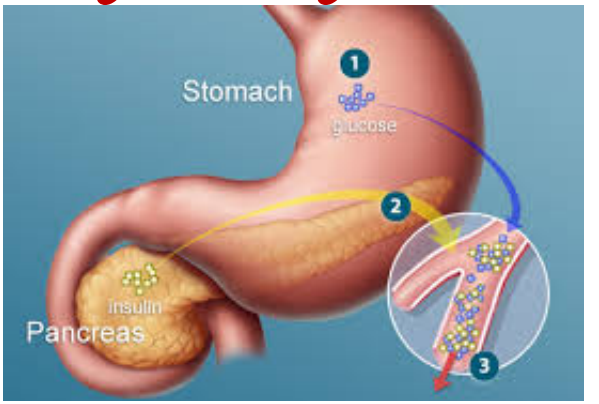
Glycolysis II



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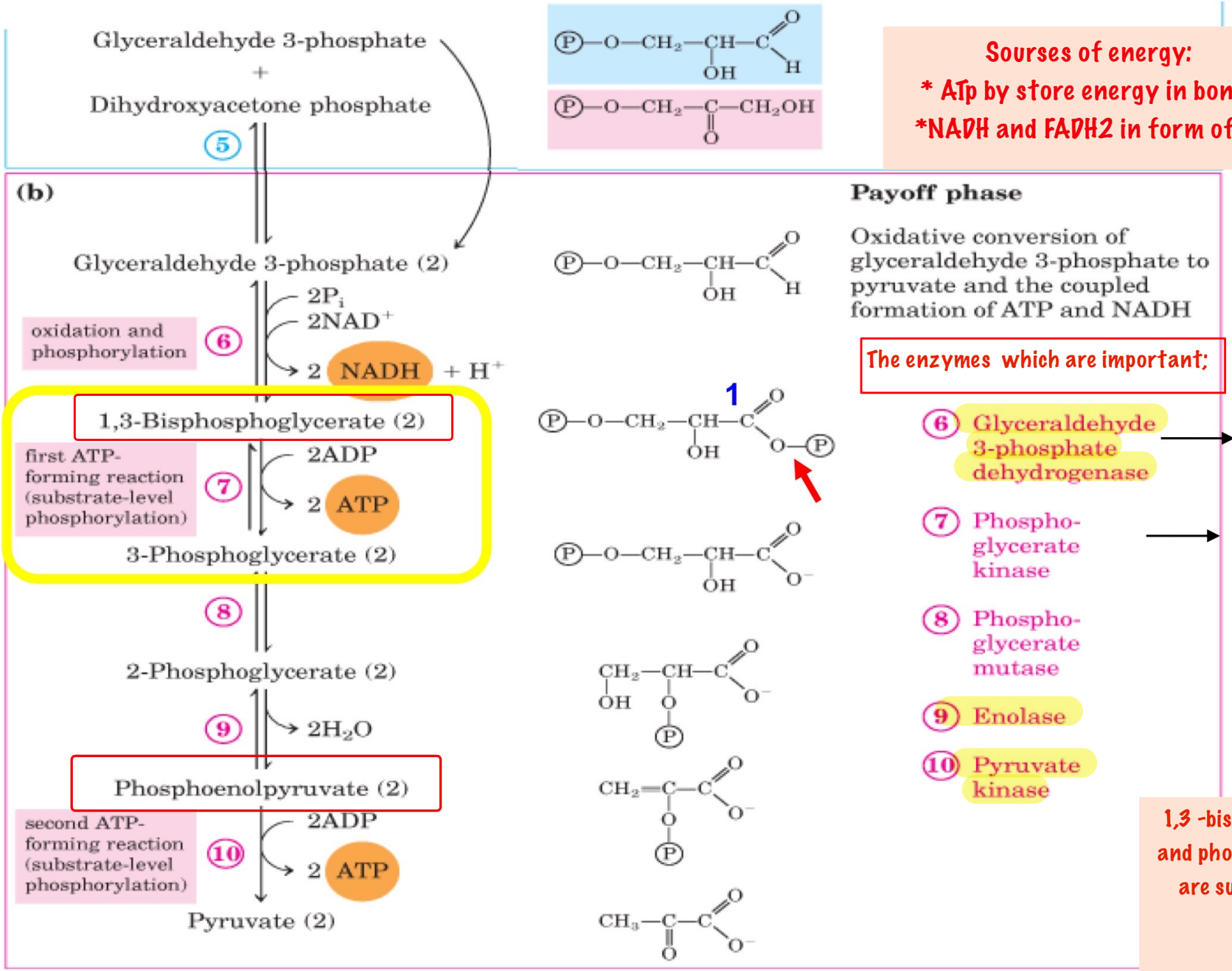
B. Pay Off Phase



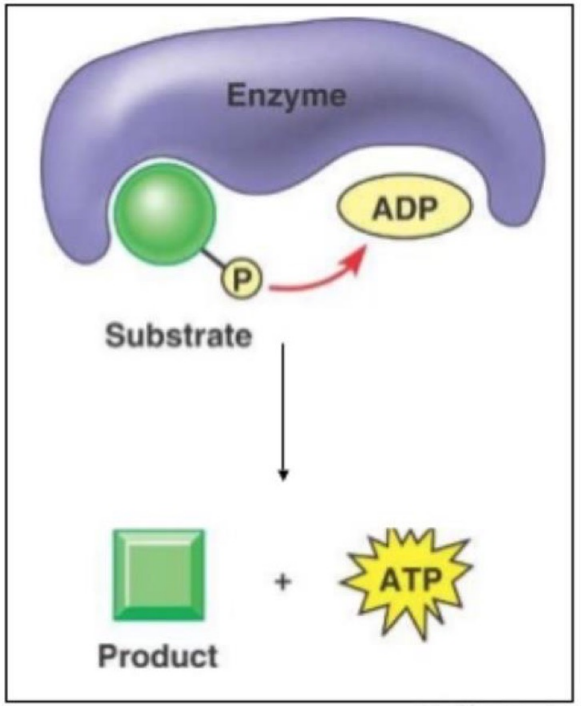
Sourses of energy:
* ATp by store energy in bonds
*NADH and FADH2 in form of e-

1,3 -bisphosphoglycerate and phosphoenolpyruvate are super high energy molecules

B. Pay Off Phase

- **Step 7:** The **first ATP** molecule is generated by the substrate-level phosphorylation process catalyzed by phosphoglycerate kinase (PGK)
- 2 ATP molecules will be generated in this step
- Methods of ATP synthesis:

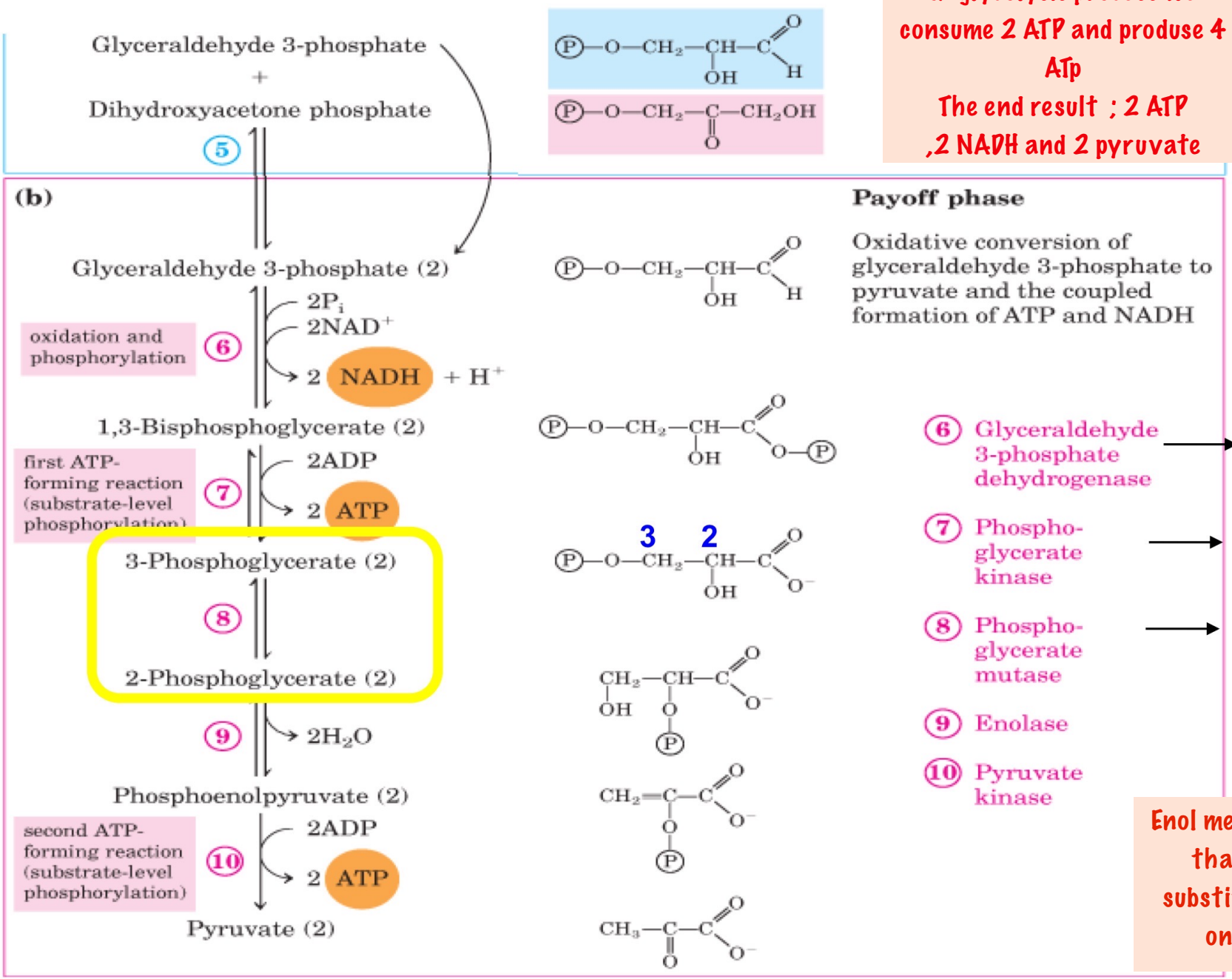
1. Substrate-level phosphorylation: it is a direct method of ATP synthesis by an enzyme which catalyzes the transfer of phosphate group from substrate to ADP
2. Oxidative phosphorylation: indirect method of ATP synthesis in which the oxidation of NADH/$FADH_2$ and the subsequently transferred electrons indirectly drive ATP synthesis from ADP



An enzyme transfers phosphate from substrate to ADP

B. Pay Off Phase

In glycolysis process we consume 2 ATP and produse 4 ATp
The end result ; 2 ATP ,2 NADH and 2 pyruvate

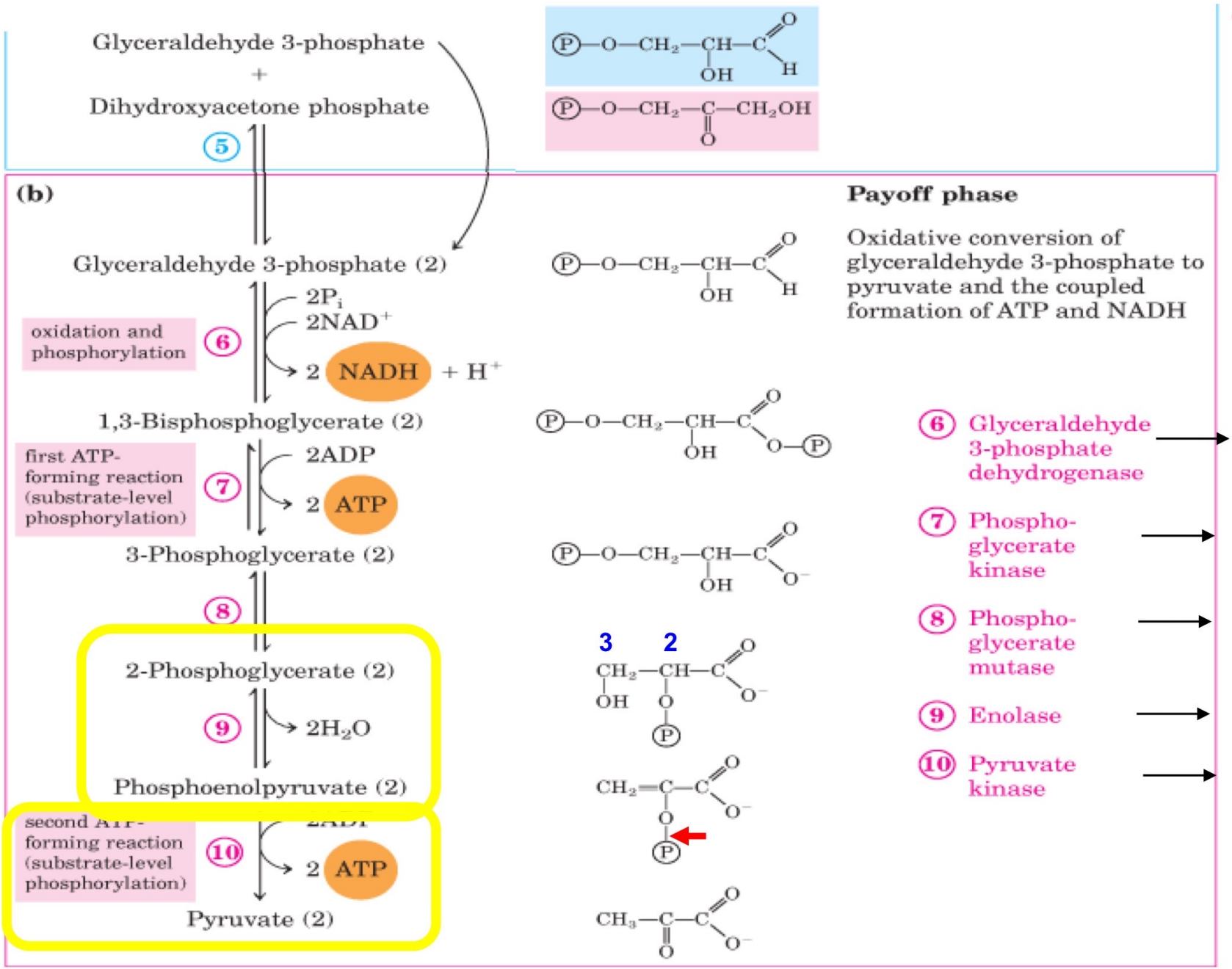


Enol means compounds that have -oH , substituted directly onto alkenes

B. Pay Off Phase

- **Step 8:** Phosphoglycerate mutase (PGM) is an isomerase which catalyzes the isomerization of 3-phosphoglycerate to 2-phosphoglycerate
- It is actually an **internal shifting of P** group from C3 to C2 within the same molecule
- The main purpose of this step is the activation of the phosphate group to prepare for the generation of the second ATP in the next reactions
- **Step 9:** The synthesis of the second super-high-energy compound **phosphoenolpyruvate (PEP)** in a simple dehydration reaction catalyzed by enolase enzyme
- Enolase acts by catalyzing the cleavage of bond between C3 and oxygen of OH group thus enhancing the formation of double bond between C3 & C2 and subsequently H atom elimination from C2

B. Pay Off Phase



B. Pay Off Phase

- The aim of this step is to increase the energy stored in the phosphate bond
- **Step 10:** The **second ATP** molecule is generated by the substrate-level phosphorylation process catalyzed by pyruvate kinase (PK). Pyruvate is the final product of glycolysis
- The activity of pyruvate kinase can be controlled (irreversible reaction) so this reaction is regulatory step

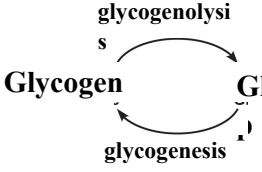
- The net result of glycolysis is the formation of:

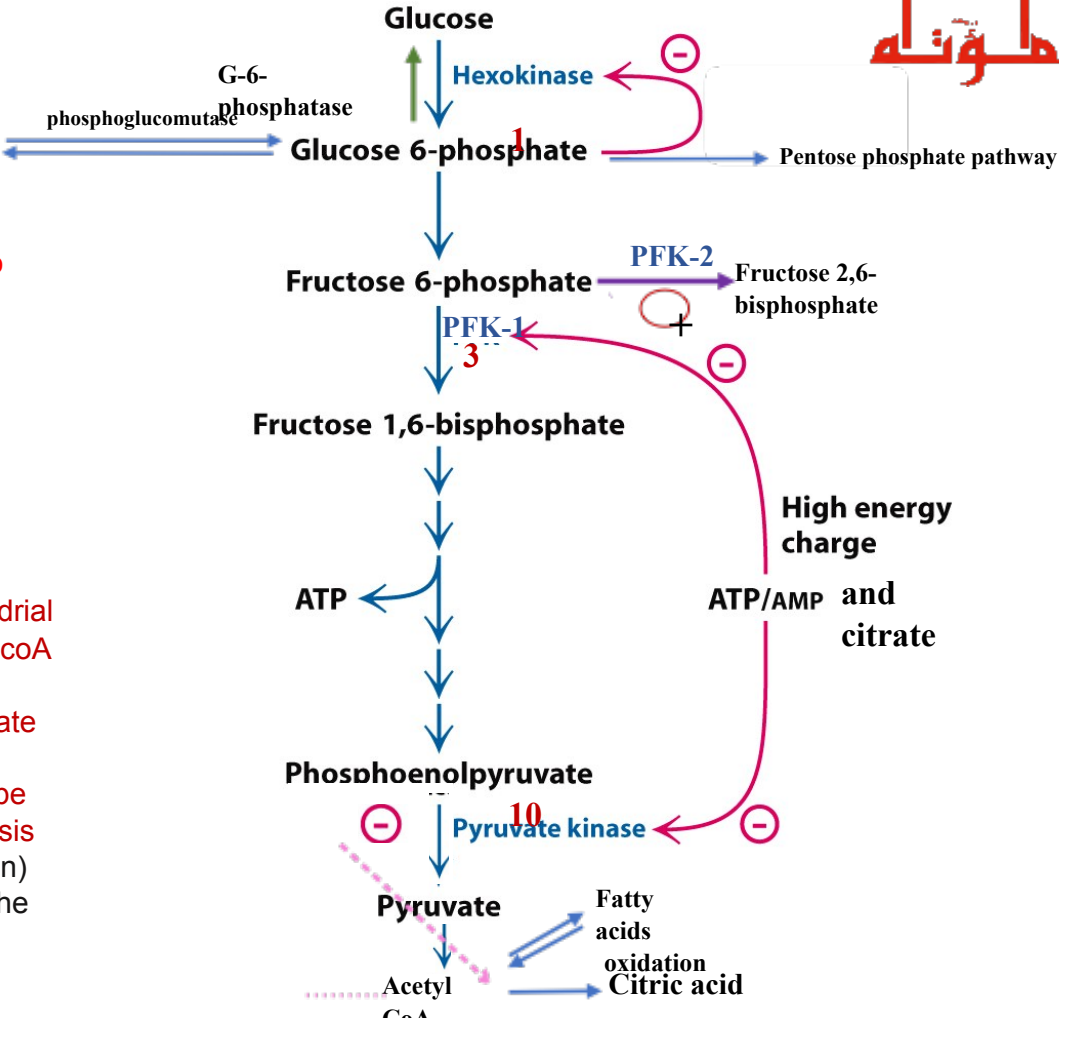
  2 pyruvate

  2 ATP

  2 NADH

Glycolysis Regulation





*Molecules that have visa to move through double layer of mitochondria

1. Citrate (initial substrate in krebs
2. pyruvate

*F.A oxidation : in mitochondrial matrix which excess Acetyl coA will move to cytosol by :

1. Citrate bind zalo celate
2. Break the previous bond & Acetyl coA will be in cytosol for fat synthesis

*beta (oxidation\ degradation) happens in the matrix and the synthesis in cytosol

Glycolysis Regulation

the converion from Acetyl CoA to carbohydate is irrevesable while from Acetyl CoA to fat is reversable

Glycolysis can be controlled at 3 points:

Step 1 which is catalyzed by hexokinase enzyme (allosteric enzyme). Hexokinase isoforms (except glucokinase) are allosterically inhibited by excess G6P **(Only in liver ,not in brain &sk.ms.)**

Step 3 which is catalyzed by phosphofructokinase-1 enzyme. It is an allosteric enzyme. Two significant inhibitors are citrate and ATP whereas AMP/ADP and recently fructose 2,6-biphosphate (in liver) are activators. Actually this is the most important control point and it is considered as the main **rate-limiting step** in glycolysis

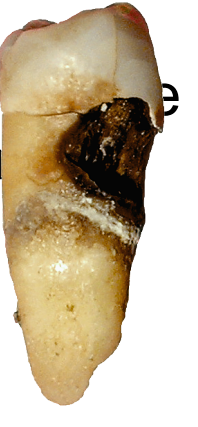
Step 10 which is catalyzed by pyruvate kinase enzyme. It is controlled by the level of ATP and Acetyl CoA (both are allosteric inhibitors). Accumulated Acetyl CoA in the cytosol is an indicator that the energy is now available from fat breakdown so no need to proceed in glycolysis (Acetyl coA Will inhibit pyruvate kinase & glycolysis)

Fluoride as Inhibitor of Enolase

Oral bacteria depends on the food debris or dietary sugars found on the tooth surface as a primary source of energy. Acids are produced through fermentation process (harmful) (For the tissue of the teeth)

Fluoride is a competitive inhibitor of enolase enzyme catalyzing Step 9

Drinking fluoridated water or using a toothpaste containing fluoride inhibit the oral bacteria enolase activity. Consequently, this disrupts bacteria glycolytic pathway and prevents form of dental caries



Fluoride will inhibit pyruvate & consequently lactic acid

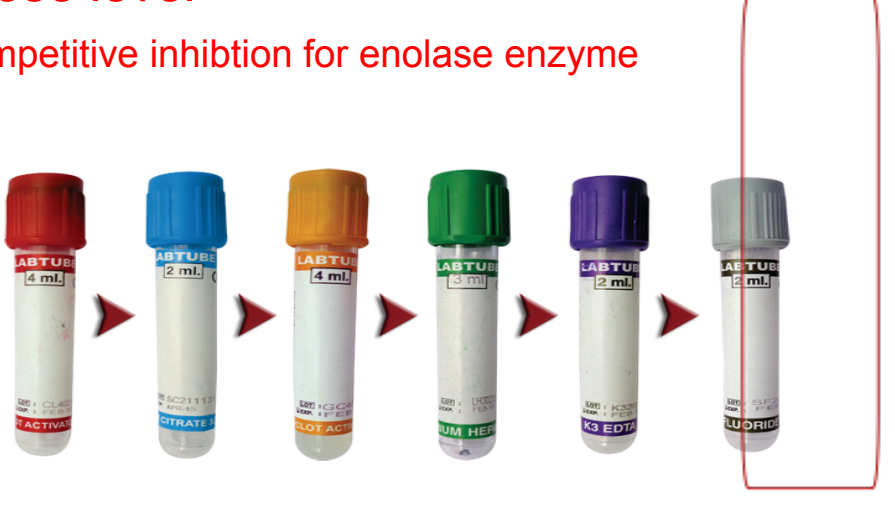
Fluoride as Inhibitor of Enolase

Sodium fluoride is known to have antiglycolytic effect that inhibits glycolysis by erythrocytes

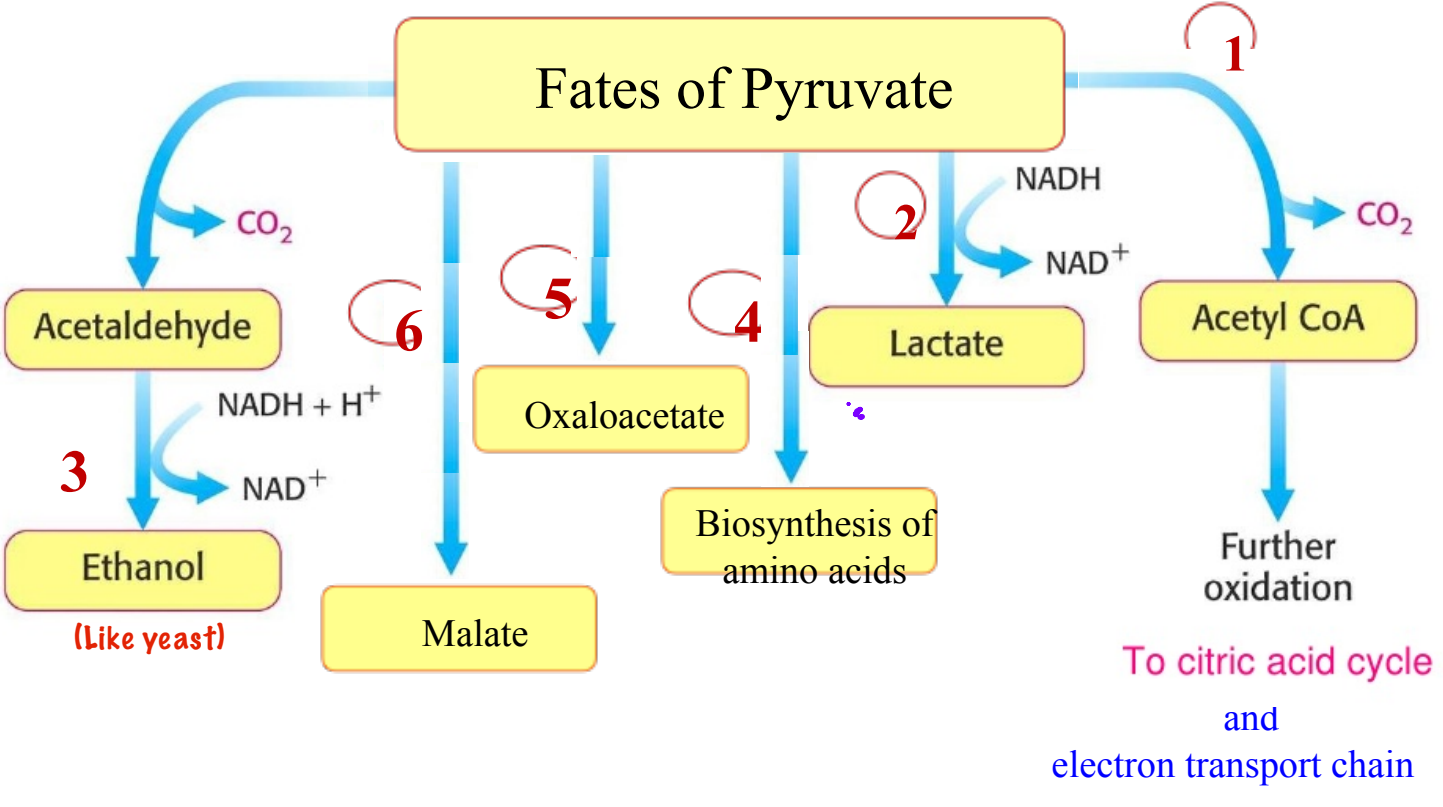
NaF tubes (gray top) are widely used for blood collection for glucose measurement

Fluoride-containing tubes are suitable for blood collection if there is a long delay in blood separation following collection (false negative result) \ ** in diabetic patients for measuring blood-glucose level

- Fluoride do competitive inhibtion for enolase enzyme



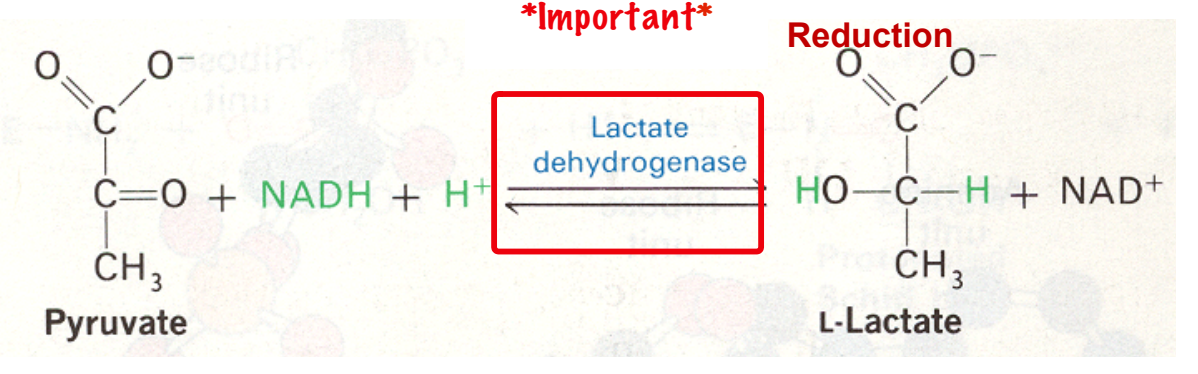
Metabolic Fates of Pyruvate



Metabolic Fates of Pyruvate

2. Lactic Acid Fermentation: **bacteria, RBCs and O2-starved muscle cells**

Anaerobic condition

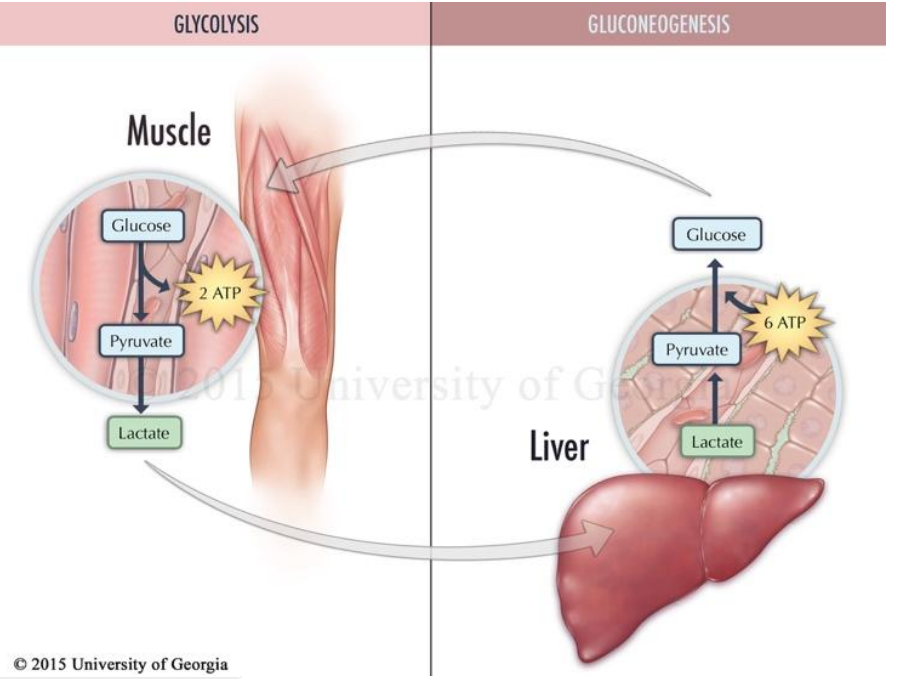


Oxidizing agent : Pyruvate
Reducing agent : NADH

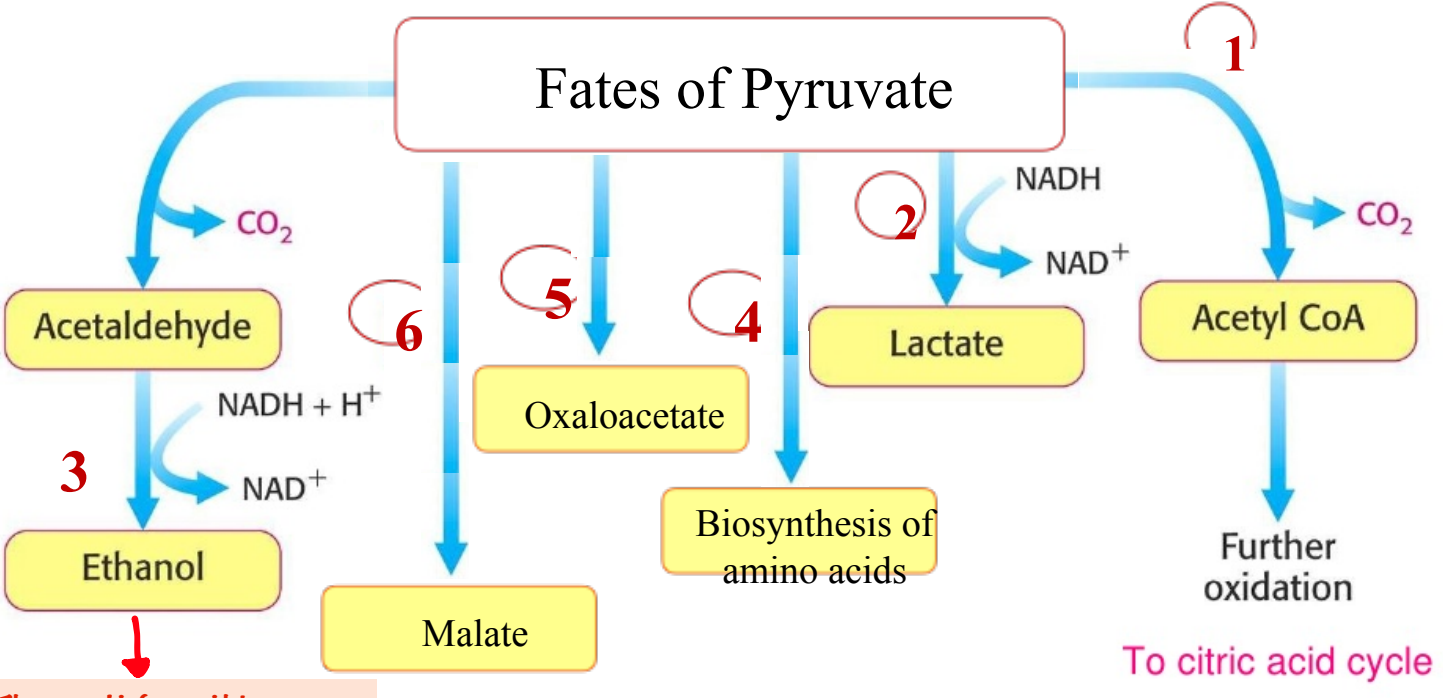
Cori Cycle

Cori cycle "lactic acid cycle" is the metabolic pathway in which lactic acid produced in muscles during the time of oxygen depletion is converted back to glucose in the liver by gluconeogene process (Non-carbohydrate source)

**cori cycle is the way To get rid of the acid

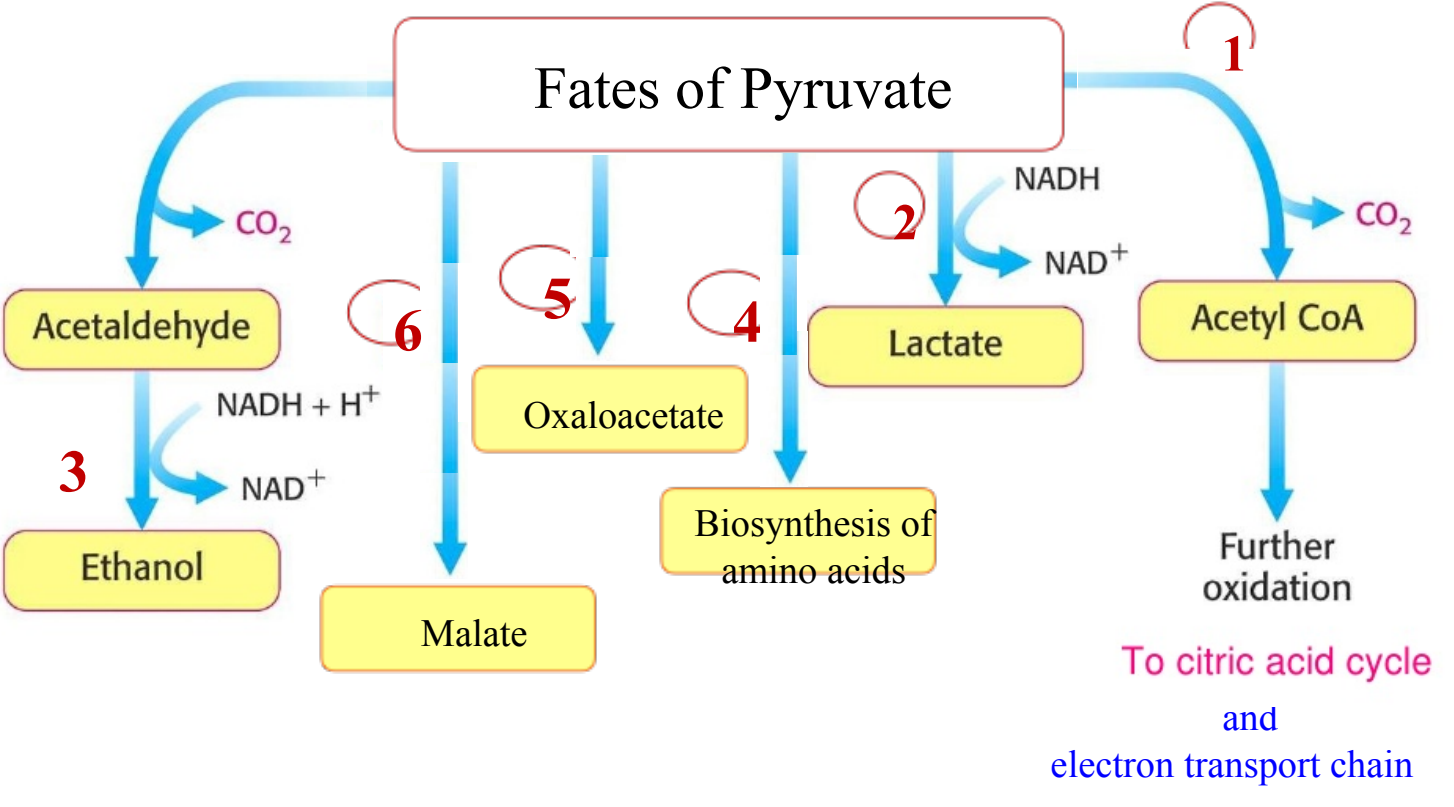


Metabolic Fates of Pyruvate



The result from this reaction :
Co2 and the ethanol will evaporate

Metabolic Fates of Pyruvate



Metabolic Fates of Pyruvate

In aerobic conditions, pyruvate is converted to acetyl CoA which enters the citric acid cycle for further oxidation to CO2 followed by oxidative phosphorylation

In anaerobic conditions like in lactic acid bacteria and some human cells (e.g. **RBCs and O2-starved muscle cells), pyruvate is reduced to lactic acid with the concomitant oxidation of NADH to NAD+ (lactic acid fermentation) (e.g. when milk curdle into youghrt)

In anaerobic conditions like in some M.O's (e.g. yeast), pyruvate is converted to ethanol (2 Steps)

Amino acid biosynthesis: pyruvate is a precursor of some amino acids like alanine

5. & 6. Pyruvate can be used for synthesis of oxaloacetate

or malate (both are TCA cycle intermediates)

Glycolysis as Anabolic Pathway

Glycolysis acts as catabolic as well as anabolic pathway. Therefore, glycolysis is very important central metabolic pathway

Glycolysis intermediates with biosynthetic roles:

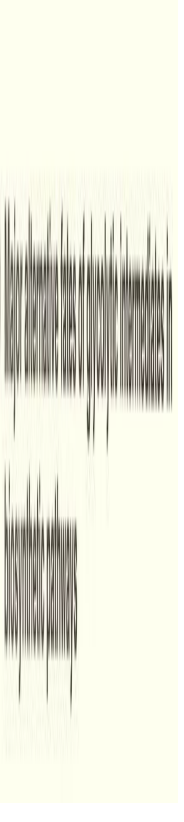
Nucleotides biosynthesis: G6P is an initial substrate in pentose phosphate pathway (metabolic pathway which generates pentoses)

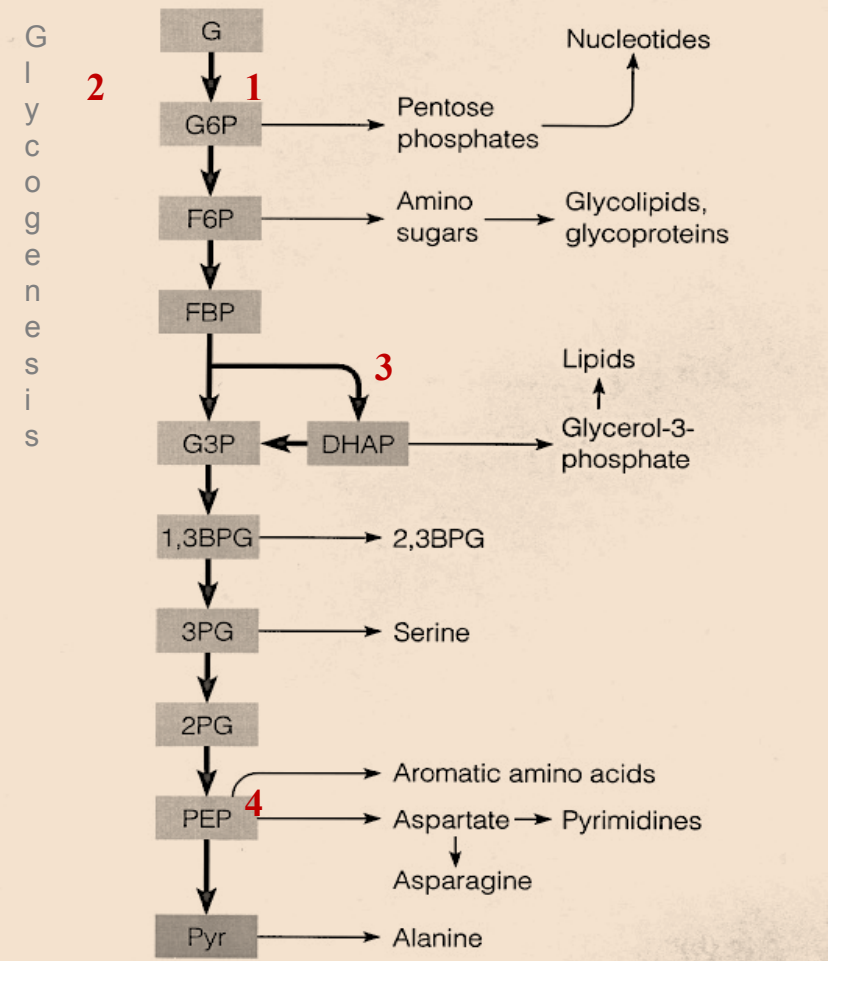
Glycogenesis via G6P

Lipids biosynthesis: DHAP is converted to glycerol

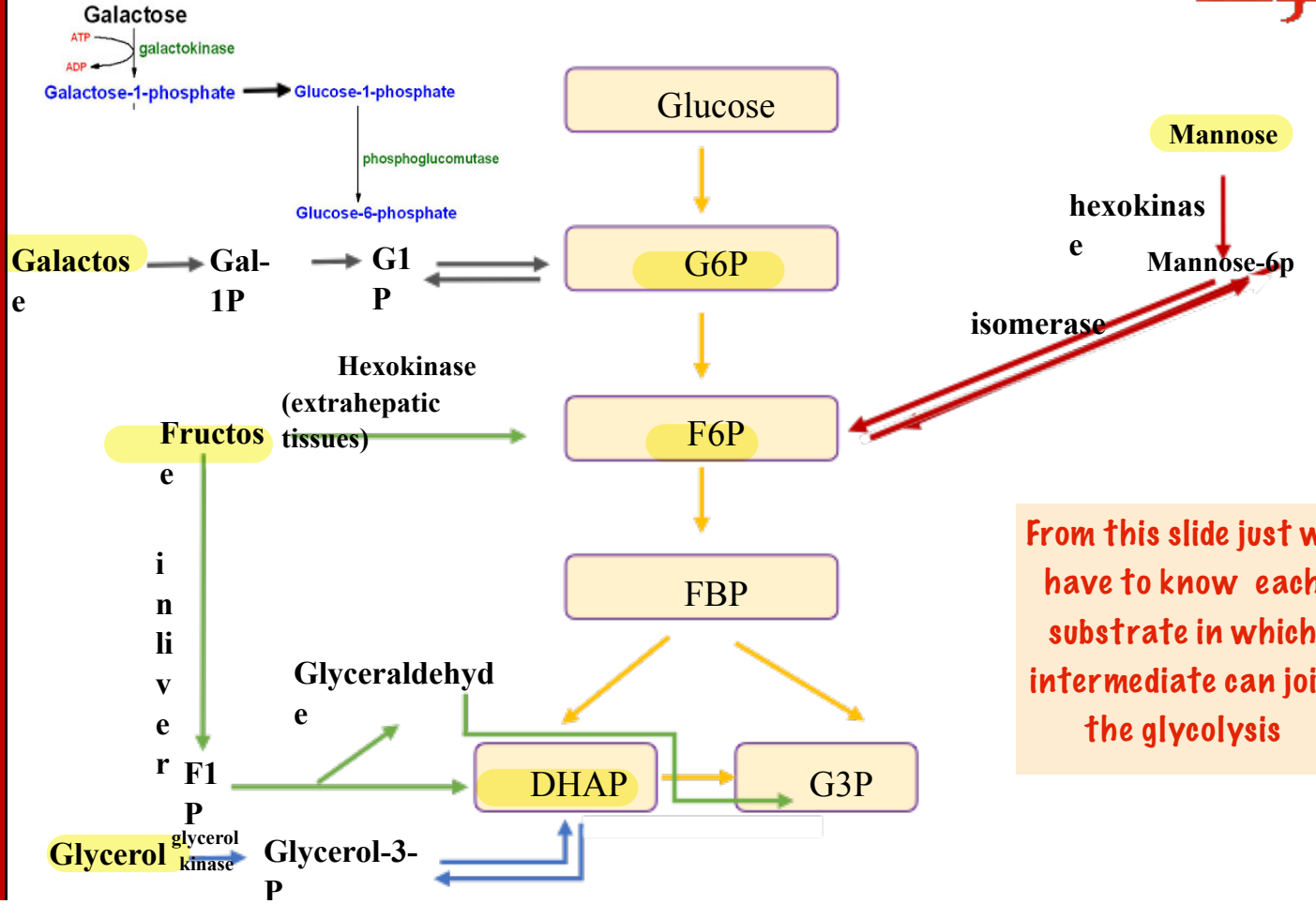
Amino acids biosynthesis: pyruvate as precursor of alanine

Glycolysis as Anabolic Pathway





Other substrates enter Glycolysis



From this slide just we have to know each substrate in which intermediate can join the glycolysis