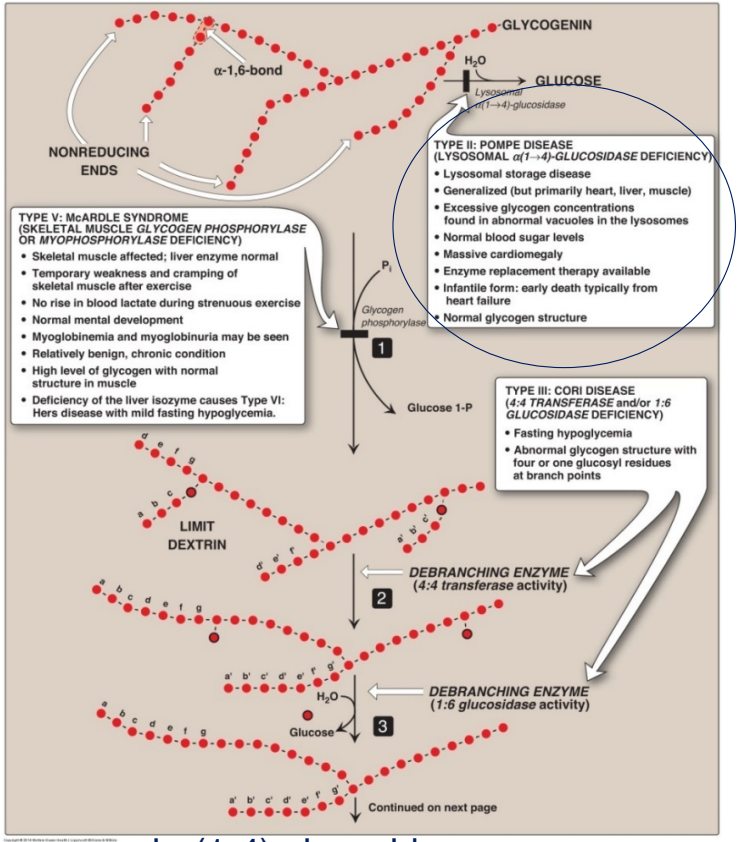
Excessive accumulation of normal glycogen in a specific tissue

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 α(1-4) glucosidase.

Reference

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