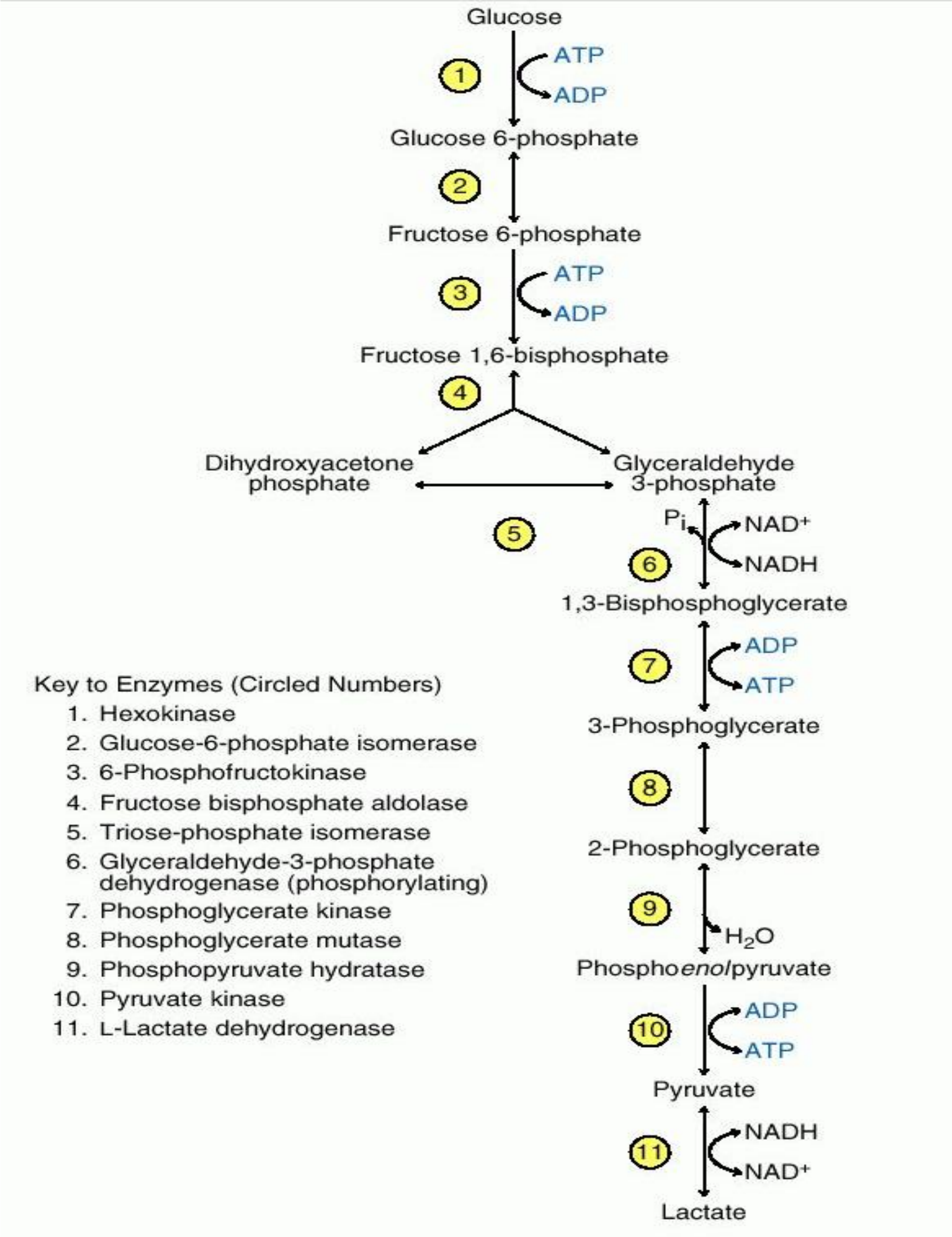
Glycolytic Pathway for ATP

RBCs take up glucose from the plasma and process it by glycolysis, which generates the ATP molecules that are used in the other cellular metabolic processes.
ATP is produced within the cytoplasm through anaerobic glycolysis for the lifetime of the cell.

Embden Meyerhof pathway



Steps in the glycolytic pathway and enzymes of glycolysis

1. Glucose is converted to Glucose 6-phosphate by the action of the enzyme **hexokinase**. An ATP is consumed in this process.
2. The second step is the conversion of G6P to Fructose 6-phosphate (F6P) by the enzyme **phosphoglucoisomerase**. It is an isomerization reaction. Fructose can also enter the EMP pathway at this step by phosphorylation.
3. F6P is converted to fructose 1,6-bisphosphate (FBP) by utilizing another molecule of ATP. The enzyme **phosphofructokinase** catalyzes the reaction. It is an irreversible reaction and is a rate-limiting step.
4. The enzyme **aldolase** converts fructose 1,6-bisphosphate into dihydroxyacetone phosphate (DHAP) and glyceraldehyde 3-phosphate.
5. The enzyme **triosephosphate isomerase** interconverts dihydroxyacetone phosphate (DHAP) with glyceraldehyde 3-phosphate (GADP).
6. Now the pay-off phase starts. Since a molecule of glucose yields two molecules of triose sugar, each reaction from this step onwards occurs twice.

   Here in this step, 3-phosphoglyceraldehyde (PGAL) is converted into 1, 3-bisphosphoglycerate (BPGA) by the action of the enzyme **Glyceraldehyde 3-phosphate dehydrogenase** (GAPDH). NAD^+ is reduced to NADH + H^+. In this step, dehydrogenation and phosphorylation take place.

7. 1, 3-bisphosphoglycerate (BPGA) is then converted into 3-phosphoglycerate (3-PGA). Phosphate is transferred from BPGA to ADP, forming ATP. This is a substrate-level phosphorylation. Two molecules of ATP are produced in this step. The enzyme **phosphoglycerate kinase** catalyzes this reaction.
8. 3-PGA is then converted into 2-PGA by the action of the enzyme **phosphoglycerate mutase.** The enzyme transfers a phosphate group from C-3 to C-2.
9. It is an elimination reaction, wherein a molecule of water is removed from 2-PGA to produce phosphoenolpyruvate (PEP). The enzyme **enolase** catalyzes this dehydration reaction.
10. It is the last step of the EMP pathway or glycolysis. **Pyruvate kinase** transfers a phosphate group from PEP to ADP, forming ATP and pyruvate or pyruvic acid. 2 ATP molecules and 2 pyruvate molecules are produced. This is also a substrate-level phosphorylation.

Notes: **Preparatory Phase or Energy-requiring Phase:** The first 5 steps of the EMP pathway are known as the investment phase. Energy is consumed in this process to produce two molecules of triose sugar phosphates. **Pay-off Phase:** The second half of glycolysis produces ATP and NADH and pyruvate.

HMP (hexose monophosphate shunt, also known as the pentose phosphate pathway)

- Aerobic glycolysis occurs through a diversion of glucose catabolism into HMP.
- The HMP drives glucose 6 phosphate to ribulose 5 phosphate by the action of G6PD.
- NADP is converted to its reduced form NADPH.
- NADPH is then available to reduce oxidized glutathione (GSSG) to reduced glutathione (GSH) in the presence of glutathione reductase.
- Reduced glutathione becomes oxidized as it reduces peroxide to water and oxygen via glutathione peroxidase.
- G6 PD provides the only means of generating NADPH for glutathione reduction. When there is a deficiency of G6PD RBCs are particularly vulnerable to oxidative damage.

Methemoglobin reductase pathway

- Heme iron is constantly exposed to oxygen and peroxide.
- Peroxide oxidizes Heme iron from Ferrous to ferric state resulting in methemoglobin.

Rapoport Luebering Pathway

- 1, 3 -BPG is diverted by bisphosphoglycerate mutase to form 2, 3- BPG.
- 2, 3-BPG regulates oxygen delivery to tissues by competing with oxygen for the oxygen binding site for hemoglobin.
- When 2, 3-BPG binds heme, oxygen is released, which enhances delivery of oxygen to the tissues.