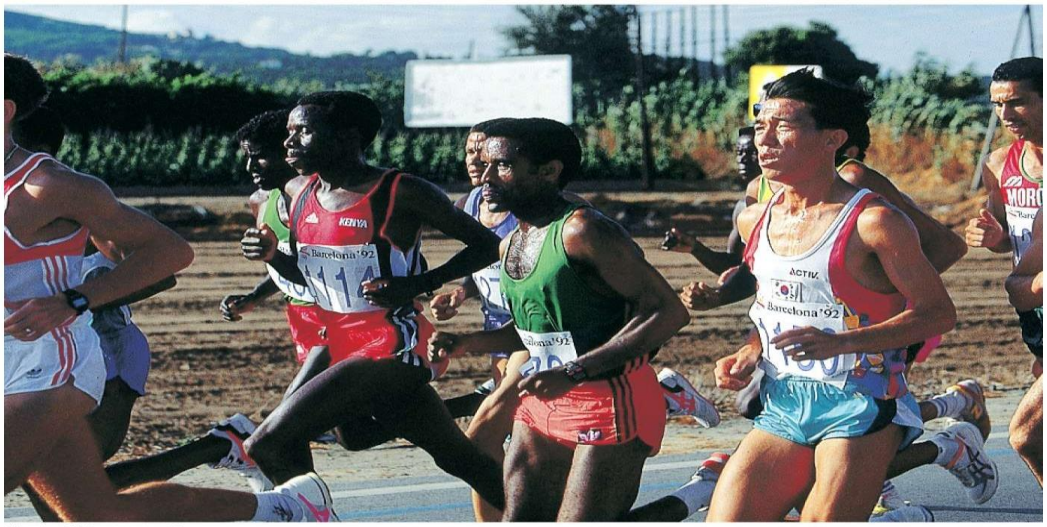
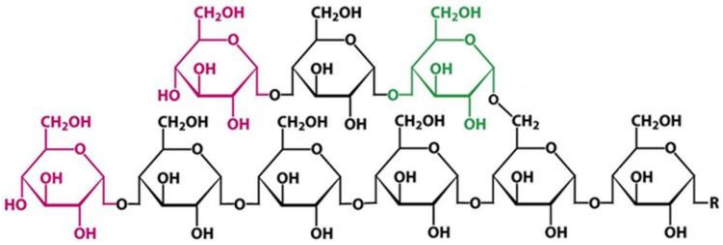
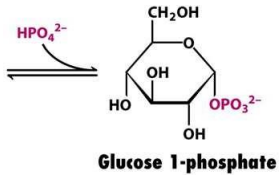
Glycogen Metabolism



Chapter 21 Opener part 1
Biochemistry, Sixth Edition

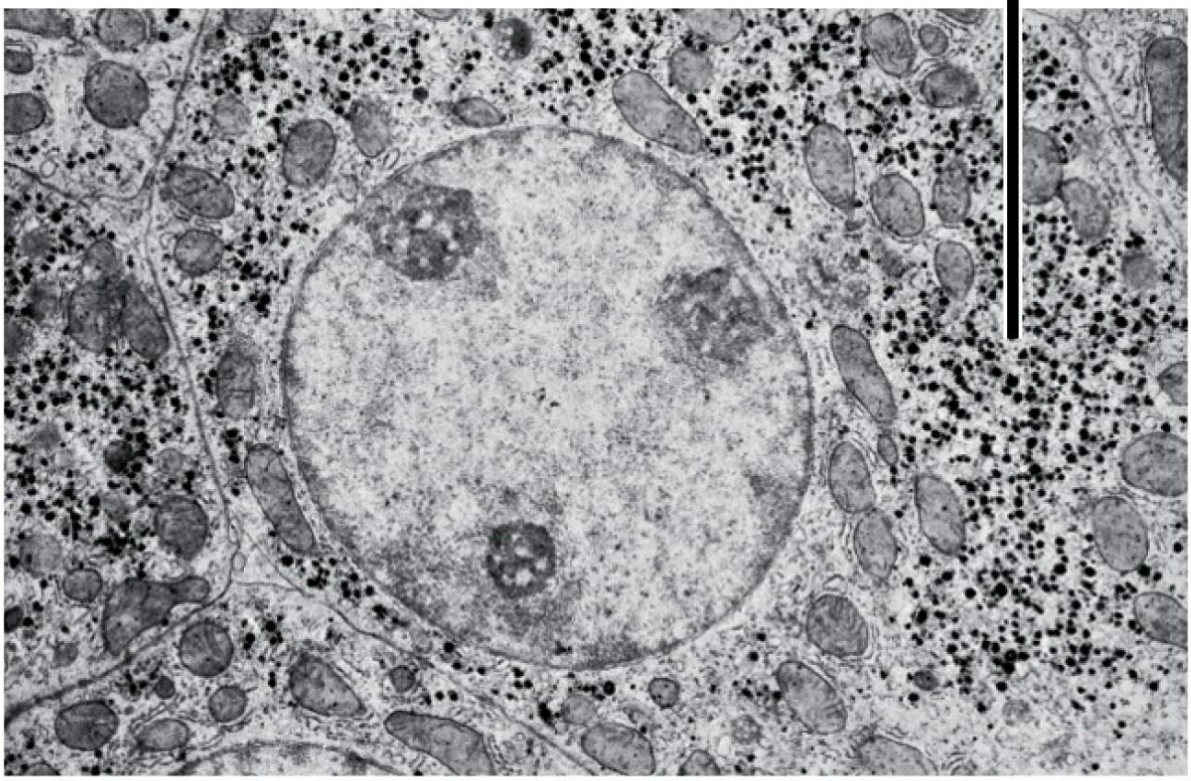
Dr:- Bariaa Ali Maki





Glucose 1-phosphate

Glycogen granules



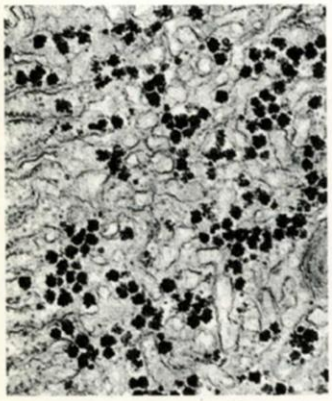
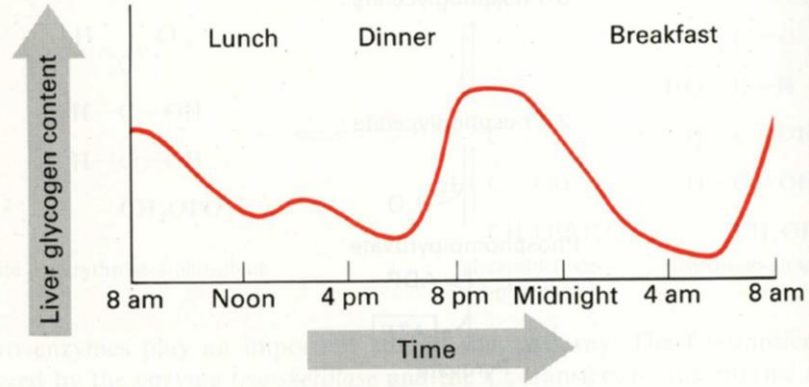
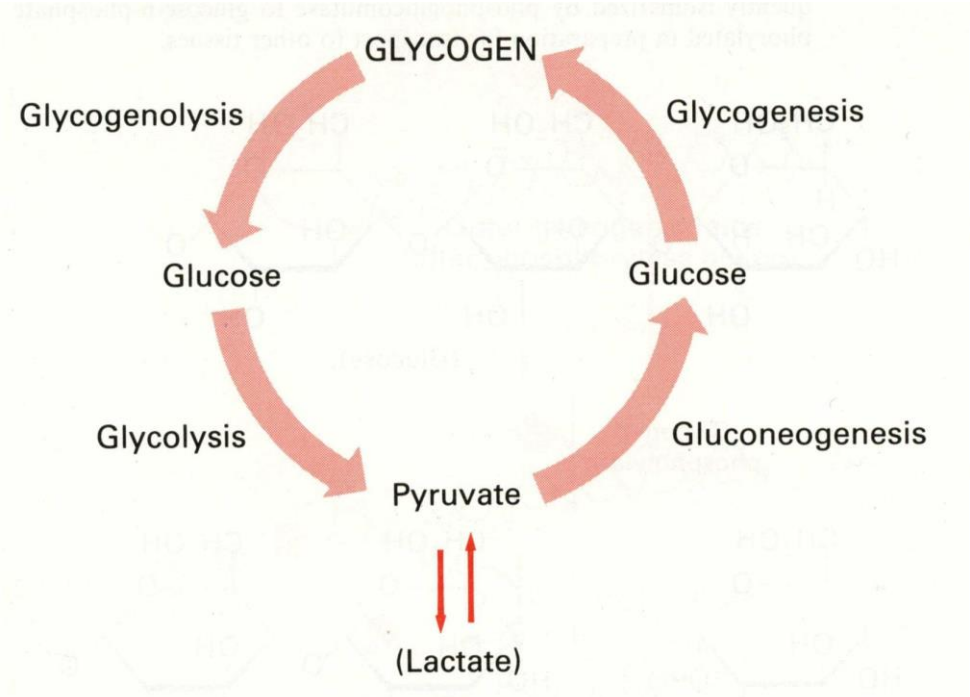


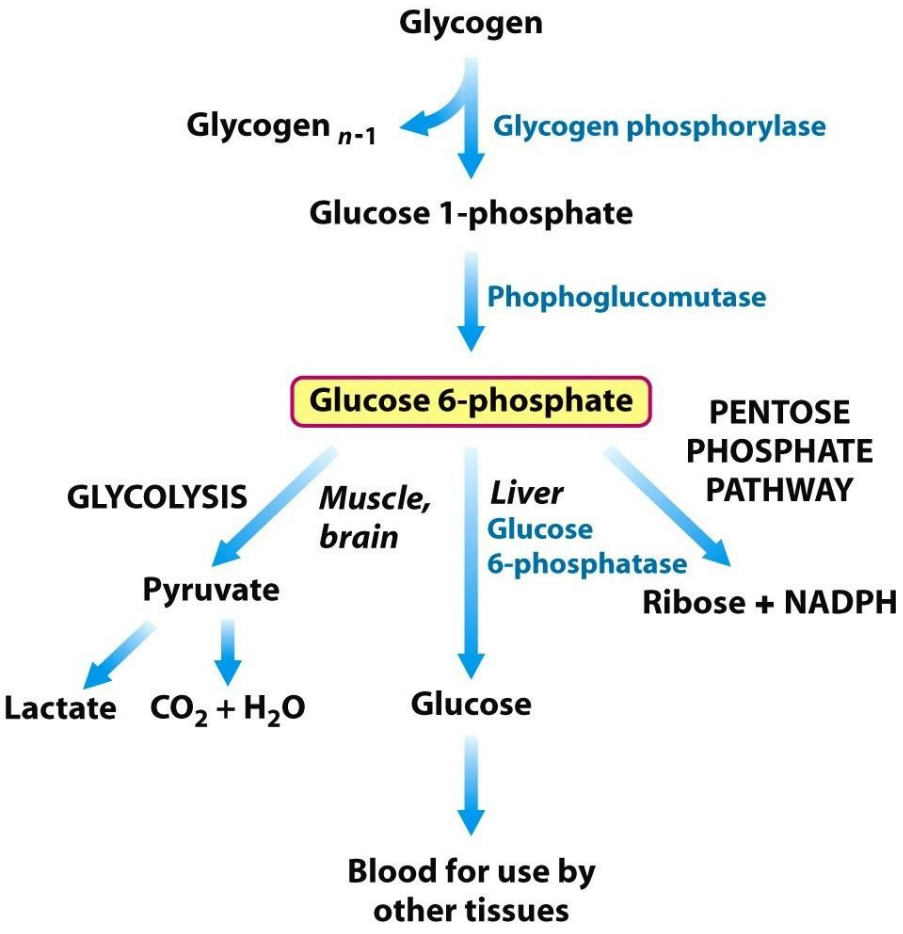
FIGURE 29–9 Electron micrographs showing glycogen granules (darkly stained material) in liver cells.

FIGURE 29–10 Variation of liver glycogen levels between meals.

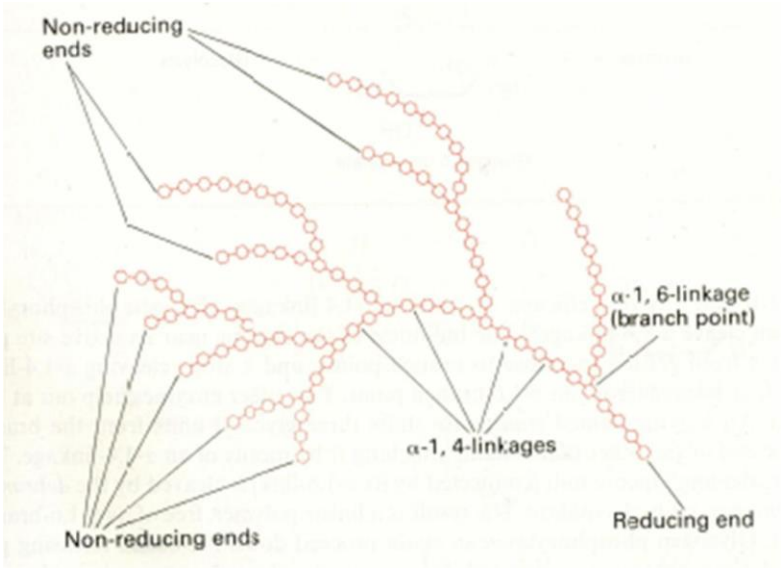


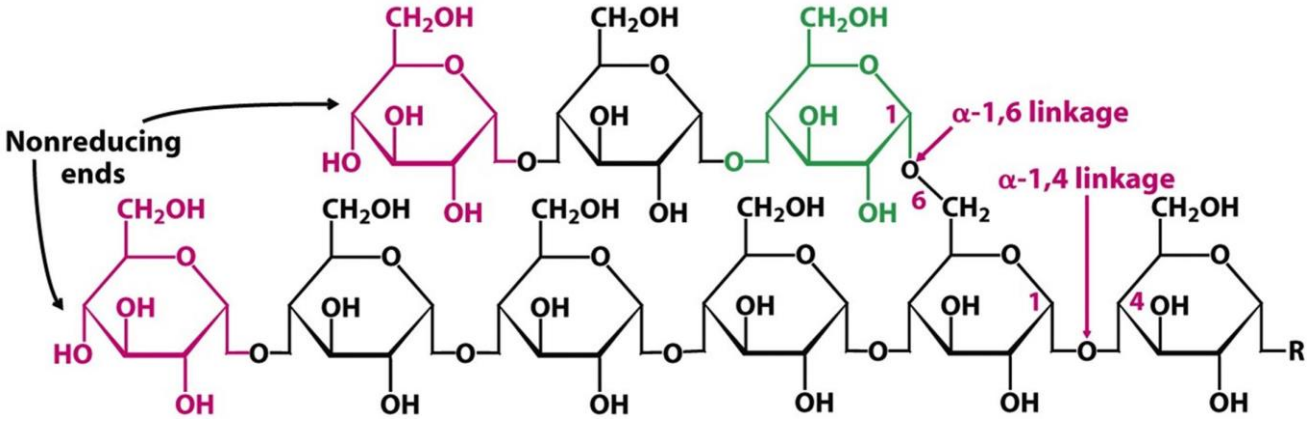
The important pathways of glucose metabolism. Note that the glycogen degradations pathways end in *-lysis*, while the glycogen synthesis pathways end with *-genesis*.





Glycogen nomenclature




Nonreducing ends
α-1,6 linkage
α-1,4 linkage
R

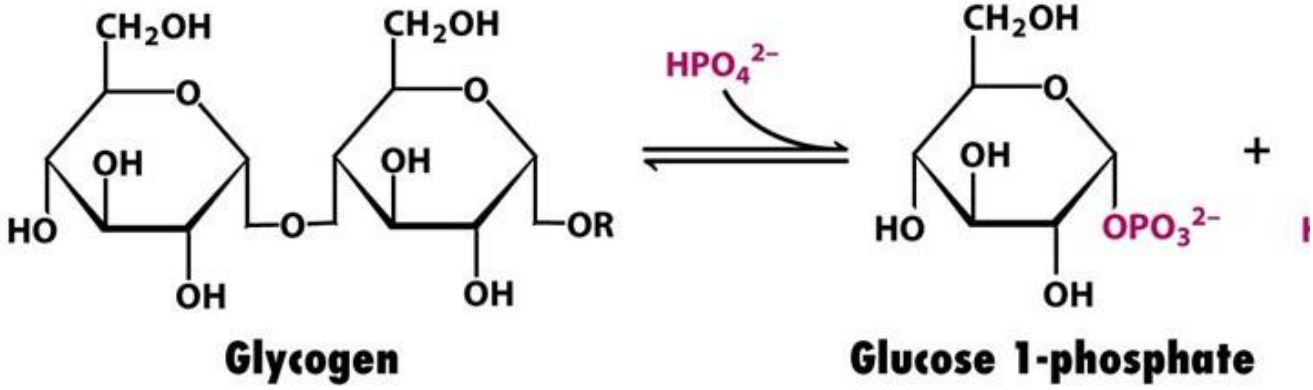
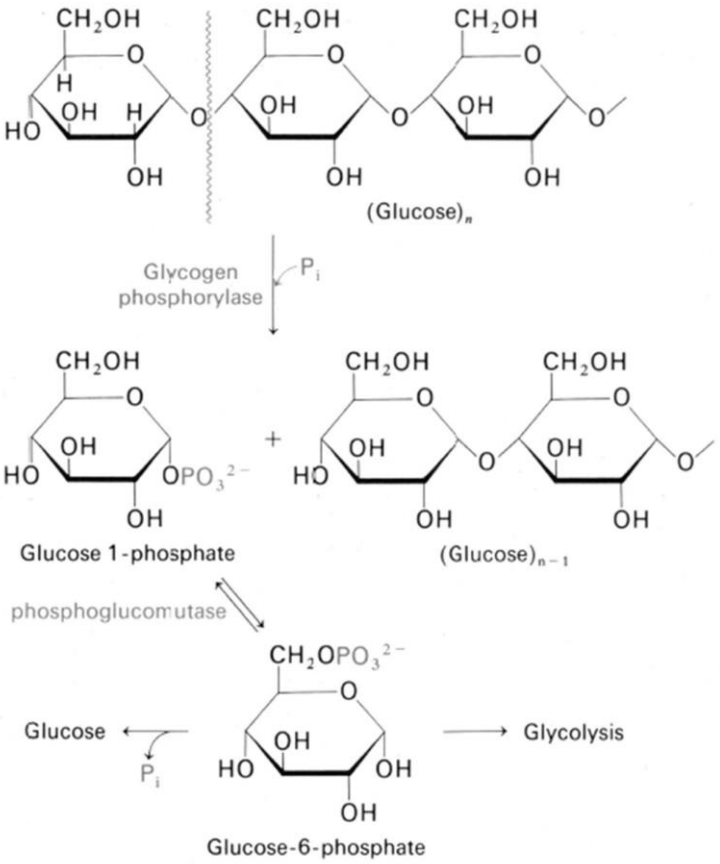
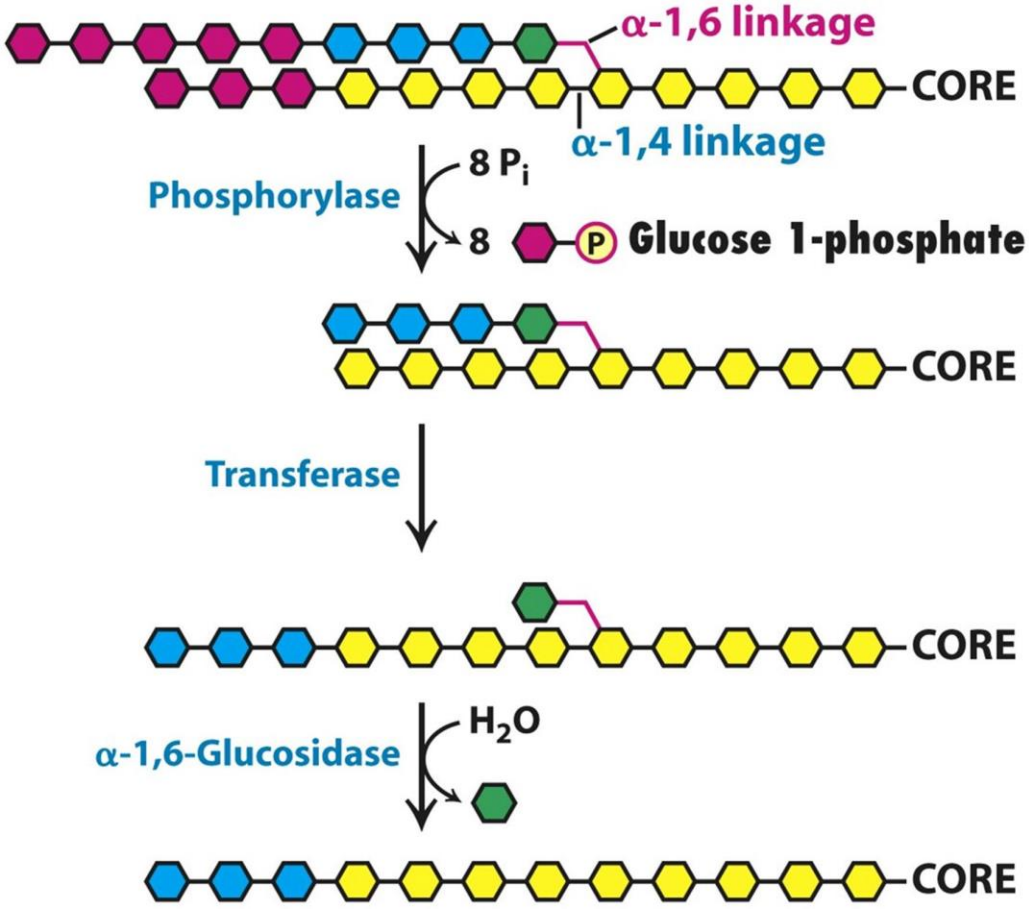
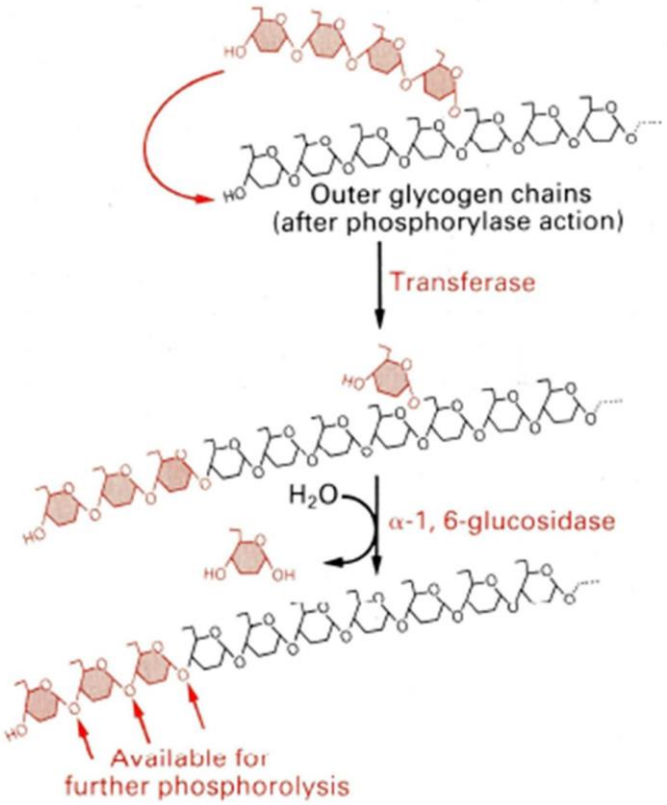

HPO4 2–
OPO3 2–
+
Glycogen
Glucose 1-phosphate

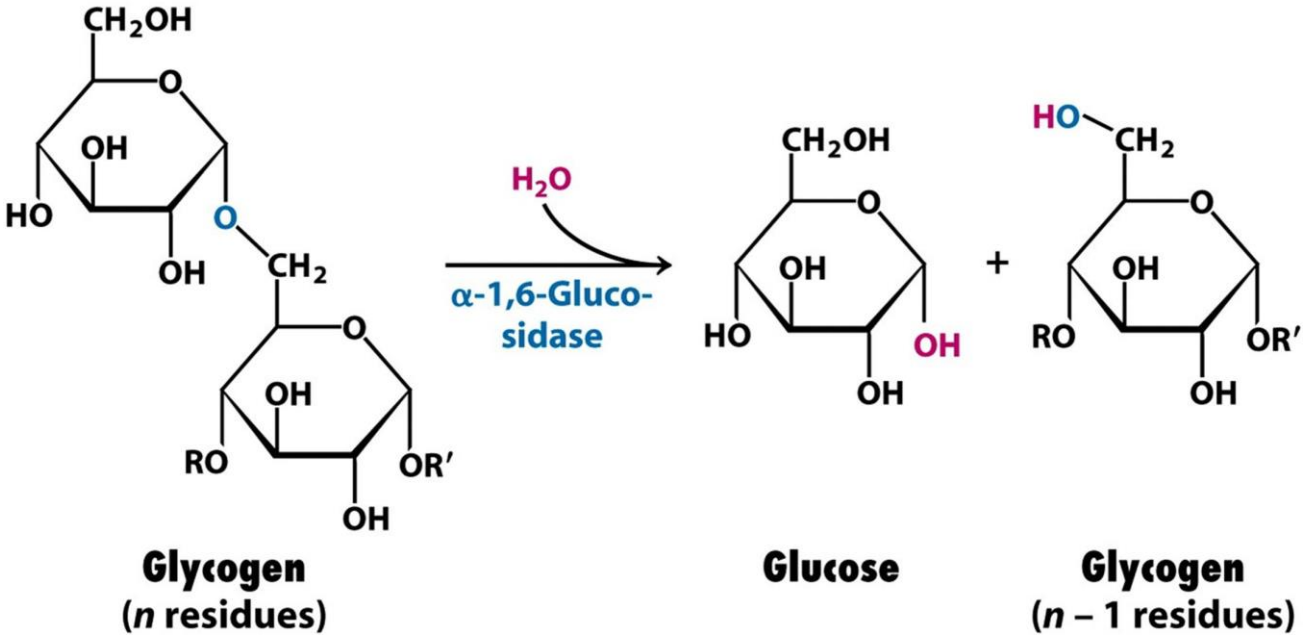
FIGURE 29–13 Glucose monomers are removed from the nonreducing ends of glycogen by the enzyme glycogen phosphorylase, which uses phosphate to split the glycosidic bond, rather than water. The resulting product, glucose-1-phosphate, is subsequently isomerized by phosphoglucomutase to glucose-6-phosphate or dephosphorylated in preparation for transport to other tissues.





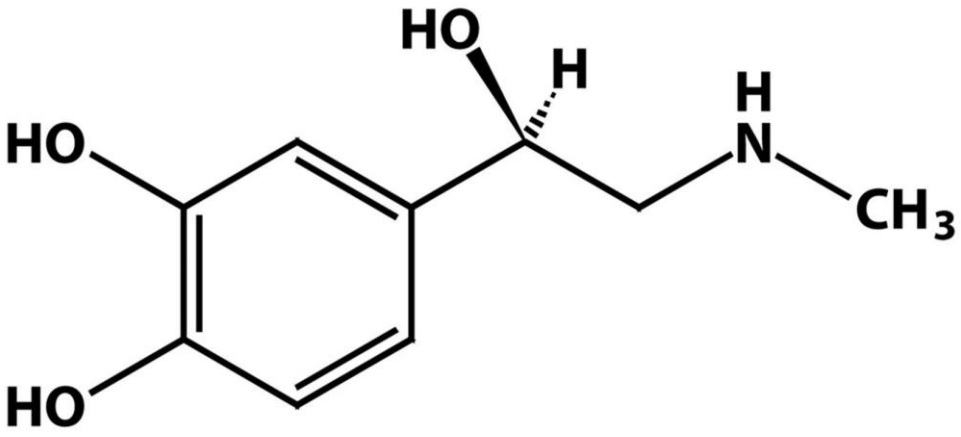
Glycogen De-branching Process





Glycogenolysis (or glycogen breakdown)
requires 3 major enzymes:
1) GLYCOGEN PHOSPHORYLASE (bond cleavage by phosphorolysis)
Glycogen
(n units)+ Pi <–––> Glycogen (n-1) + G-1-P
inorginic phosphate Glucose-1-phosphate
2) GLYCOGEN DEBRANCHING ENZYME (Fig. 15-6)
3) PHOSPHOGLUCOMUTASE (Fig. 15-7):
G-1-P <–––> G-1,6-P <–––> G-6-P
Glucose-1,6-bisphosphate Glucose-6-phosphate

G-6-P has several fates.
In LIVER, it is hydrolyzed to glucose + P i
by GLUCOSE-6-PHOSPHATASE.



Epinephrine

(β-phenylethylamine)

5 10

$^{+}H_3N$–His–Ser–Glu–Gly–Thr–Phe–Thr–Ser–Asp–Tyr–

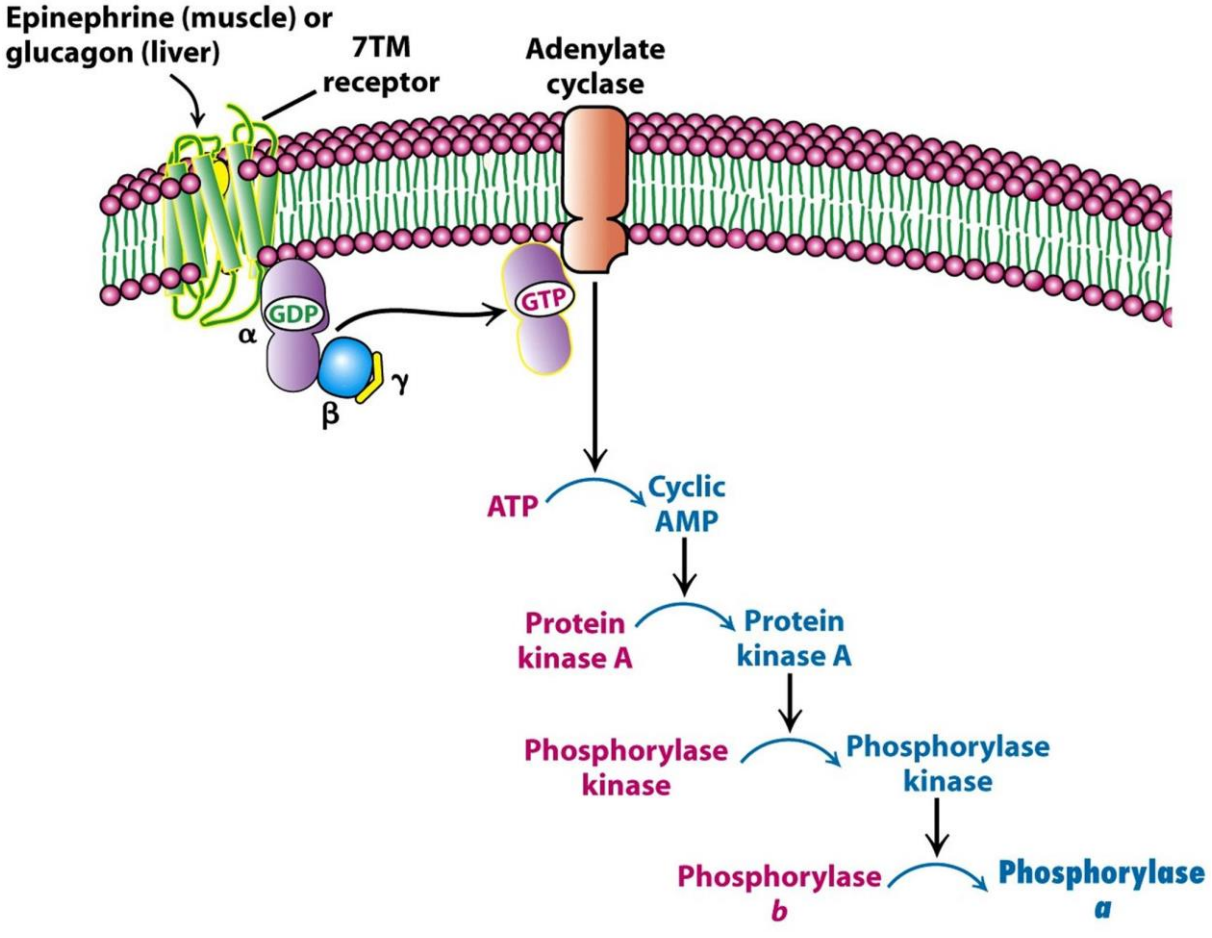
15 20

–Ser–Lys–Tyr–Leu–Asp–Ser–Arg–Arg–Ala–Gln–

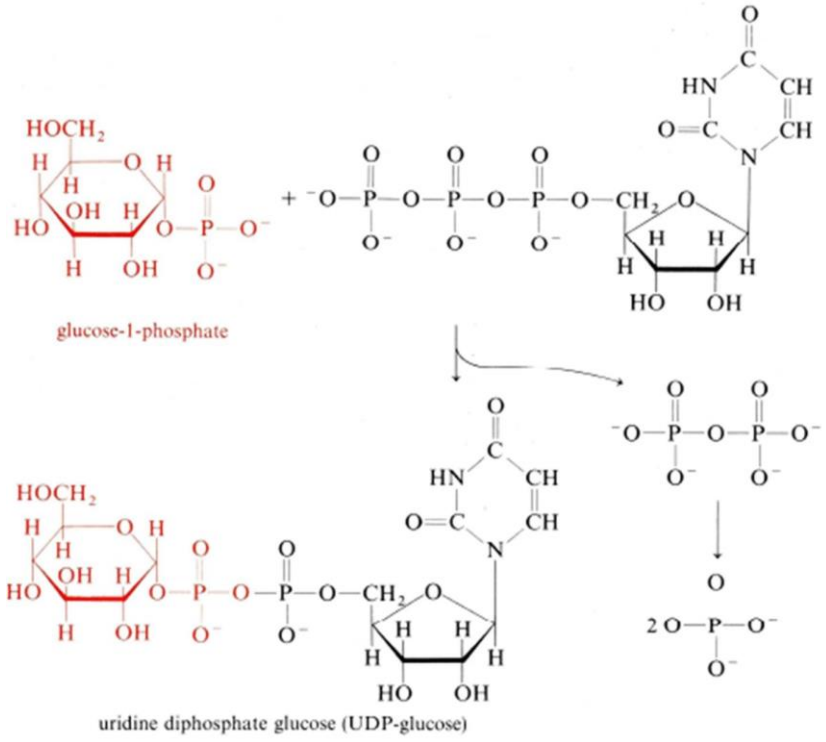
25 29

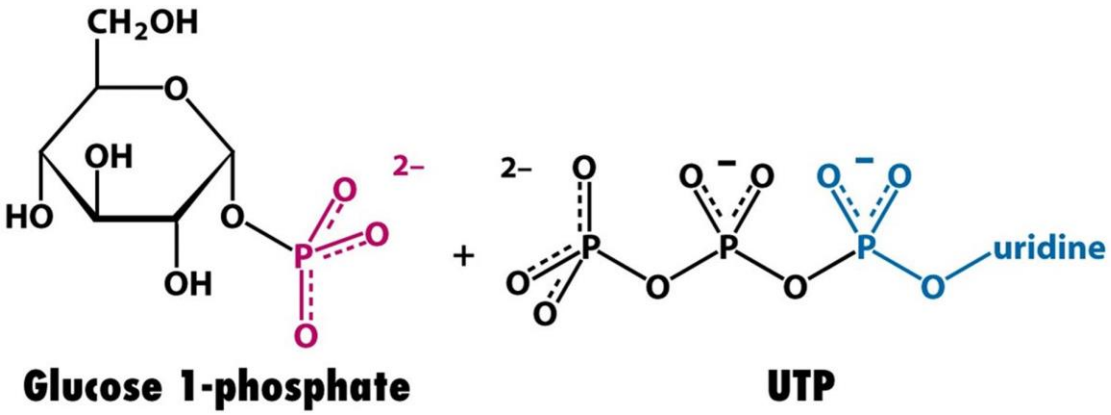
–Asp–Phe–Val–Gln–Trp–Leu–Met–Asn–Thr–COO^{-}

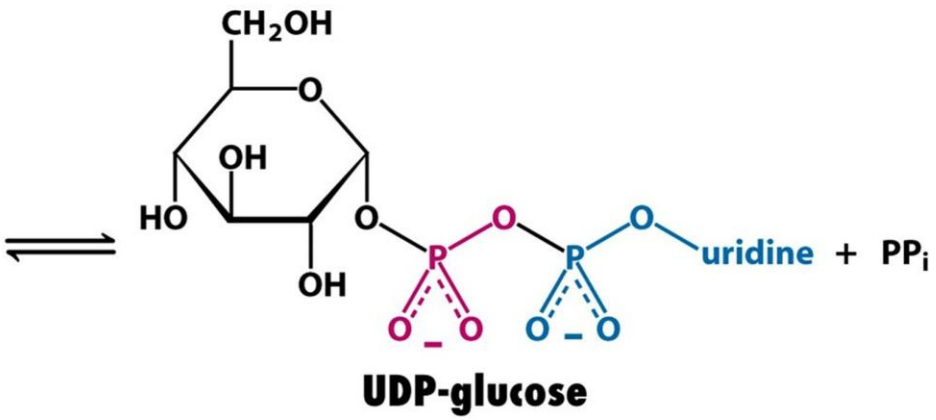
Glucagon

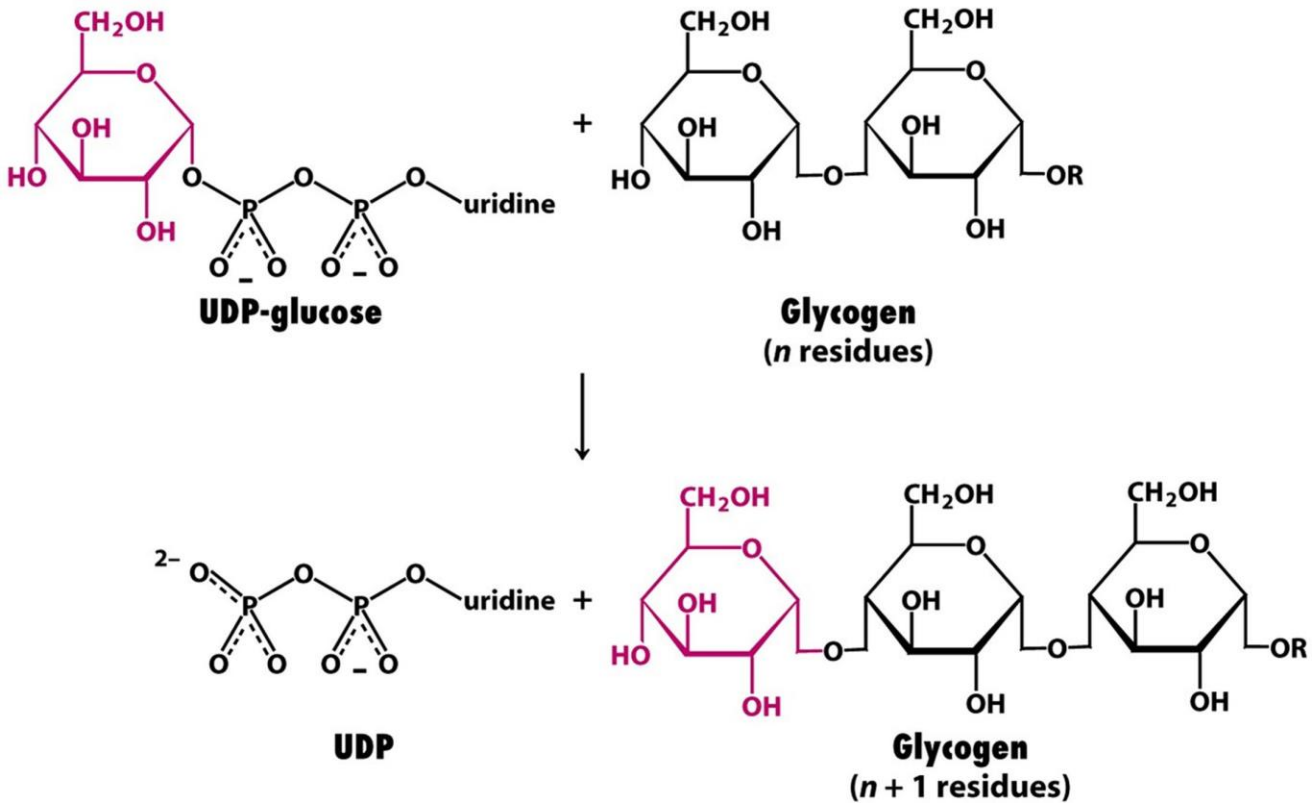


Glycogen Synthesis starts with the activation of glucose-1-P to UDP-glucose:

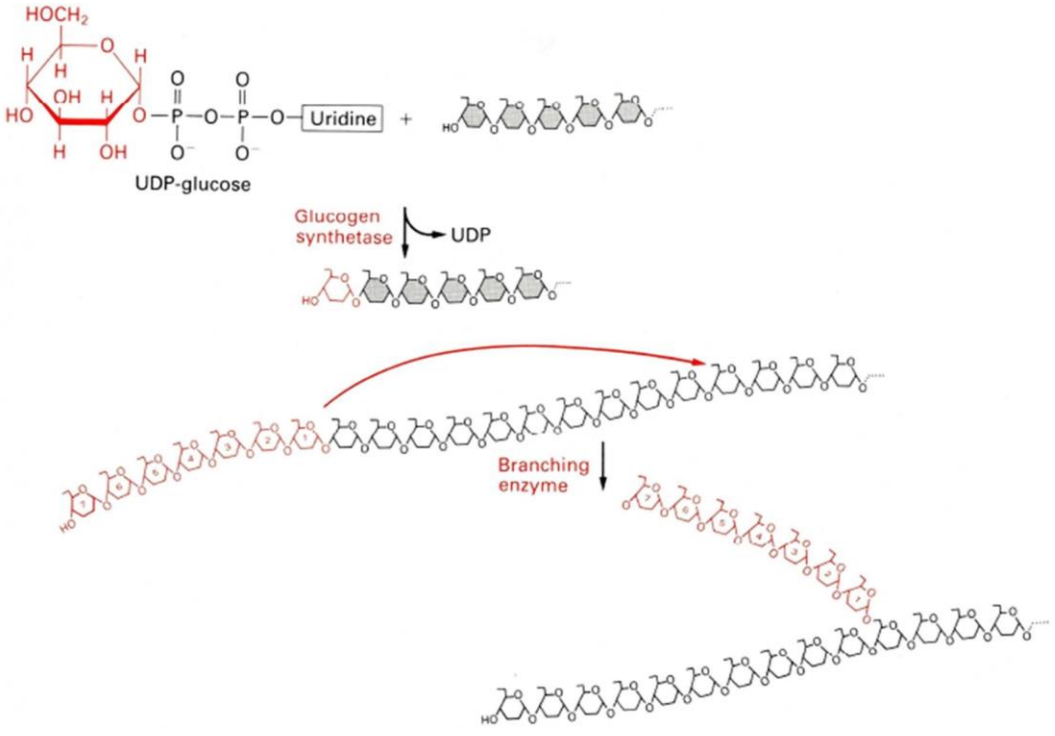


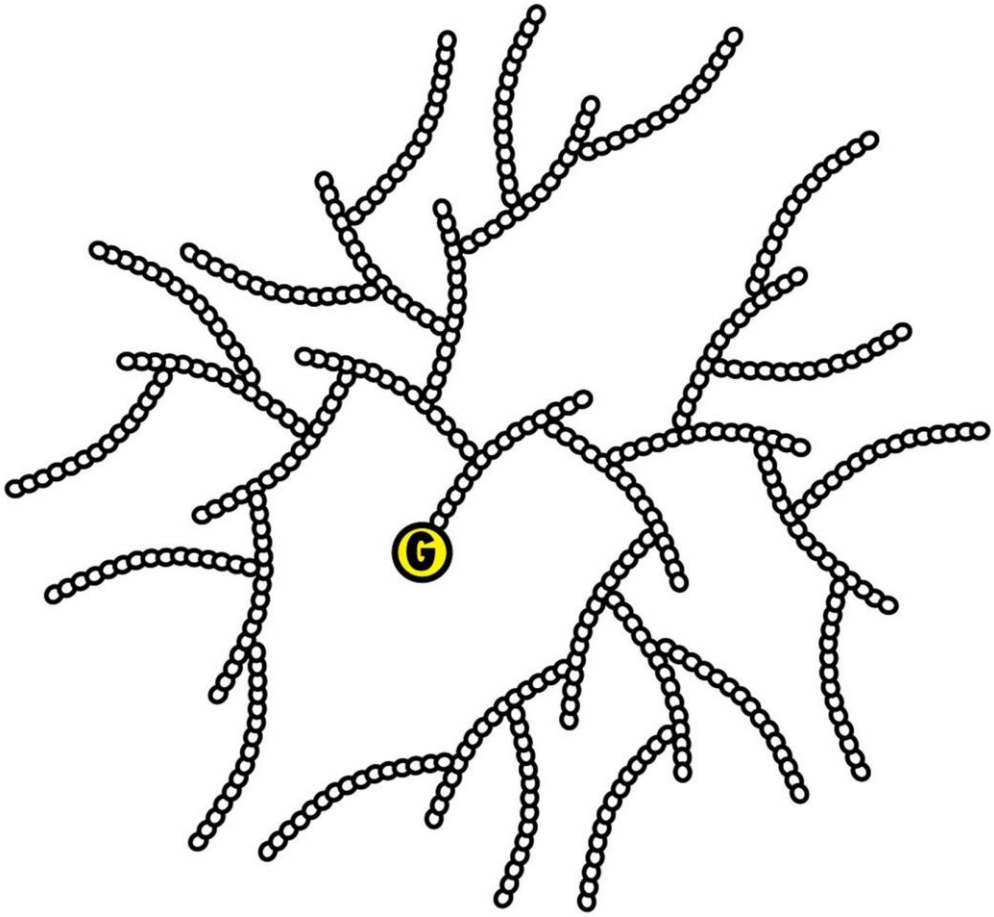






Glycogen Synthesis: Elongation & Branching

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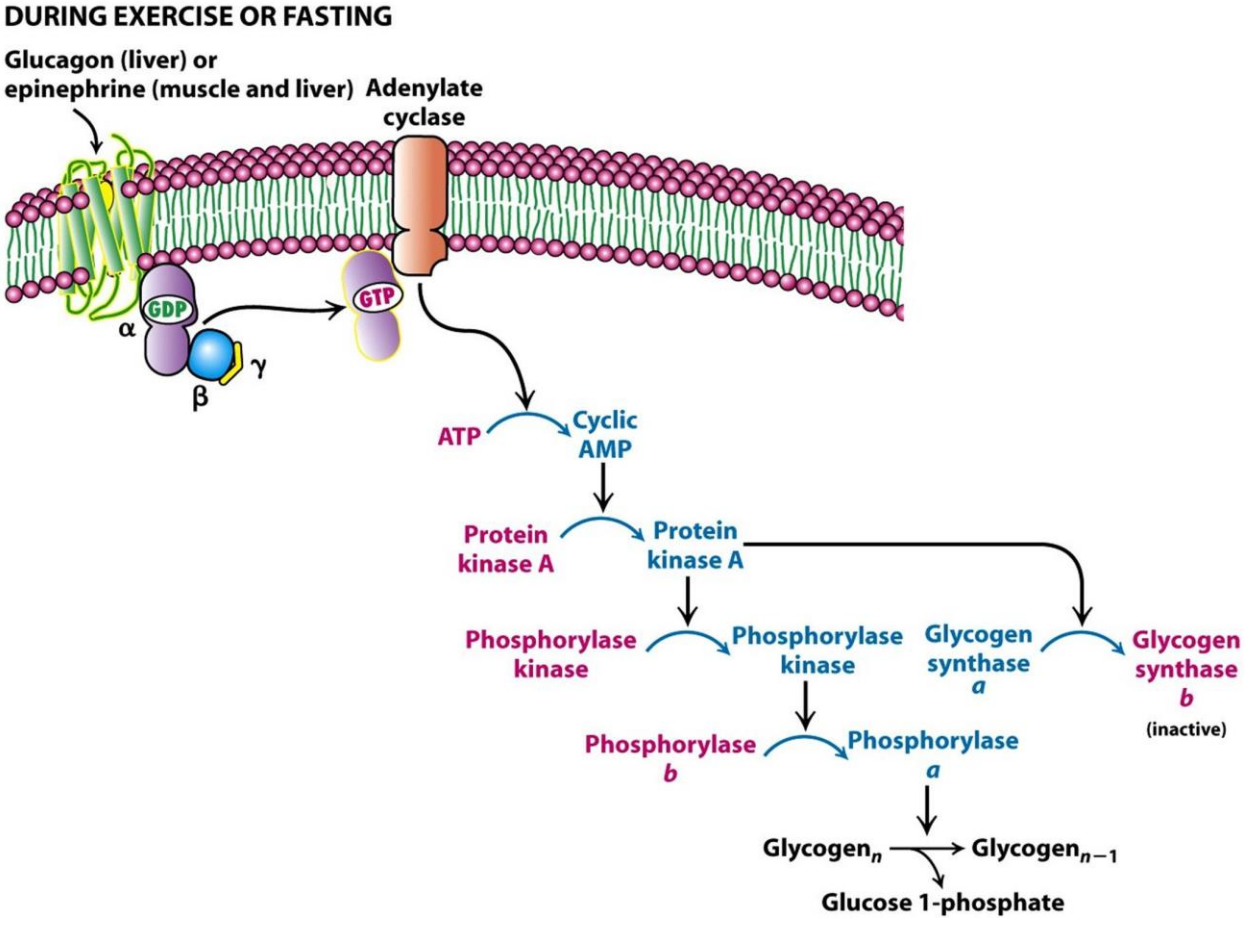
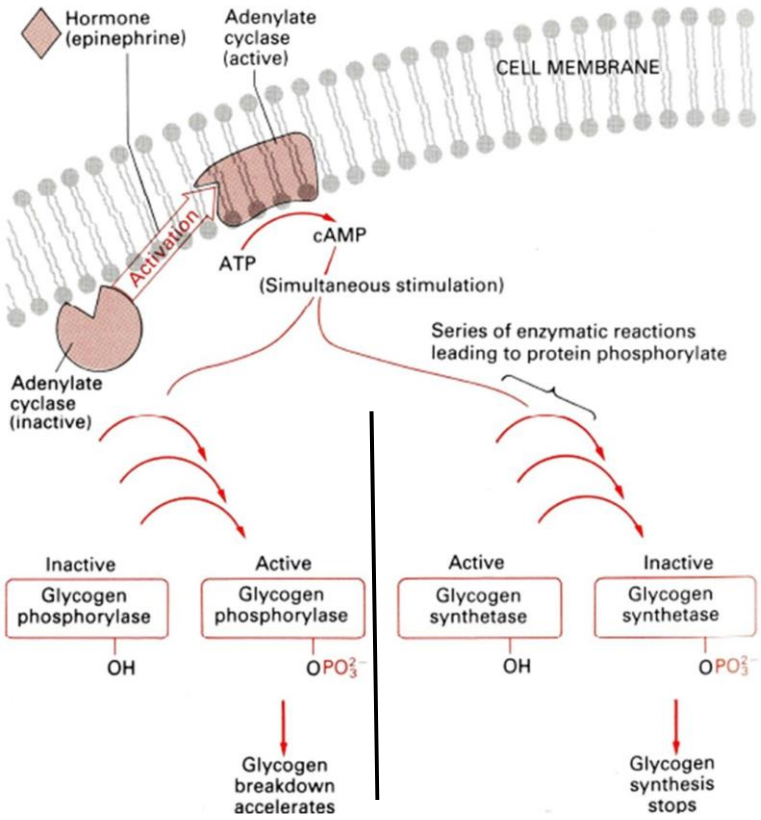
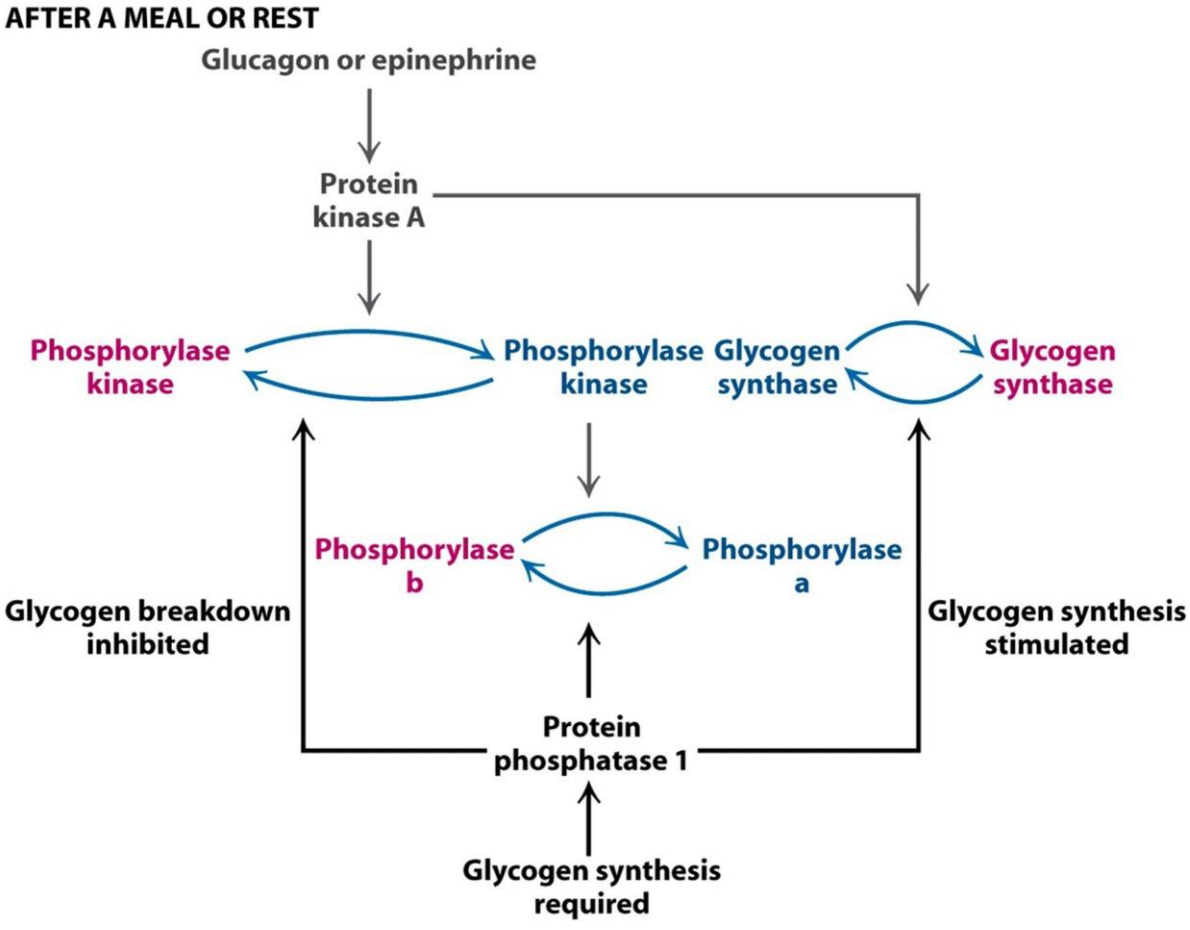
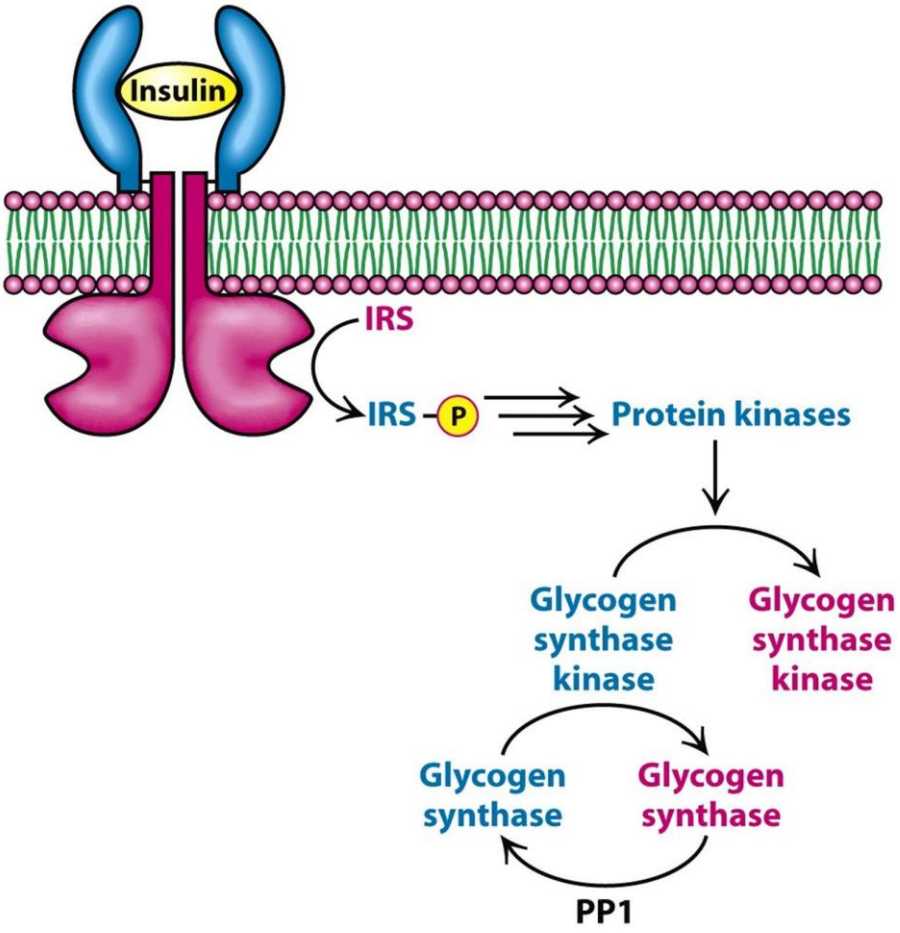

DURING EXERCISE OR FASTING
Glucagon (liver) or
epinephrine (muscle and liver)
Adenylate
cyclase
GDP
GTP
α
β
γ
ATP
Cyclic
AMP
Protein
kinase A
Protein
kinase A
Phosphorylase
kinase
Phosphorylase
kinase
Glycogen
synthase
a
Glycogen
synthase
b
(inactive)
Phosphorylase
b
Phosphorylase
a
Glycogen$_n$
Glycogen$_{n-1}$
Glucose 1-phosphate

Hormonal regulation of Glycogen Metabolism







Hormonal regulation of Glycogen Metabolism

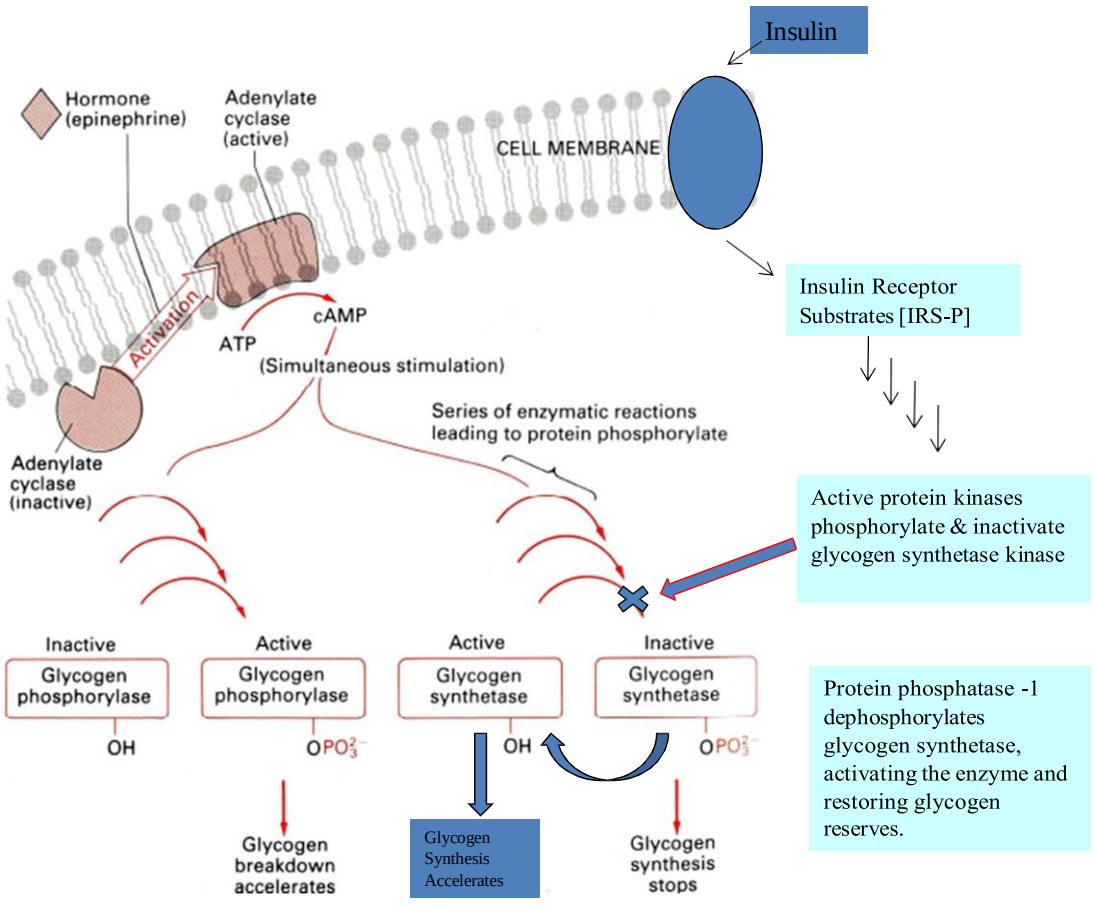


TABLE 21.1 Glycogen-storage diseases

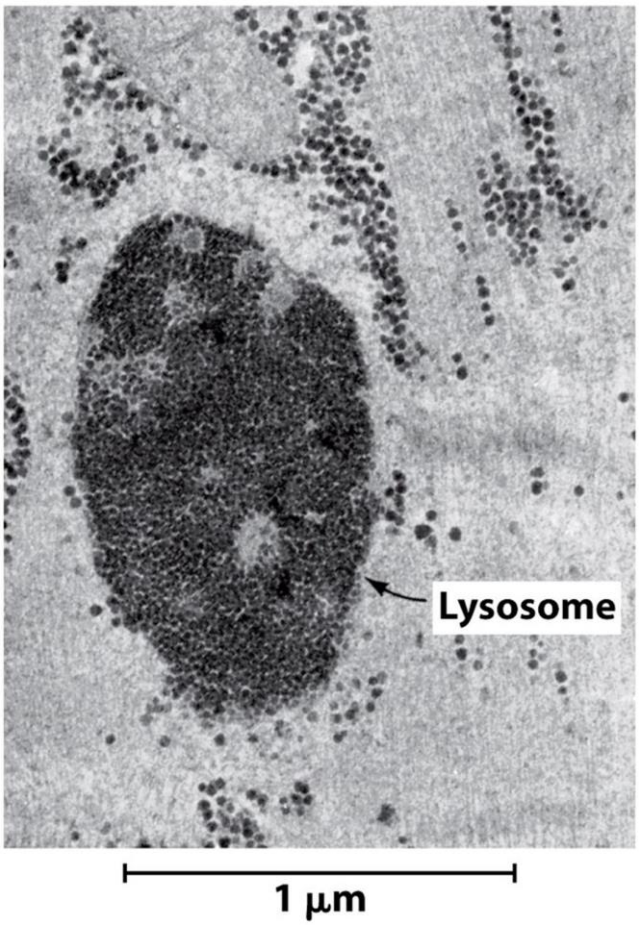
Type	Defective enzyme	Organ affected	Glycogen in the affected organ	Clinical features
I Von Gierke disease	Glucose 6-phosphatase or transport system	Liver and kidney	Increased amount; normal structure.	Massive enlargement of the liver. Failure to thrive. Severe hypoglycemia, ketosis, hyperuricemia, hyperlipemia.
II Pompe disease	α-1,4-Glucosidase (lysosomal)	All organs	Massive increase in amount; normal structure.	Cardiorespiratory failure causes death, usually before age 2.
III Cori disease	Amylo-1,6-glucosidase (debranching enzyme)	Muscle and liver	Increased amount; short outer branches.	Like type I, but milder course.
IV Andersen disease	Branching enzyme (α-1,4 ⟶ α-1,6)	Liver and spleen	Normal amount; very long outer branches.	Progressive cirrhosis of the liver. Liver failure causes death, usually before age 2.
V McArdle disease	Phosphorylase	Muscle	Moderately increased amount; normal structure.	Limited ability to perform strenuous exercise because of painful muscle cramps. Otherwise patient is normal and well developed.
VI Hers disease	Phosphorylase	Liver	Increased amount.	Like type I, but milder course.
VII	Phosphofructokinase	Muscle	Increased amount; normal structure.	Like type V.
VIII	Phosphorylase kinase	Liver	Increased amount; normal structure.	Mild liver enlargement. Mild hypoglycemia.

Note: Types I through VII are inherited as autosomal recessives. Type VIII is sex linked.

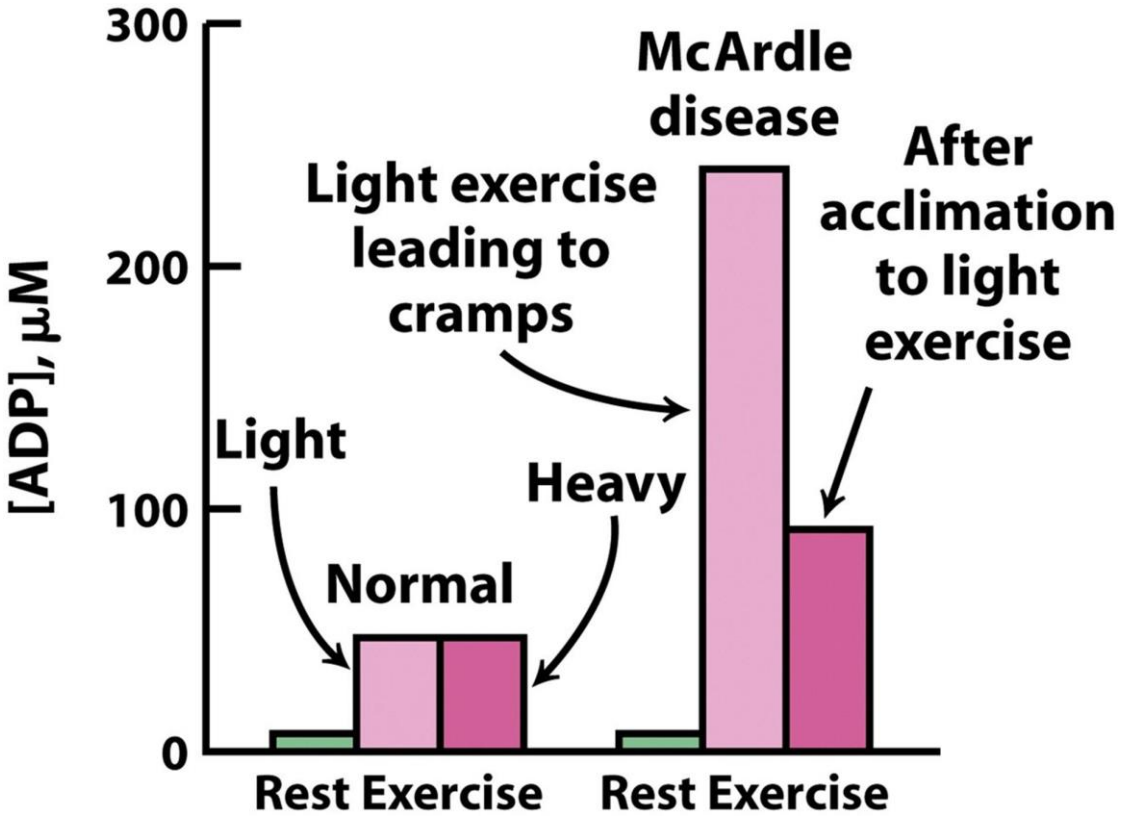
Glycogen-engorged lysosome:

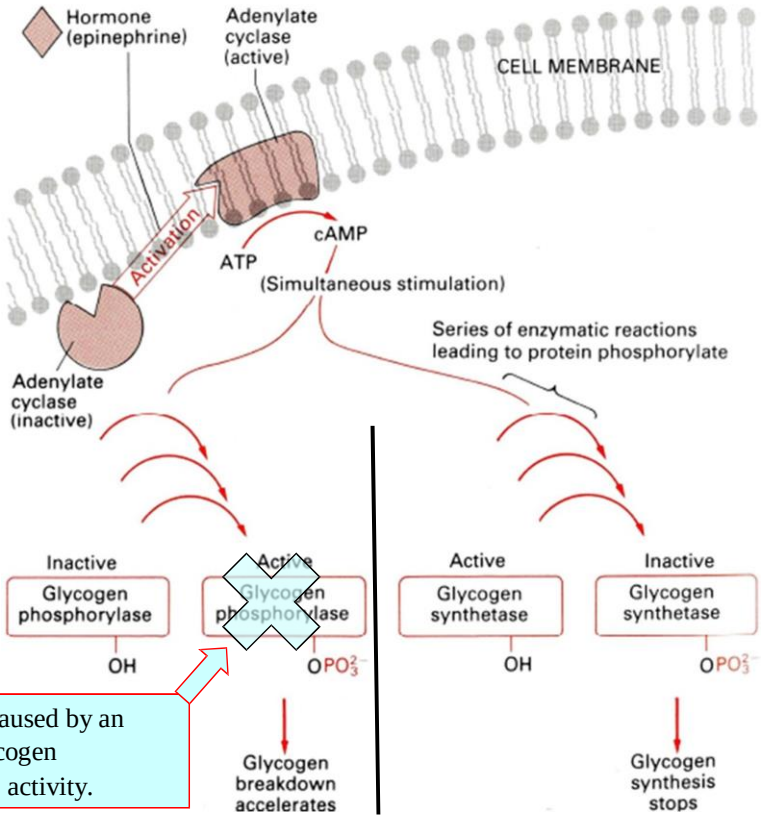
Pompe's disease is caused by a deficiency in α-1,4-glycosidase in lysosomes.

Although cytoplasmic glycogen levels are normal, polymers of glycogen can not escape from the lysosome.



MRI (^{31}P-NMR) studies show high levels of ADP in muscle cells of patients with McArdle's disease.





McArdles' disease is caused by an absence of muscle glycogen phosphorylase enzyme activity.

Subsequently, glycolytic activity slows and ADP accumulates. Creatine phosphate is hydrolyzed during strenuous exercise, yielding a more alkaline environment in muscle cells.

End of Glycogen Metabolism Lecture