Carbohydrate Metabolism

Tishk International University,

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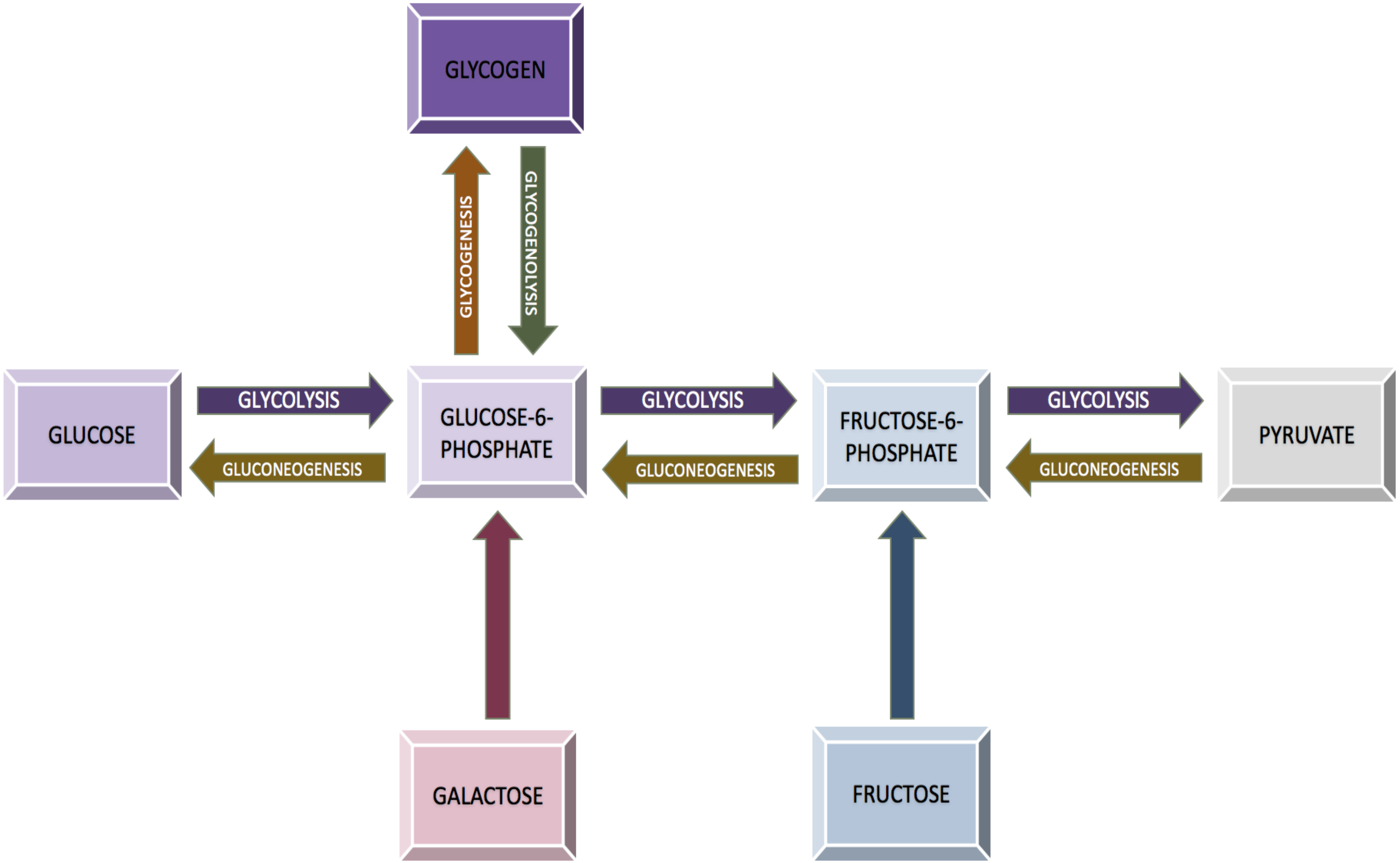
Biochemistry, 1st Semester

- Carbohydrates are central to many essential metabolic pathways.
- Plants synthesize carbohydrates from carbon dioxide and water through photosynthesis, allowing them to store energy absorbed from sunlight internally.
- When animals consume plants, they use cellular respiration to break down these stored carbohydrates to make energy available to cells.
- Both animals and plants temporarily store the released energy in the form of high energy molecules, such as ATP, for use in various cellular processes.

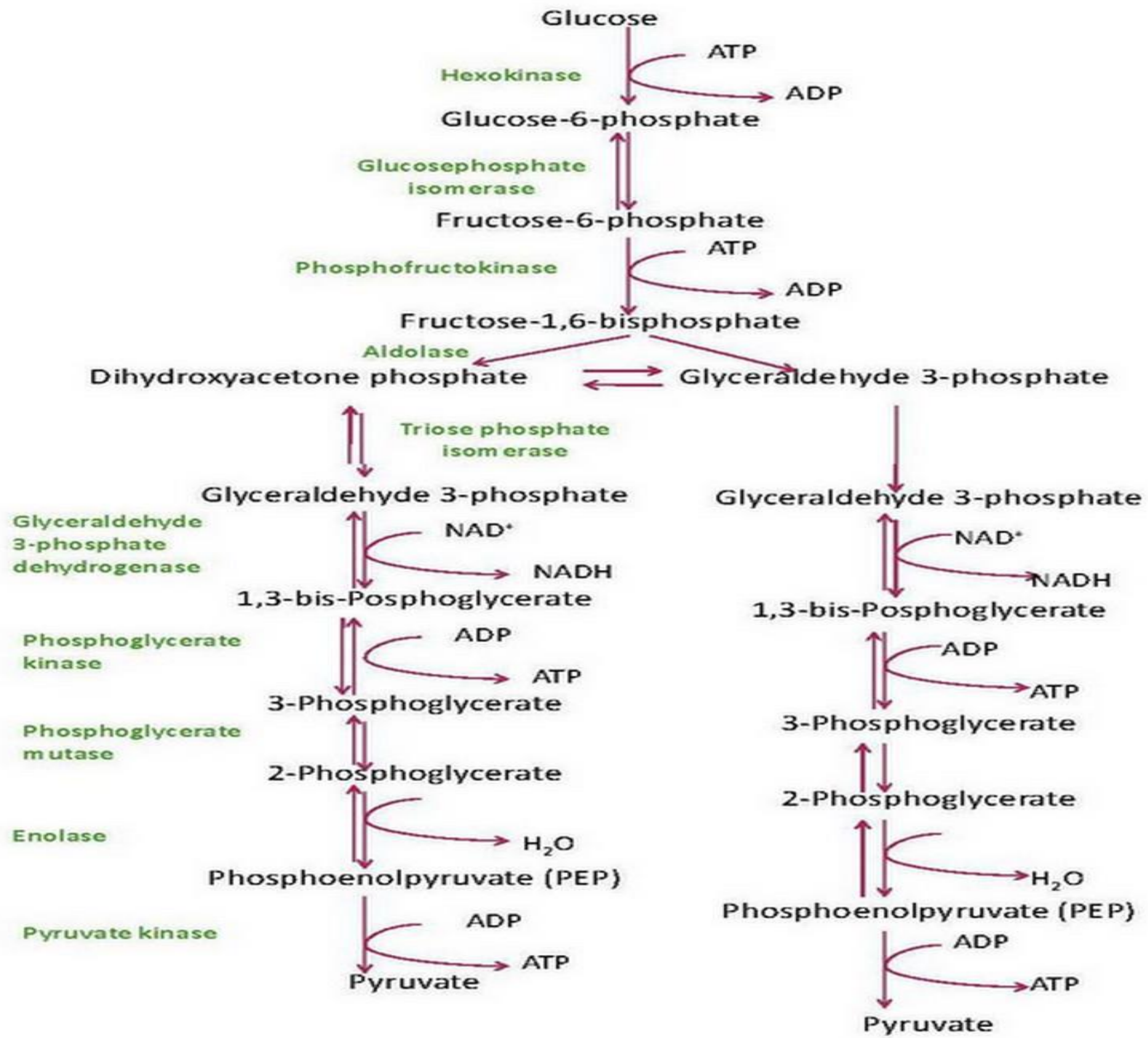
- In humans carbohydrate metabolism begins in the mouth with the action of **salivary amylase** on starches (polysaccharides),
- and it converts to glucose (monosaccharides), absorbed into the blood stream from the epithelium of the small intestine.
- the absorbed monosaccharides are transported to the tissues, which transports them to the liver, and the process of **cellular respiration** begins.
- In the liver, hepatocytes either pass the glucose on through the circulatory system or store excess glucose as glycogen.

- **Carbohydrate metabolism** is a fundamental biochemical process that ensures a constant supply of energy to living cells.
- The most important carbohydrate is glucose, which can be broken down via glycolysis, enter into the Kreb's cycle and **oxidative phosphorylation** to generate ATP.
- Further important pathways in carbohydrate metabolism include the pentose phosphate pathway (conversion of hexose sugars into pentoses),
- glycogenesis (conversion of excess glucose into glycogen, stimulated by insulin),
- glycogenolysis (conversion of glycogen polymers into glucose, stimulated by glucagon),
- gluconeogenesis (*de novo* glucose synthesis).


GLYCOGEN
GLYCOGENESIS
GLYCOGENOLYSIS
GLUCOSE
GLYCOLYSIS
GLUCONEOGENESIS
GLUCOSE-6-PHOSPHATE
GLYCOLYSIS
GLUCONEOGENESIS
FRUCTOSE-6-PHOSPHATE
GLYCOLYSIS
GLUCONEOGENESIS
PYRUVATE
GALACTOSE
FRUCTOSE

1) Glycolysis

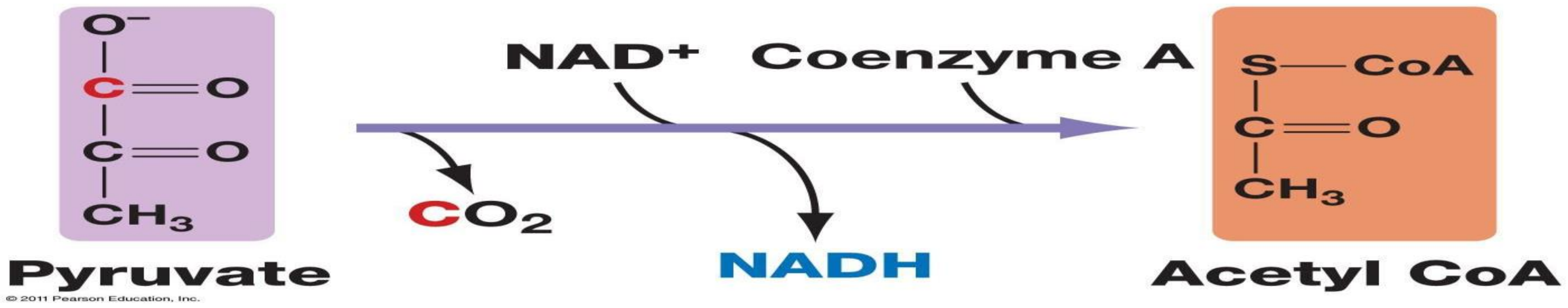
- Glycolysis is such a catabolic reaction, it breaks down glucose to the pyruvate to generate ATP.
- Cells in the body take up the circulating glucose in response to insulin and, through a series of reactions called **glycolysis**, transfer some of the energy in glucose to ADP to form ATP.


Glucose
ATP
Hexokinase
ADP
Glucose-6-phosphate
Glucosephosphate isomerase
Fructose-6-phosphate
ATP
Phosphofructokinase
ADP
Fructose-1,6-bisphosphate
Aldolase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate
Triose phosphate isomerase
Glyceraldehyde 3-phosphate
Glyceraldehyde 3-phosphate
Glyceraldehyde 3-phosphate dehydrogenase
NAD+
NADH
1,3-bis-Posphoglycerate
Phosphoglycerate kinase
ADP
ATP
3-Phosphoglycerate
Phosphoglycerate mutase
2-Phosphoglycerate
Enolase
H2O
Phosphoenolpyruvate (PEP)
Pyruvate kinase
ADP
ATP
Pyruvate
NAD+
NADH
1,3-bis-Posphoglycerate
ADP
ATP
3-Phosphoglycerate
2-Phosphoglycerate
H2O
Phosphoenolpyruvate (PEP)
ADP
ATP
Pyruvate

- Glycolysis can be divided into two phases: energy consuming (also called chemical priming) and energy yielding.
- The first phase is the **energy-consuming phase**, so it requires 2ATP molecules to start the reaction for each molecule of glucose. However, the end of the reaction produces 4 ATPs, resulting in a net gain of 2 ATP energy molecules.

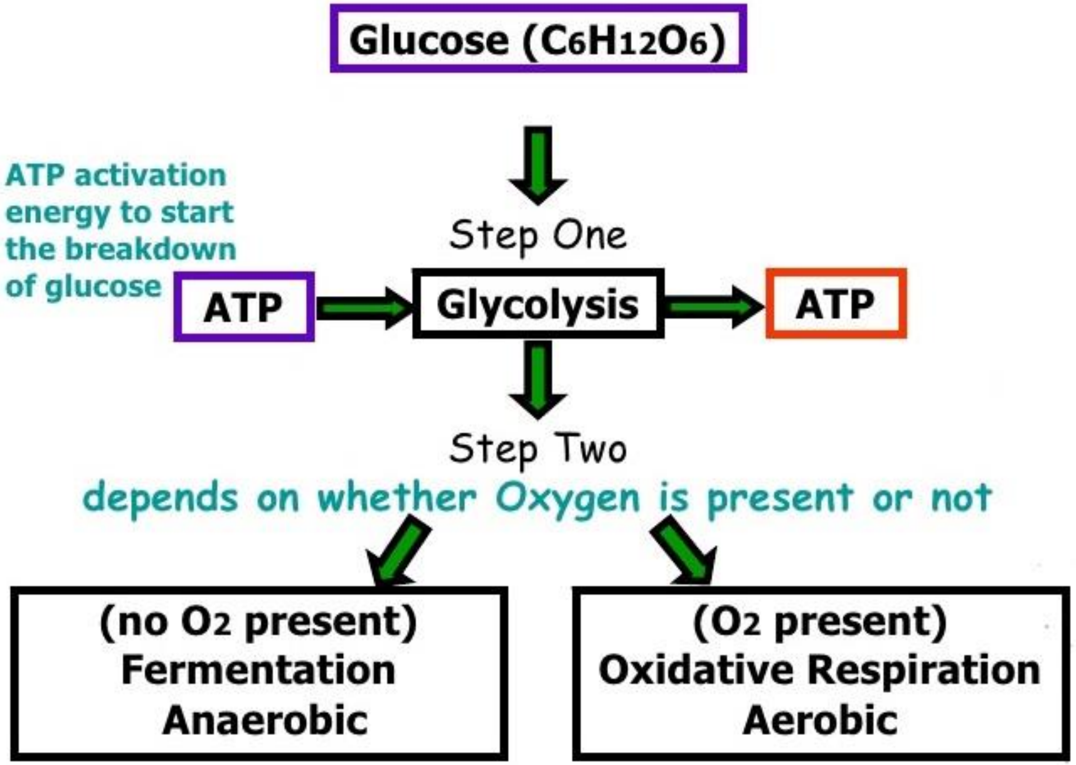
- Glucose+2ATP+2NAD++4ADP+2P*i*→Pyruvate+4ATP+2NADH+2H+

- The last step in glycolysis produces the product **pyruvate**. After producing pyruvate there is two pathway to continue which are aerobic and anaerobic.
- Transformation pyruvate to Acetyl CoA;



- 1) aerobic respiration; In the presence of oxygen, pyruvate continues on to the Krebs cycle (also called the **citric acid cycle** or **tricarboxylic acid cycle (TCA)**,
- 2) anaerobic respiration;
- oxygen is limited or absent, pyruvate can be converted into lactic acid.
- Occurs in most cells of the body when oxygen is limited or mitochondria are absent or nonfunctional.
- For example, , when a person exercises, muscles use ATP faster than oxygen can be delivered to them. They depend on glycolysis and lactic acid production for rapid ATP production.

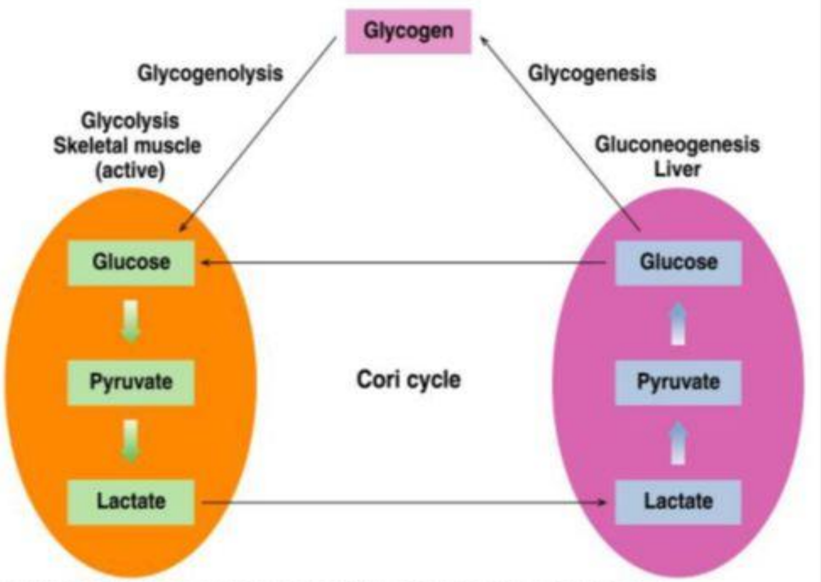
Cellular Respiration



Anaerobic respiration- Cori Cycle

Cori Cycle

- When anaerobic conditions occur in active muscle, glycolysis produces lactate.
- The lactate moves through the blood stream to the liver, where it is oxidized back to pyruvate.
- Gluconeogenesis converts pyruvate to glucose, which is carried back to the muscles.
- The Cori cycle is the flow of lactate and glucose between the muscles and the liver.



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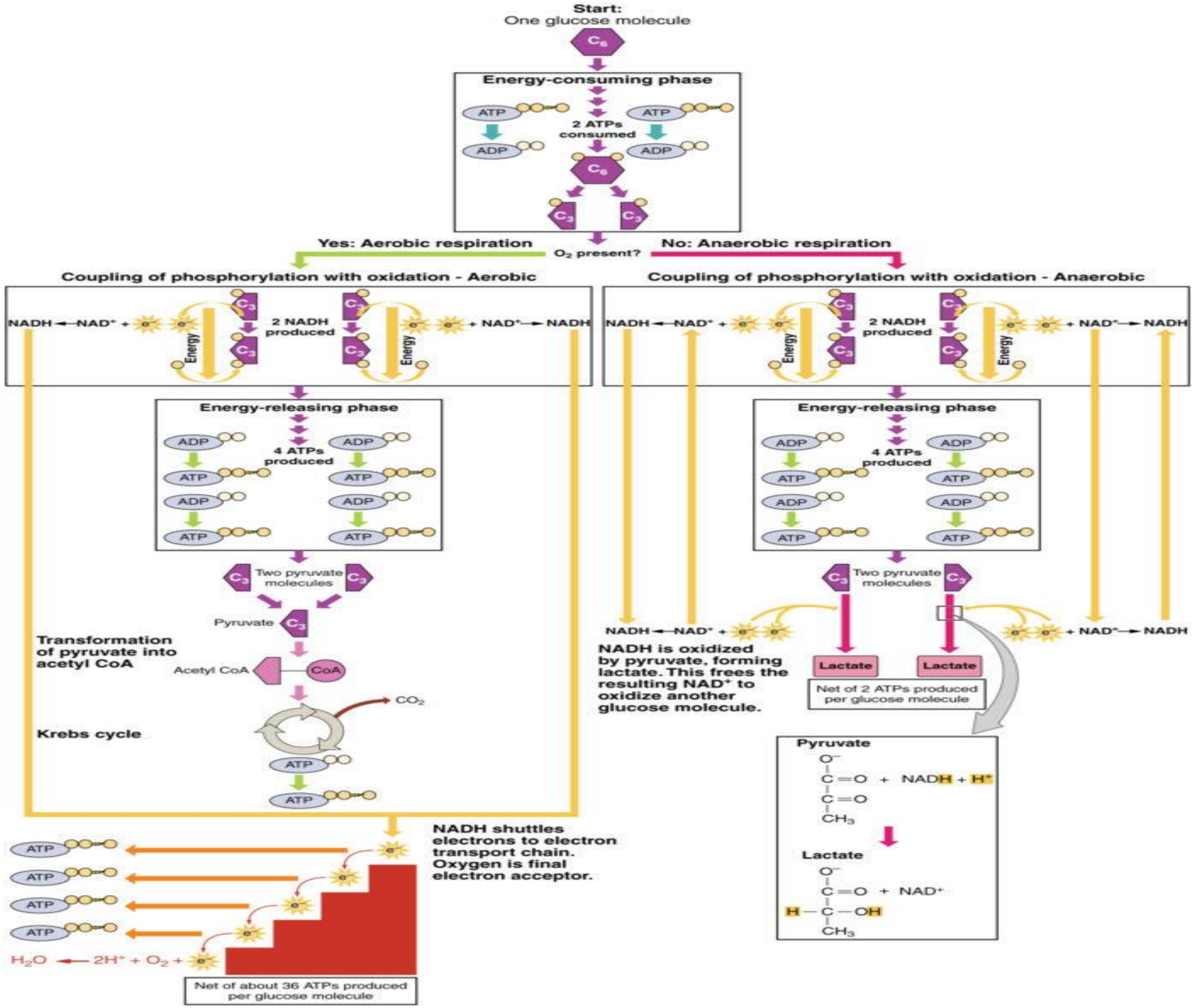
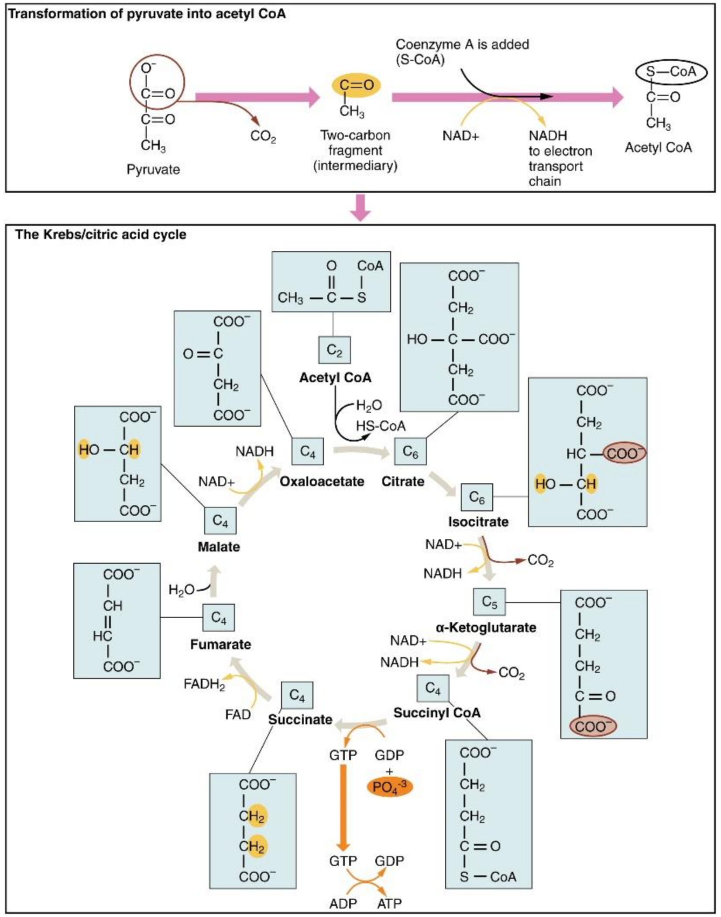


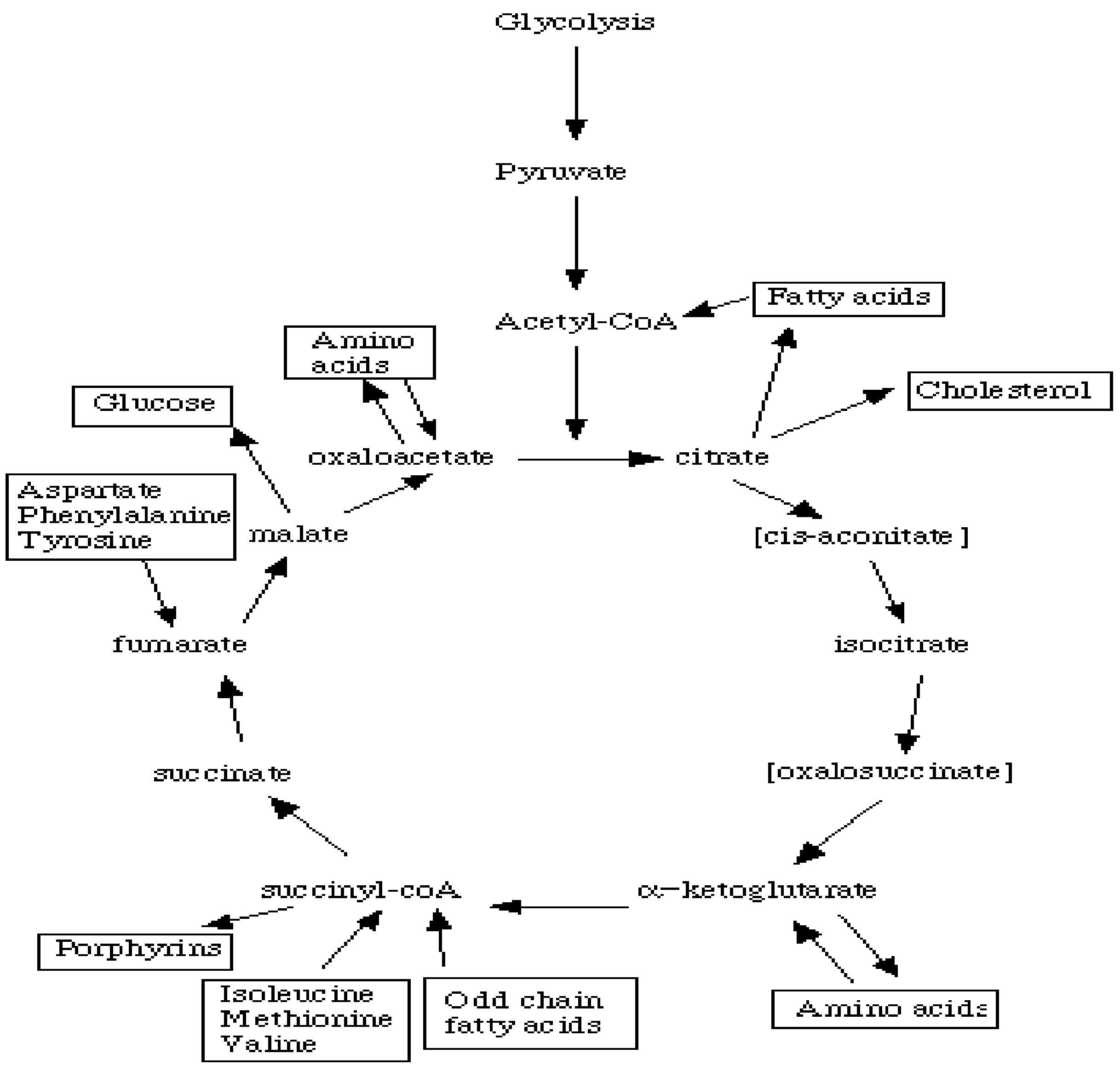
Figure: The process of anaerobic respiration converts glucose into two lactate molecules in the absence of oxygen or within erythrocytes that lack mitochondria. During aerobic respiration, glucose is oxidized into two pyruvate molecules.

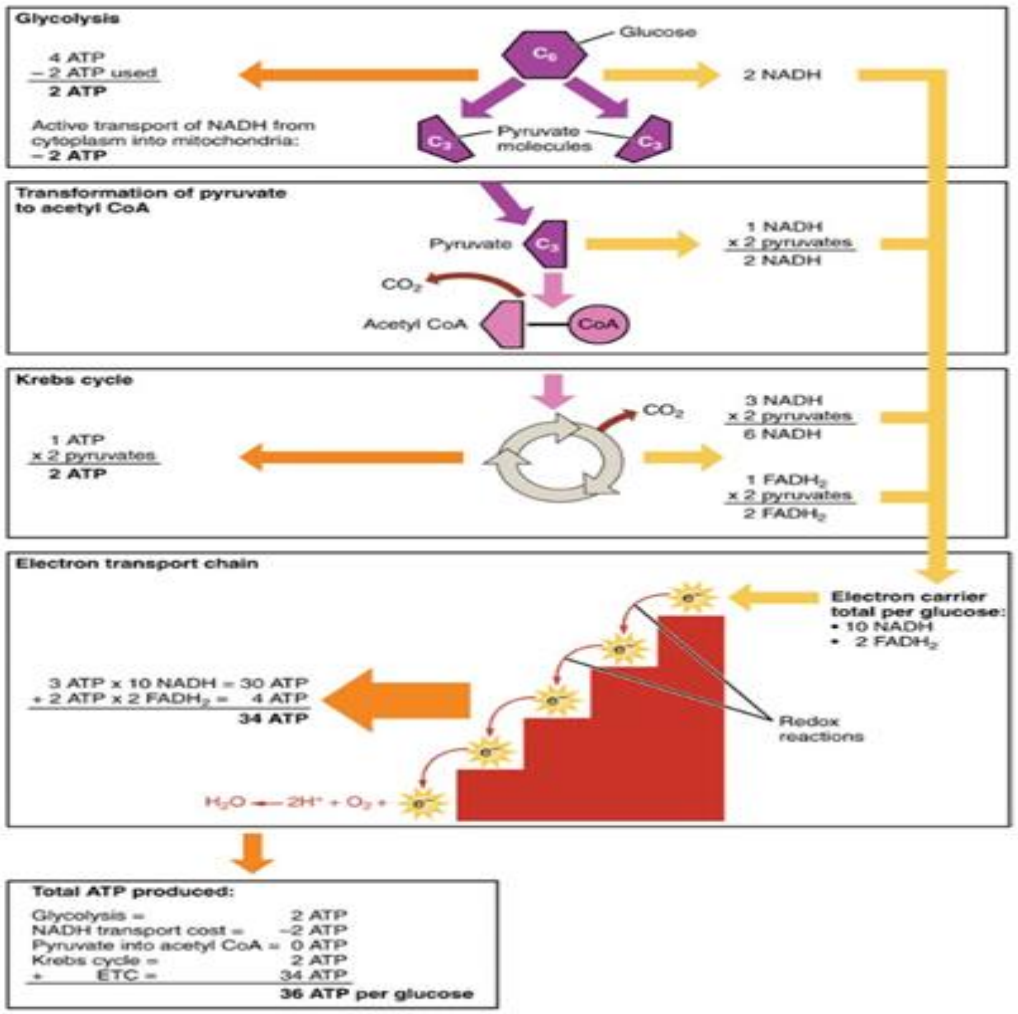
Aerobic Respiration- Krebs Cycle

- The three-carbon pyruvate molecule generated during glycolysis moves from the cytoplasm into the mitochondrial matrix, where it is converted by the enzyme pyruvate dehydrogenase into a **two-carbon acetyl coenzyme A (acetyl CoA)** molecule.
- This reaction is an oxidative decarboxylation reaction.
- It converts the (3C) pyruvate into a (2C) acetyl CoA molecule, releasing carbon dioxide and transferring two electrons that combine with NAD^+ to form NADH.
- Acetyl CoA enters the Krebs cycle by combining with a 4C oxaloacetate, to form the 6C molecule citrate, or citric acid, at the same time releasing the coenzyme A molecule.

- The six-carbon citrate molecule is systematically converted to a five-carbon molecule and then a four-carbon molecule, ending with oxaloacetate, the beginning of the cycle.
- Along the way, each citrate molecule will produce one ATP, one FADH2, and three NADH.
- The FADH2 and NADH will enter the oxidative phosphorylation system (Electron Transport Chain-ETC) located in the inner mitochondrial membrane.
- In addition, the Krebs cycle supplies the starting materials to process and break down proteins and fats. Krebs cycle occur in the mitochondria cytoplasm (matrix).
- Every glucose molecule that enters aerobic respiration, a net total of 36 ATPs are produced.


Transformation of pyruvate into acetyl CoA
Pyruvate
CO_2
Two-carbon fragment (intermediary)
Coenzyme A is added (S-CoA)
NAD+
NADH to electron transport chain
Acetyl CoA
The Krebs/citric acid cycle
Acetyl CoA
H_2O
HS-CoA
Oxaloacetate
Citrate
Isocitrate
NAD+
NADH
CO_2
α-Ketoglutarate
NAD+
NADH
CO_2
Succinyl CoA
GTP
GDP
+
PO_4^{-3}
GTP
GDP
ADP
ATP
Succinate
FAD
$FADH_2$
Fumarate
H_2O
Malate
NAD+
NADH

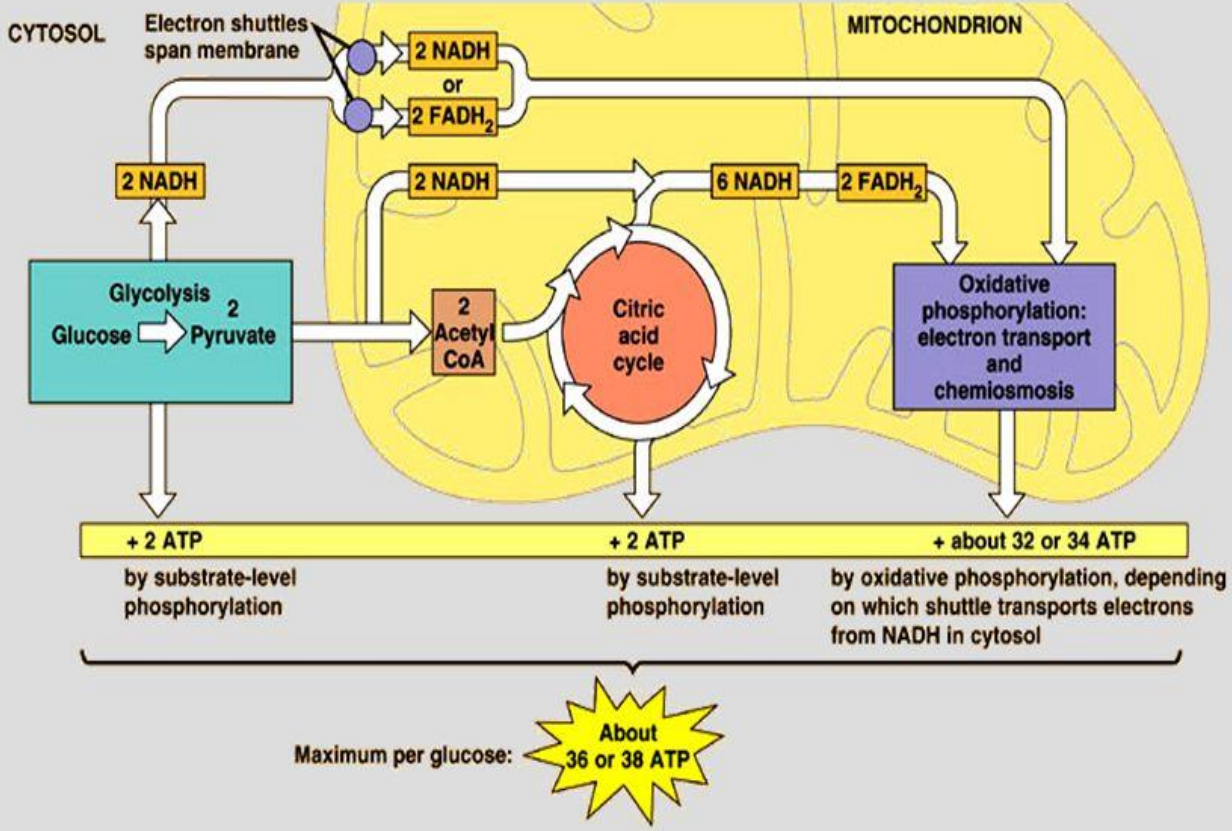

Glycolysis
Pyruvate
Acetyl-CoA
Fatty acids
Amino acids
Cholesterol
Glucose
oxaloacetate
citrate
Aspartate
Phenylalanine
Tyrosine
malate
[cis-aconitate]
fumarate
isocitrate
succinate
[oxalosuccinate]
succinyl-coA
α−ketoglutarate
Porphyrins
Isoleucine
Methionine
Valine
Odd chain fatty acids
Amino acids



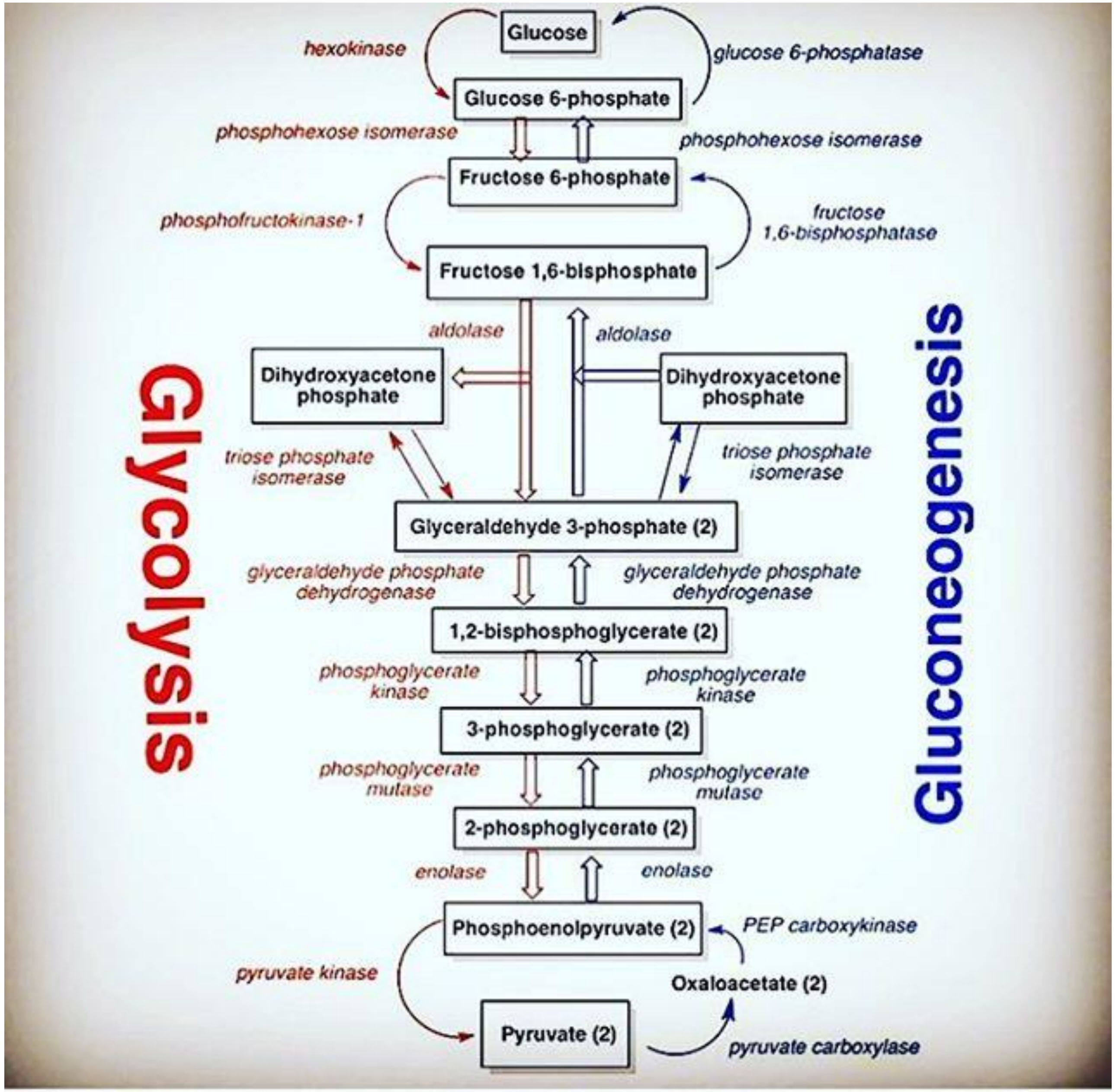
Figure; Carbohydrate metabolism involves glycolysis, the Krebs cycle, and the electron transport chain.

Cellular Respiration

Summary of respiration



KNOW THIS DIAGRAM – EXCELLENT SUMMARY ☺



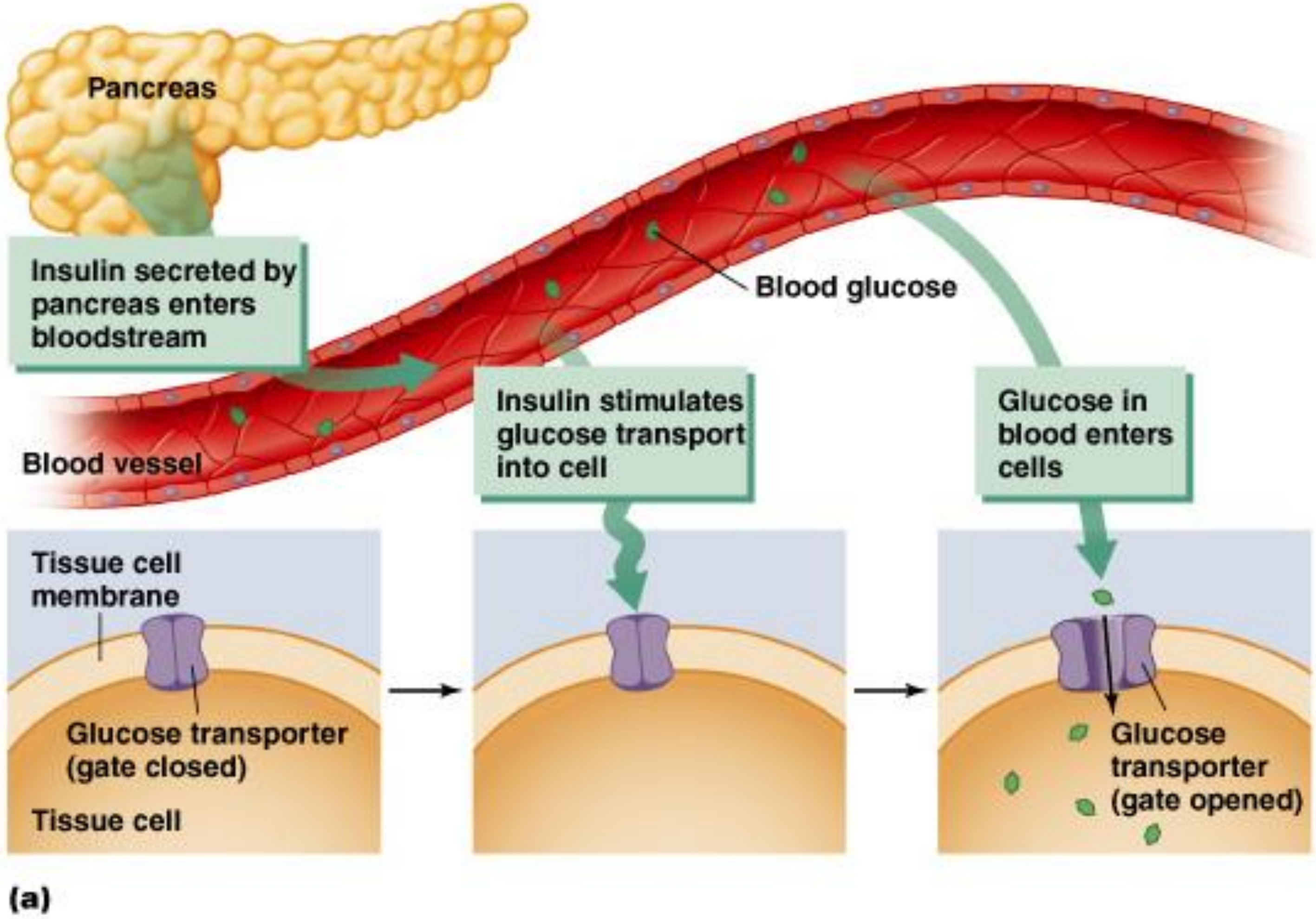
Glucose
hexokinase
glucose 6-phosphatase
Glucose 6-phosphate
phosphohexose isomerase
phosphohexose isomerase
Fructose 6-phosphate
phosphofructokinase-1
fructose 1,6-bisphosphatase
Fructose 1,6-bisphosphate
aldolase
aldolase
Dihydroxyacetone phosphate
Dihydroxyacetone phosphate
triose phosphate isomerase
triose phosphate isomerase
Glyceraldehyde 3-phosphate (2)
glyceraldehyde phosphate dehydrogenase
glyceraldehyde phosphate dehydrogenase
1,2-bisphosphoglycerate (2)
phosphoglycerate kinase
phosphoglycerate kinase
3-phosphoglycerate (2)
phosphoglycerate mutase
phosphoglycerate mutase
2-phosphoglycerate (2)
enolase
enolase
Phosphoenolpyruvate (2)
PEP carboxykinase
pyruvate kinase
Oxaloacetate (2)
Pyruvate (2)
pyruvate carboxylase
Glycolysis
Gluconeogenesis

Carbohydrate Metabolism Disorders

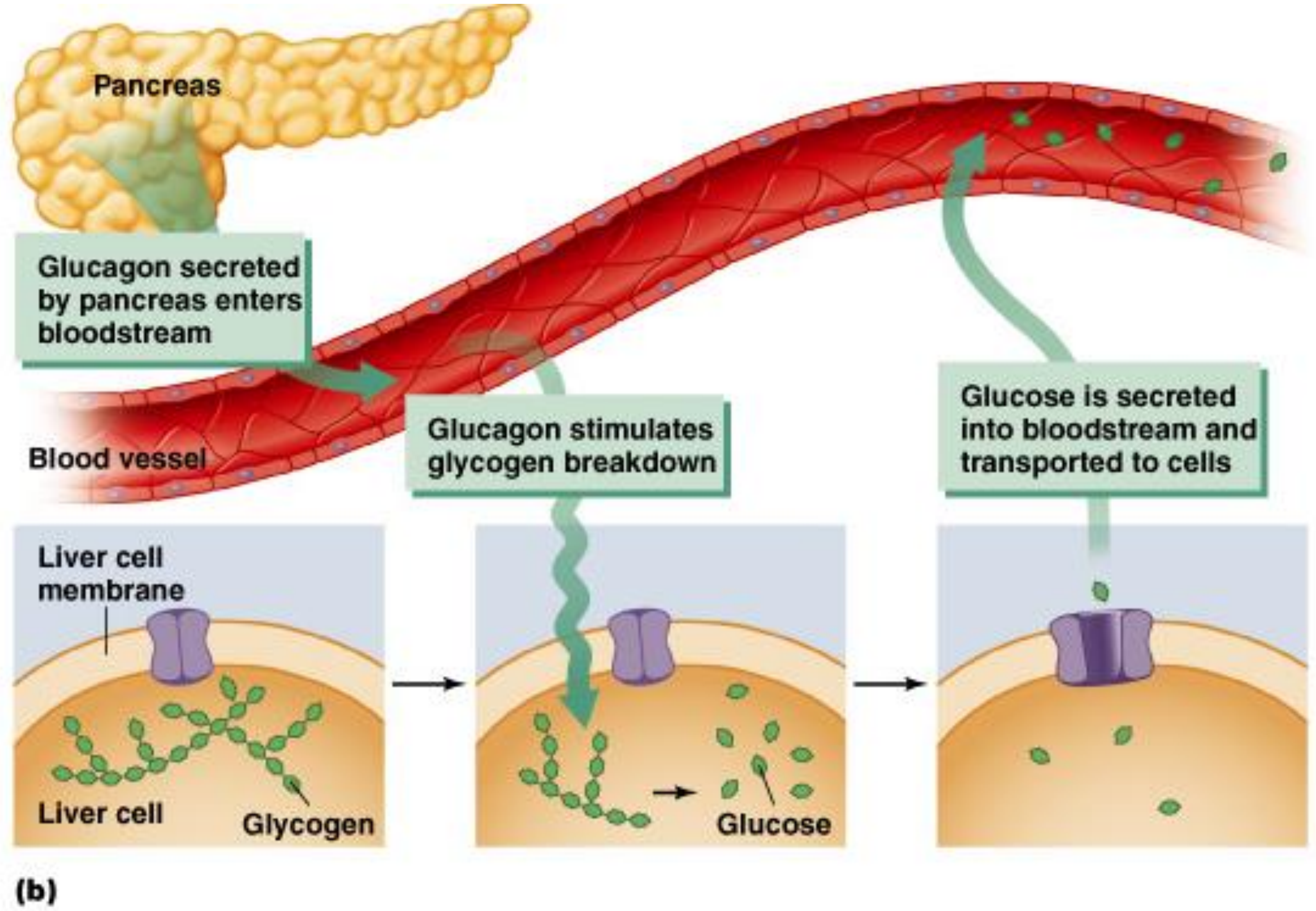
- There are multiple diseases that arise from improper carbohydrate metabolism. Diabetes mellitus is caused by a lack of, or a resistance to, insulin leading to hypoglycemia or hyperglycemia.
- Lactose intolerance is a common allergy in adults and results from a lack of the enzyme lactase, which converts lactose disaccharides (found in dairy products) into glucose monosaccharides.
- Much rarer diseases such as galactosemia and Von Gierke's diseases are caused by congenital mutations in enzymes involved in glucose metabolic pathways.

- Blood sugar concentrations are controlled by three hormones: insulin, glucagon, and epinephrine. If the concentration of glucose in the blood is too high, insulin is secreted by the pancreas.
- Insulin stimulates the transfer of glucose into the cells, especially in the liver and muscles, although other organs are also able to metabolize glucose.
- If blood glucose levels are low, then epinephrine and glucagon hormones are secreted to stimulate the conversion of glycogen to glucose.

Regulation of Blood Glucose: Insulin



Regulation of Blood Glucose: Glucagon



- The glucose in blood must be kept within a normal range for the body to work properly (70-90mg/100ml).
- If it rises or falls significantly, the body can usually bring it back to normal. This process is called homeostasis.
- If these hormones (insulin and glucagon) do not work properly lead to some disorders:
  - ✓ Hypoglycemia: usually due to the presence of excessive amounts of insulin,
  - ✓ Hyperglycemia: When the pancreas does not secrete enough insulin.

Hypoglycemia

- Condition resulting from a lower than the normal blood-sugar level (below 70mg/100ml)
- Extreme hypoglycemia, usually due to the presence of excessive amounts of insulin,
- Symptoms:
- Headache, anxiety, confusion, sweating, slurred speech, etc.

Hyperglycemia

- Higher than the normal level (above 120mg/100ml)
- When the pancreas does not secrete enough insulin,
- May temporarily exist as a result of eating a meal rich in carbohydrates,
- Extreme hyperglycemia, the renal threshold (160-170mg/100ml) is reached and excess glucose is excreted in the urine.
- *Untreated diabetes can cause nerve damage, kidney damage, blindness, and death*

Classification of Diabetes Mellitus

- Metabolic diseases
- Characterized by hyperglycemia
- Divided into 2 groups
- IDDM
- NIDDM

Insulin dependent diabetes mellitus (IDDM)

- Type 1 Diabetes- Juvenile onset diabetes
- *Accounts for 10% of all cases*
- Usually diagnosed in childhood
- The pancreas makes little or no insulin, so sugar cannot get into the body's cells for use as energy.
- Frequently called the insulin-needed group
- must use insulin injections to control their blood glucose daily to survive.

Non-insulin dependent diabetes mellitus

- Type-2 diabetes- Adult onset diabetes
- Most common, 80-90% of diabetic population
- Occur in adults (over 40 age)
- Commonly occurs in obese individuals
- However, treatment also may include oral glucose-lowering medications (taken by mouth) or insulin injections (shots).

Risk factors for diabetes

- Type 1 diabetes:
  - family history/genetics;
  - viral infection.

- Type 2 diabetes:
  - family history/genetics;
  - overweight or obesity, especially central obesity;
  - adults aged over 40;
  - people of Asian or African-Caribbean origin;
  - lower socio-economic status;
  - low birth weight;
  - previous gestational diabetes (during pregnancy).

Gestational Diabetes

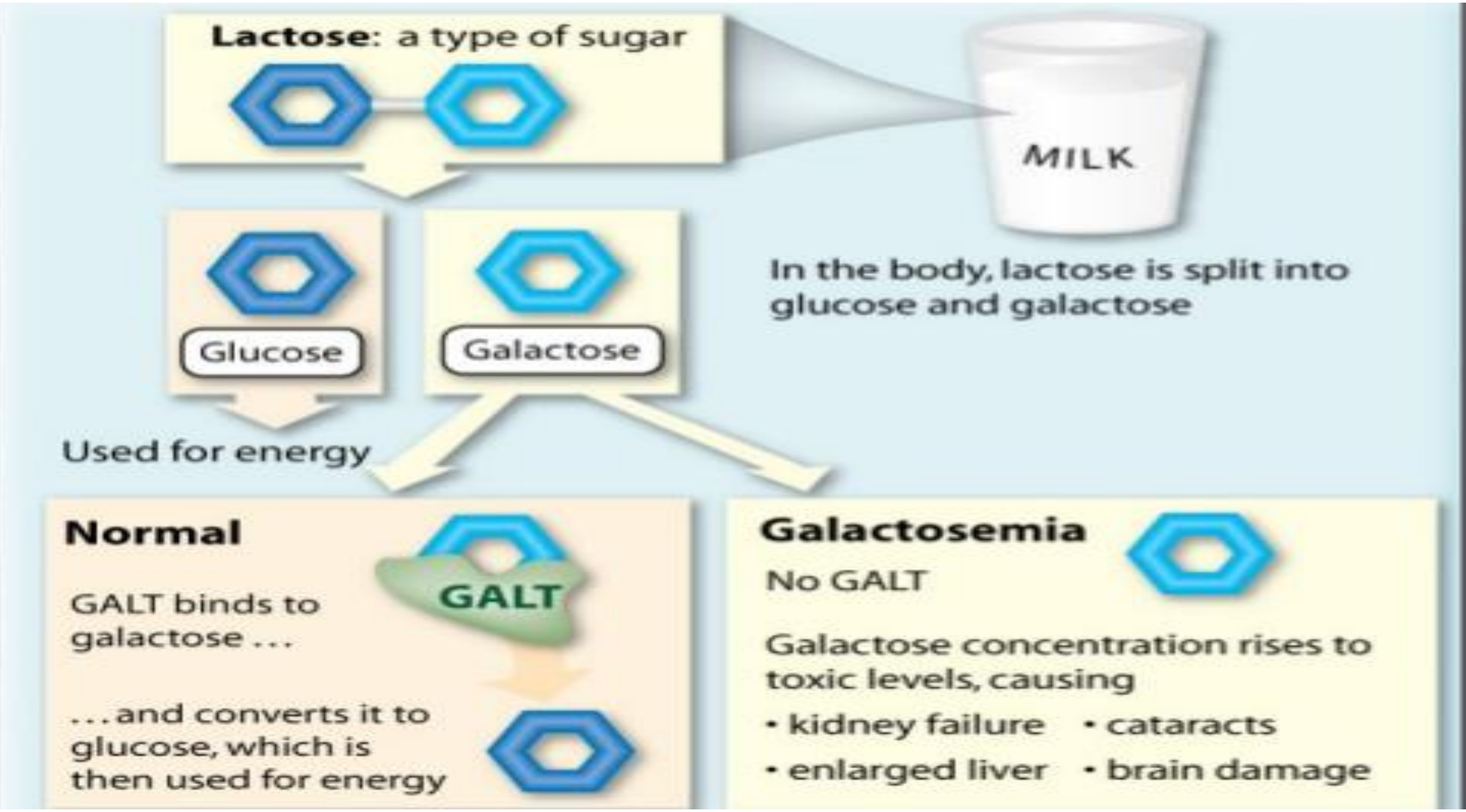
- Blood sugar levels are high during pregnancy in women
- During pregnancy, many physiological changes take place. Change in metabolism can be seen.
- In order to keep metabolism normal during pregnancy, the body has to make three times more insulin than normal to offset the hormones made by the placenta.
- Increased sugar levels in the blood can lead to many problems;
    - High risk of type 2 diabetes and cardiovascular disease

Who’s at Risk for Gestational Diabetes?

- Women over 25 years age
- Women who are overweight
- Women with a family history of diabetes
- Women who are members of high risk ethnic groups (Hispanic, African American, Native American)
- Women who’ve had a past stillbirth or a very large baby (over 9 Ibs).

What is Galactosemia?

- It is inborn error of metabolism when body is unable to break galactose
- There is deficiency of enzyme ***galactose-3-phosohateuridyltransferase.***
- Due to block of this enzyme galactose-3-phosphate will accumulate in liver and this will inhibit galactokinase as well as glycogen phosphate.



Lactose: a type of sugar
MILK
Glucose
Galactose
In the body, lactose is split into glucose and galactose
Used for energy
Normal
GALT binds to galactose ...
GALT
...and converts it to glucose, which is then used for energy
Galactosemia
No GALT
Galactose concentration rises to toxic levels, causing
• kidney failure
• cataracts
• enlarged liver
• brain damage