Glycolysis

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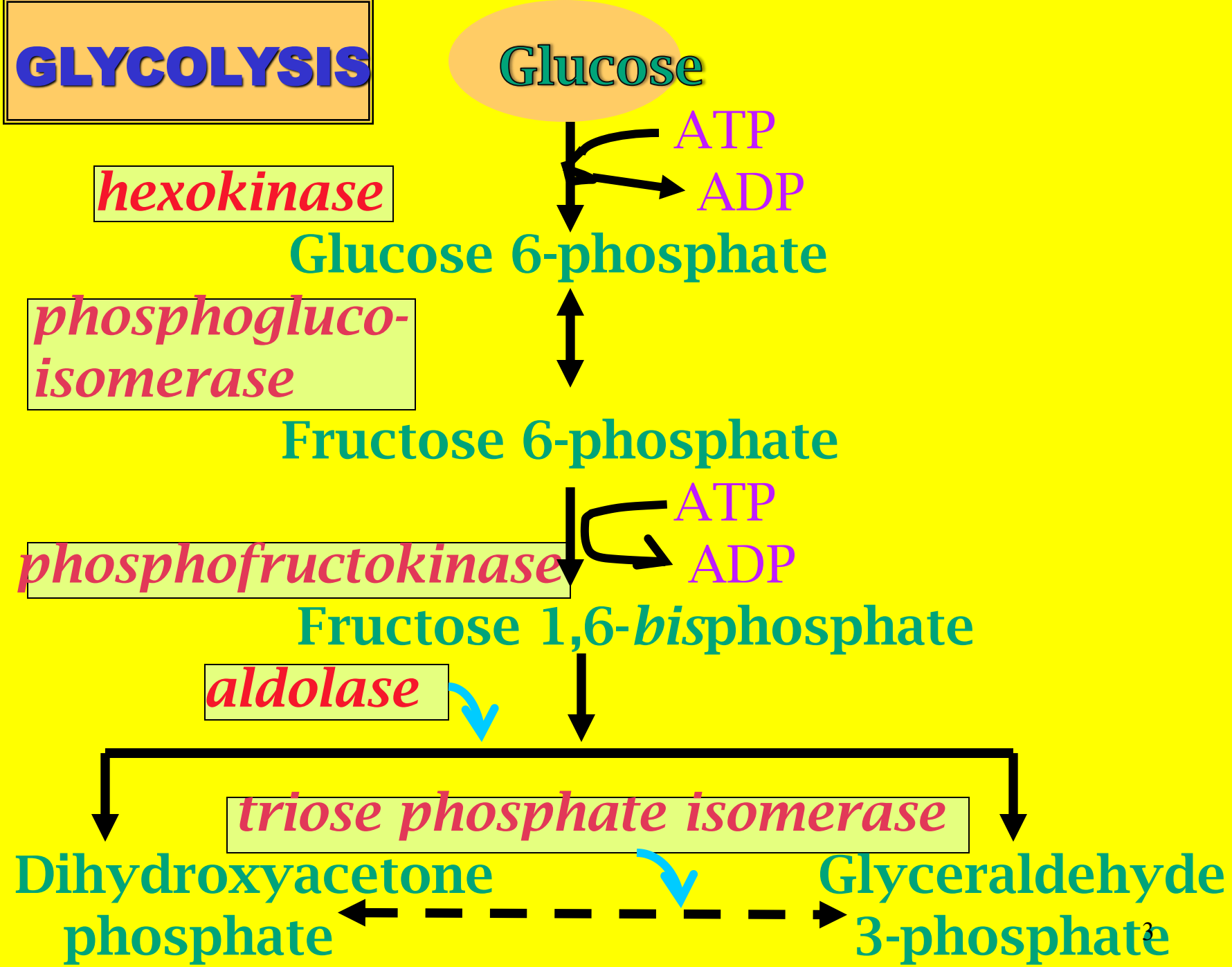
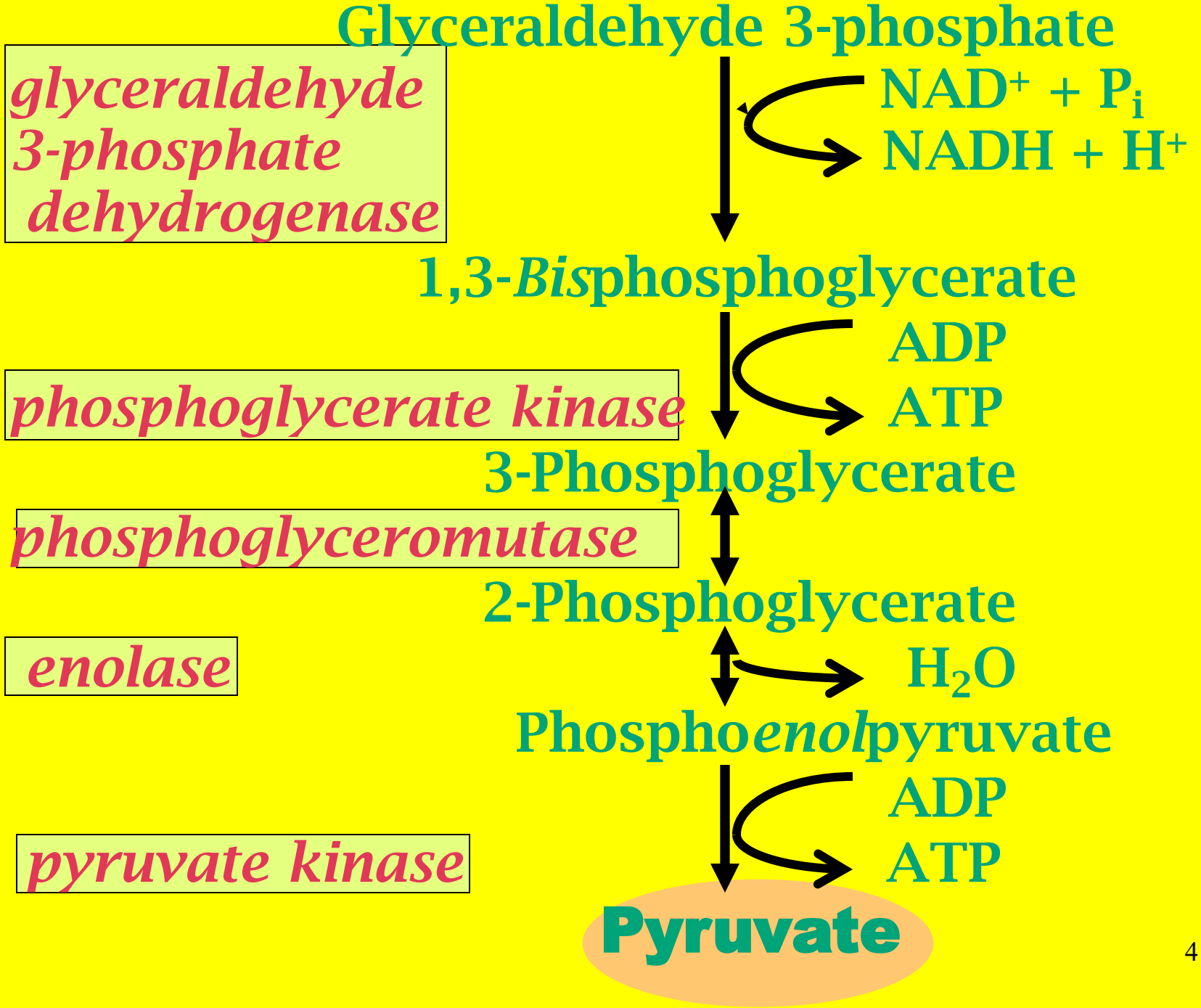
biochemistry

Glycolysis is a cytoplasmic pathway which one molecule of glucose is converted to a series of intermediates leading to formation of two molecules of pyruvic acid to generate energy (in the form of ATP) and intermediates that are used in the body for biosynthesis .

In muscle , as oxygen becomes used up through activity , pyruvic acid , so formed ,can be converted to lactic acid under anaerobic conditions by the lactate dehydrogenase reaction .

Mature RBCs or erythrocytes contain no mitochondria , so they are totally dependent upon glycolysis for ATP production .


GLYCOLYSIS
Glucose
ATP
ADP
hexokinase
Glucose 6-phosphate
phosphogluco-
isomerase
Fructose 6-phosphate
ATP
ADP
phosphofructokinase
Fructose 1,6-bisphosphate
aldolase
triose phosphate isomerase
Dihydroxyacetone
phosphate
Glyceraldehyde
3-phosphate


Glyceraldehyde 3-phosphate
glyceraldehyde 3-phosphate dehydrogenase
NAD+ + Pi
NADH + H+
1,3-Bisphosphoglycerate
ADP
ATP
phosphoglycerate kinase
3-Phosphoglycerate
phosphoglyceromutase
2-Phosphoglycerate
enolase
H2O
Phosphoenolpyruvate
ADP
ATP
pyruvate kinase
Pyruvate

Summary of Energy Relationships for Glycolysis

Input = 2 ATP

1. glucose + ATP → glucose-6-P
2. fructose–6-P + ATP → fructose-1,6-*bis*phosphate

Output = 4 ATP + 2 NADH

1. 2 glyceraldehyde-3-P + 2 P_i + 2 NAD^+ →
   2 (1,3-*bis*phosphoglycerate) + 2 NADH

2. 2 (1,3-*bis*phosphoglycerate) + 2 ADP →
   2 (3-P-glycerate) + 2 ATP

3. 2 PEP + 2 ADP → 2 pyruvate + 2 ATP

Net = **2ATP and 2NADH**

The fate of pyruvate

*Pyruvate can be converted in the cytosol by lactate dehydrogenase to lactate .

*Pyruvate can enter mitochondria and be converted by pyruvate dehydrogenase to acetyl CoA , which can enter TCA cycle .

*Pyruvate can also be converted to oxaloacetate by pyruvate carboxylase , an enzyme found in tissues such as the liver and brain , but not in muscle .

*Pyruvate can be transaminated to form the amino acid alanine .

Conversion of pyruvate to Lactate

Enzyme = *Lactate Dehydrogenase*

Pyruvate + NADH + H^+ = lactate + NAD^+

Notes :

* Pyruvate reduced in the cytosol by NADH (which is produced by glycolysis) forming Lactate and regenerating NAD .

* In patients with acidosis , such as in diabetes or hyperventilation , lactate is converted to pyruvate , therefore , the reaction of lactate dehydrogenase is reversible and depends on the levels of oxygen in vivo .

* The function of LDH in muscle is mainly conversion of pyruvic acid to lactic acid , so it is activated by high level of pyruvic acid and inhibited by high level of lactic acid .

In the heart , the reverse occurs , it act for conversion of lactic acid to pyruvic acid in order to supply high energy , so it is inhibited by high level of pyruvic acid and stimulated by high level of lactic acid .

LDH consist of four subunits that can be either of the muscle (M) or the heart (H) type .

Five isozymes occur (MMMM , MMMH , MMHH , MHHH , HHHH) , which can be separated by electrophoresis . Different tissues have different mixtures of these isozymes .

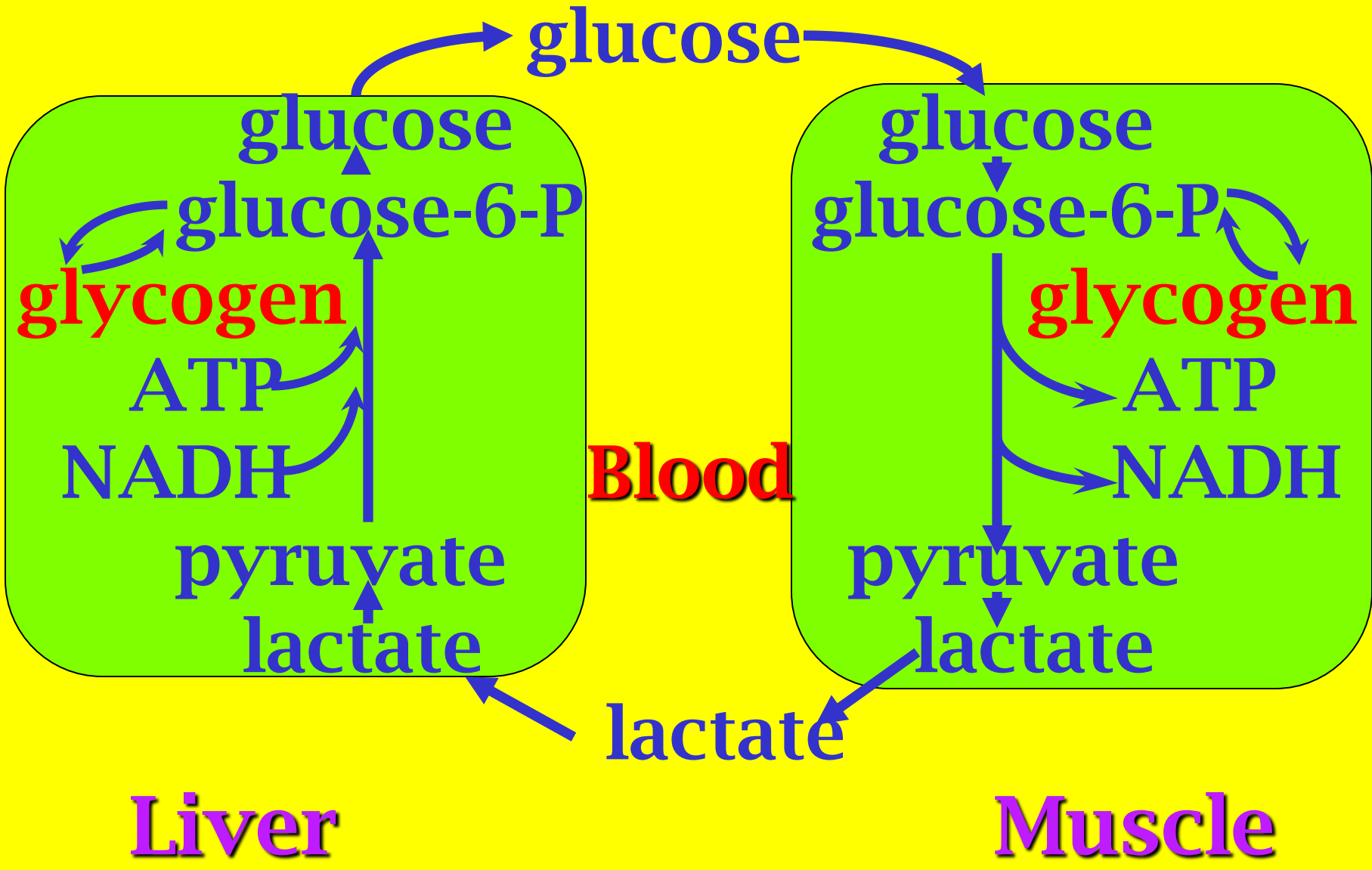
Lactate is released by tissues (e.g. RBCs or exercising muscle) and is used by the liver for gluconeogenesis or by tissues such as the heart and kidney where it is converted to pyruvate and oxidized for energy .

* Skeletal muscle and liver contain Predominantly the "**M**" forms ; heart the "**H**" forms .

During and after myocardial infarction (heart attack) , heart cells die releasing LDH into the circulation .

* Diagnostic .

LACTIC ACID (CORI) CYCLE



REGULATION OF GLYCOLYSIS

Three irreversible kinase reactions primarily drive glycolysis forward.

1 . Hexokinase .
2 . Phosphofructokinase (PFK) .
3 . Pyruvate kinase .

Metabolism of Fructose

Fructose is metabolized mainly in the liver where it is converted to pyruvate or under fasting conditions to glucose .

1 . Fructose is phosphorylated by ATP to form fructose –1– phosphate by the enzyme fructokinase . Fructose -1 – phosphate is cleaved by aldolase to form dihydroxyacetone phosphate (DHAP) and glyceraldehyde , which is phosphorylated by ATP to form glyceraldehyde – 3 – phosphate . DHAP and G-3-P are intermediates of glycolysis .

2 . In tissues other than liver , the major fate of fructose is phosphorylation by hexokinase to form fructose-6-phosphate , which enters glycolysis .

3 . Production of fructose from glucose include :

- Glucose is reduced to sorbitol by aldose reductase , which reduces the aldehyde group to an alcohol .
- Sorbitol is then reoxidized at carbon 2 by sorbitol dehydrogenase to form fructose .
- Fructose , derived from glucose in seminal vesicles , is the major energy source for sperm cells .

Notes :

* PFK is inhibited in high concentration of ATP (when ATP is high , the cell dose not need ATP and glycolysis inhibited) and citrate (high level of citrate indicate the adequate amount of substrate are entering TCA cycle , therefor , glycolysis slow down) .

* The serum aldolase level are elevated in poly myocytosis , multiple seclerosis and poly neuritis .

* In RBCs , 1 , 3 – bisphosphoglycerate can be converted to 2,3 – bisphosphoglycerate , a compound that decreases the affinity of hemoglobin for oxygen .

2,3 – Bisphosphoglycerate is dephosphorylated to form inorganic phosphate and 3-phosphoglycerate , an intermediate that reenters the glycolytic pathway .