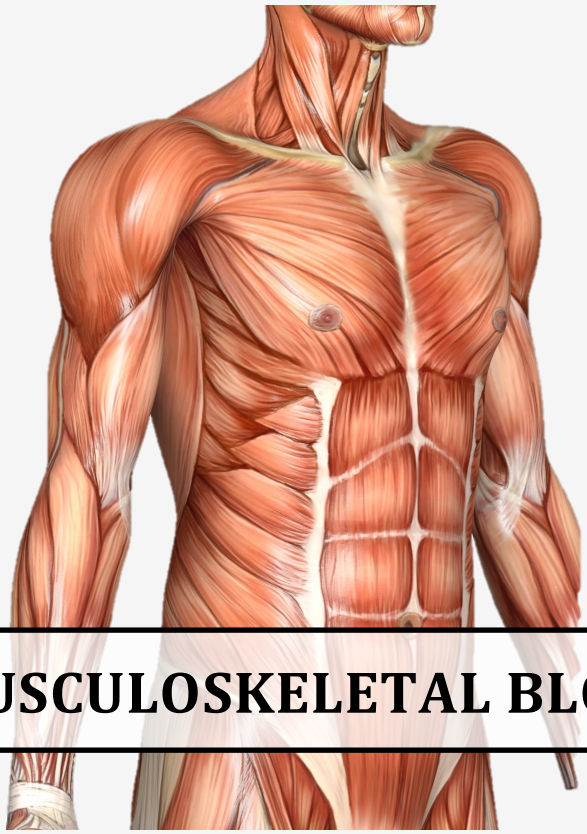

MUSCULOSKELETAL BLOCK

Lecture Title: Glycogen Metabolis

Lecture 1

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Color index:

Red= important

Purple = addition

Orange = Explanation

Objectives:

- Storage of carbohydrates in liver & muscle.
- Carbohydrates storage as glycogen.
- Overview of glycogen synthesis (Glycogenesis).
- Overview of glycogen breakdown (Glycogenolysis).
- Key elements in regulation of both Glycogenolysis and Glycogenesis.

Keywords:

- Glycogen
- Glycogenesis
- Glycogenolysis

Abbreviations

- G-6-P = Glucose 6-Phosphate

Location of glycogen

- 400g in muscles (1-2% of resting muscles weight)
- 100g in liver (~10% of well-fed liver)

Function of glycogen

- **Muscle:** fuel reserve (ATP) (during muscular exercise)
- **Liver:** a source for blood glucose (especially during early stages of fasting)

In liver when there is a tendency to hypoglycemia, the breakage of glycogen starts and when glycogen is consumed, gluconeogenesis will take place.

The end product for glycogenolysis in liver is **Glucose**; Because the enzyme glucose-6-phosphatase (convertor enzyme for glucose 6-p to free glucose) is found in the liver.

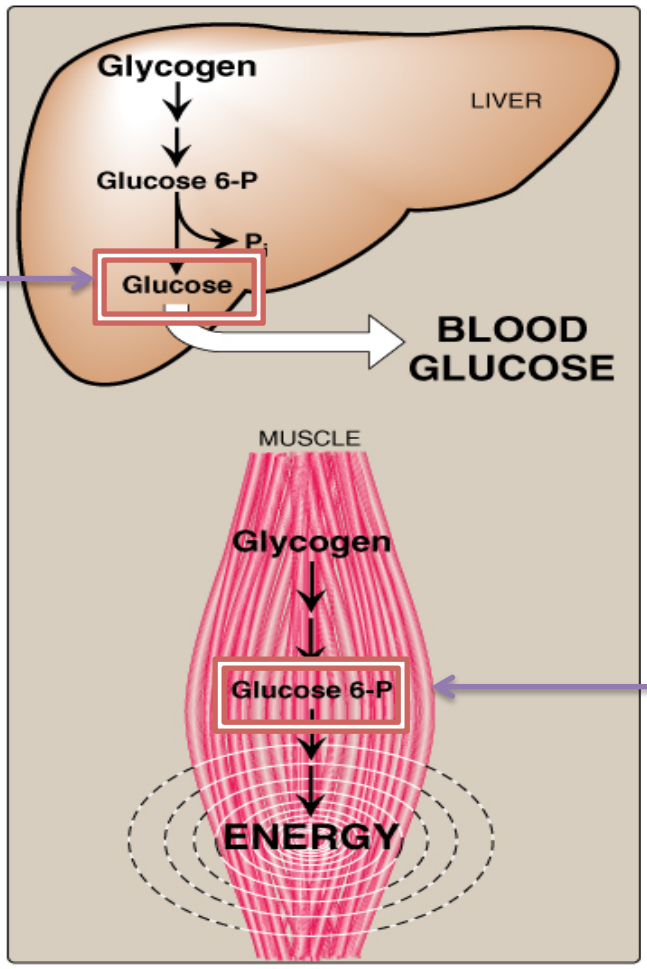


Figure 11.2
Functions of muscle and liver glycogen.

The end product for glycogenolysis in muscle is **Glucose 6-P**; Because the enzyme glucose-6-phosphatase can NOT be found in muscles (found only in liver and kidney).

Structure of Glycogen:

Glycogen is a branched chain "Homo-poly-saccharide" exclusively α - D-Glucose.

- Sugar
- The same
- More than 10

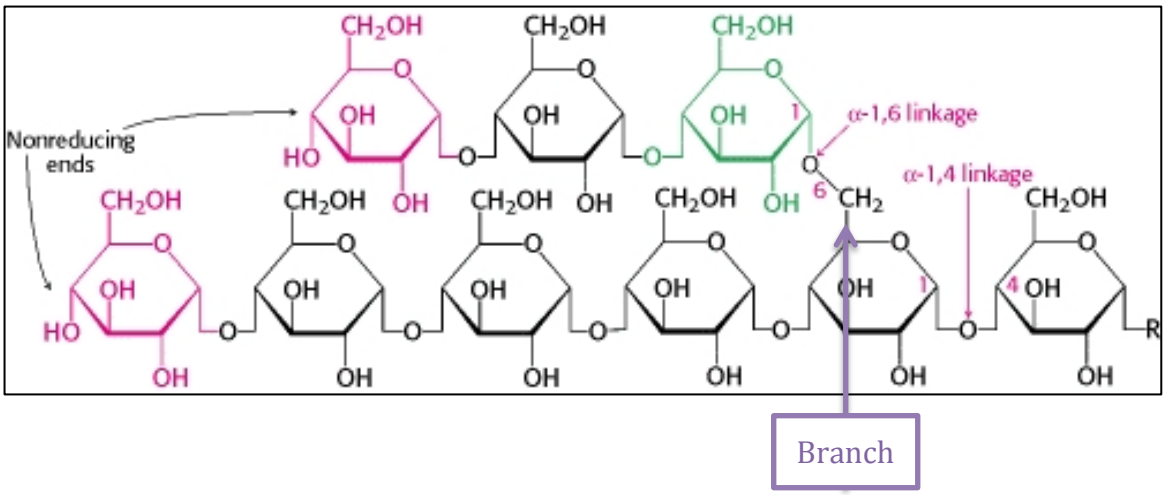
- **Glucose residues** (compound) are bound by ∝ [1 – 4] glucosidic linkage.

1st carbon atom binds to 4th carbon atom in the next glucose

- **Branches** (every 8–10 residue) are linked by ∝ [1–6] glucosidic linkage.

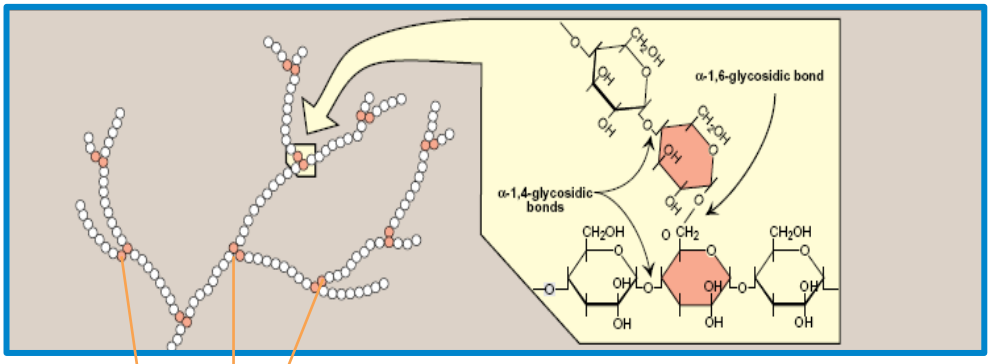
1st carbon atom binds to 6th carbon atom in the next glucose

In this structure of two outer branches of a glycogen molecule, the residues at the non-reducing ends are shown in red and residue that starts a branch is shown in green. The rest of the glycogen molecule is represented by R "side chain".

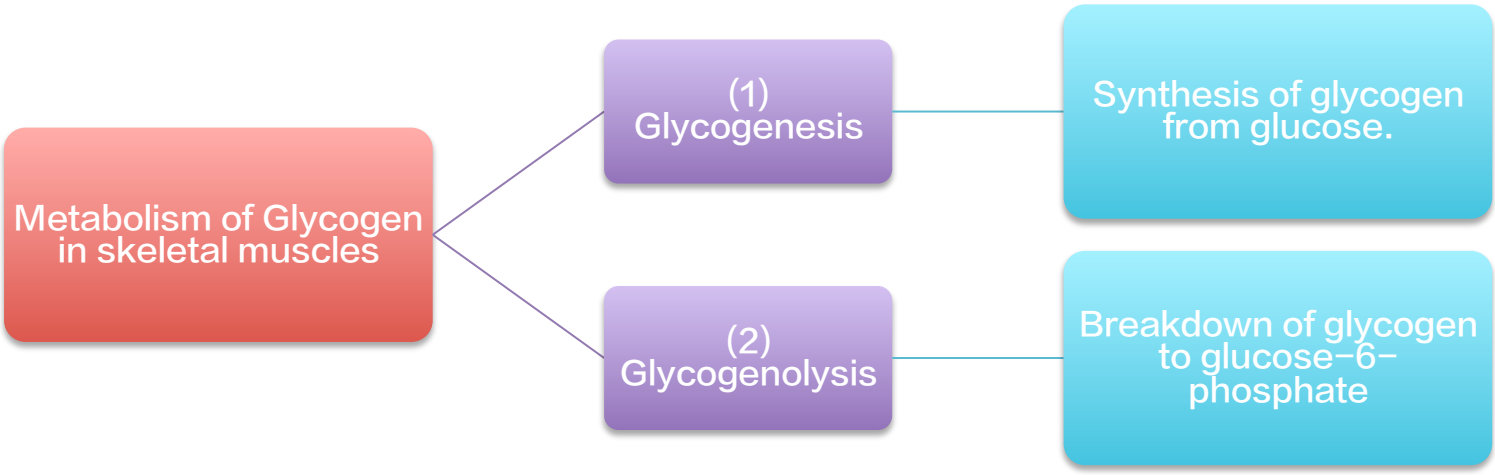


Why are Carbohydrates stored as glycogen?

1) Highly branched and that allows glycogen to be a readily source of glucose.
2) Easily add or remove glucose.



Branches point



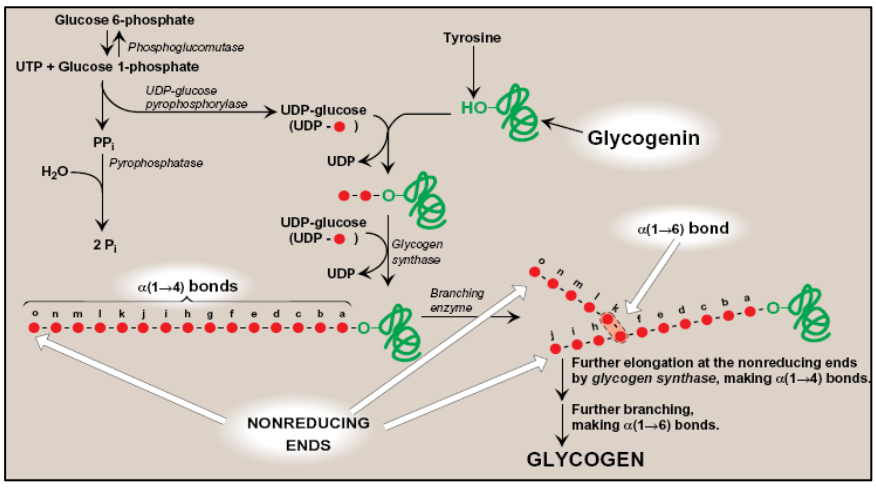
- Glycogen present in cytoplasm in the form of **granules** which contain most of the enzymes necessary for Glycogen synthesis and degradation.

(1) GLYCOGENESIS

- Building blocks: UDP-GLUCOSE.

Uredines DiPhosphate (UDP) is activator enzyme. It is important step to start glycogenesis

- Initiation of synthesis by
  i. Elongation of pre-existing glycogen fragment
  OR
  ii. The use of glycogen primer (glycogenin)



- ELONGATION by enzyme: Glycogen synthase (for α 1-4 linkages)
  Glycogen synthase (Rate-limiting enzyme) cannot initiate synthesis but only elongates pre-existing glycogen fragment or glycogen primer (glycogenin).

- BRANCHING: Branching enzyme (for a1-6 linkages).

(2) 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)

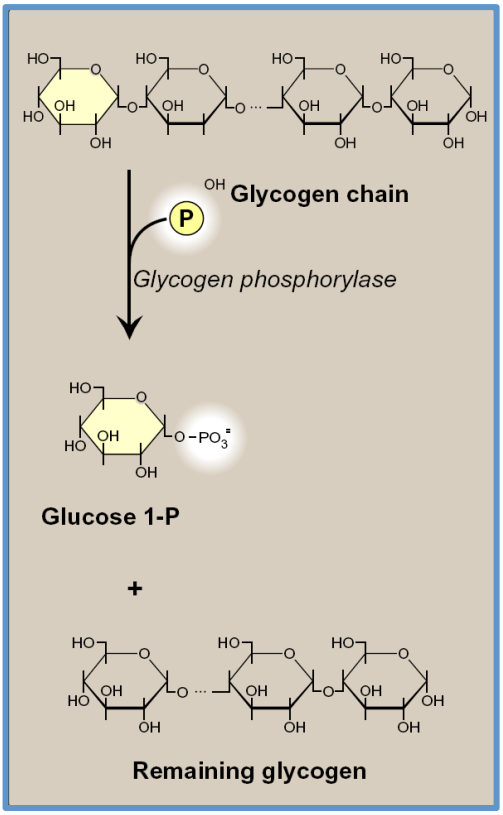
(Pyridoxal phosphate) is co-enzyme for glycogen phosphorylase. Derived from vitamin B.

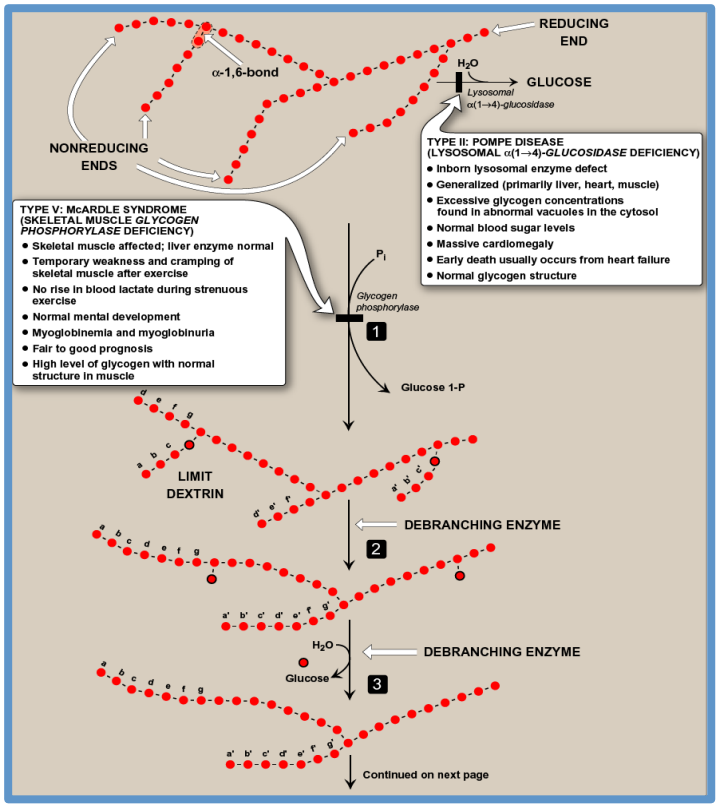
2- Removal of branches : by debranching enzymes

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)

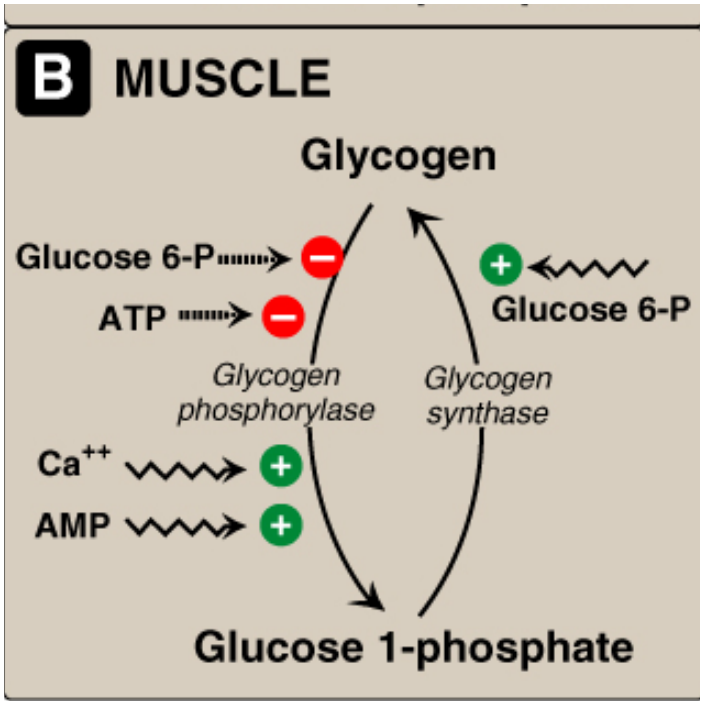
The end-product in muscle is energy by glycolysis of glucose-6-P and the net ATP will be 9 ATPs

UDP-Glucose → elongation of pre-existing OR glycogenin → Glycogen synthase → branching enzyme

Regulation of Glycogen Metabolism

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

1- ALLOSTERIC REGULATION

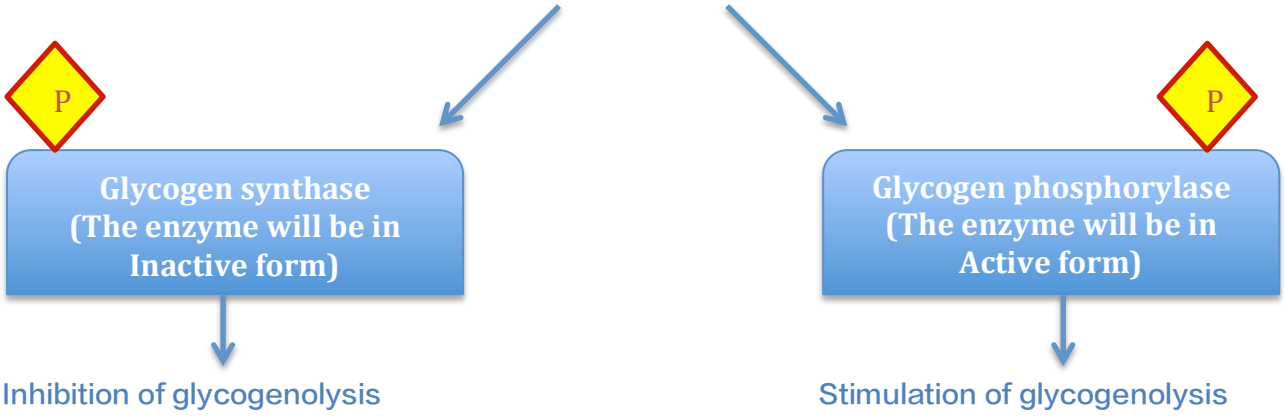


Glycogen phosphorylase		Glycogen synthase	
Inhibitors	**Stimulators**	**Inhibitors**	**stimulators**
Glucose 6-P	Ca++	–	Glucose 6-P
ATP	AMP		

- Increase of calcium during muscle contraction ➔ Formation of Ca^{2+}-calmodulin complex
  ➔ Activation of Ca^{2+}-dependent enzymes,
  e.g., glycogen phosphorylase

2- HORMONAL REGULATION BY EPINEPHRINE

Muscle contraction
↓
Epinephrine release
↓
Skeletal muscle: Epinephrine/receptor binding
↓
Second messenger: cAMP
↓
Response: Enzyme phosphorylation



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.

Type V: McARDLE SYBDROME (Skeletal muscle glycogen phosphorylase deficiency)

- Skeletal muscle affected; liver enzyme normal
- Temporary weakness and cramping of skeletal muscle after exercise
- No rise in blood lactate durning strenuous exercise
- Normal mental development
- Myoglobinemia (pigment found in blood which indicates muscle disease) and Myoglobinuria (pigment found in urine which indicates muscle disease)
- Fair to food prognosis

QUIZ

1- which one of these has the highest glycogen percentage in it?

a) Stomach
b) Liver
c) Muscles
d) Brain

2- the function of the liver glycogen is:

a) Provide ATP for muscles
b) Production of liver enzymes
c) Source for blood glucose
d) None of the following

3- The net ATP produced from glycogenlysis in the muscles:

a) 9
b) 8
c) 2
d) No energy it's energy consuming.

4- The end product for glycogenlysis is:

a) Glucose
b) Glycogen
c) Glucose 6-P
d) Glycogen 6-P

5- Glucose-1-P is converted to glucose-6-P by:

a) Phosphorylation
b) Mutase enzyme
c) PFK-1
d) Pyridoxal phosphate

6- Glycogen chain is converted to glucose-1-phosphate by:

a) Glycogen phosphorylase
b) Mutase enzyme
c) Phosphorylation
d) PFK-1

7- Glycogen _____ begins when the muscle is at rest:

a) Degradation
b) Synthesis
c) Carboxylation
d) Phosphorylation

8- Which one of the following is a glycogen storage disease:

a) Anemia
b) Mcardle syndrome
c) Métabolique syndrome
d) Marfan syndrome

ANSWERS:
1- B
2- C
3- A
4- C
5- B
6- A
7- B
8- B

GOOD LUCK