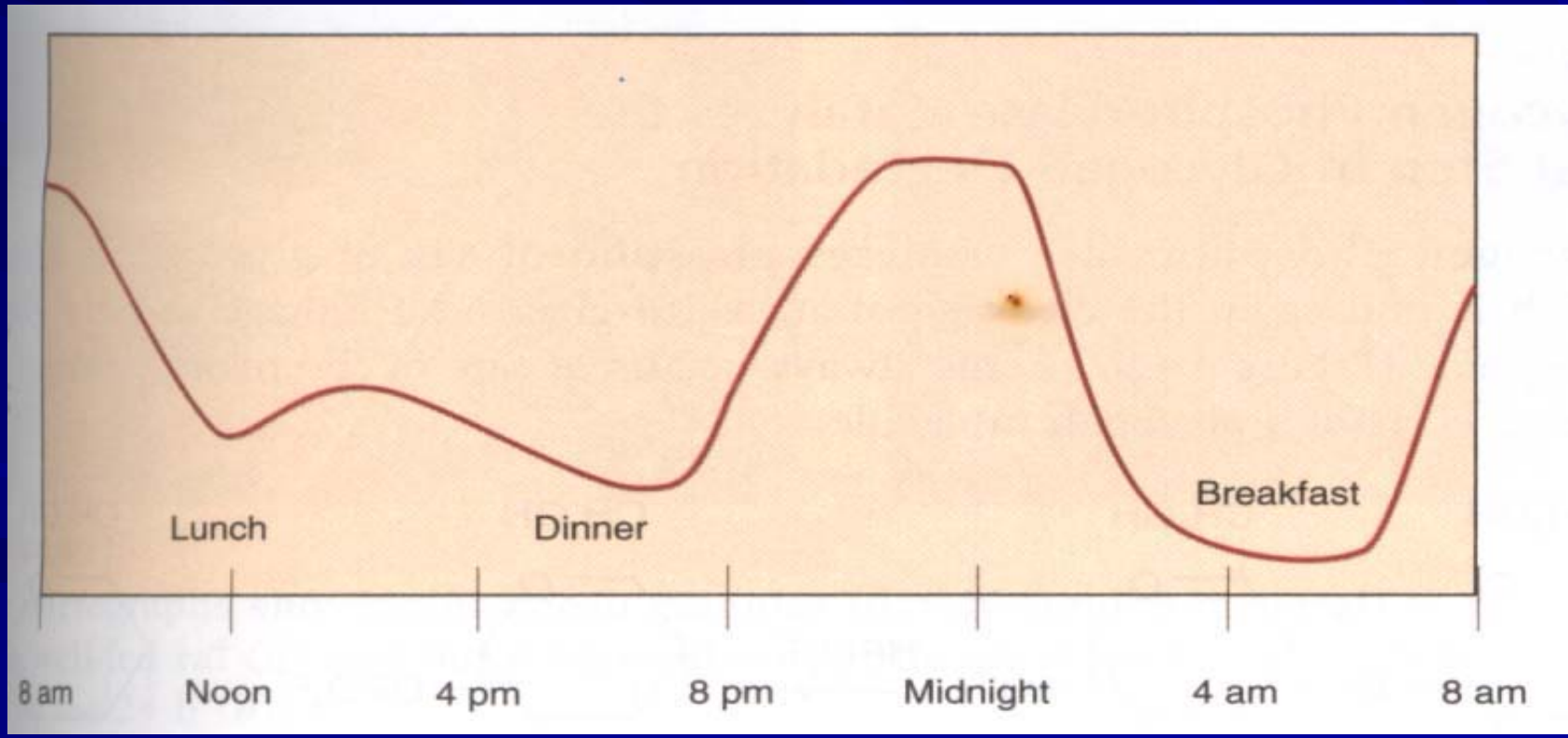
GLYCOGENESIS

- Glycogen synthesis occurs after a meal, when blood glucose level are high
- Glycogen is stored in muscle and liver for quite different reasons
- Muscle glycogen is a readily available source of glucose for glycolysis within the muscle itself
- Liver glycogen functions to store and export glucose to maintain blood glucose between meals
- Liver glycogen levels vary greatly in response to intake of food

GLYCOGENESIS

- It’s accumulating to high levels shortly after a meal
- Then it’s decreasing slowly as it is mobilized to help maintain a nearly constant blood glucose level

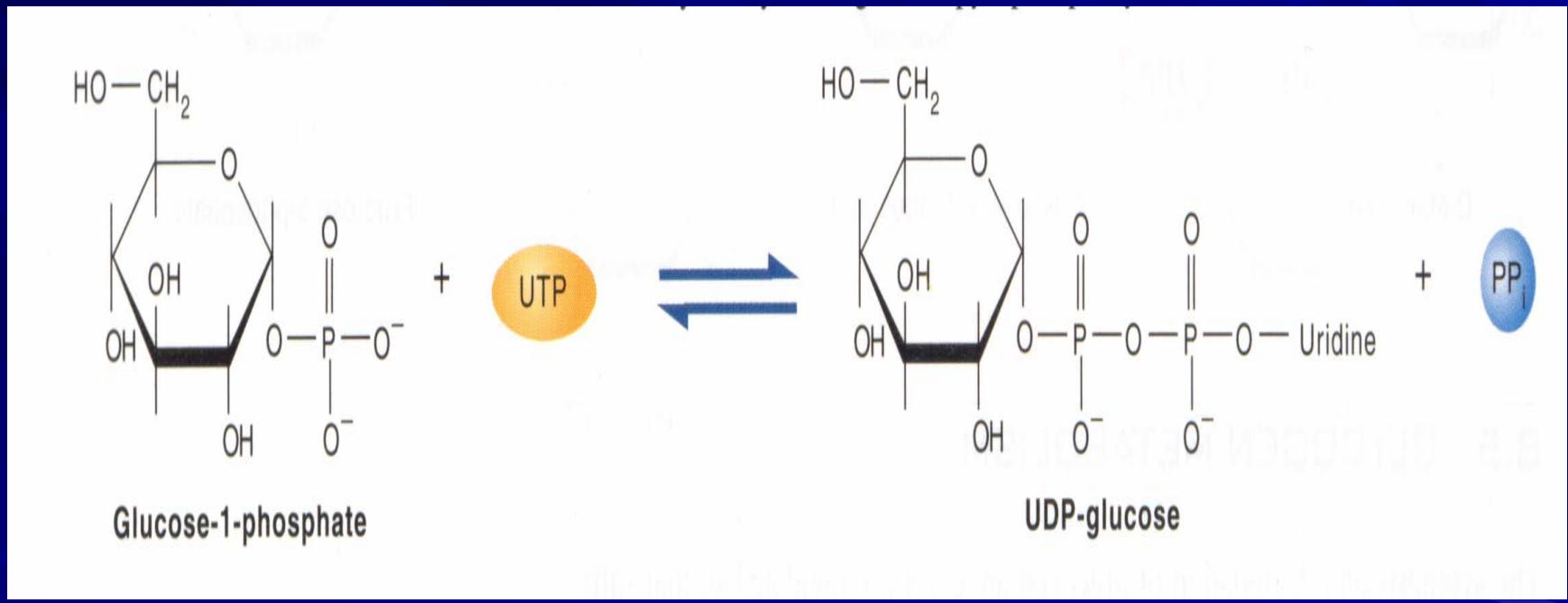


REACTIONS OF GLYCOGENESIS

- Glycogen synthesis from of α D glucose
- The process occurs in the cytosol
- The process requires energy supplied by ATP and Uridine triphosphate (UTP)
- Glycogenesis involves the following set of reactions :

  - Phosphorylation of glucose to form glucose 6 phosphate by hexokinase or glucokinase
  - Synthesis of glucose 1 phosphate by phosphoglucomutase from glucose 6 phosphate
  - Synthesis of UDP-glucose by action of glucose 1-phosphate uridylyltransferase

REACTIONS OF GLYCOGENESIS



REACTIONS OF GLYCOGENESIS

- Synthesis of glycogen from UDP-glucose

This process requires two enzymes:

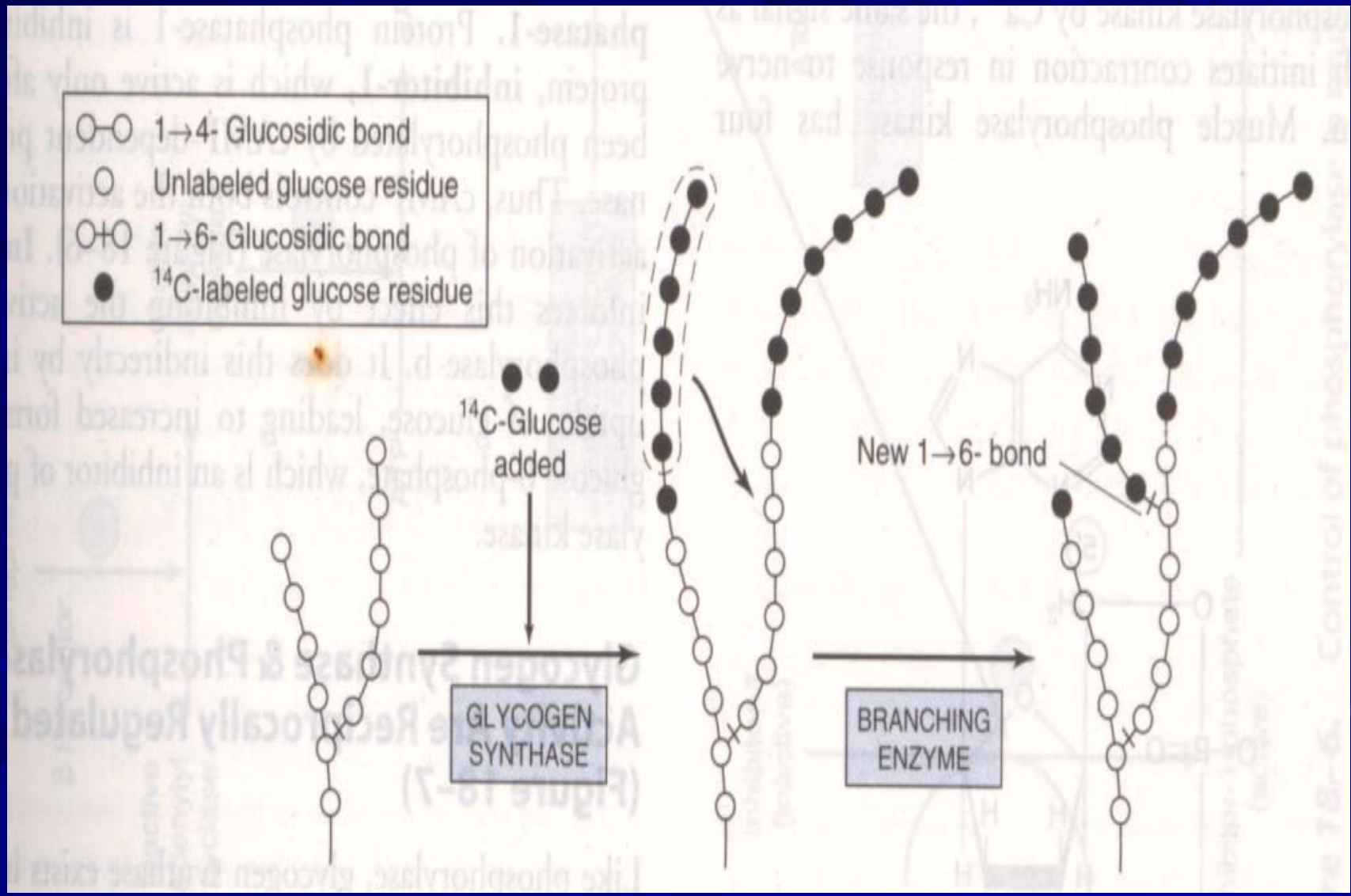
a. Glycogen Synthase

→creates chains of glucose molecules with α-1,4 glycosidic linkages

b. Amylo-α (1,4→1,6)-glucosyl transferase (branching enzyme)

→removes a block of about seven glucosyl residues from a growing chain and transfers it to another chain to produce an α-1,6-glycosidic

Glycogenolysis



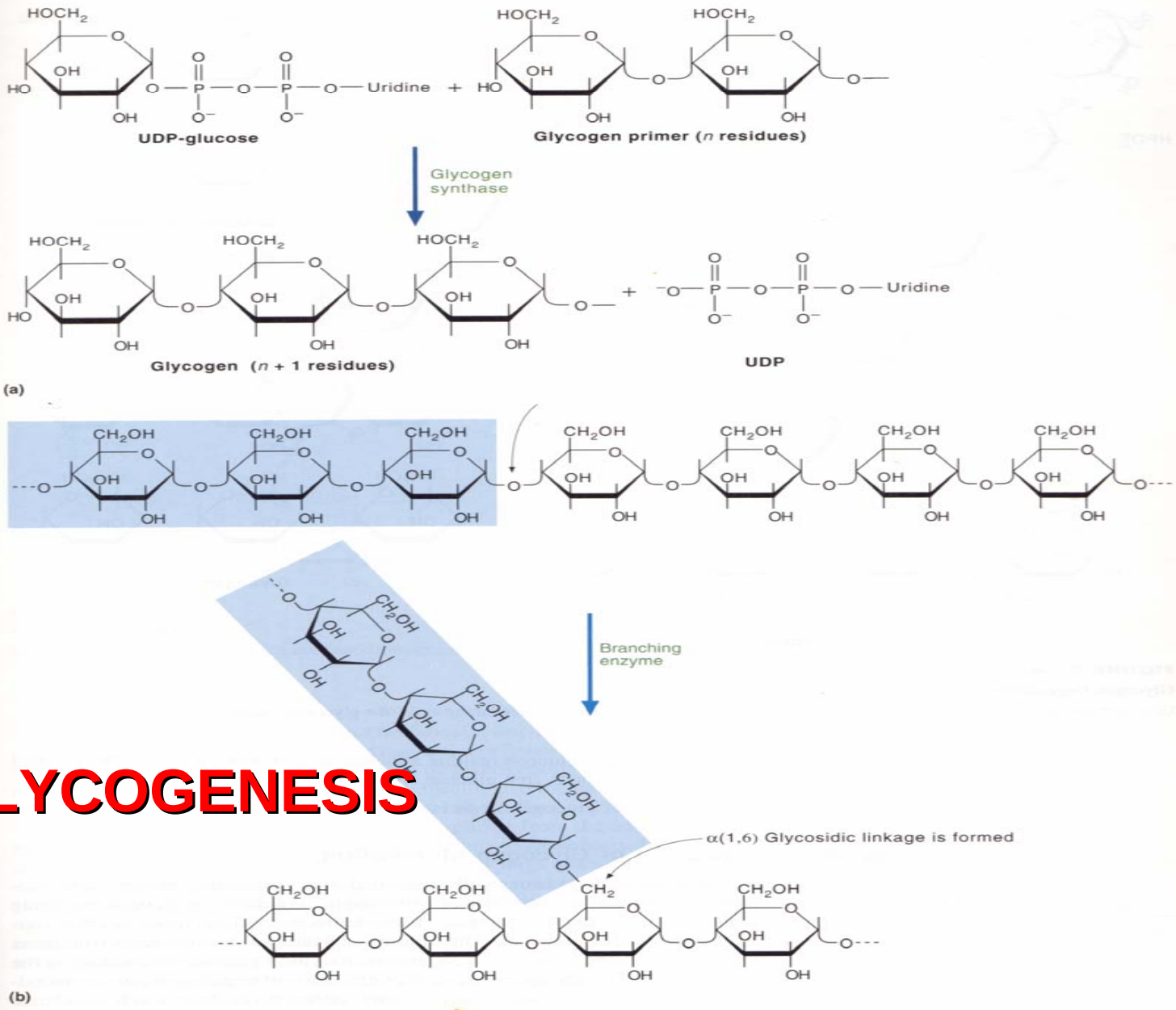
Synthesis of Primer to Initiate Glycogen Synthesis

- A primer is needed for glycogen synthesis
- Glycogen synthase cannot initiate chains synthesis using free glucose as an acceptor of a molecule of glucose from UDP-glucose
- A fragment of glycogen can serve as a primer in cells whose glycogen store are not totally depleted
- In the absence of a glycogen fragment, a spesific protein, called glycogenin can serve as an acceptor of glucose residues

Synthesis of Primer to Initiate Glycogen Synthesis

- Glycogenin is now known that a polypeptide of 332 amino acids
- Transfer of the first molecule of glucose from UDP-glucose to glycogenin is catalyzed by glycogen initiator synthase
- Glycogenin itself can then transfer a few additional glucosyl units to the growing α-1,4 glucosyl chain

  →Glycogenin is aself glucosylating enzyme



GLYCOGENESIS

GLYCOGENOLYSIS

- Glycogenolysis refers to breakdown of glycogen to glucose or glucose 6 phosphate in response to low blood glucose
- This process occurs in the cytosol
- It is not a reversal of the synthetic reactions
- In humans, the store of liver glycogen lasts somewhere between 12 and 24 hour during fasting

GLYCOGENOLYSIS

Glycogen degradation requires the following reactions :

- Shortening of chains

  - Using inorganic phosphate (Pi), glycogen phosphorylase cleaves the $\alpha(1,4)$ linkages on the outer branches of glycogen

  - Glycogen phosphorylase stops when it comes within four glucose residus of branch point

  - A glycogen molecule that has been degraded to its branch points is called a limit dextrin

  - Phosphorylase cannot degrade it any further

GLYCOGENOLYSIS

- Removal of branches

  - Oligo-(α-1,4→ α-1,4)-glucantransferase removes the outer three of the four glucose residues attached at a branch and transfer them to nonreducing end of another chain

  - It cause exposing the 1,6 branch point

  - Amylo-α(1,6)-glucosidase (debranching enzyme), begins the removal of α(1,6)

  - With the removal of the branch, further action by phosphorylase can proceed

GLYCOGENOLYSIS

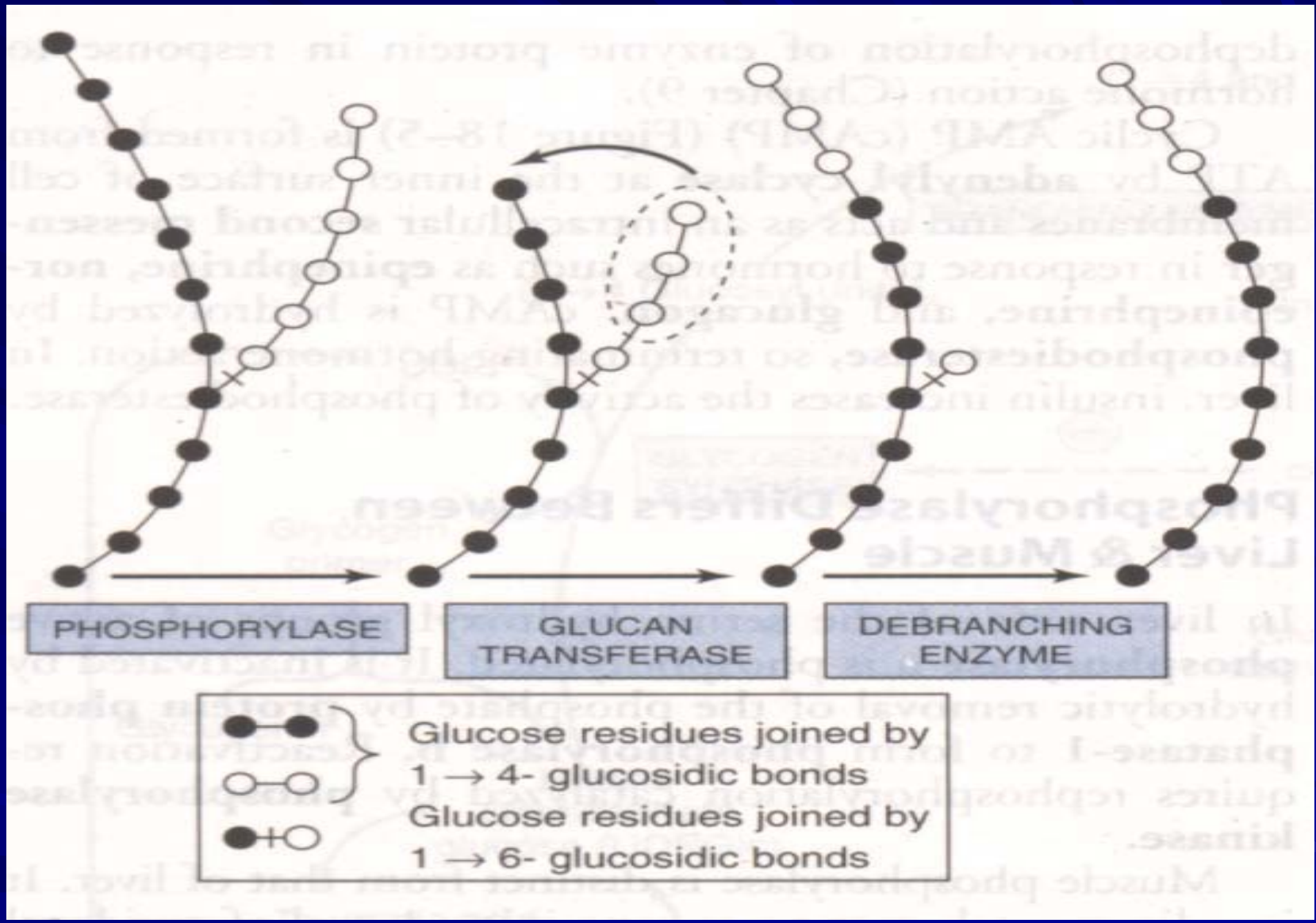
- Conversion of glucose 1 phosphate to glucose 6 phosphate

  - glucose 1 phosphate, produced by glycogen phosphorylase is converted to glucose 6 phosphate

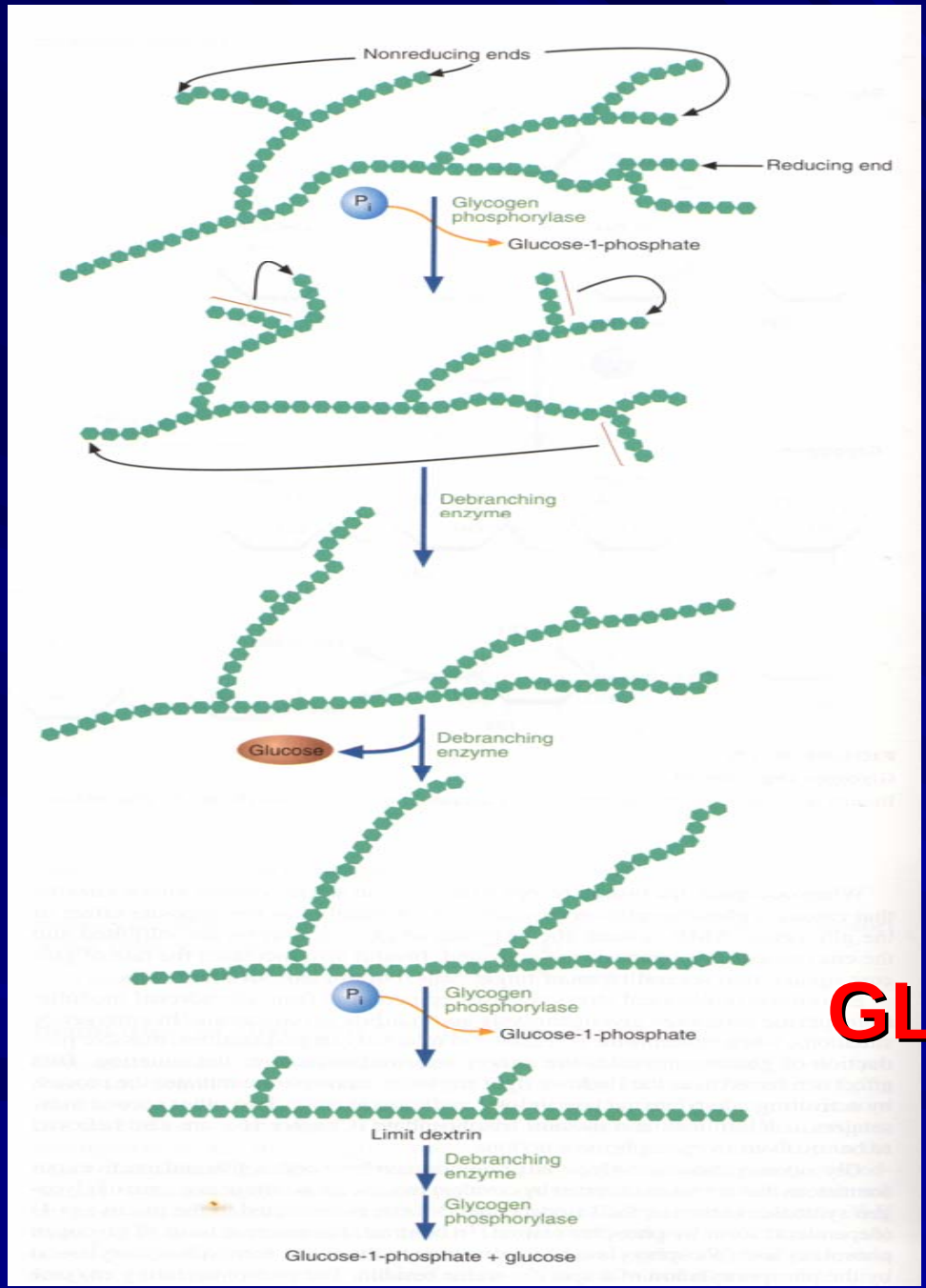
  - It catalyzed by phosphoglucomutase

  - In liver and kidney but not in muscle , glucose 6 phosphatase, removes phosphate from glucose 6 phosphate

  - It enabling glucose to be formed and diffuse from the cell into the blood

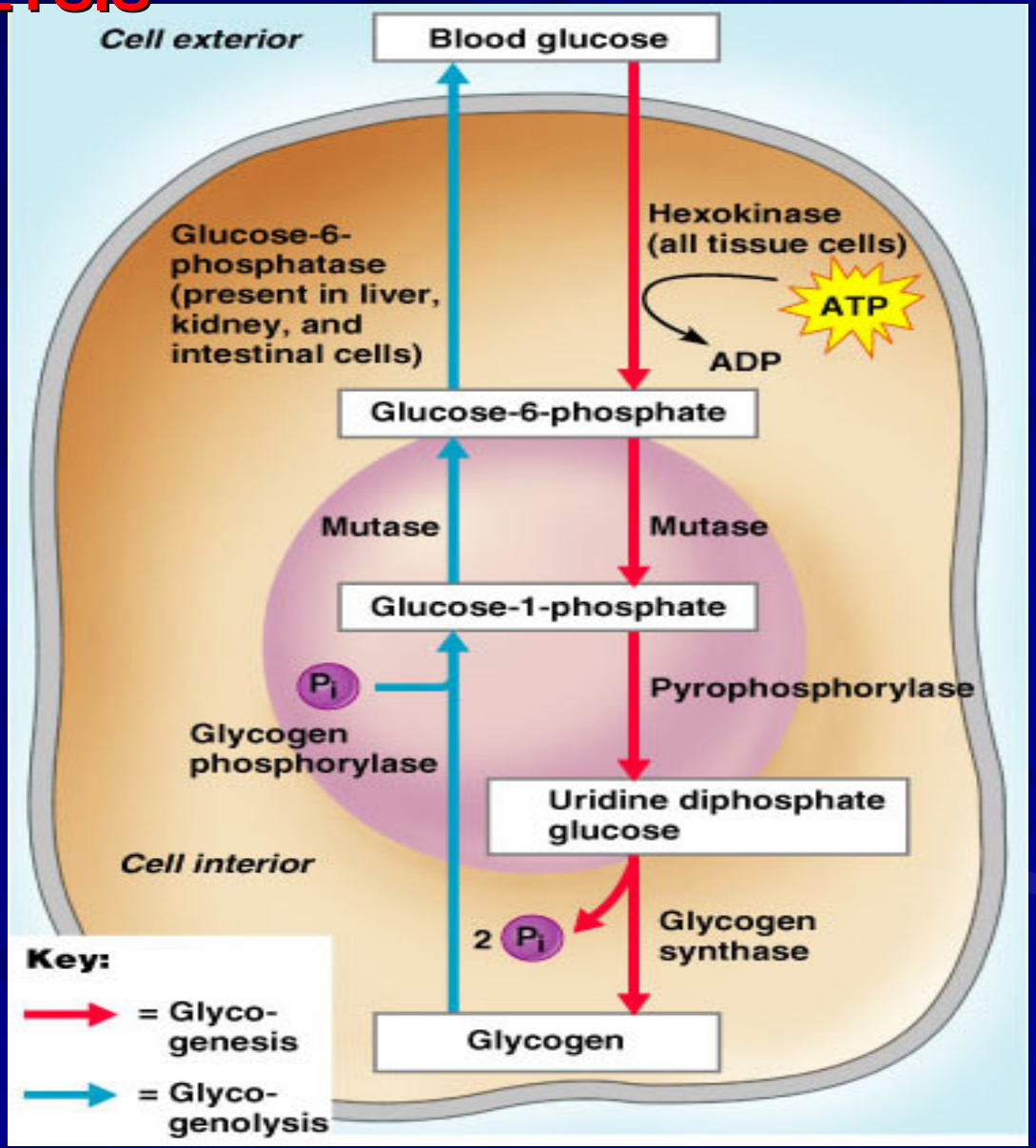


Glycogenolysis



GLYCOGENOLYSIS

PATHWAY OF GLYCOGENESIS AND OF GLYCOGENOLYSIS



GLYCOGEN STORAGE DISEASES

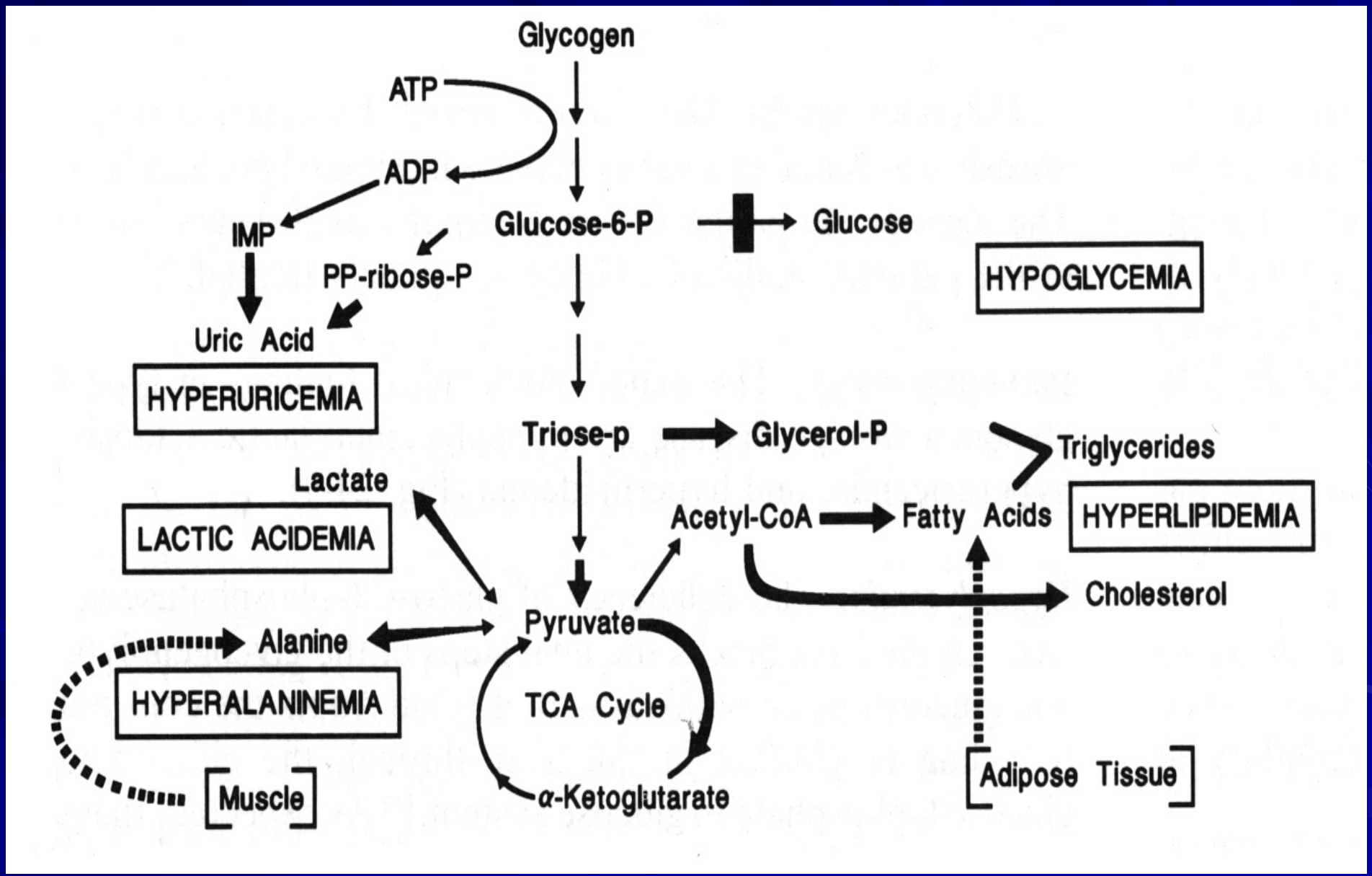
- A group of genetic disease that result from a defect in an enzyme required for either glycogen synthesis or degradation
- The result in either formation of glycogen that has an abnormal structure or the accumulation of excessive amounts of normal glycogen in specific tissue
- A particular enzyme may be defective in a single tissue
- The severity of disease may range from fatal infancy to mild disorders that are not life threatening

GLYCOGEN STORAGE DISEASES

Some of the more prevalent glycogen storage diseases :

- Von Gierke's disease
  - Called type I glycogen storage disease
  - Caused by deficiency glucose 6 phosphatase
  - Affects liver, kidney and intestine
  - Fasting hypoglycemia-severe
  - Fatty liver, hepatomegaly
  - Hyperlacticacidemia and hyperuricemia
  - Normal glycogen structure, increased glycogen stored

Type I : Von Gierke's disease



GLYCOGEN STORAGE DISEASES

Some of the more prevalent glycogen storage diseases :

- Pompe's disease
  - Called type II glycogen storage disease
  - Inborn lysosomal enzyme defect
  - Excessive glycogen concentrations found in abnormal vacuoles in the cytosol
  - Normal blood sugar level
  - Severe cardiomegaly
  - Early death usually occurs

GLYCOGEN STRORAGE DISEASES

- Cori's disease

  - Called type III glycogen storage disease

  - Caused by deficiency of glycogen debrancher enzyme

  - Glycogen accumulates because only the outer branches can be removed from the molecule by phosphorylase

  - Hepatomegaly occurs, but diminishes with age

GLYCOGEN STRORAGE DISEASES

- McArdle's Syndrome

  - Called type V glycogen storage disease

  - Caused by skeletal muscle glycogen phosphorylase deficiency (liver enzyme normal)

  - Temporary weakness and cramping of skeletal muscle after exercise

  - No rise blood lactate during strenuous exercise

  - Normal mental development

  - Myoglobinuria in later life

  - High level of glycogen with normal structure in muscle

Glycogen Storage Diseases

TABLE 17-1. HEREDITARY GLYCOGEN STORAGE DISEASES[a]

Type	Enzyme Deficiency	Tissue	Common Name	Glycogen Structure
I	Glucose-6-phosphatase	Liver	von Gierke's disease	Normal
II	α-1,4-Glucosidase	All lysosomes	Pompe's disease	Normal
III	Amylo-1,6-glucosidase (debranching enzyme)	All organs	Cori's disease	Outer chains missing or very short
IV	Amylo-(1,4 → 1,6)-transglycosylase (branching enzyme)	Liver, probably all organs	Andersen's disease	Very long unbranched chains
V	Glycogen phosphorylase	Muscle	McArdle's disease	Normal
VI	Glycogen phosphorylase	Liver	Hers' disease	Normal
VII	Phosphofructokinase	Muscle		Normal
VIII	Phosphorylase kinase	Liver	Tarui's disease	Normal
IX	Glycogen synthase	Liver		Normal, deficient in quality

[a] All types but Type VIII are autosomal recessive; Type VIII is sex linked.