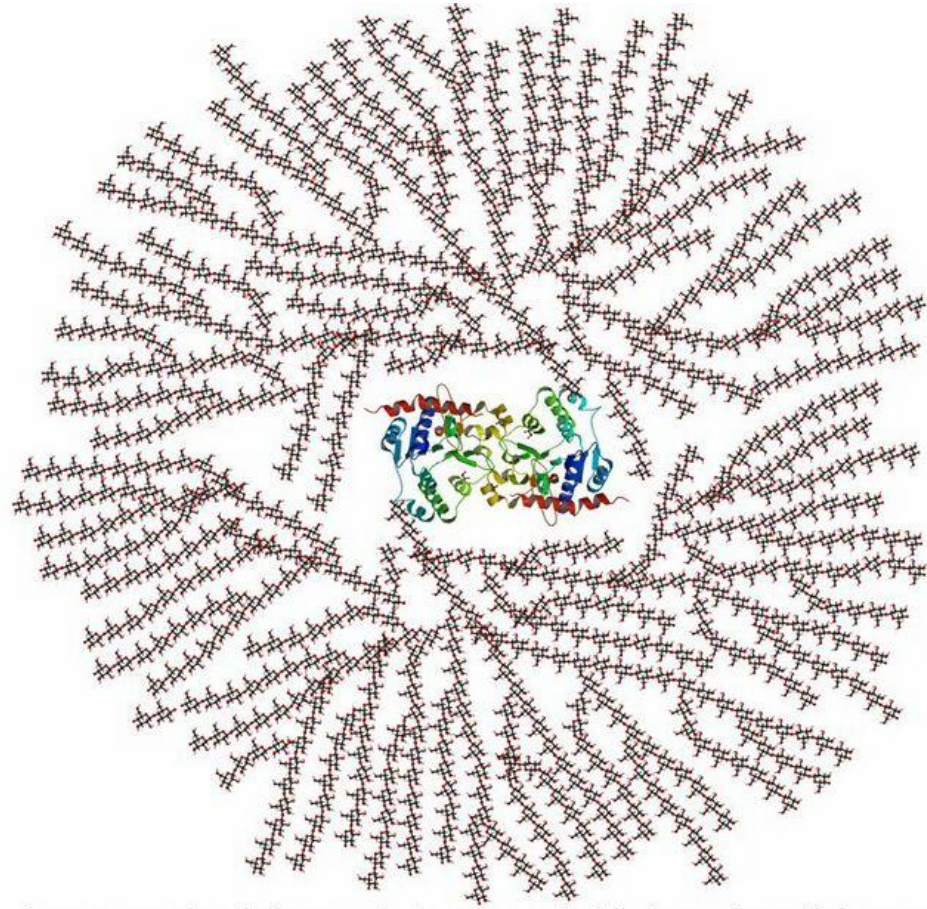


# Glycogen Metabolism



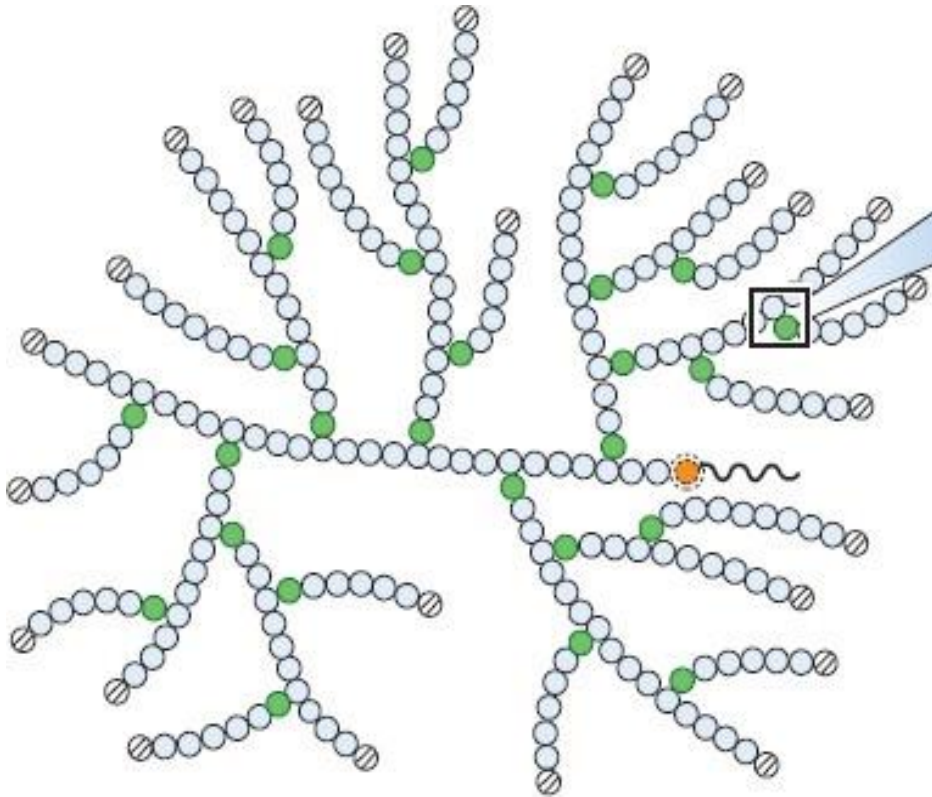
A core protein of glycogenin is surrounded by branches of glucose units.  
The entire globular complex may contain approximately 30,000 glucose units.

Dr. Diala Abu-Hassan

# Sources of Blood Glucose

- Diet
  - Starch, mono and disaccharides, glucose
  - Sporadic, depend on diet
- Glycogen
  - Storage form of glucose
  - Rapid response
  - Limited amount
  - Important energy source for exercising muscle
- Gluconeogenesis
  - Sustained synthesis
  - Slow in responding to falling blood glucose level

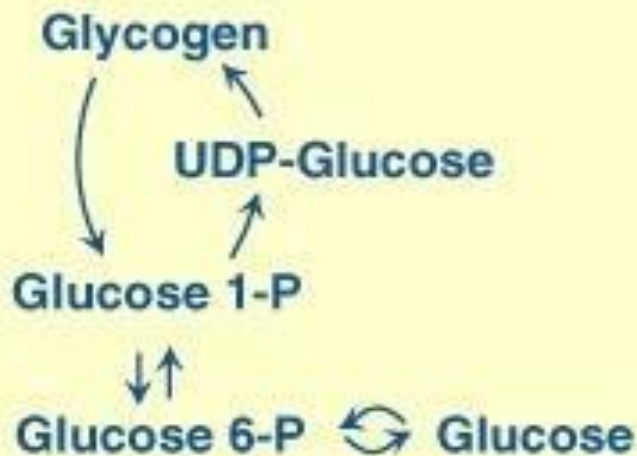
# Glycogen Structure



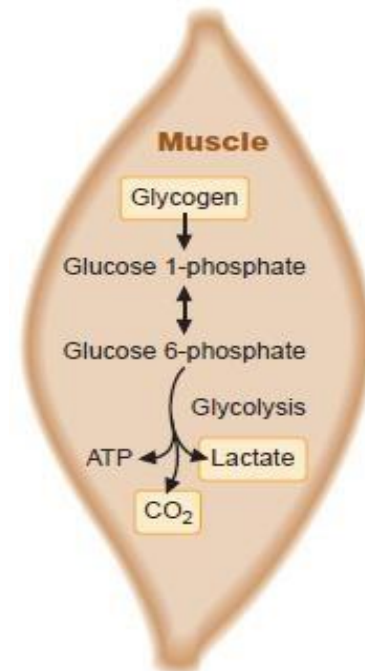
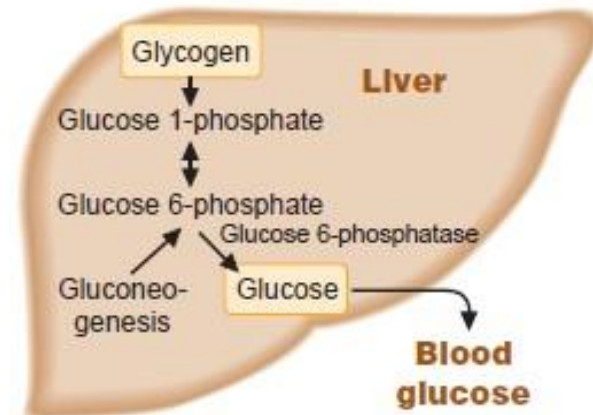
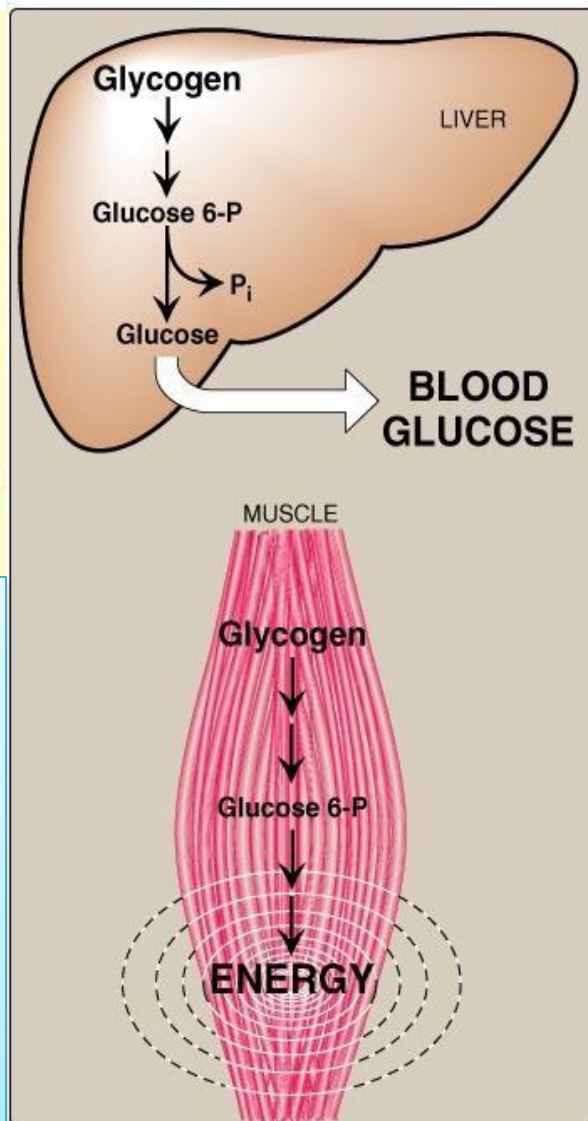
\*Extensively branched homopolysaccharide

\*One molecule consists of hundreds of thousands of glucose units

# Glycogen synthesis & degradation

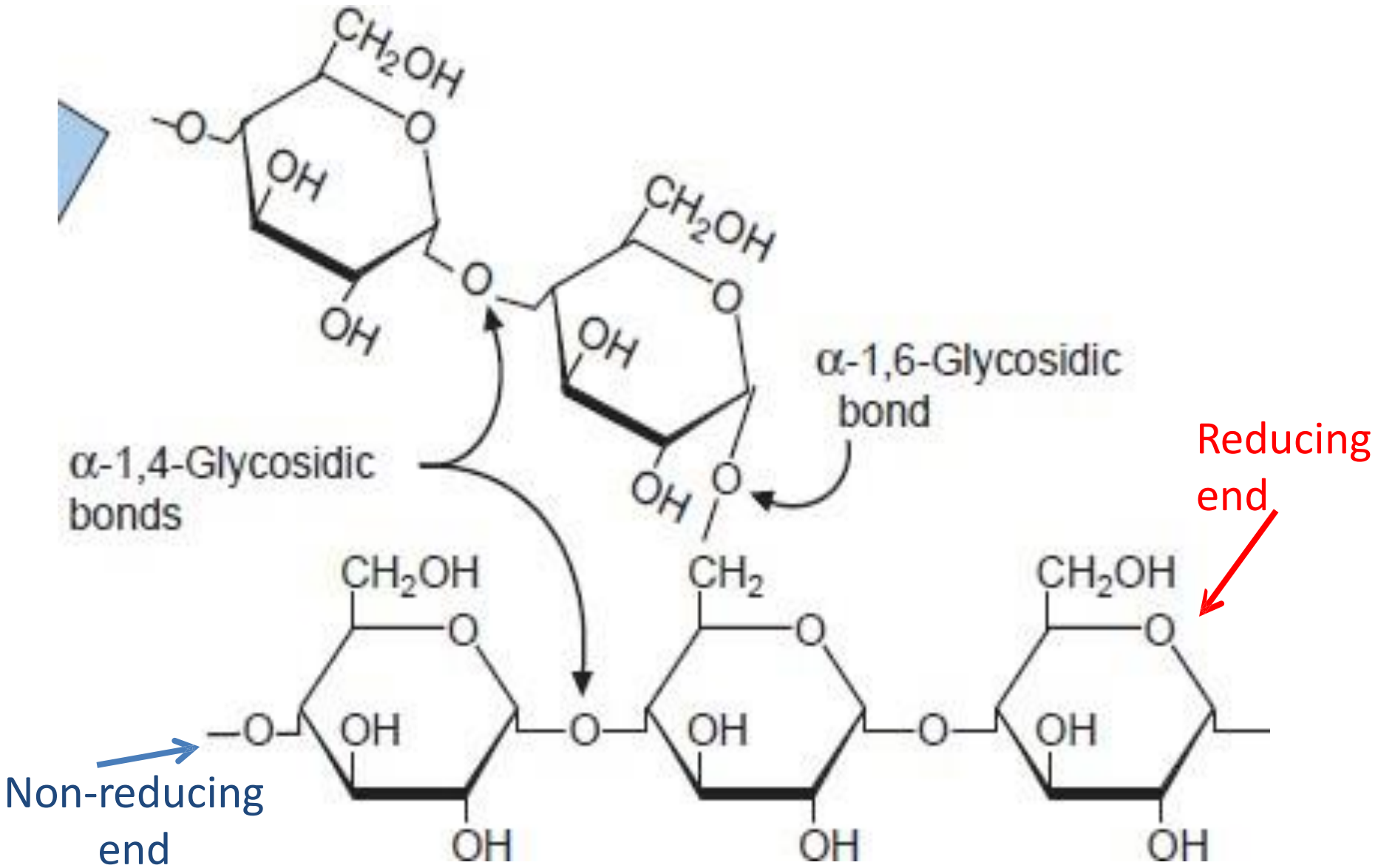


- Liver glycogen stores increase during the well-fed state and are depleted during fasting
- Muscle glycogen is not affected by short periods of fasting (a few days) and is only moderately decreased in prolonged fasting (weeks).



Fates of Glucose that results from glycogen degradation

# Direction of Glycogen Degradation

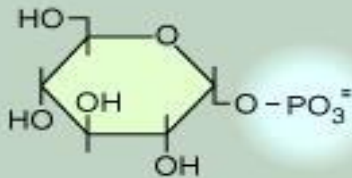
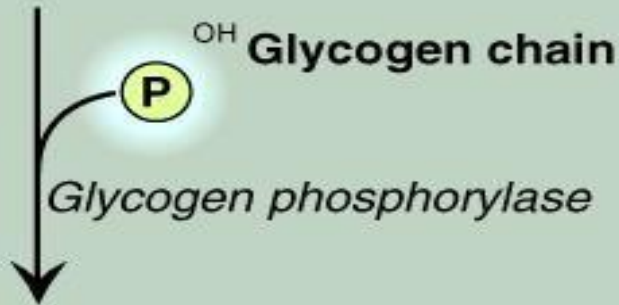
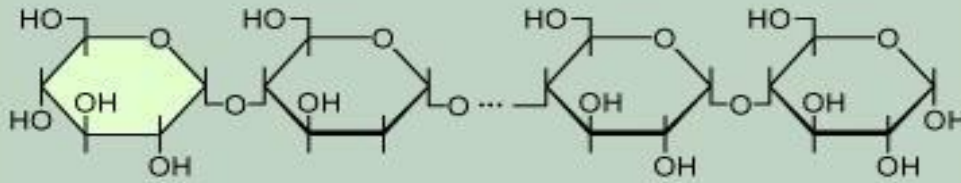


# Degradation of glycogen (Glycogenolysis)

Degradation of glycogen  
One glucose unit is removed at a time

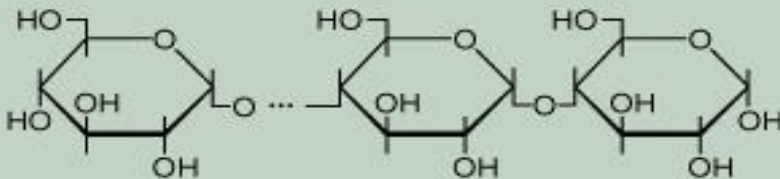
Starts from the non-reducing ends

Released in the form of glucose 1-phosphate



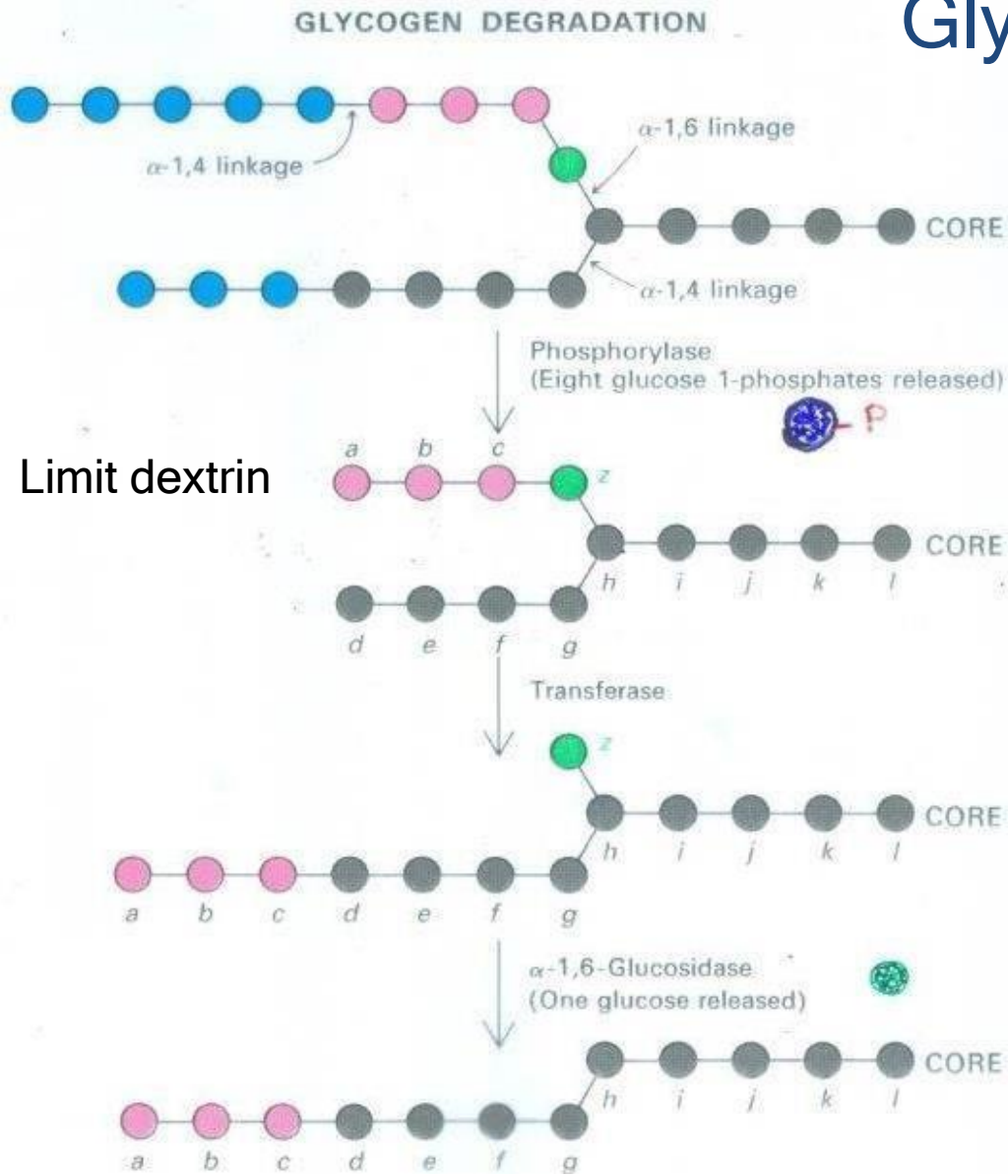
**Glucose 1-P**

+



**Remaining glycogen**

# Glycogen Degradation



Limit dextrin

Debranching enzyme

G-1-P is converted in the cytosol to G-6-P by phosphoglucomutase

# Lysosomal degradation of glycogen

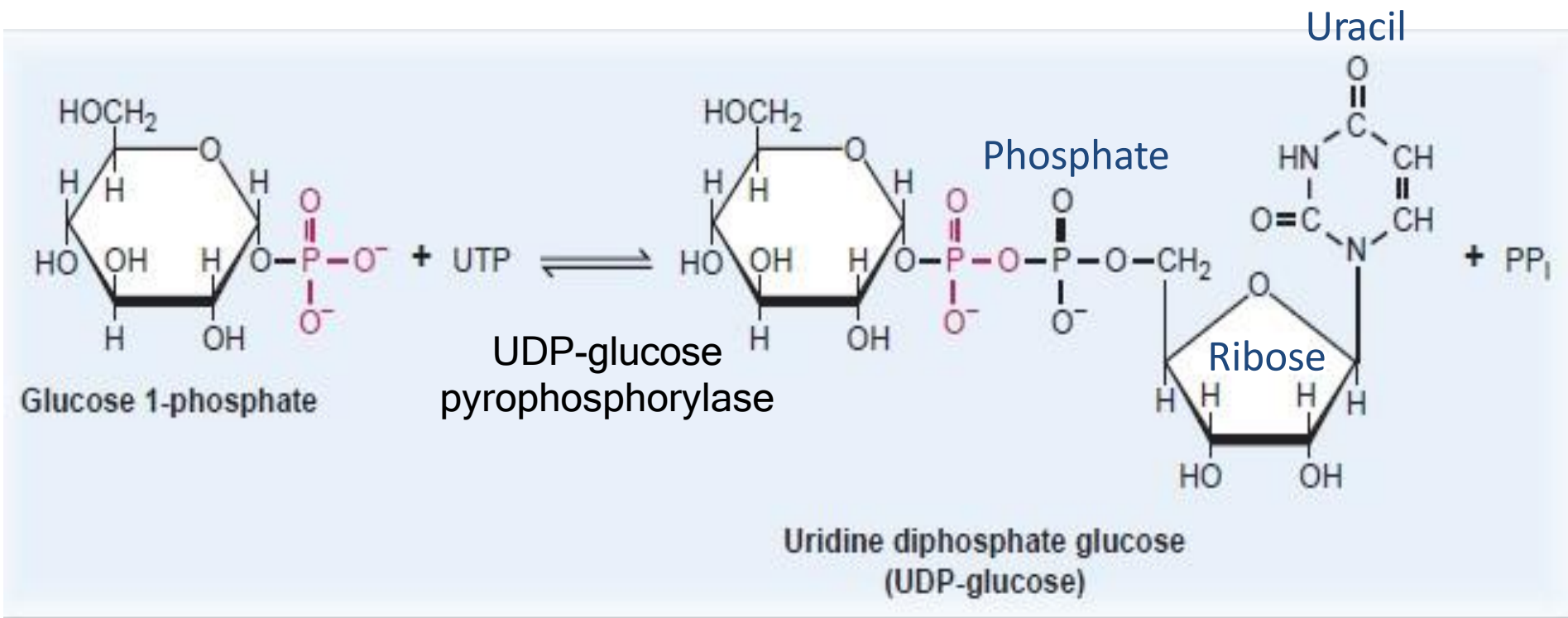
- A small amount (1-3%) of glycogen is degraded by the lysosomal enzyme,  $\alpha(1-4)$ -glucosidase (acid maltase).
- The purpose of this pathway is unknown.
- A deficiency of this enzyme causes accumulation of glycogen in vacuoles in the lysosomes (Type II: Pompe disease)



# Glycogen Synthesis (glycogenesis)

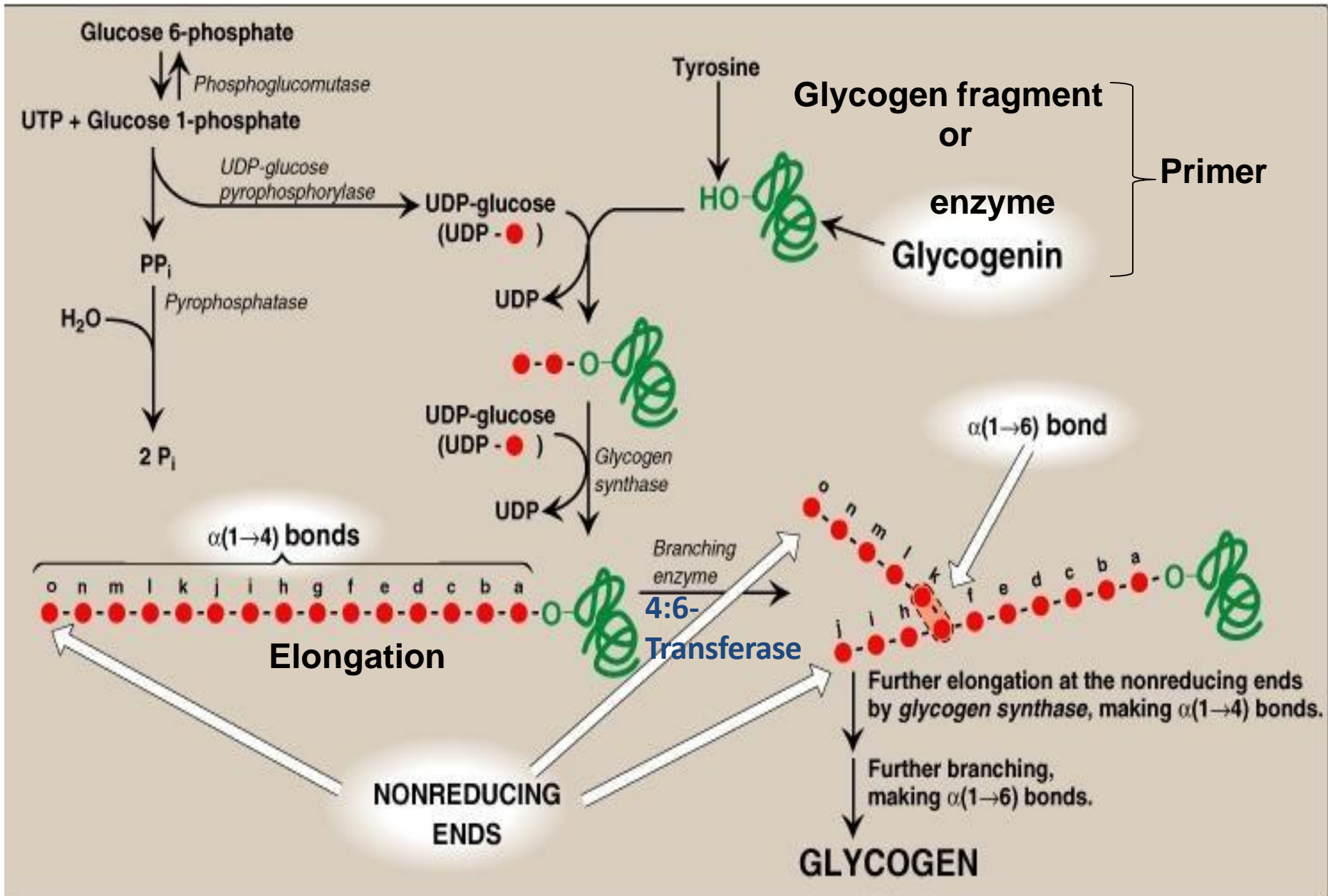
# Glycogenesis-Glycogen synthesis

Glycogen is synthesized by adding glucose one by one  
UDP-Glucose is the active donor of glucose units

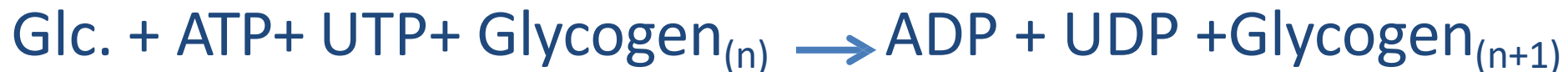
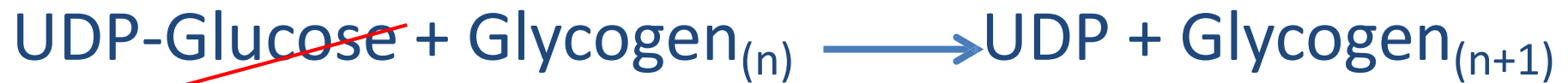
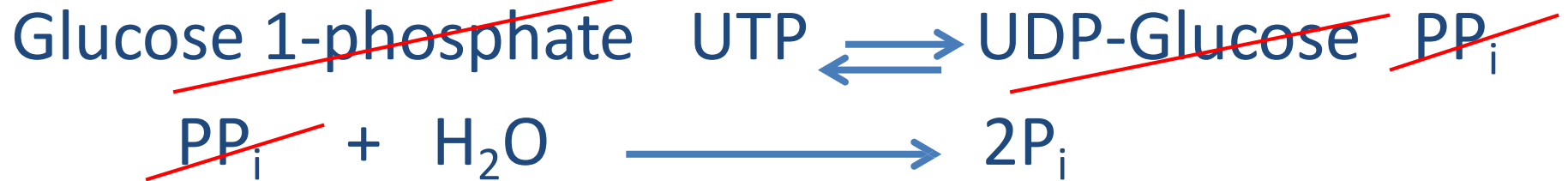


Formation of UDP-Glucose

# Glycogen Synthesis



# Energy needed for glycogen synthesis

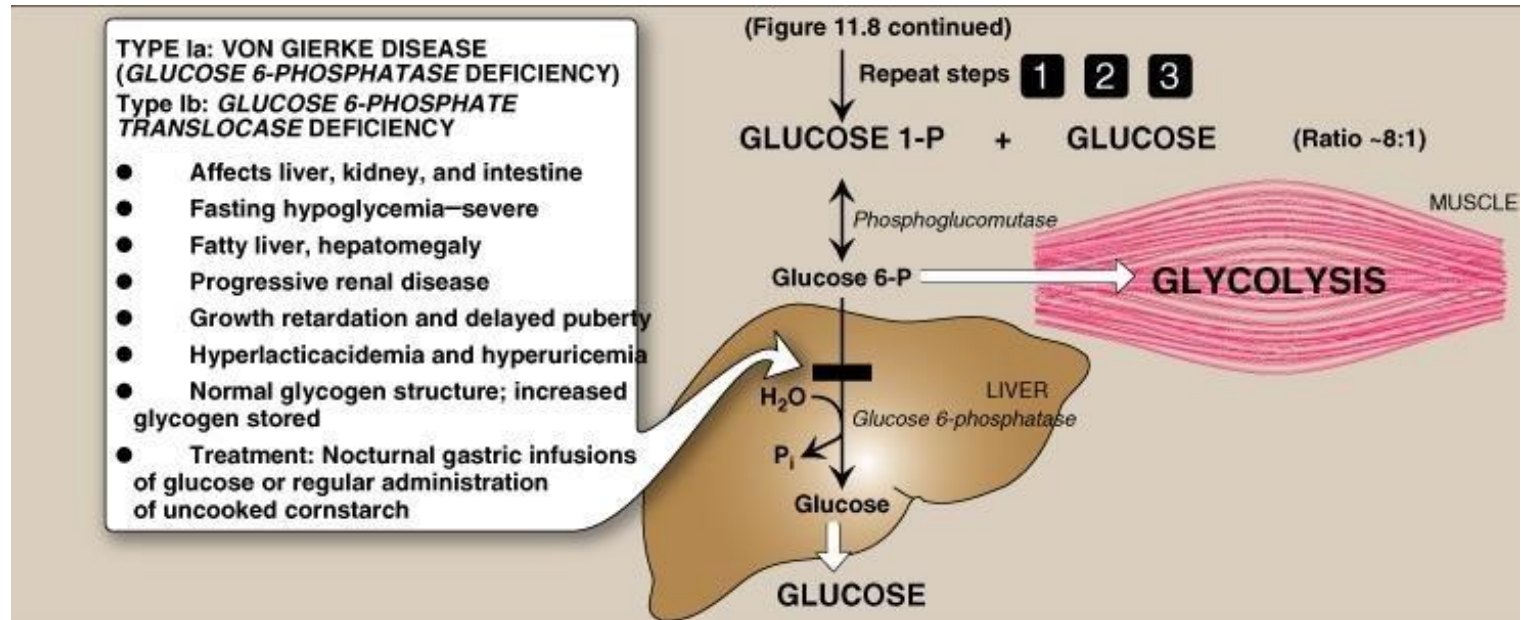


# Glycogen Storage Diseases

- Genetic diseases
- Defect in an enzyme required for synthesis or degradation →
- Accumulation of excessive amount of abnormal glycogen (synthesis) or normal glycogen (degradation)
- In one or more tissue
- Severity: FATAL in Infancy..... Mild disorder

# Glycogen Storage Diseases

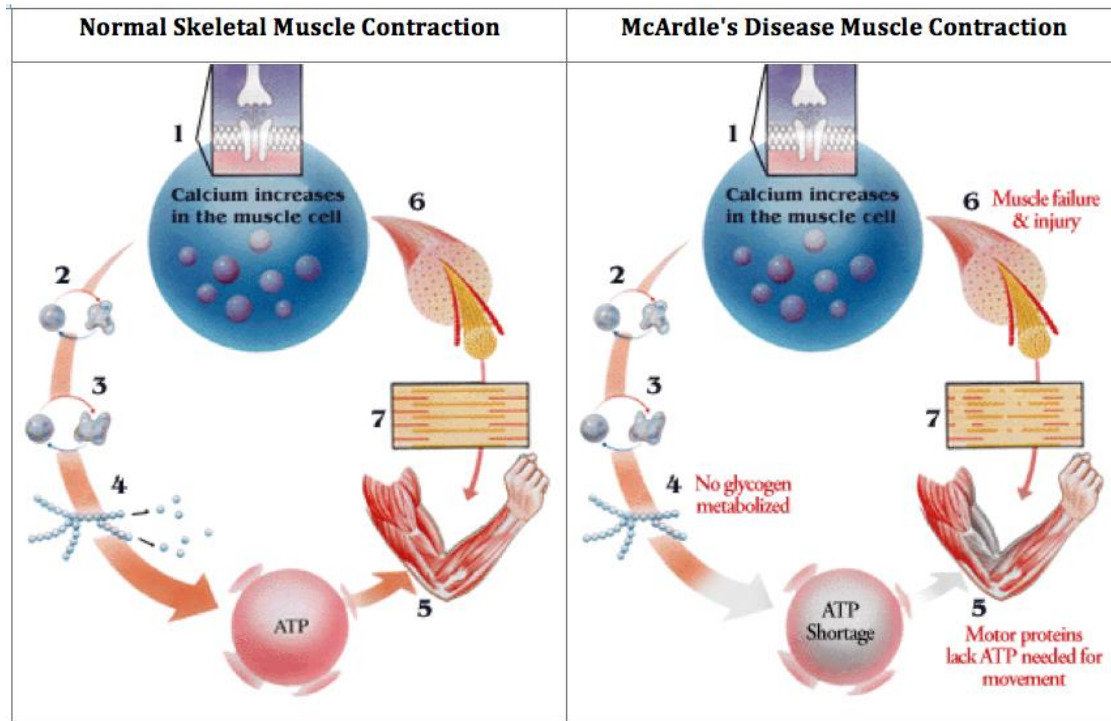
- I Glucose-6-phosphatase (von Gierke disease)



- Liver, kidney and intestine.
- Severe fasting hypoglycemia
- Hepatomegaly fatty liver.
- Normal glycogen structure.
- Progressive renal disease.
- Growth retardation.

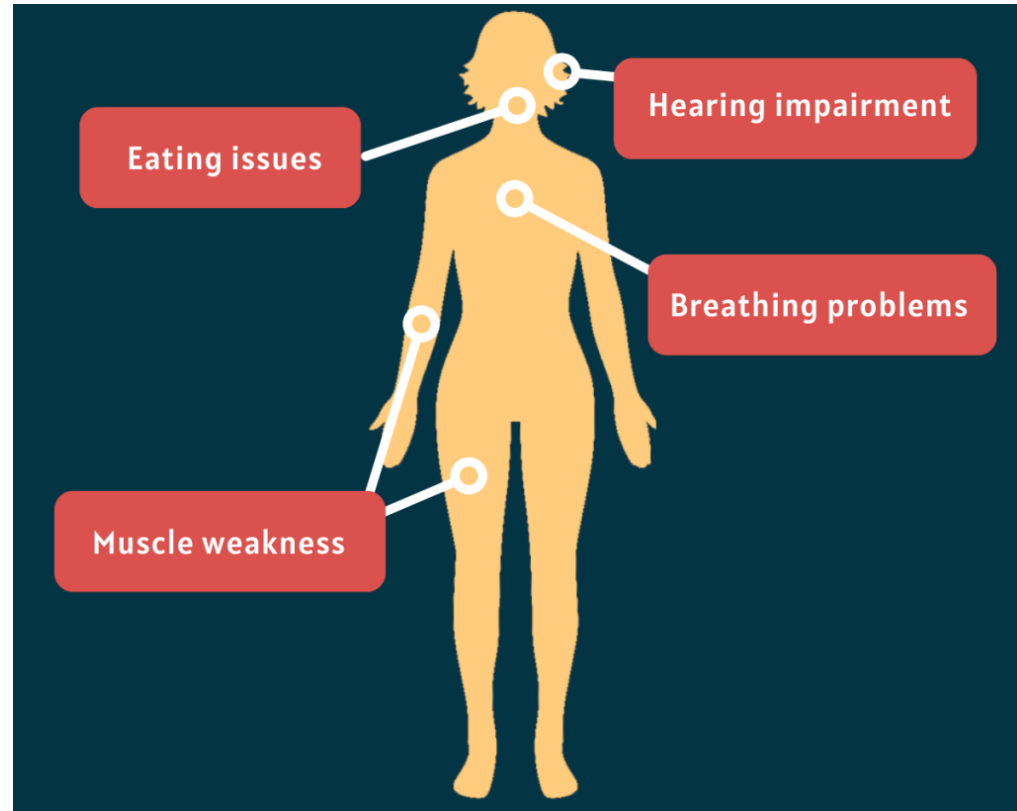
# Glycogen Storage Diseases

- V Muscle glycogen phosphorylase (McArdle syndrome)
- Skeletal muscle glycogen phosphorylase deficiency
  - Only muscle is affected;
  - Weakness and cramping of muscle after exercise
  - no increase in [lactate] during exercise



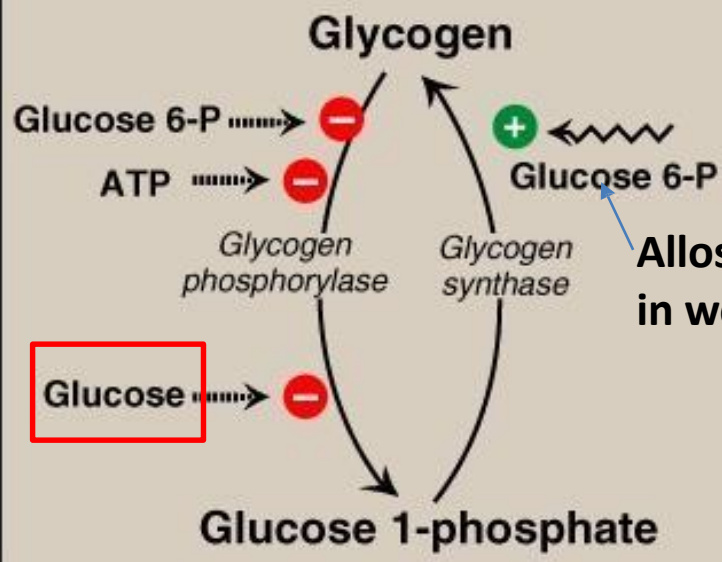
# Glycogen Storage Diseases

- II Lysosomes  $\alpha$  (1 $\rightarrow$ 4) glucosidase  $\rightarrow$  POMPE Disease
- Degradation of glycogen in the lysosomes
- $\approx$  3% of glycogen is degraded in the lysosomes
- Affects liver, heart and muscle
- Excessive glycogen in abnormal vacuoles in the lysosomes
- Massive cardiomegaly
- Normal blood sugar, normal glycogen structure
- Early death from heart failure.





# A LIVER

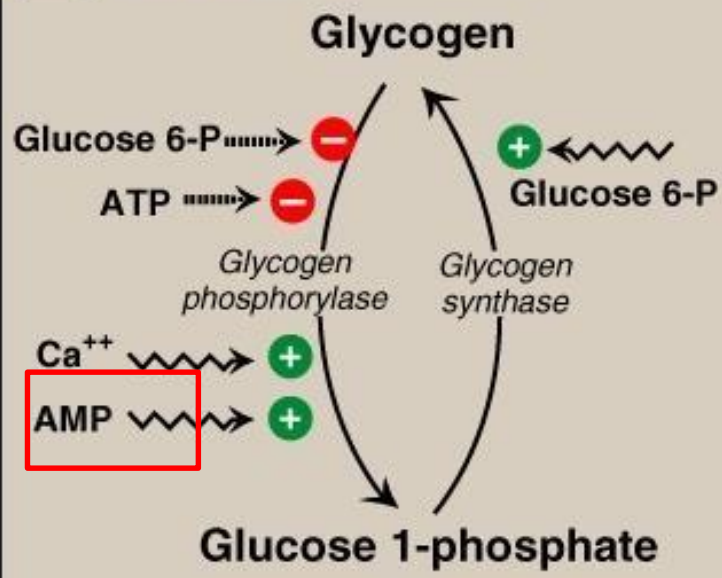


Allosteric activator in well-fed state

# Allosteric Regulation of Glycogen Metabolism

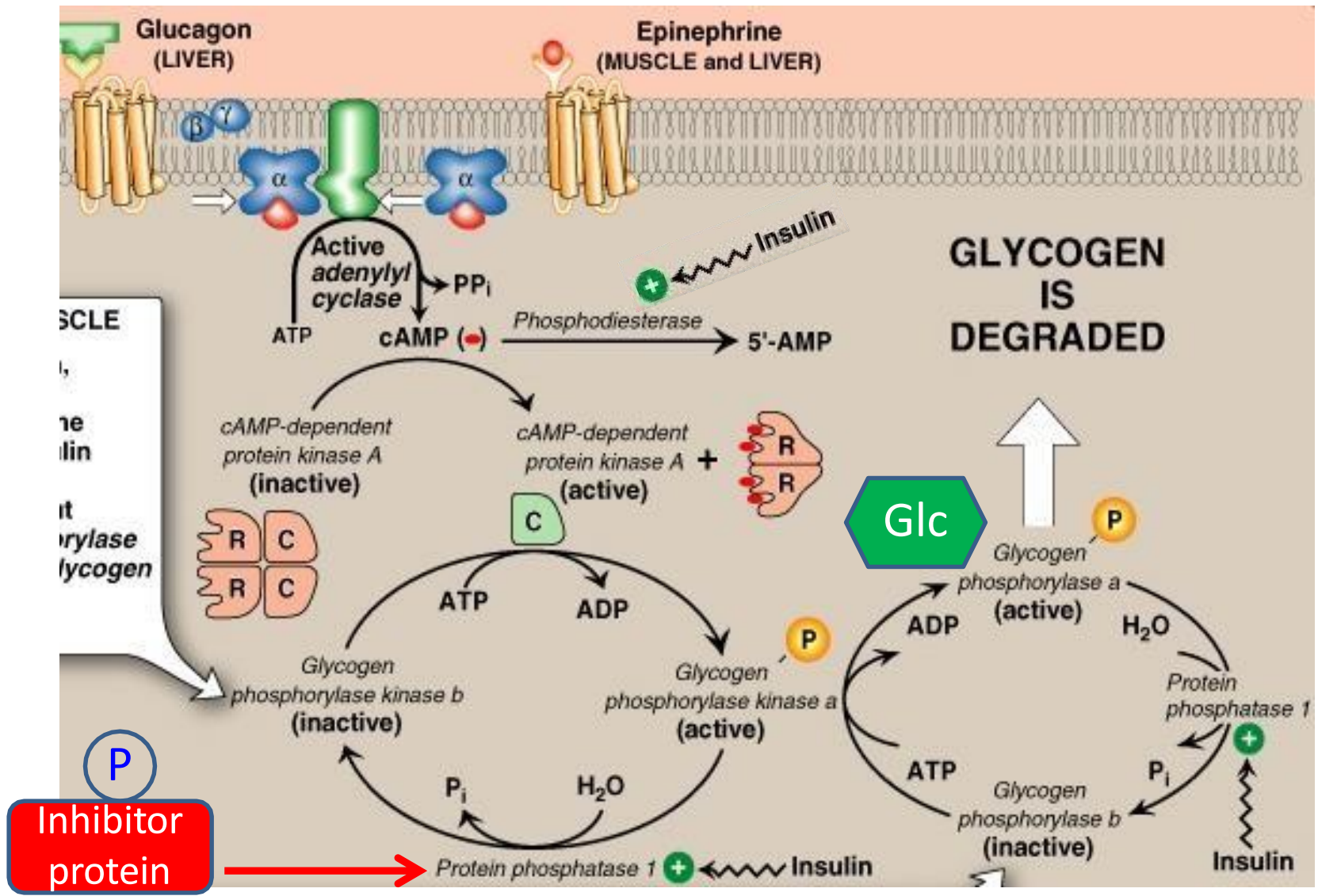
Rapid response to cell's needs  
Available substrate and ATP → synthesis

# B MUSCLE



↓↓ Glucose and ↓ ATP → Glycogenolysis

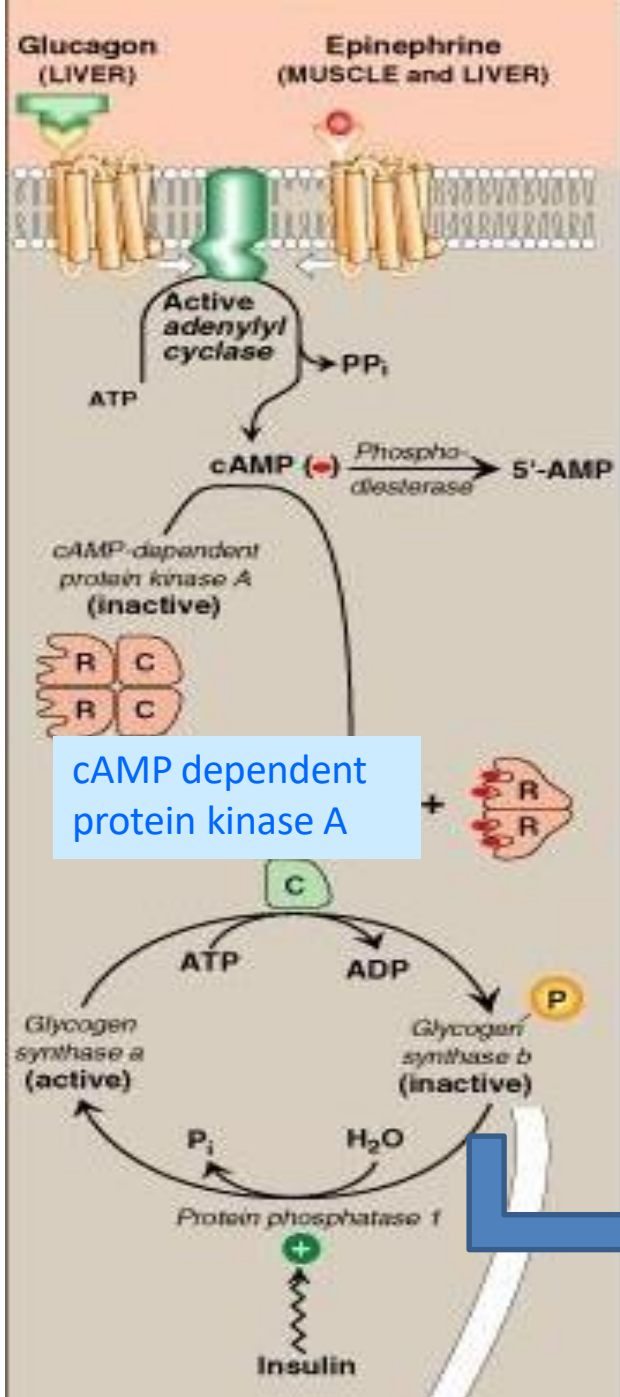
# Hormonal Regulation of Glycogen Metabolism



# Regulation of Glycogen Synthesis

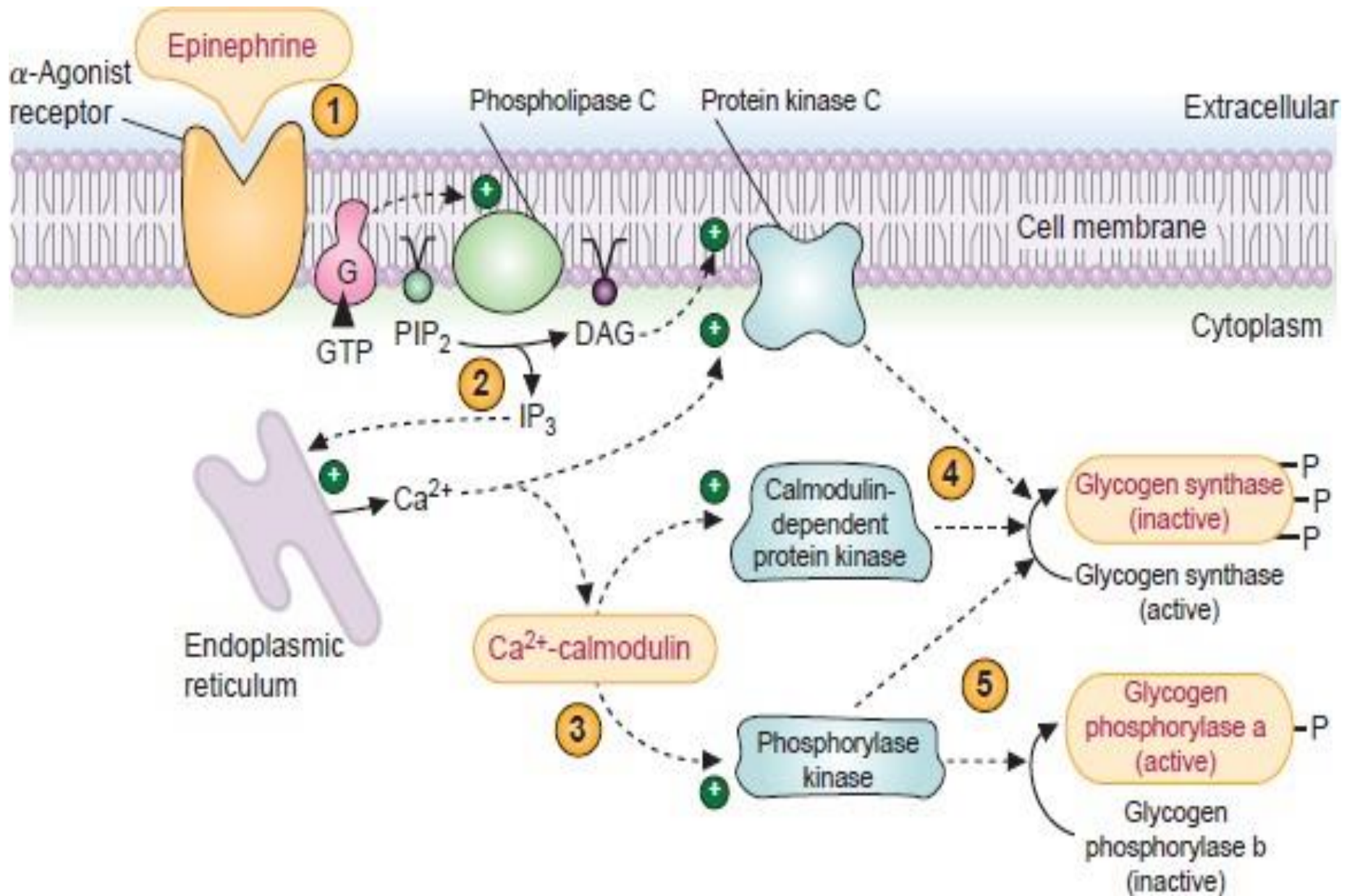
Phosphorylation at several sites

Inhibition is proportional to the degree of phosphorylation



GLYCOGEN SYNTHESIS IS INHIBITED

# Hormonal Regulation of Glycogen Metabolism



# Ca<sup>2+</sup> -Calmodulin Complex Function

