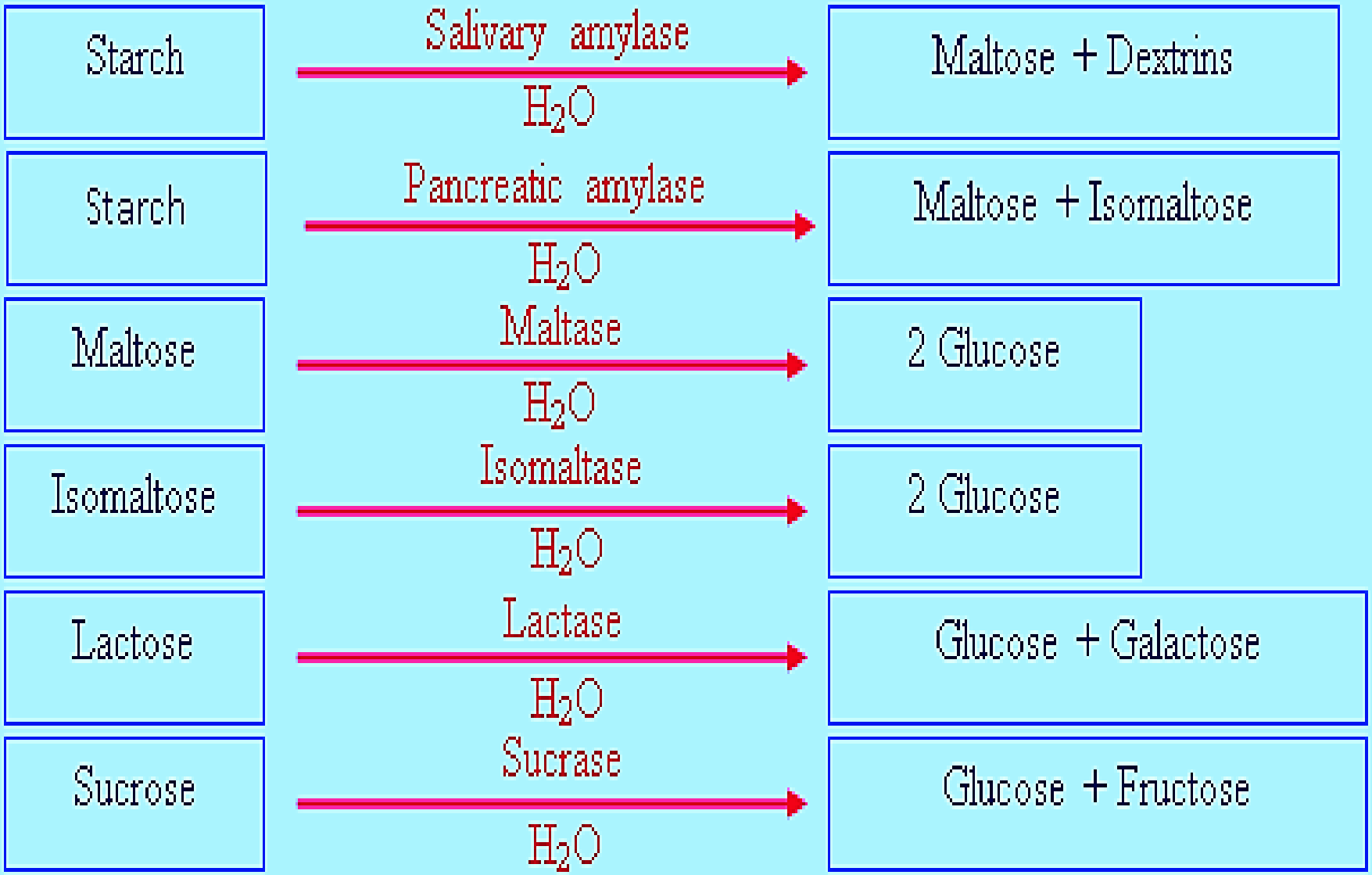
Carbohydrate Metabolism

Digestion of Dietary Carbohydrates



Absorption of Monosaccharides

1- Simple Diffusion

- According to concentration gradient.
- Fructose & pentoses.

2- Facilitated Transport

GLUT5: glucose, galactose & fructose.

3- Active Transport

Sodium glucose transporter (SGLT)I: glucose & galactose.

Fate of Absorbed Sugars

- Absorbed **Fructose and galactose** → liver → glucose → uptake by tissues

Pathways for glucose utilization

1- Oxidation for production of energy

2- Provides other compounds:

Carbohydrates: i.e. fructose, galactose & pentoses.

Glycerol 3-phosphate: triacylglycerol and phospholipids

Acetyl CoA: cholesterol and fatty acids

Non essential amino acids.

3- Storage: glycogen in liver & triacylglycerol in adipose tissue.

4- Excretion in urine.

Oxidation of glucose

I- The Major Pathways: **for energy production.**

A) Glycolysis: produces pyruvate under aerobic condition lactate under anaerobic condition.

B) Krebs' cycle: under aerobic condition, pyruvate is converted to active acetate for oxidation through Krebs' cycle.

II- The Minor Pathways: **for synthesis of other derivatives.**

A) Hexose monophosphate pathway (HMP): For production of pentoses and NADPH.

B) Uronic acid pathway: For production of uronic acids.

GLYCOLYSIS

- **Oxidation of glucose to pyruvate in presence of O_2 or lactate in absence of O_2.**
- **Site:** cytosol of all cells.
- **Steps:**

Phase I (Energy utilization phase):

Glucose is cleaved to two molecules of glyceraldehyde 3-phosphate. This phase consumes 2 molecules of ATP.

Phase II (Energy recovery phase):

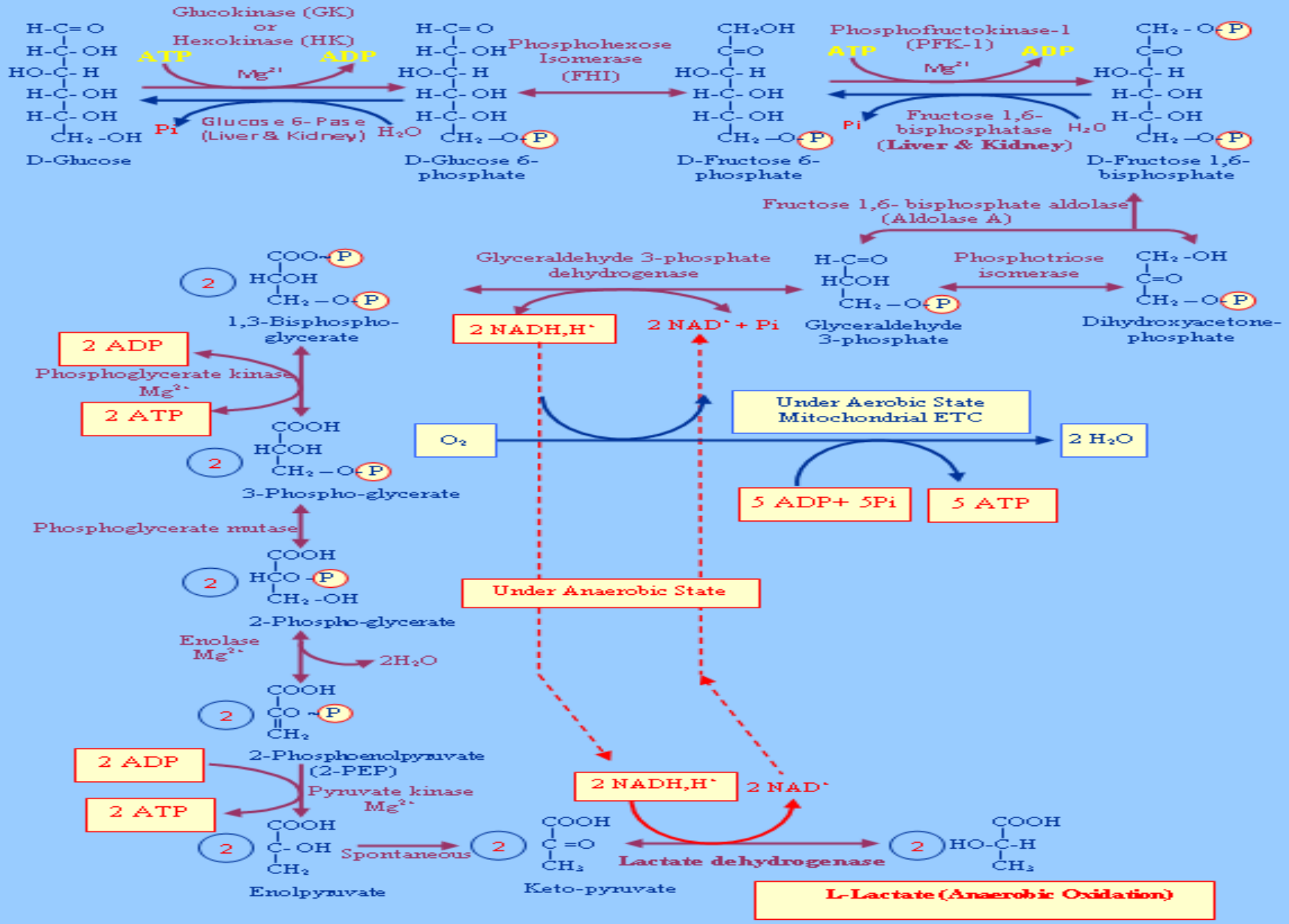
The two molecules of glyceraldehyde 3-phosphate are converted to pyruvate under aerobic state with generation of 10 ATPs.

Or lactate under anaerobic state with generation of 4 ATPs.

- All reactions are reversible except GK, PFK, PK.

	Hexokinase	Glucokinase
Site	Extrahepatic	Liver & pancreatic β cells
K_m	Low (high affinity)	High (low affinity)
G6P	Allosteric inhibitor	No effect
Glucagon	No effect	Inhibitor
Insulin	No effect	Stimulator

Steps of Glycolysis



Importance of Glycolysis

I. Energy production

Reaction catalyzed by	Aerobic state	Anaerobic state
Hexokinase or Glucokinase	-1	-1
Phosphofructokinase-1	-1	-1
Glyceraldehyde 3-phosphate dehydrogenase	+6	0
Phosphoglycerate kinase	+2	+2
Pyruvate kinase	+2	+2
Net energy gain	**8 ATP**	**2 ATP**

II. Importance of Intermediates

Pyruvate: active acetate, oxaloacetate, and lactate.

DHAP ⟶ glycerol 3-phosphate which is used in triacylglycerol and phospholipid synthesis.

Non essential aa : Pyruvate ⟶ alanine

3Phosphoglycerate ⟶ serine.

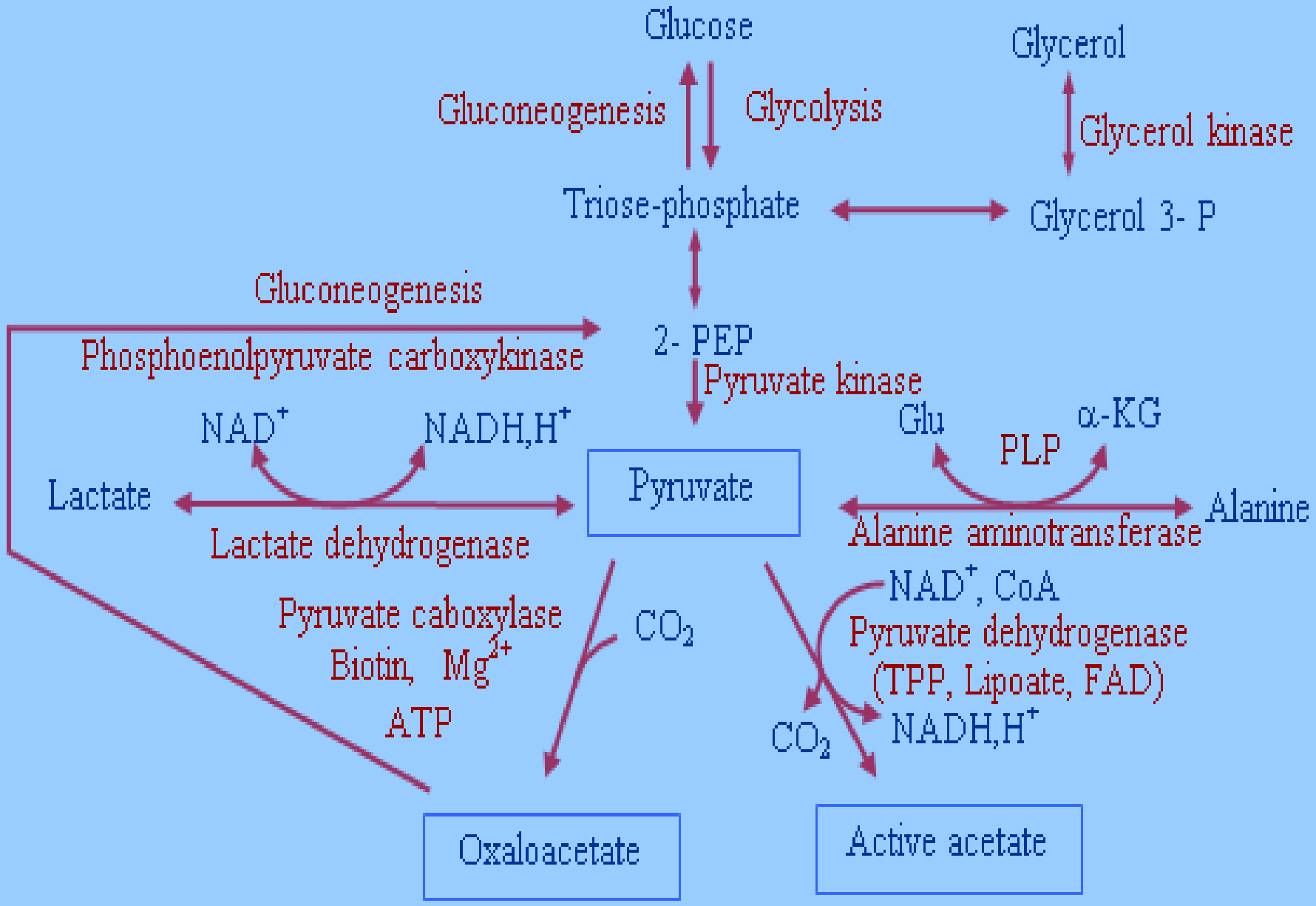
Regulation

Key enzymes: GK, PFK, PK

Stimulated by: insulin, AMP, F6P

Inhibited by: glucagon, ATP, citrate

Summary Diagram for Metabolism of Pyruvate



Energy Yield from Glucose Oxidation

Pathway	Products	ATP
Glycolysis	2 X pyruvate	8
Oxidative decarboxylation of pyruvate	2 X Acetyl CoA	2 x 3 = 6
TCA, ETC		2 x 12 = 24
Net energy gain		**38**

Hexose Monophosphate Pathway (HMP)

alternative route for glucose oxidation not for energy production.

- **Site:** cytosol of liver, adipose tissue, ovaries, testes, RBCs & retina.
- **Steps:**

Oxidative irreversible phase:

Glucose 6-phosphate undergoes dehydrogenation & decarboxylation to yield ribulose 5-phosphate.

Nonoxidative reversible phase:

6 molecules of ribulose 5-P are converted to 5 molecules of glucose 6-P by two enzymes: **transketolase** & **transaldolase.**

Importance of HMP pathway

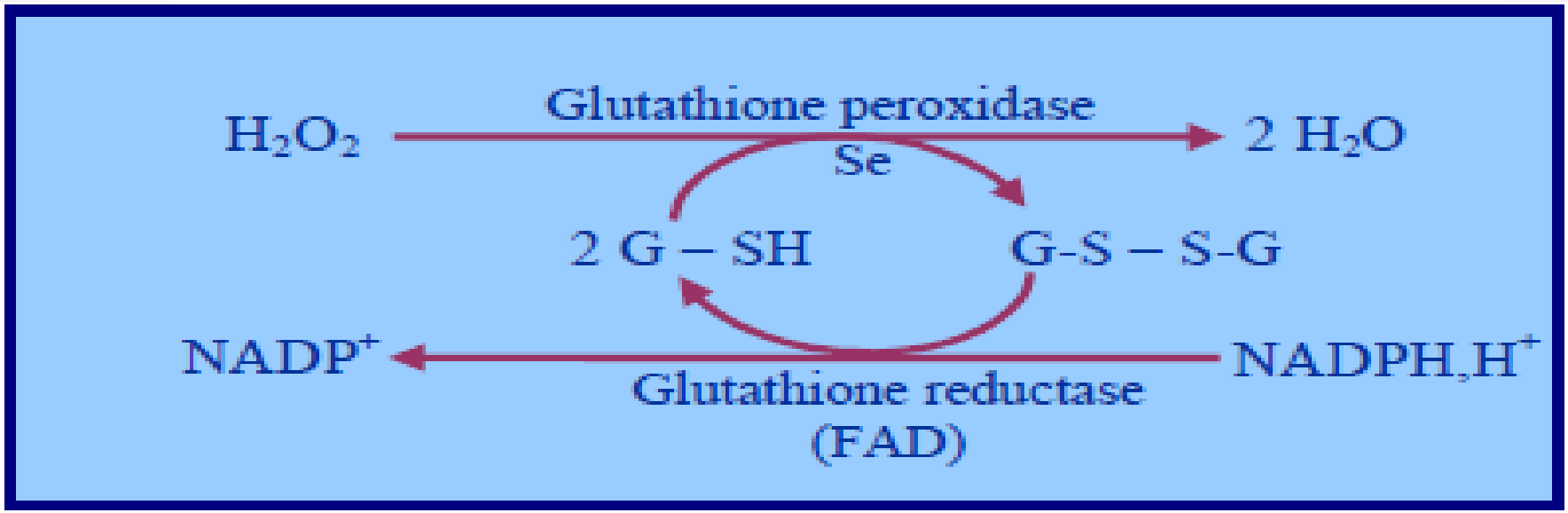
I- It provides *ribose 5-phosphate*

required for synthesis of nucleotides and nucleic acids.

II- Main source of *NADPH*, required for:

A) Reductases

1. Glutathione reductase



2. Folate, retinal reducatase

3. Reducatases of FA, steroid synthesis.

B) Hydroxylases

e.g. Steroids hydroxylase

C) NADPH Oxidase: phagocytosis (respiratory burst).

Favism

Genetic deficiency of glucose-6-phosphate dehydrogenase (G6PD).

- ***Precipitating factors:***

  Certain drugs (premaquine, aspirin), Fava beans

- ***Symptoms:***

  Asymptomatic: in between attacks.

  Hemolytic crisis: on exposure to above factors.

- ***Mechanism:***

G6PD deficiency → HMP inhibition → ↓ NADPH →

Inhibition of glutathione reductase → ↓ reduced glutathione

→ failure to protect cells from oxidative damage by H_2O_2

→ Lysis of red cells → hemolytic anemia, jaundice.

- ***Managment:***

- Avoid drugs, fava beans.

- Blood transfusion during attacks

Uronic acid Pathway

is an alternative route for glucose oxidation.

- **Site:** cytosol of liver

Importance of Uronic acid pathway:

- Main function is formation of ***UDP-glucuronate***:

1- Glycosaminoglycans (GAGs) synthesis.

2- Synthesis of L-ascorbic acid (not in human)

3- Conjugation reactions: with bilirubin, steroids to make them: more soluble, easily excreted i.e. Detoxication.

GLUCONEOGENESIS

It is the synthesis of glucose and /or glycogen from non-carbohydrate sources.

Site: Liver, kidney.

Steps: reversal of glycolysis, the irreversible reactions are reversed by 4 enzymes:

Glycolytic Key Enzymes	*Gluconeogenic Key Enzymes*
Glucokinase	Glucose 6-phosphatase
Phosphofructokinase-1	Fructose 1,6-bisphosphatase
Pyruvate kinase	Pyruvate carboxylase
	Phosphoenolpyruvate carboxykinase.

Sources:

1. Lactate.
2. Pyruvate.
3. Glucogenic aa
4. Glycerol
5. Odd chain FA

Regulation:

Insulin: ⇓⇓ gluconeogenesis, ⇑⇑ glycolysis

Anti-insulin: ⇑⇑ gluconeogenesis, ⇓⇓ glycolysis

Importance:

1. Source of blood glucose during fasting & starvation.
2. Removal of waste products e.g. lactate, glycerol.

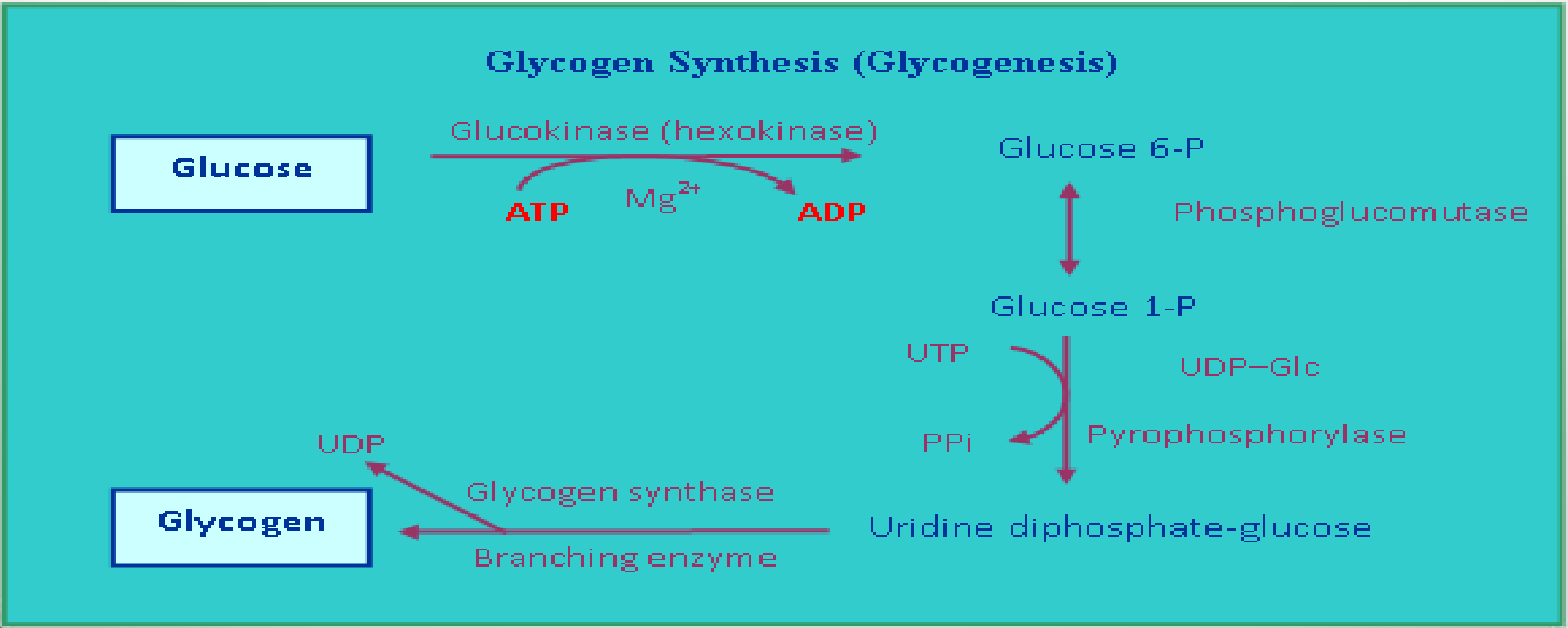
Glycogen Metabolism

Glycogenesis

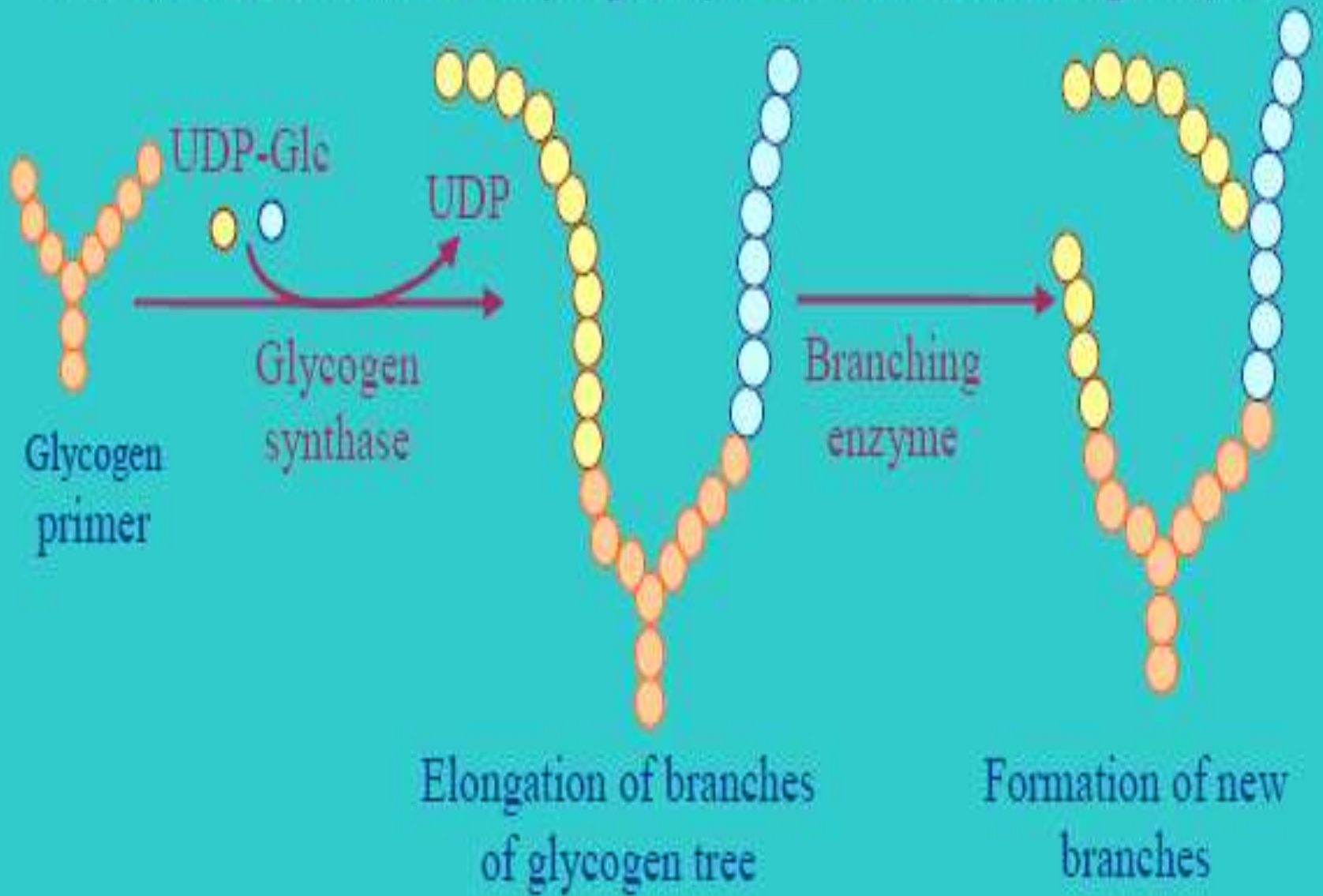
Definition: synthesis of glycogen from glucose.

Site: cytosol of liver & muscles.

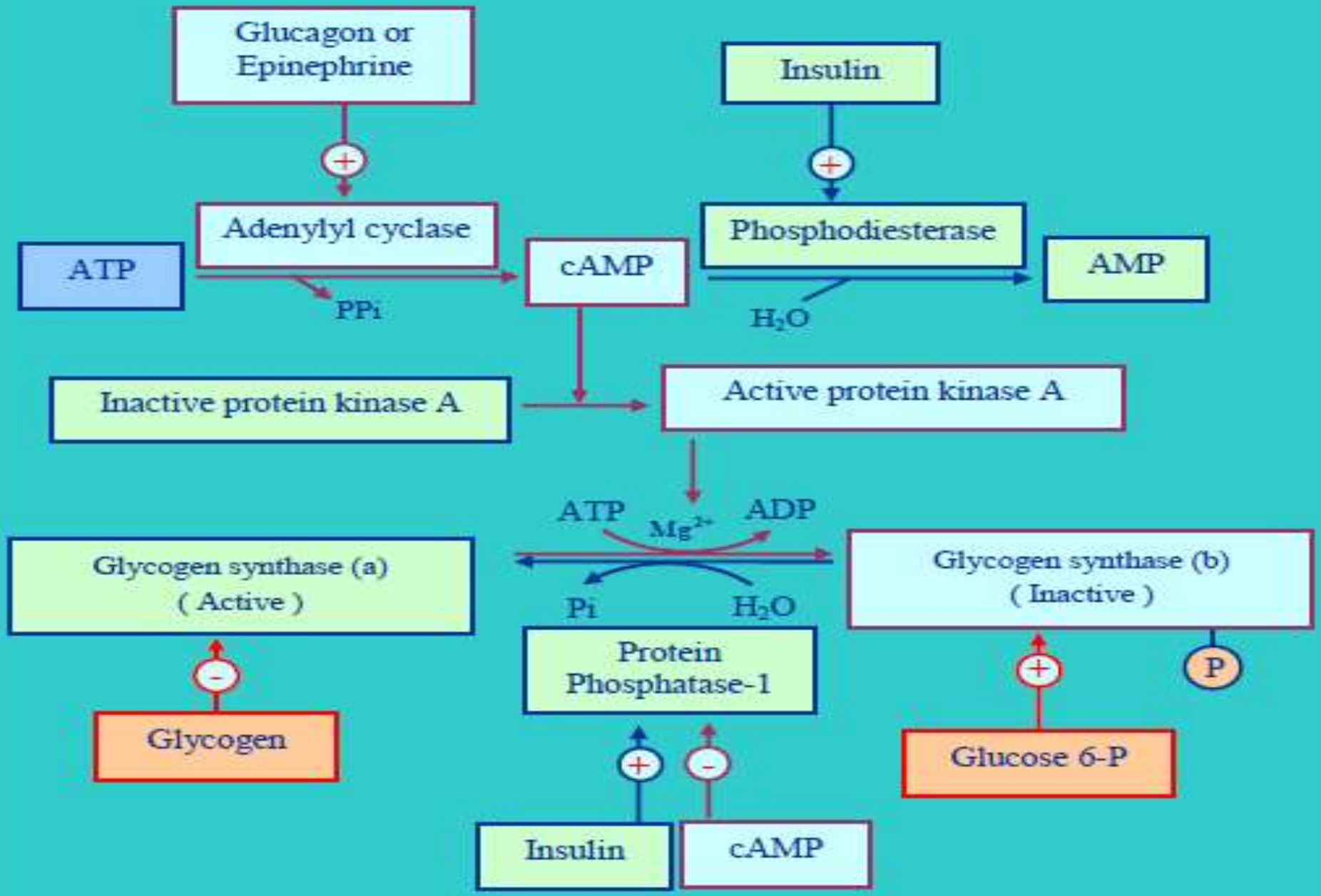
Steps:



Mechanism of Action of Glycogen Synthase and Branching Enzyme



Regulation of Activity of Glycogen Synthase



Glycogenolysis

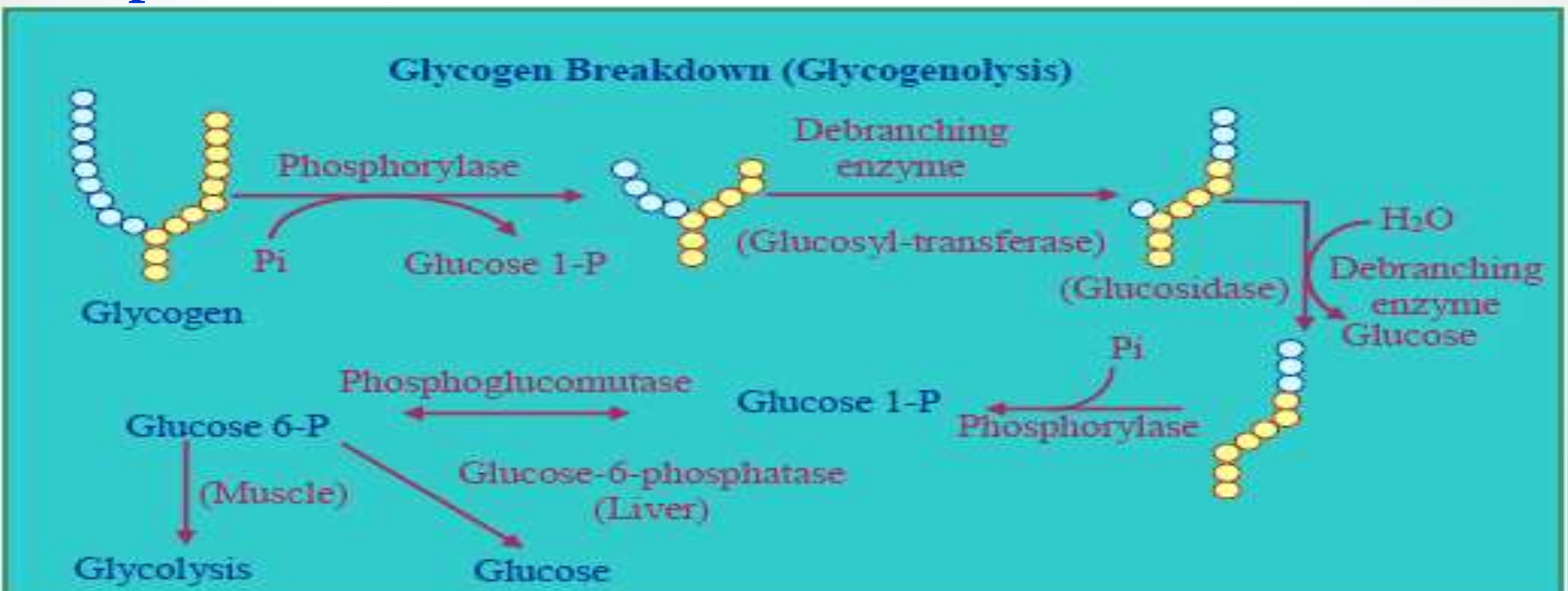
Definition: breakdown of glycogen to glucose in liver or G6P in muscles (due to absence of G6 phosphatase in muscles).

Importance:

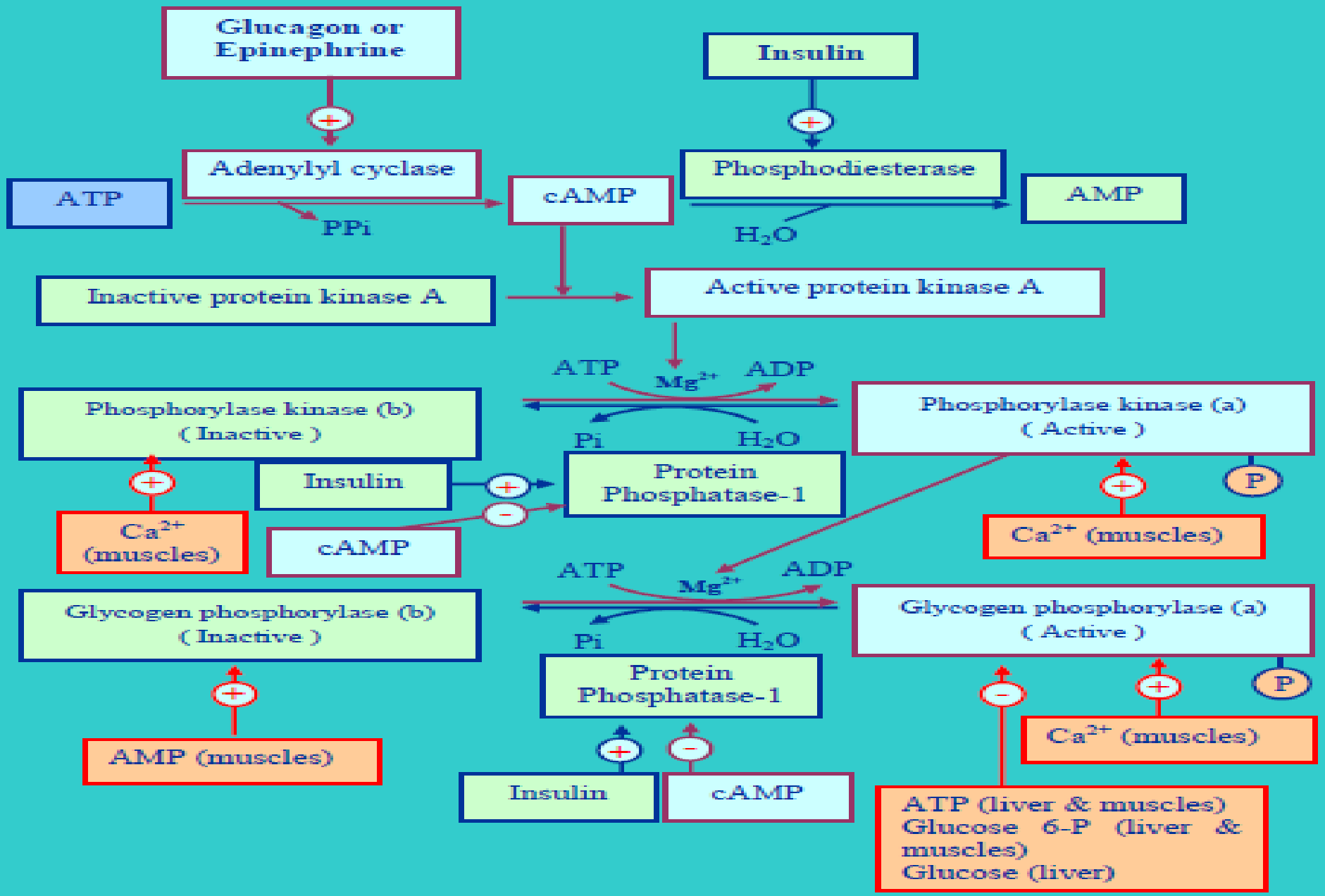
In muscles: source of energy during exercise.

In liver: source of blood glucose during 18 hours starvation.

Steps:



Regulation of Activity of Glycogen Phosphorylase

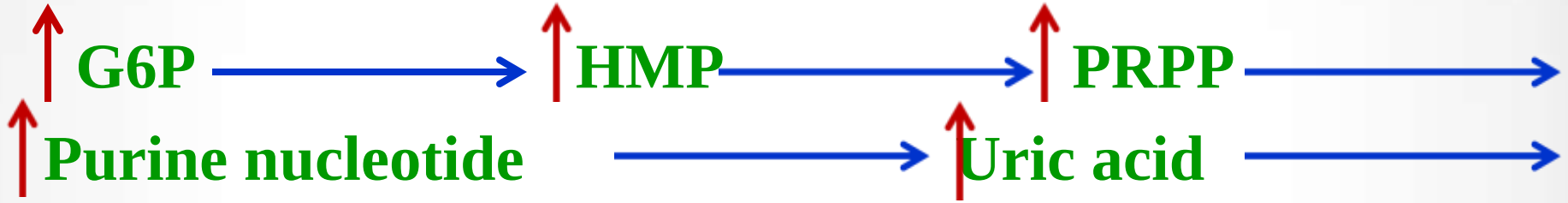


Von Gierke's disease

Genetic disease due to deficiency of ***G6 phosphatase***

Accumulation of ***glycogen*** in ***liver& kidney***

Hepatomegaly, ***renal failure*** & ***fasting hypoglycemia.***



Hyperuricemia (Gout).