Glycogen Metabolism

Glycogen is a storage form of glucose ,found in most type of cells . The liver and muscle contain the largest glycogen stores .

Liver glycogen is a source of blood glucose while muscle glycogen use for its energy needs .

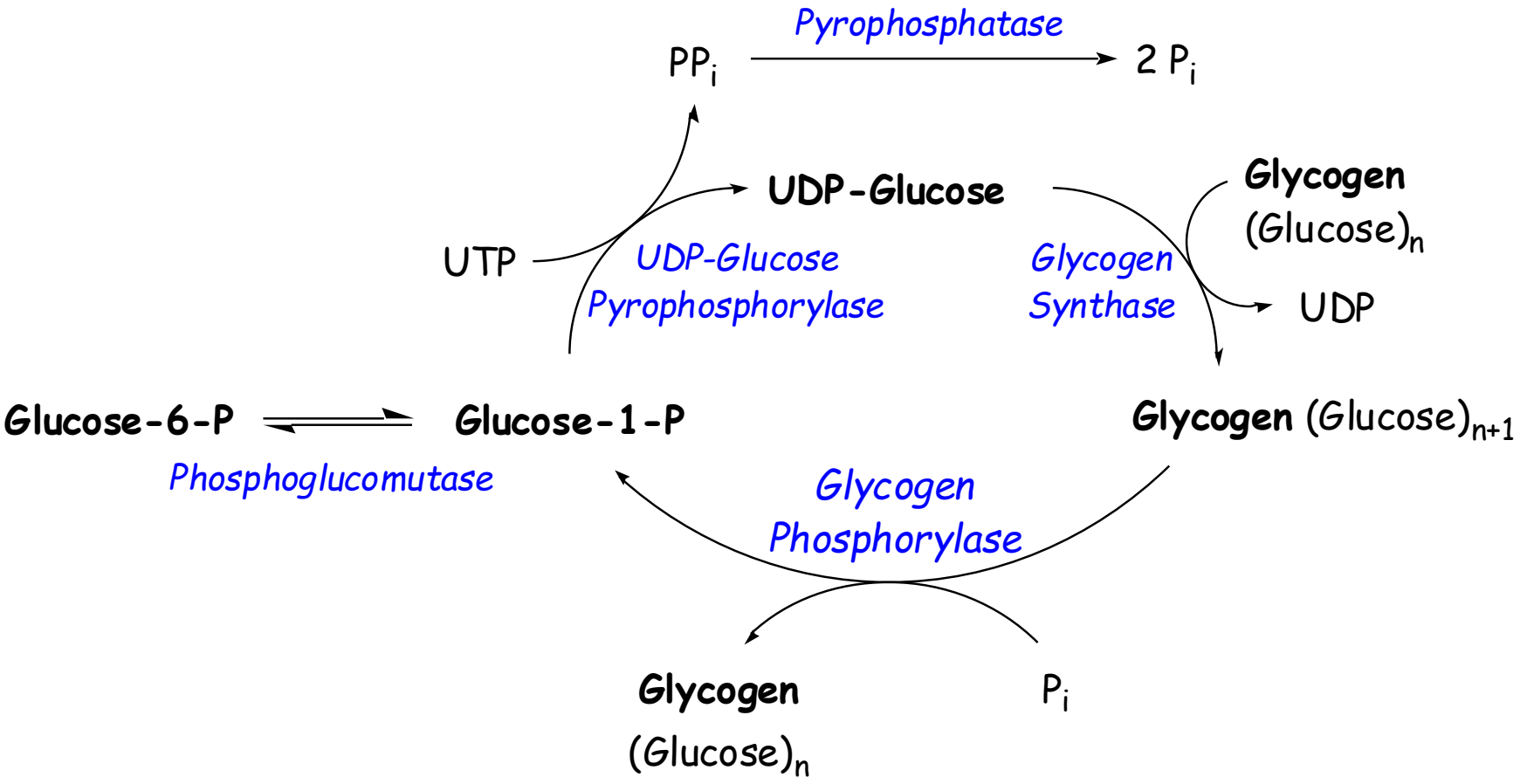
The body maintains blood glucose level at about 80 mg / dl to ensure that the brain and other tissues which are dependent on glucose for the generation of ATP have a continous supply .

Glycogen synthesis and degradation are regulated in liver by hormonal changes which signal the need for blood glucose .

Cyclic AMP integrates the regulation of glycogenesis and glycogenolysis by promoting stimultaneous activation of glycogen phosphorylase and inhibition of glycogen synthase .

cAMP is formed from ATP by adenylate cyclase at the inner surface of cell membrane and act as an intracellular second messenger in response to hormones such as glucagon, epinphrine and norepinephrine .

Glycogen Metabolism



- Duration of liver glycogen storage is about 12 hours (enough for about 12 hrs) then gluconeogenesis starts .

- Glucose can be rapidly delivered to the blood stream when needed upon degradation of glycogen.
= **glycogenolysis**

- Enough glucose and energy triggers synthesis of glycogen.
= **glycogenesis**

Hormones regulated glycogen metabolism :

1 . *Glucagon*
2 . *Epinephrine*
3 . *Insulin*

◆ Primary enzymes targets in glycogen metabolism are : ***glycogen phosphorylase*** and ***glycogen synthase***. The actions of the hormones are indirect.

======= HORMONES =========

1 . Glucagon

-A linear polypeptide hormone produced in **α-cells** of the islets of Langerhans of the **pancreas**.

- Act on **liver** cells .It has no action in muscle .

-Stimulates glycogenolysis and inhibits glycogenesis.

-Inhibit glycolysis and stimulates gluconeogenesis .

-Depresses glycogen synthesis .

2 . Epinephrine

- Stimulates glycogenolysis in liver and muscle cells .

-It is secreted by the adrenal medulla in response to hypoglycemia .

- Decrease glucose utilization .

3 . Insulin

-- *Peptide hormone produced by B-cell of islets of langerhans of the pancrease.It is anabolic hormone .*

-- Insulin composed of 51 amino acids arrange in two peptide chain linked together by 2 disulfide bridges .

-- Bind to receptors on the cells membrane of liver and muscle cells.

-- Increases glycogenesis .

-- Stimulate the uptake of glucose into tissues .

-- Inhibits gluconeogenesis and glycogenolysis .

-- Promote the conversion of glucose to glycogen or fat for storage .

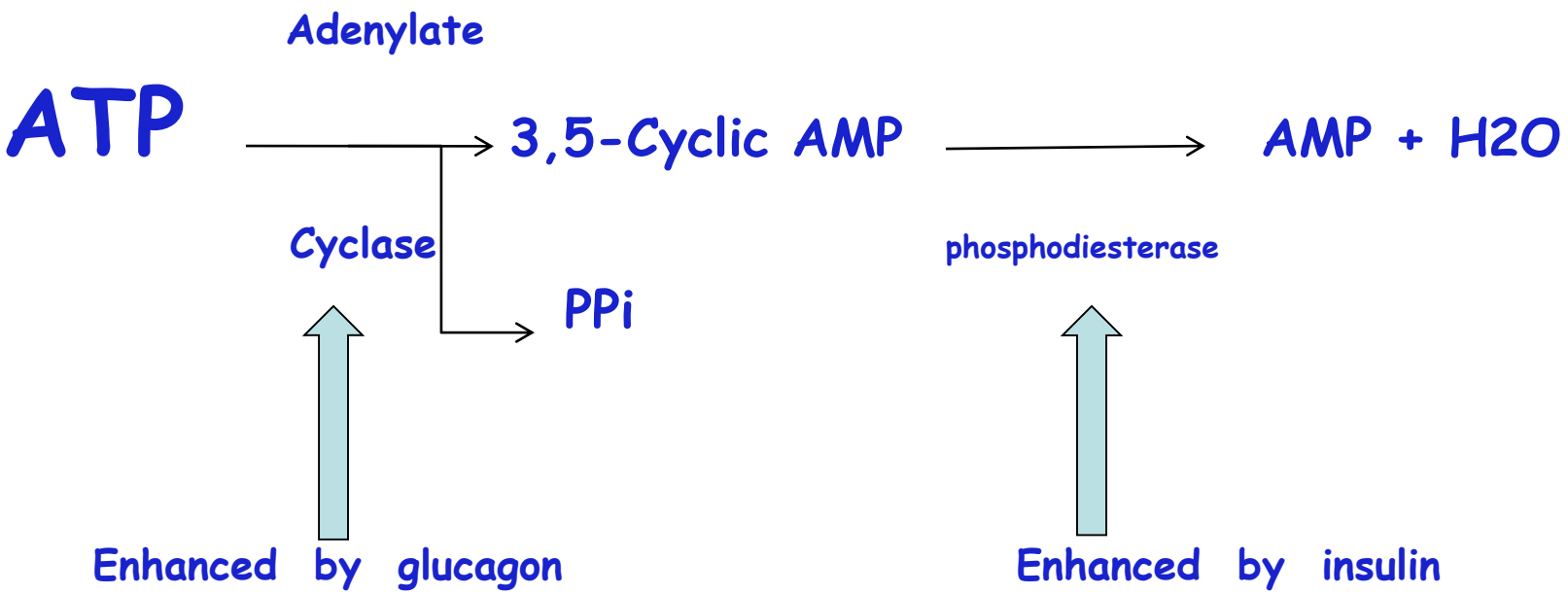
(Biosynthesis of insulin)

This involves two inactive precursors :

Preproinsulin (inactive) —(Endoplasmic Reticlum)→ proinsulin (inactive) —(Golgi apparatus)→ A and B chain (active)

Preproinsulin is cleaved by protolysis to form proinsulin which is further cleaved to form active insulin .

Formation of Cyclic AMP (cAMP)



Glycogen Storage Diseases:

Caused by genetic dificiencies of certain enzymes of glycogen metabolism that lead to accmulation of glycogen or inability to use that glycogen as a feul source .

Types of Glycogen Storage Diseases

Type	Enzyme Deficiency	Name	Tissues	Characteristics
0	Glycogen Synthase		Liver	Less glycogen in liver Hypoglycemia Hyperketonemia
1	Glucose-6-phosphatase	Von Gierke's Disease	Liver,Kidney	Enlarged liver and Kidney,Growth failure Severe hypoglycemia Hyperlipmia
2	Lysosomal Glycosidase		Liver,Heart, Muscle	Glycogen accumulates in lysosomes , Infantile form
3	Amylo-1,6-Glucosidase (Debranching Enzyme)	Pompe's Disease	Liver,Muscle	Fasting hypoglycemia Short-chainedglycogen
4	Amylo-4,6-Glucosidase (Branching Enzyme)	Cori's Disease	Liver	Long unbranched glycogen
5	Muscle Glycogen Phosphorylase	McArdle's Disease	Muscle	Little glycogen in muscle , Cramps Myoglobinuria
6	Liver Glycogen Phosphorylase	Her's Disease	Liver	Hepatomegaly Mild hypoglycemia Good prognosis
7	Phosphofructokinase	Tarui's Disease	Muscle	More glycogen accumulates in muscle
8	Phosphorylase Kinase		Liver	Hepatomegaly