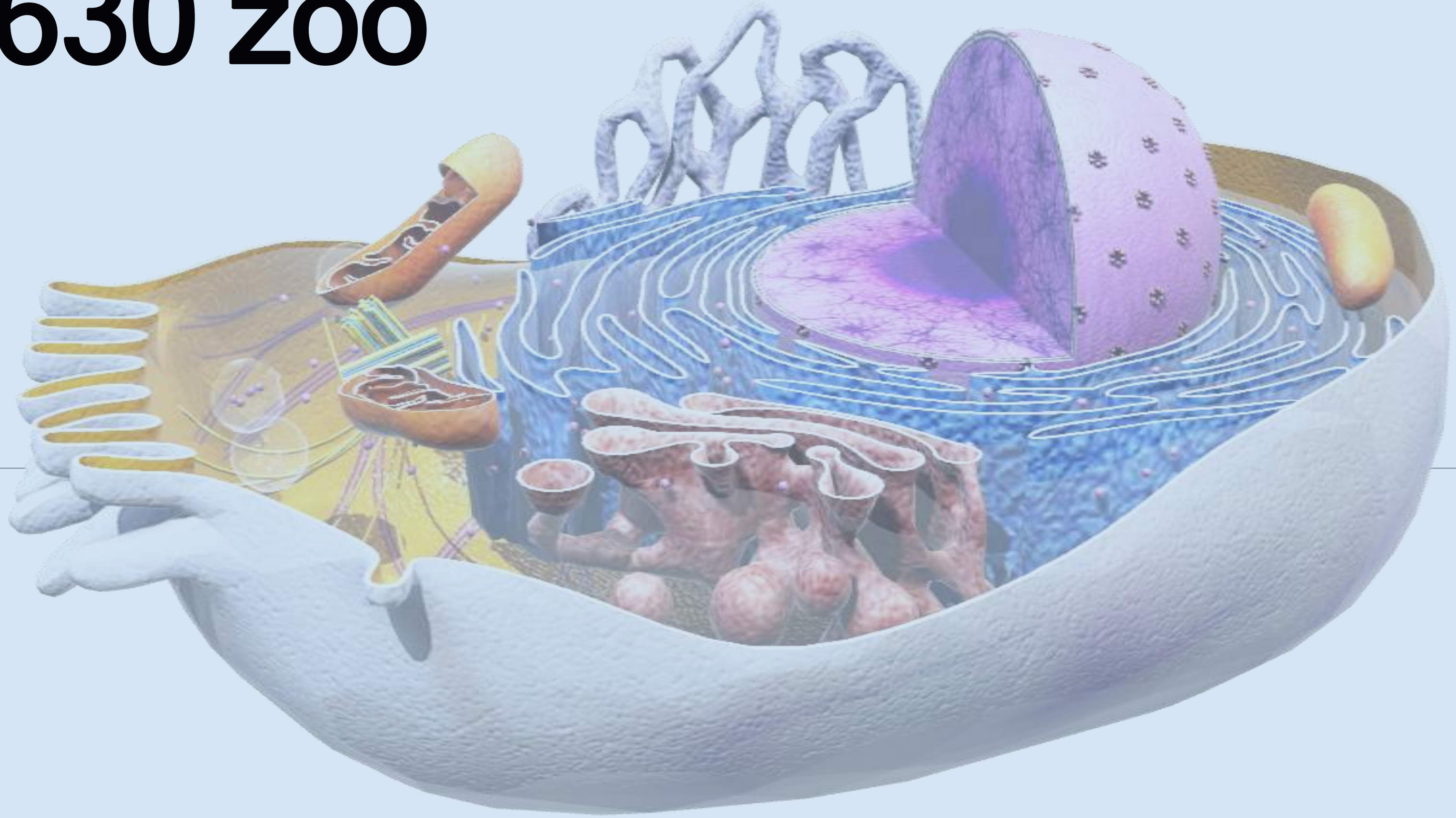
Carbohydrate Metabolism
630 zoo

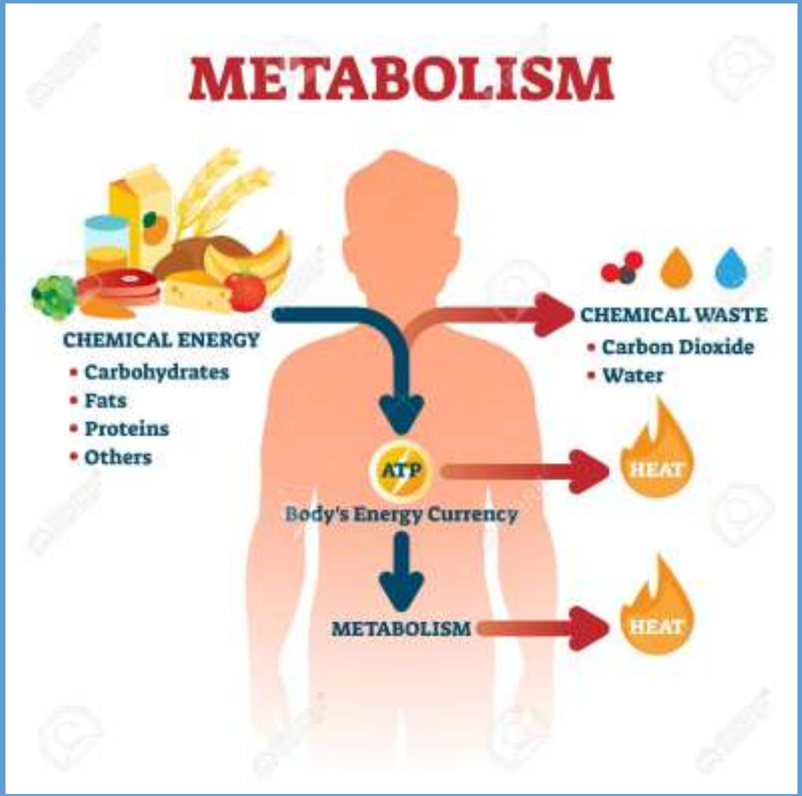


Release of Energy From Foods and "Free Energy"

Many of the chemical reactions in the cells are **aimed at** making the energy in foods available to the various physiological systems of the cell.

For instance, energy is required for:

1. Muscle activity
2. Secretion by the glands
3. Maintenance of membrane potentials by the nerve and muscle fibers
4. Synthesis of substances in the cells
5. Absorption of foods from the gastrointestinal tract



Coupled Reactions

- All the energy in the food—carbohydrates, fats, and proteins—can be oxidized in the cells, and during this process, large amounts of energy that can be used by the body's cells are released.
- To provide this energy, the chemical reactions must be “coupled” with the systems responsible for these physiologic functions.
- This coupling is accomplished by special cellular enzymes and energy transfer systems

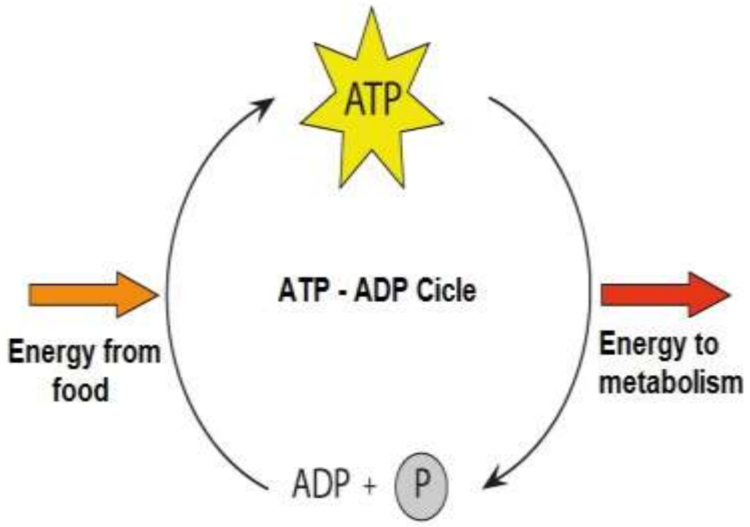
“Free Energy”

- The amount of energy liberated by complete oxidation of a food is called the free energy of oxidation of the food
- This free energy is captured in our body by Adenosine Triphosphate (ATP)
- ATP is an essential link between energy-utilizing and energy-production of the body.
- For this reason, it has been called the energy currency of the body, and it can be gained and spent repeatedly.

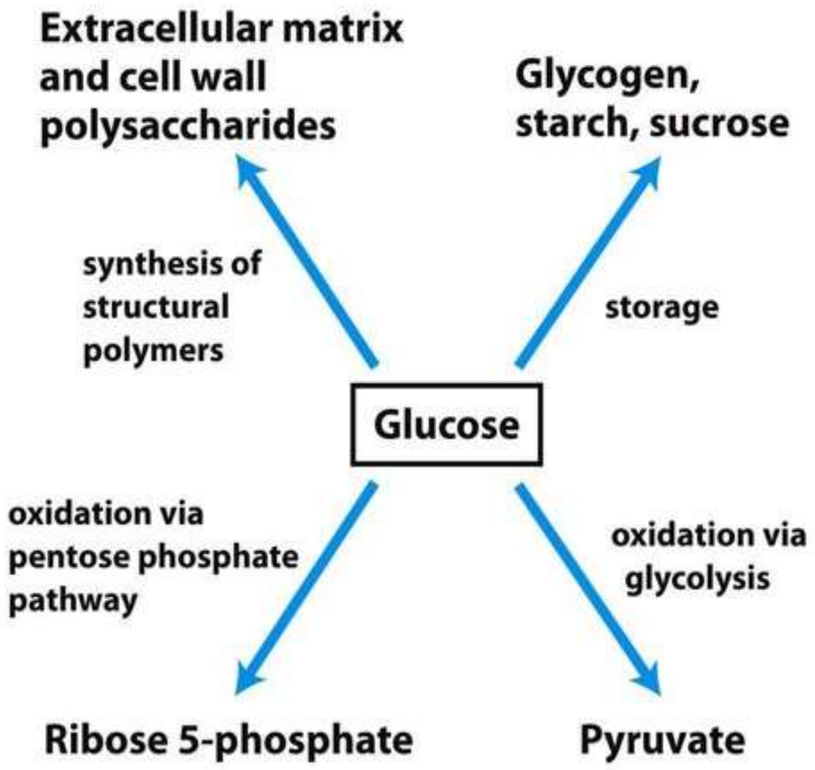
- ATP is present everywhere in the cytoplasm and nucleoplasm of all cells, and essentially all the physiological mechanisms that require energy for operation obtain it directly from ATP.
- In turn, the food in the cells is gradually oxidized, and the released energy is used to form new ATP, so, the body always needs to keep a supply of this substance.

The free energy derived from the oxidation of carbohydrates, proteins, and fats is used to convert adenosine diphosphate (ADP) to ATP, which is then consumed by the various reactions of the body that are necessary for many functions including:

1) Active transport of molecules across cell membranes;
2) Contraction of muscles
3) Various synthetic reactions that create hormones, cell membr essential molecules of the body;
4) Conduction of nerve impulses;
5) Cell division and growth;



CENTRAL ROLE OF GLUCOSE IN CARBOHYDRATE METABOLISM



- The final products of carbohydrate digestion in the alimentary tract are almost entirely **glucose, fructose, and galactose**—with glucose representing, on average, about 80 percent of these products.
- After absorption from the intestinal tract, much of the fructose and almost all the galactose are rapidly **converted into glucose** in the liver.
- Glucose then becomes the final common pathway for the transport of almost all carbohydrates to the tissue cells.

TRANSPORT OF GLUCOSE THROUGH THE CELL MEMBRANE

- Before glucose can be used by the body's tissue cells, it must be transported through the cell membrane into the cellular cytoplasm.

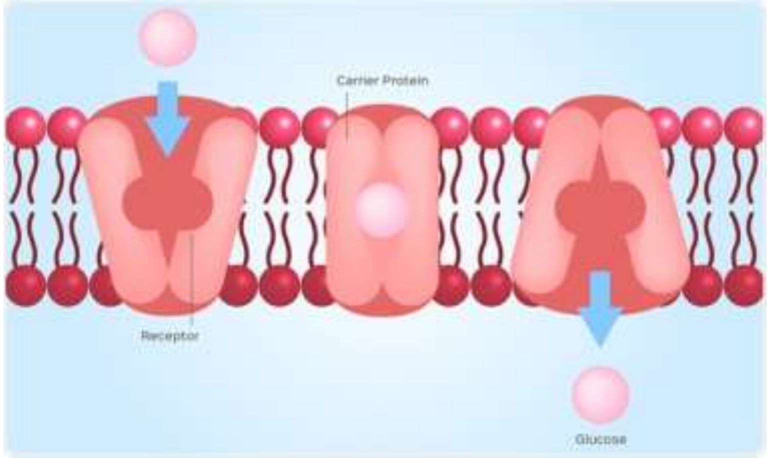
- However, glucose cannot easily diffuse through the pores of the cell membrane because of its large molecular weight.

- So, glucose does pass to the interior of the cells easily by the mechanism of facilitated diffusion.

TRANSPORT OF GLUCOSE THROUGH THE CELL MEMBRANE

FACILITATED DIFFUSION

The principles of facilitated diffusion are the following:



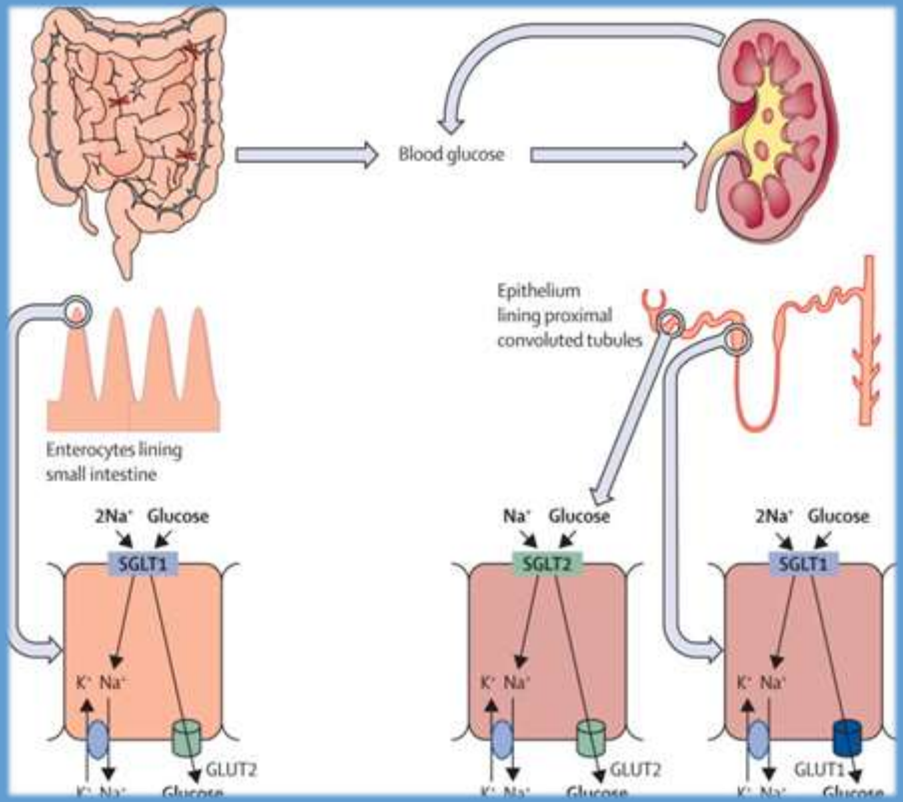
1. Glucose binds with the protein carrier molecules that are found in the lipid matrix of the cell membrane.
2. After this bound, the glucose can be transported by the carrier from one side of the membrane to the other side and then released.
3. Therefore, if the concentration of glucose is greater on one side of the membrane than on the other side, more glucose will be transported from the high-concentration area to the low concentration area.

TRANSPORT OF GLUCOSE THROUGH THE CELL MEMBRANE

In the gastrointestinal membrane or through the epithelium of the renal tubules, the transport of glucose is different.

- Through gastrointestinal membrane or the epithelium of the renal tubules, the glucose is transported by the mechanism of **active sodium-glucose co-transport.**

- At other cell membranes, glucose is transported only from higher concentration toward lower concentration by **facilitated diffusion**.

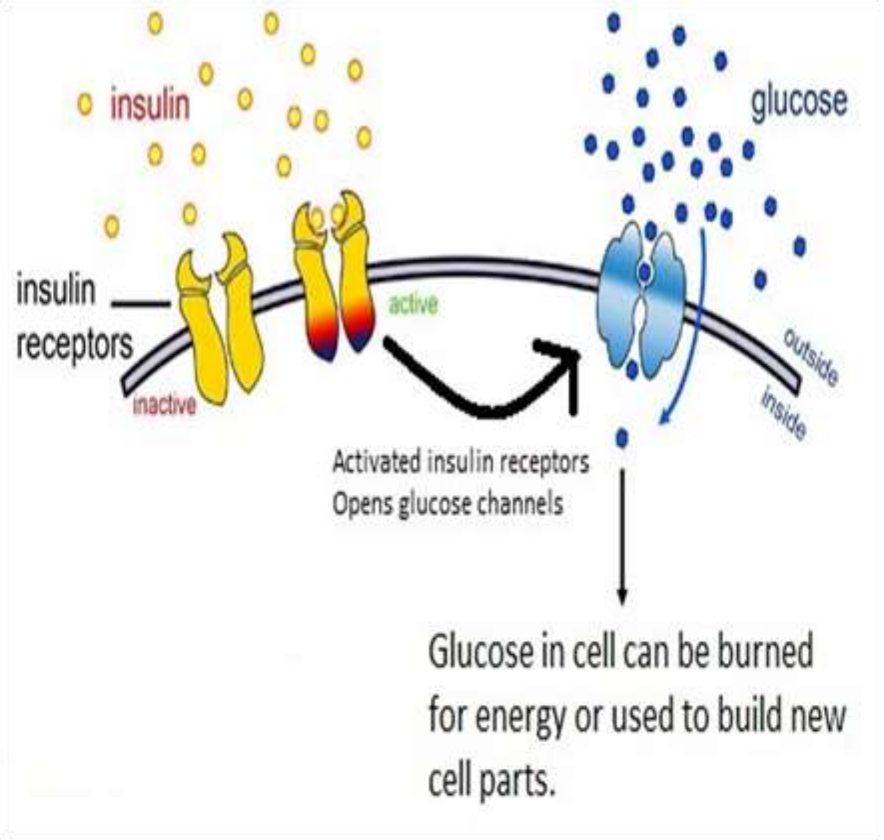


INSULIN INCREASES FACILITATED DIFFUSION OF GLUCOSE

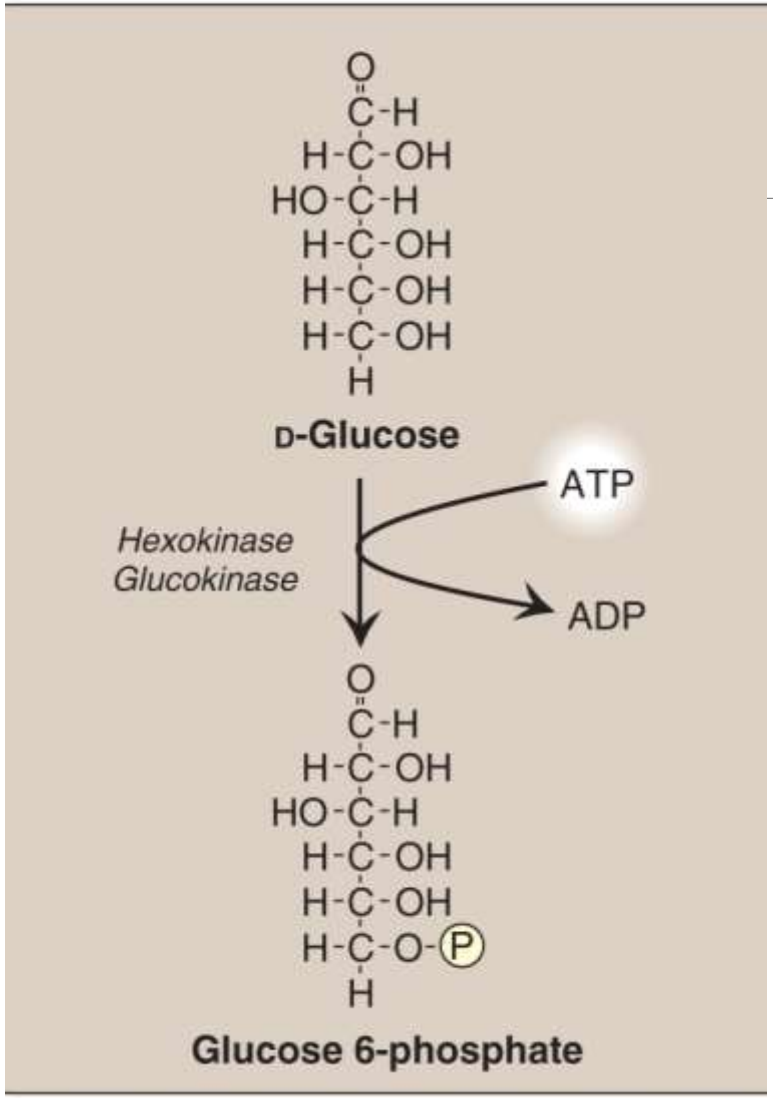
- The rate of glucose transport, as well as transport of some other monosaccharides, is greatly **increased** by insulin.

- When large amounts of insulin are secreted by the pancreas, the rate of glucose transport into most cells increases to 10 or more times the rate of transport when no insulin is secreted.

- Conversely, the amounts of glucose that can diffuse to the insides of most cells of the body in the absence of insulin, with the exception of liver and brain cells, are far too little to supply the amount of glucose normally required for energy metabolism.



PHOSPHORYLATION OF GLUCOSE



Immediately upon entry into the cells, glucose combines with a phosphate radical

This phosphorylation is promoted mainly by:

- Glucokinase enzyme in the liver
- Hexokinase enzyme in most other cells

PHOSPHORYLATION OF GLUCOSE

- The phosphorylation of glucose is almost completely irreversible

except,

- in liver cells, renal tubular and intestinal epithelial cells

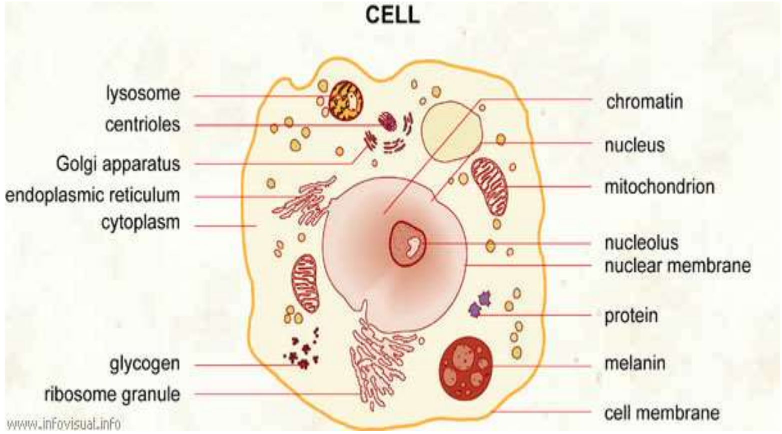
- In these cells, another enzyme, called glucose phosphatase, is available, and when activated, it can reverse the reaction.

Purpose of glucose phosphorylation

In most tissues of the body, phosphorylation serves to capture the glucose in the cell, because glucose almost immediately bind with phosphate, it will not diffuse back out, except from those special cells.

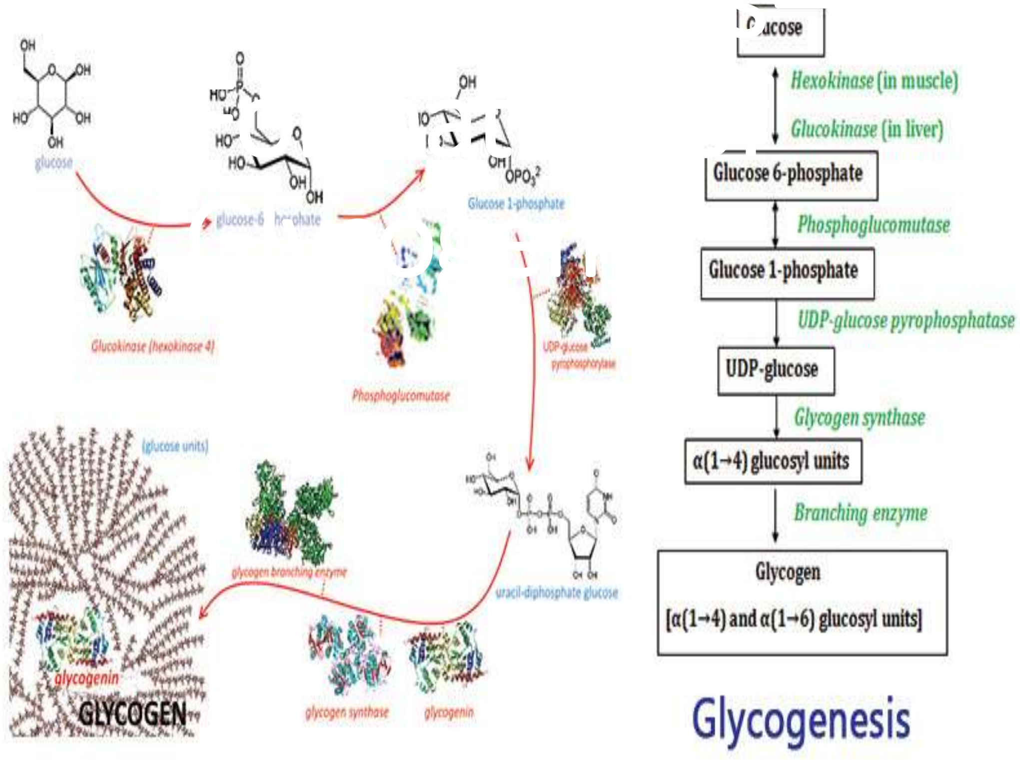
GLYCOGEN IS STORED IN THE LIVER AND MUSCLE

- After absorption into a cell, glucose can be used immediately for release of energy to the cell, or it can be stored in the form of glycogen, which is a large polymer of glucose.
- All cells of the body are capable of storing at least some glycogen, but certain cells can store large amounts, especially liver and muscle cells.
- The glycogen molecules can be polymerized to almost any molecular weight; most of the glycogen are accumulated in the form of solid granules.

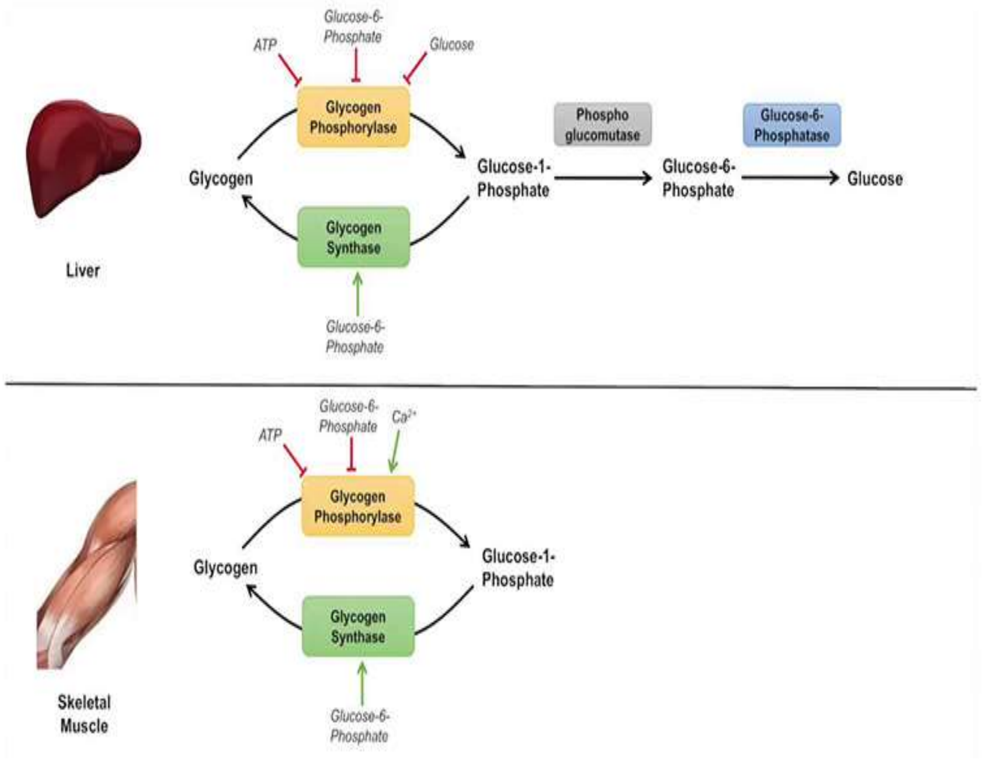


GLYCOGENESIS
FORMATION OF GLYCOGEN

- Glucose-6- phosphate can become glucose-1-phosphate; this substance is converted to uridine diphosphate glucose, which is finally converted into glycogen.
- Several specific enzymes are required to cause these conversions
- Certain smaller compounds, including lactic acid, glycerol, pyruvic acid can also be converted into glucose or closely allied compounds and then converted into glycogen.



GLYCOGENOLYSIS
BREAKING OF GLYCOGEN



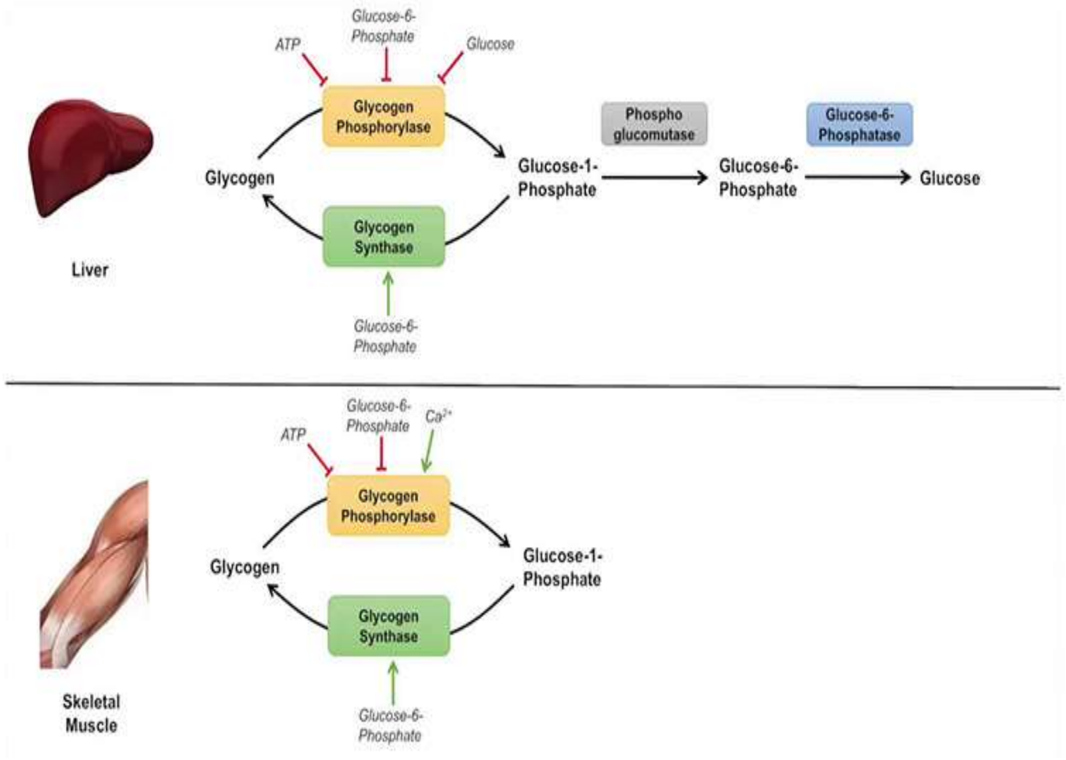
Glycogenolysis: the breakdown of the cell's stored glycogen to re-form glucose in the cells, which can then be used to provide energy.

- Glycogenolysis does not occur by reversal of the same chemical reactions that form glycogen;

<u>instead,</u>

- each subsequent glucose molecule on each branch of the glycogen polymer is split away by phosphorylation, catalyzed by the enzyme phosphorylase.

GLYCOGENOLYSIS
BREAKING OF GLYCOGEN



- Under resting conditions, the phosphorylase is in an inactive form, and thus glycogen remains stored.
- When it is necessary to re-form glucose from glycogen, the phosphorylase must first be activated.
- This activation can be accomplished in several ways, including activation by epinephrine or by glucagon.

ACTIVATION OF PHOSPHORYLASE BY EPINEPHRINE OR BY GLUCAGON.

- Two hormones, epinephrine and glucagon, can activate phosphorylase and thereby cause rapid glycogenolysis.

- Epinephrine is released by the adrenal medullae when the sympathetic nervous system is stimulated.

- Glucagon is secreted by the alpha cells of the pancreas when the blood glucose concentration falls too low.

RELEASE OF ENERGY FROM GLUCOSE

Three major steps:

1- Glycolysis

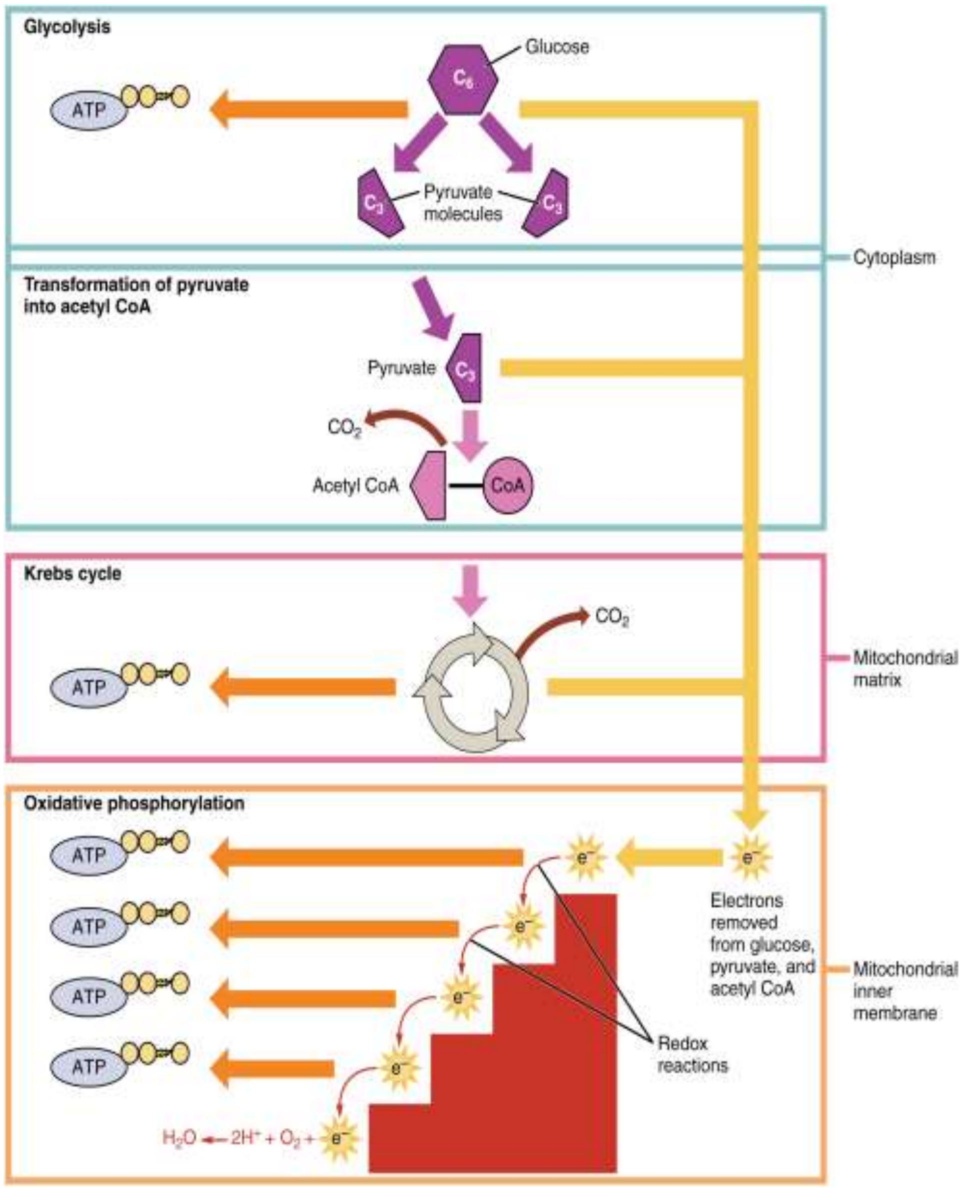
2-Cretic Acid cycle (kerbs)

3-Oxidative phosphorylation

- Cells of the body contain special enzymes that cause the glucose molecule to split a little at a time in many successive steps,

So, that its energy is released in small packets to form one molecule of ATP at a time,

Thus, forming a total of 38 moles of ATP for each mole of glucose metabolized by the cells.

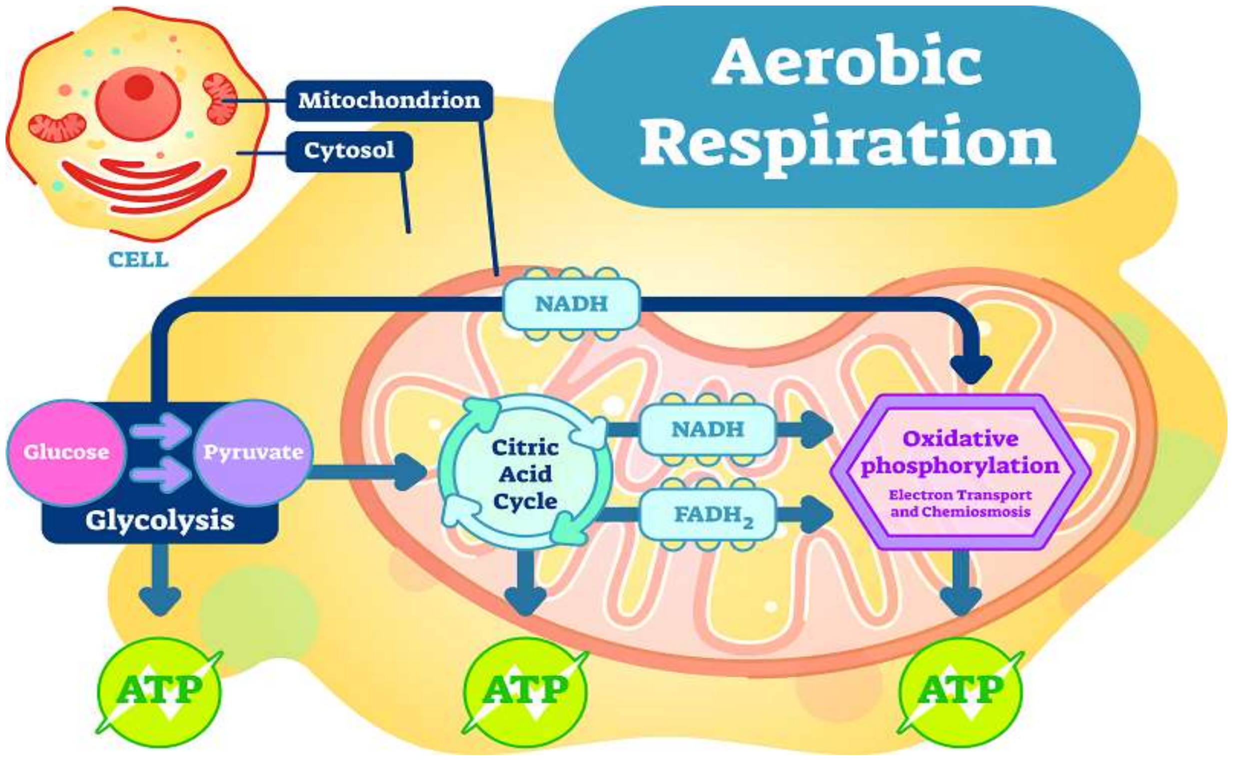


1- GLYCOLYSIS

Releasing energy from the glucose molecule is initiated by glycolysis.

The purpose of glycolysis:

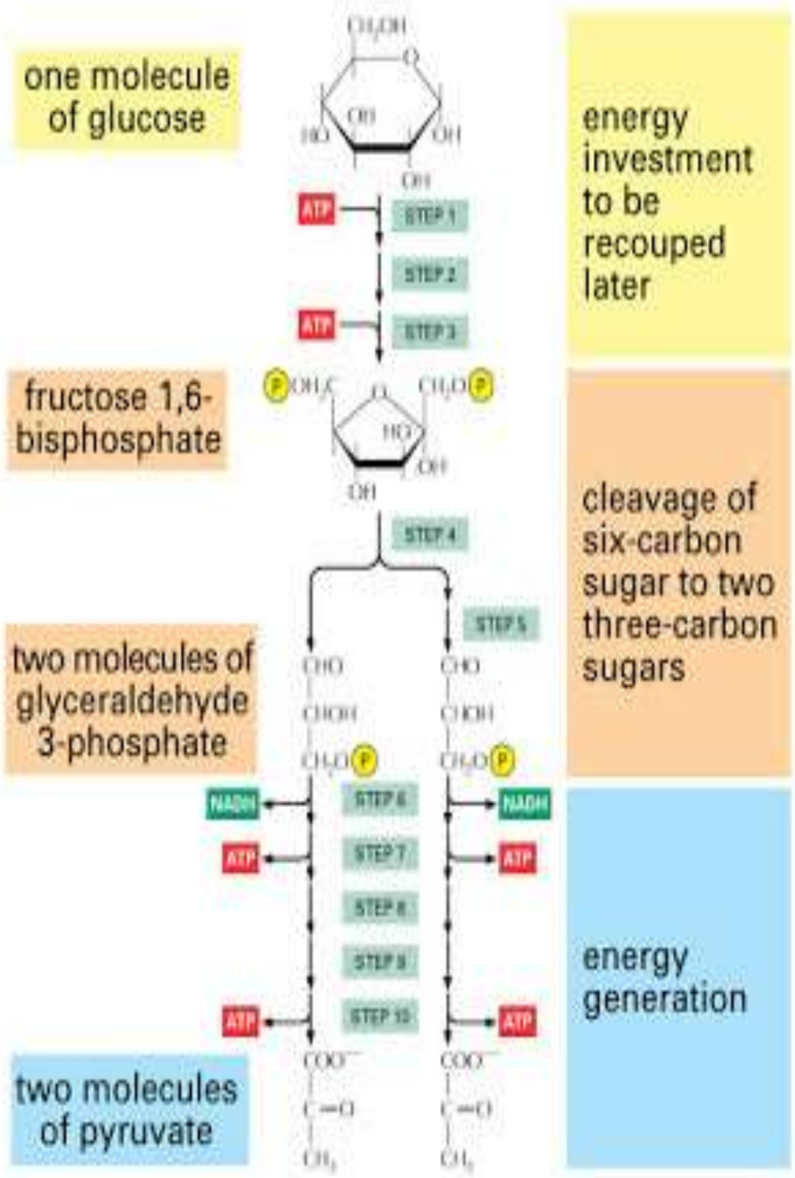
- Splitting Glucose to Form two molecules Pyruvic Acid.
- It happens in the cytoplasm.
- Glycolysis occurs by 10 sequent chemical reactions.
- Each step is catalyzed by at least one specific protein enzyme.



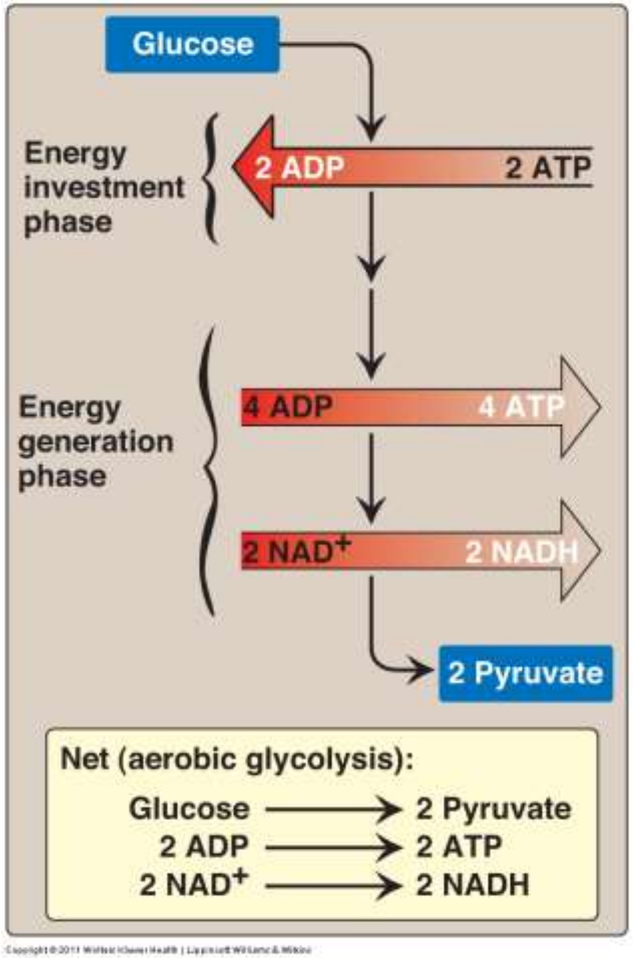
1- GLYCOLYSIS

The steps of glycolysis:

1. Glucose is first converted into fructose-1,6 diphosphate.
2. Fructose-1,6-diphosphate split into two glyceraldehyde-3- phosphate.
3. Each of which is then converted through five additional steps into pyruvic acid.



FORMATION OF ATP DURING GLYCOLYSIS



Despite the many chemical reactions in the glycolytic series, only a small portion of the free energy in the glucose molecule is released at most steps.

A total of 4 moles of ATP are formed in glycolysis

But, 2 moles of ATP are used in the first half of glycolysis.

So, the final net gain in ATP molecules by the entire glycolytic process is only 2 moles for each mole of glucose utilized.

Glycolysis produces:

Net energy :2 ATP

Net electron transfer: 2 NADH

Net reaction**:** 2 pyruvate molecules

pyruvate enters the **citric acid cycle** to produce more energy.

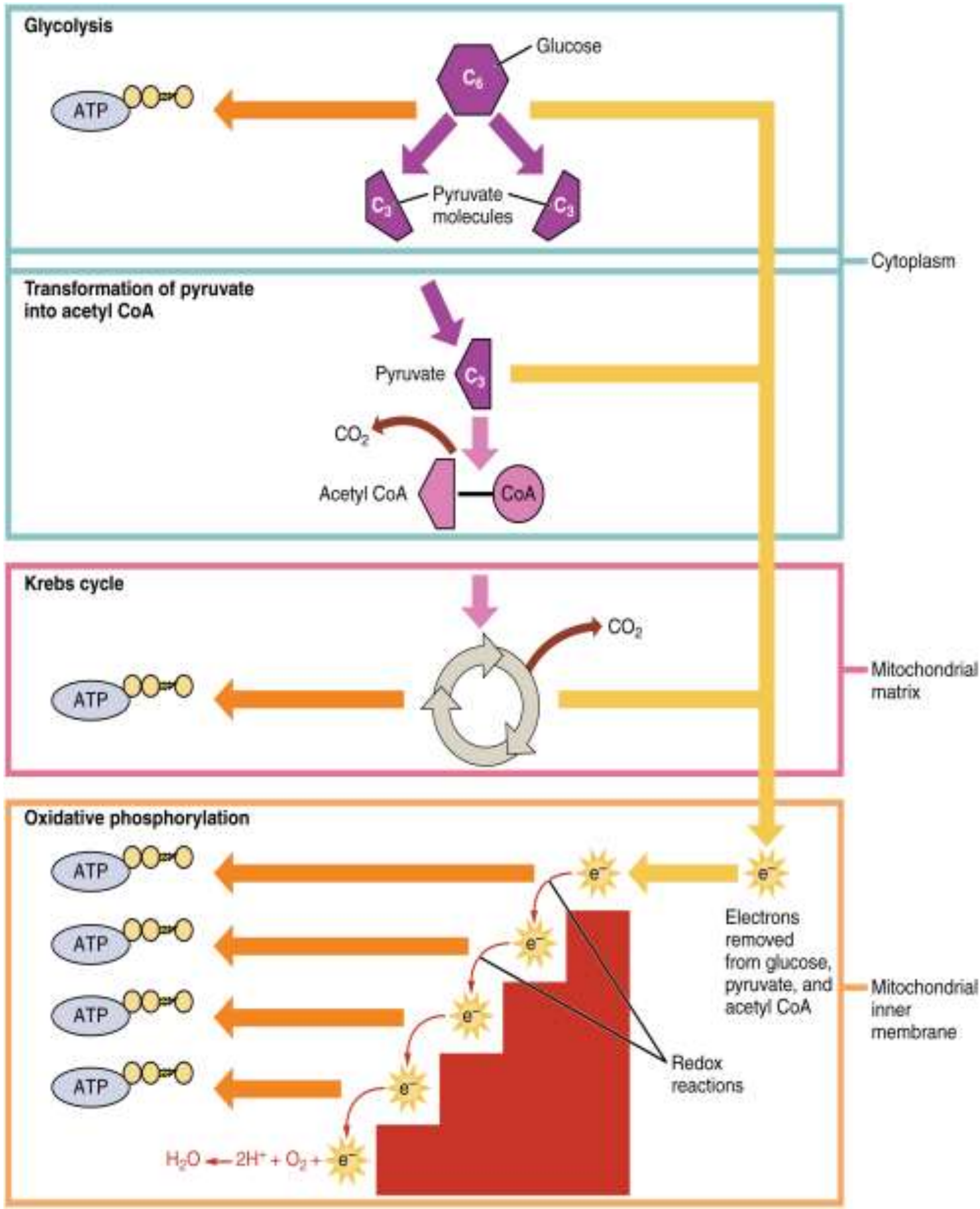
CONVERSION OF PYRUVIC ACID TO ACETYL COENZYME A

Connected stage

- Before pyruvate enters the citric acid cycle, it must be oxidized first.
- Pyruvate oxidation is the next step, it is a key connector that links glycolysis to the following stage
- **What happens in this stage?**

a two-step conversion of the two pyruvic acid molecules into two molecules of acetyl coenzyme A (acetylCoA)

This reaction occurs in mitochondrial matrix.

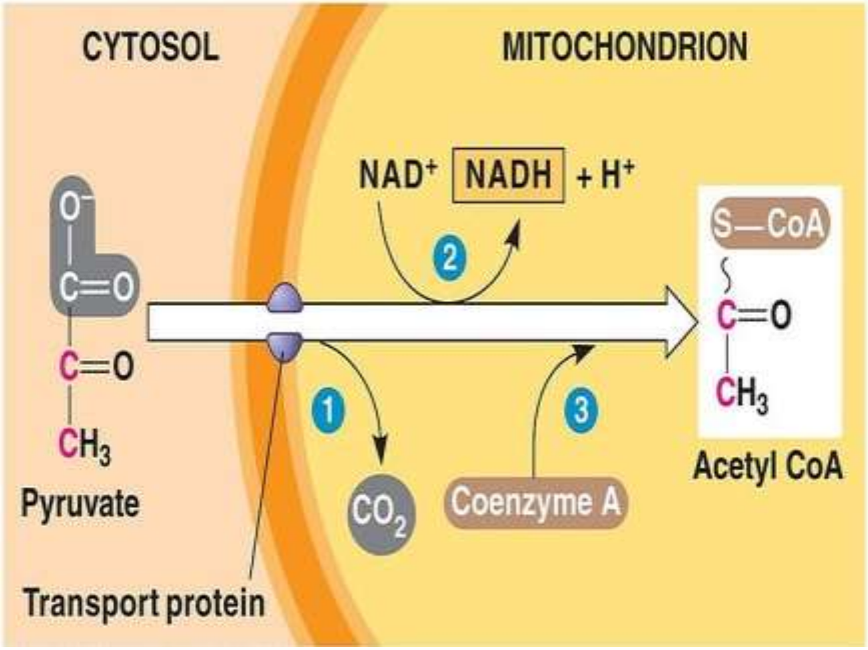


CONVERSION OF PYRUVIC ACID TO ACETYL COENZYME A

A Connected stage

The final product:

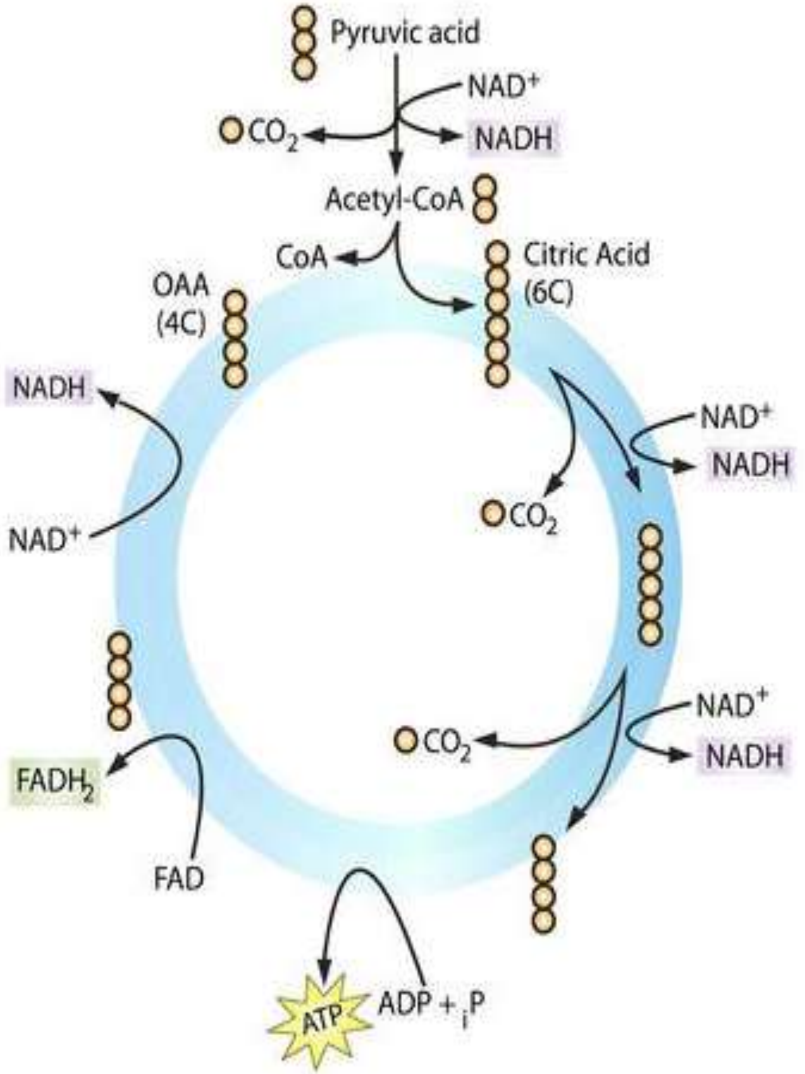
- Two carbon dioxide molecules
- Two NADH
- two molecules of acetyl-CoA



NO ATP produced here

2-CITRIC ACID CYCLE (KREBS CYCLE)

- The next stage in the degradation of the glucose molecule is called the **citric acid cycle**
- These reactions all occur in the matrix of mitochondria.
- The cycle includes eight major steps.
- The citric acid cycle is a sequence of chemical reactions in which the acetyl portion of acetyl-CoA is degraded to carbon dioxide and hydrogen atoms.

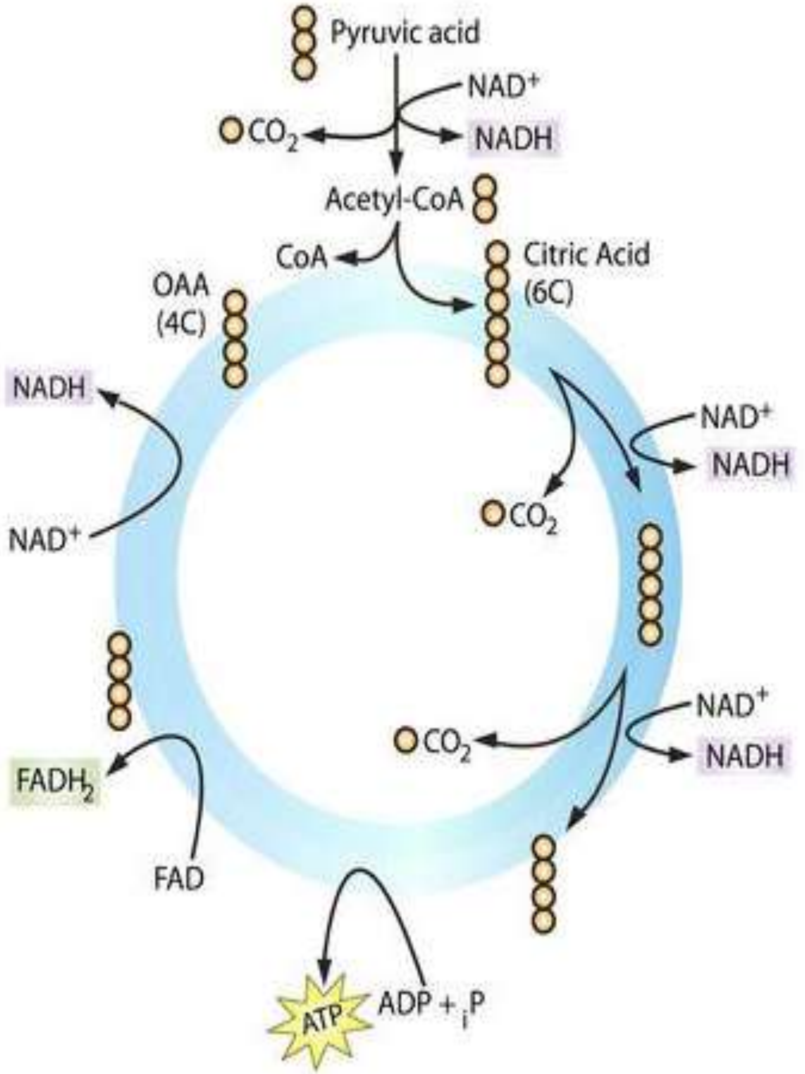


2-CITRIC ACID CYCLE (KREBS CYCLE)

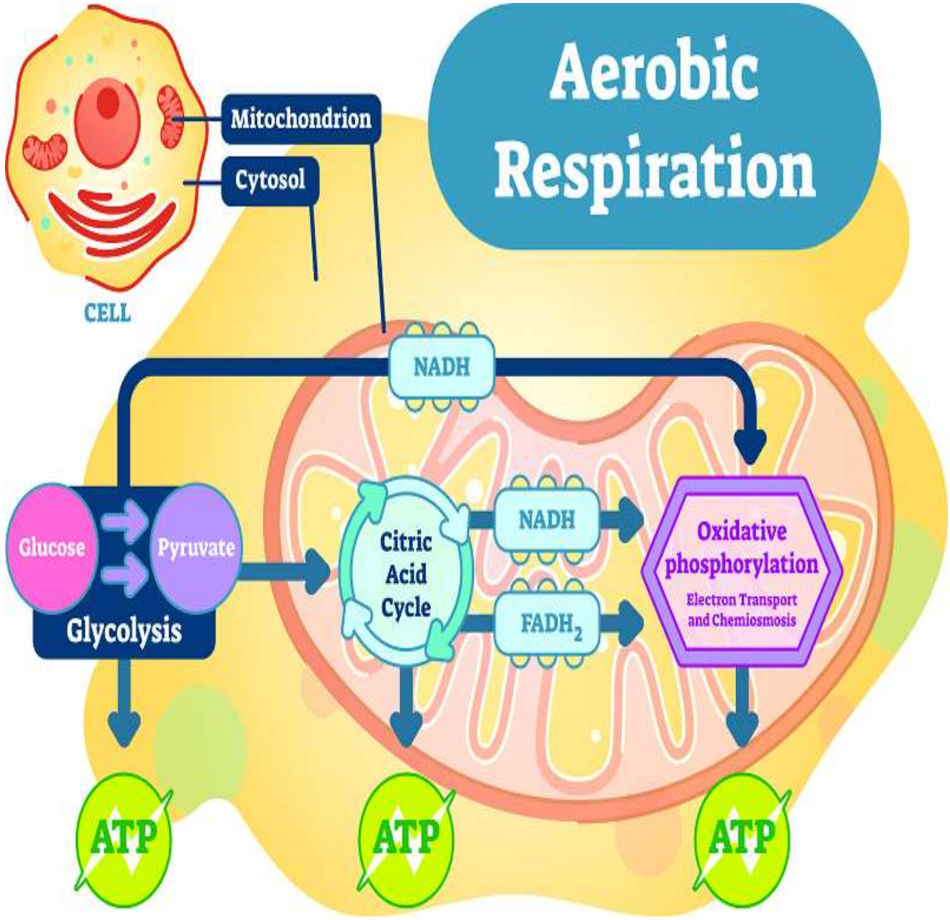
Citric acid cycle steps:

- The citric acid begins when acetyl-CoA combines with OAA (oxaloacetate) to produce citric acid
- After citric acid produced, it goes through a series of reactions that release energy. The energy is captured in molecules of NADH, ATP, and FADH2.
- The final step of the cycle regenerates OAA, the molecule that began the citric acid cycle.

Two turns are needed because glycolysis produces two pyruvate molecules when it splits glucose



2-CITRIC ACID CYCLE (KREBS CYCLE)

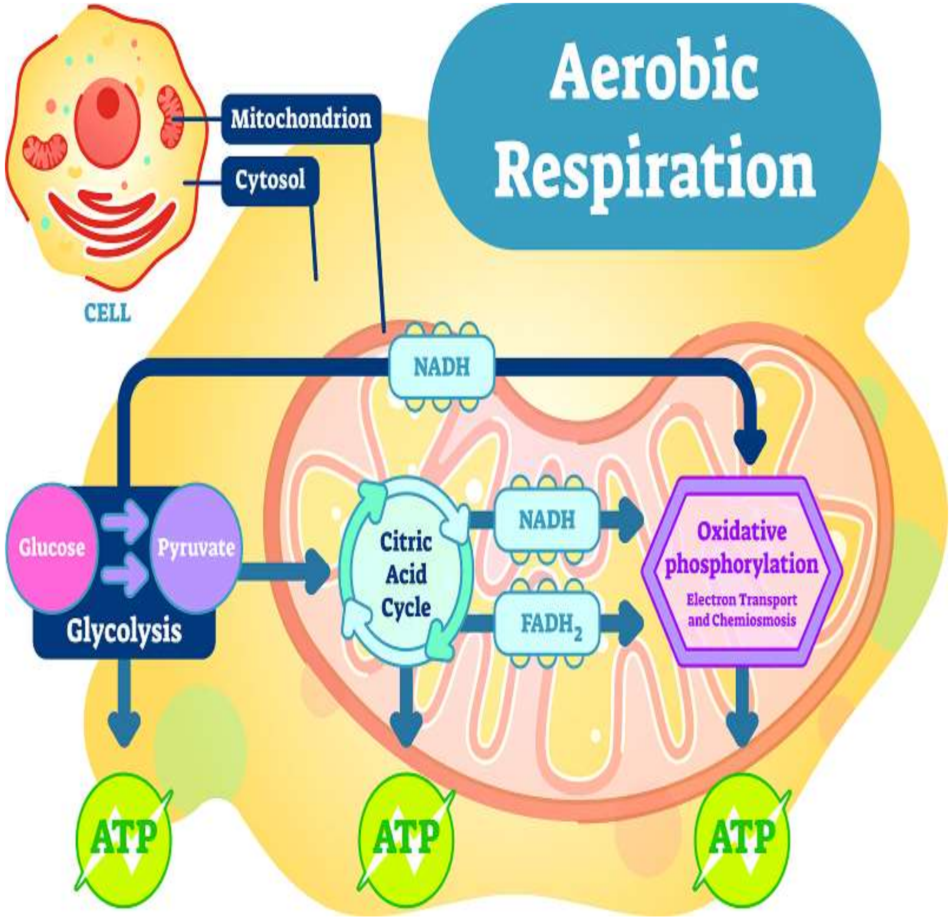


The net results of the entire citric acid cycle

After the second turn through the citric acid cycle, the original glucose molecule has been broken down completely, which results in the production of:

- 2 ATP
- 8 NADH
- 2 $FADH_2$
- 4 carbon dioxide molecules

2-CITRIC ACID CYCLE (KREBS CYCLE)



Formation of ATP in the Citric Acid Cycle:

- The citric acid cycle itself does not cause a great amount of energy to be released, only a total of two molecules of ATP are formed in this stage .
- **But,** it can generate a lot of ATP indirectly, through the release of NADH and FADH2.
- These electron carriers (NADH and FADH2) will connect with the last portion of cellular respiration, **Oxidative Phosphorylation** to produce more of ATP molecules.

FUNCTION OF DEHYDROGENASES AND NICOTINAMIDE ADENINE DINUCLEOTIDE (NAD) IN CAUSING RELEASE OF HYDROGEN ATOMS

How are the NADH produced in the above stages?

Hydrogen atoms released during the three above stages:

- 4 H during glycolysis
- 4 H during formation of acetyl-CoA from pyruvic acid
- 16 H during in the citric acid cycle

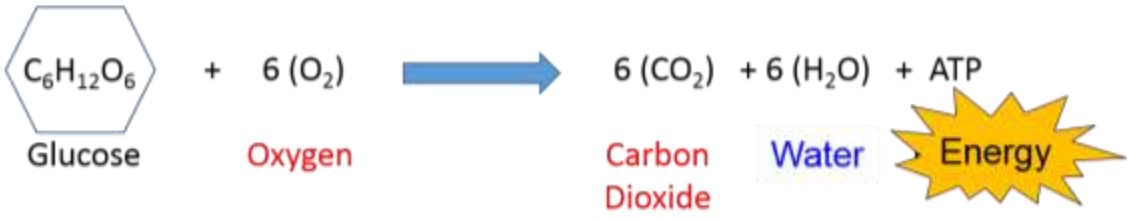
Thus, a total of 24 hydrogen atoms are released for each original molecule of glucose.

- The release of these hydrogen atoms is catalyzed by a specific protein enzyme called a **dehydrogenase**.

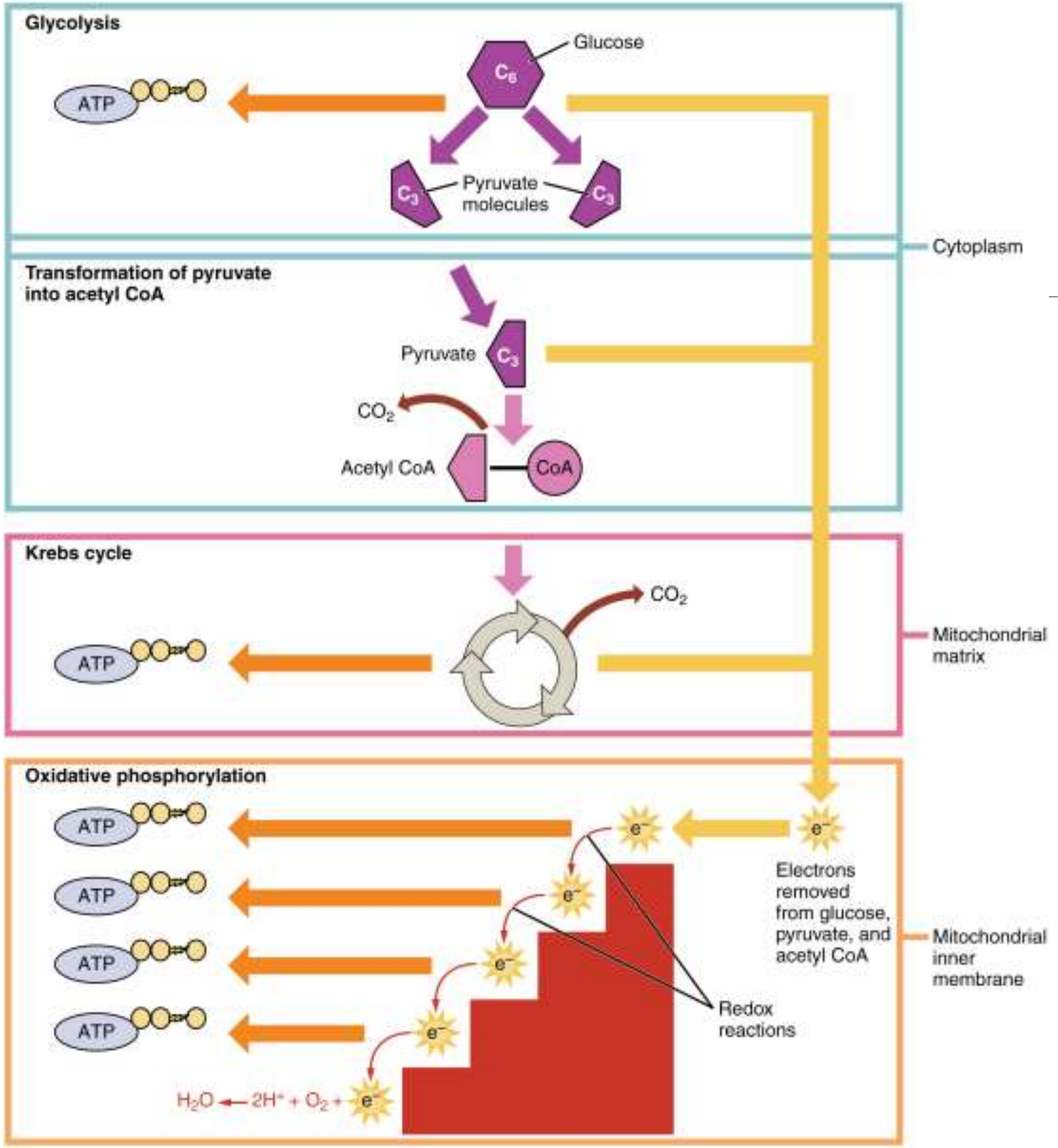
FUNCTION OF DEHYDROGENASES AND NICOTINAMIDE ADENINE DINUCLEOTIDE (NAD) IN CAUSING RELEASE OF HYDROGEN ATOMS

- 20 of the 24 hydrogen atoms immediately combine with nicotinamide adenine dinucleotide (NAD+), which form NADH
- Both the four remaining hydrogen ion and the 20 hydrogen atoms combined with NAD+ later enter the next oxidative chemical reactions that form large quantities of ATP.

FUNCTION OF DECARBOXYLASES IN CAUSING RELEASE OF CARBON DIOXIDE



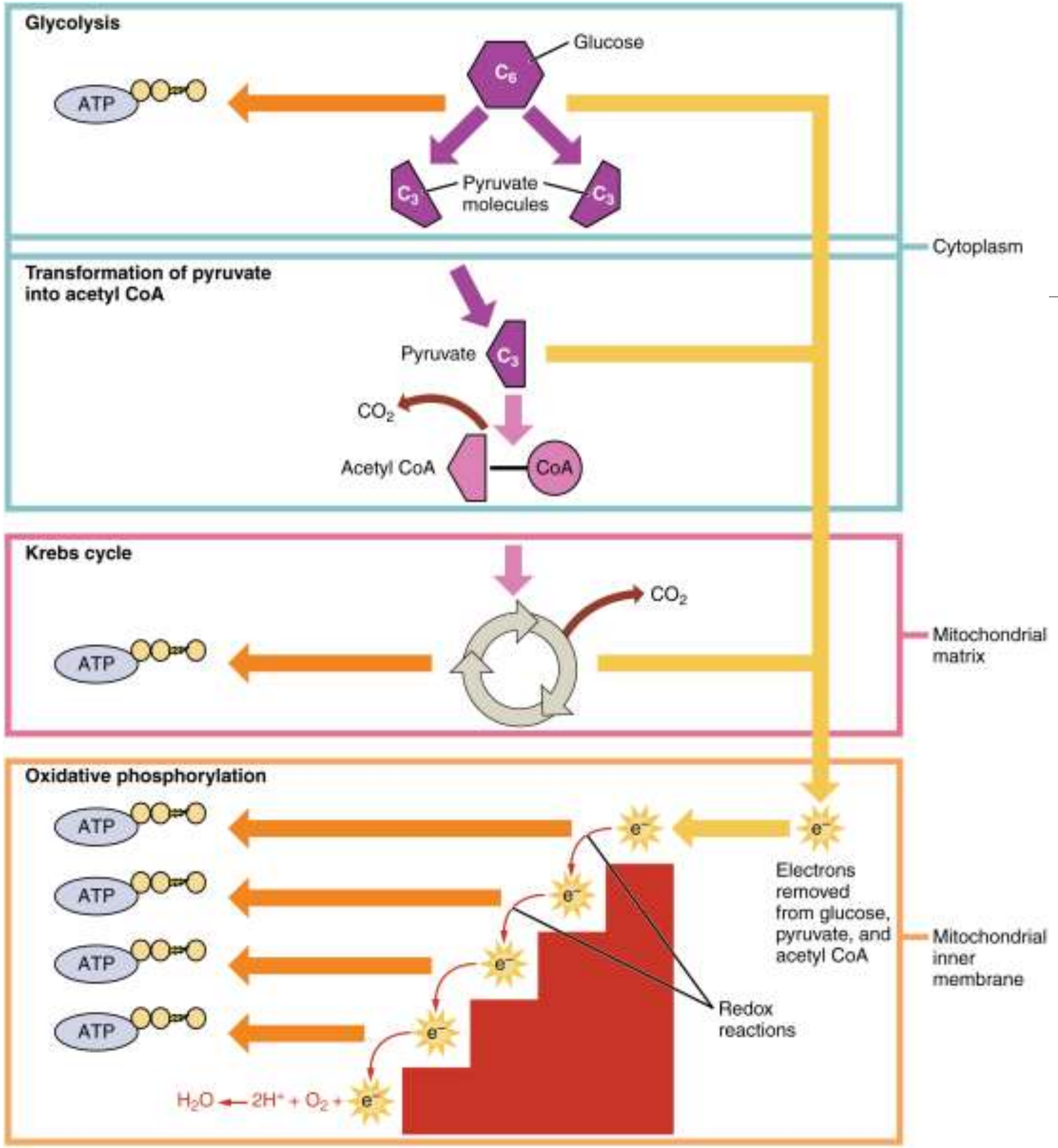
- Carbon dioxide is released as a result of the chemical reactions of the above stages.
- Specific protein enzymes, called **decarboxylases** cause the release of carbon dioxide.
- This carbon dioxide is then dissolved in the body fluids and transported to the lungs, where it is expired from the body.



3- OXIDATIVE PHOSPHORYLATION

FORMATION OF LARGE QUANTITIES OF ATP BY OXIDATION OF HYDROGEN:

- Almost 90 percent of the total ATP created through glucose metabolism is formed during subsequent oxidation of the hydrogen atoms that were released at early stages of glucose degradation.
- Indeed, the principal function of all these earlier stages is to make the hydrogen of the glucose molecule available in forms that can be oxidized.



3- OXIDATIVE PHOSPHORYLATION

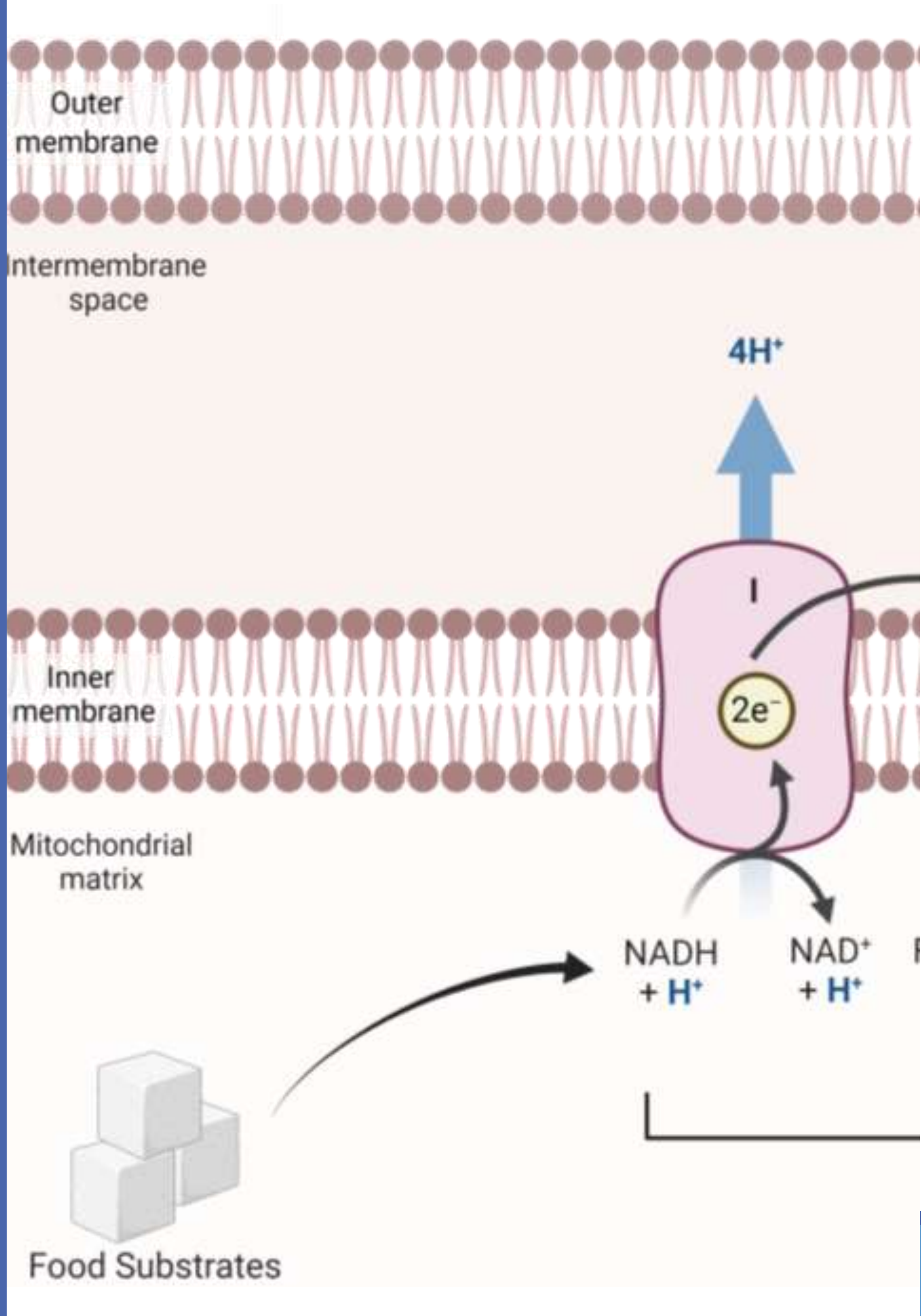
FORMATION OF LARGE QUANTITIES OF ATP BY OXIDATION OF HYDROGEN:

- A sequence of oxidation reaction release a tremendous amount of energy to form ATP in process called **oxidative phosphorylation** in the **mitochondria** by a highly specialized process called **chemiosmotic mechanism**

CHEMIOSMOTIC MECHANISM OF THE MITOCHONDRIA TO FORM ATP

Stage (1): Ionization of Hydrogen, the Electron Transport Chain, and Formation of Water:

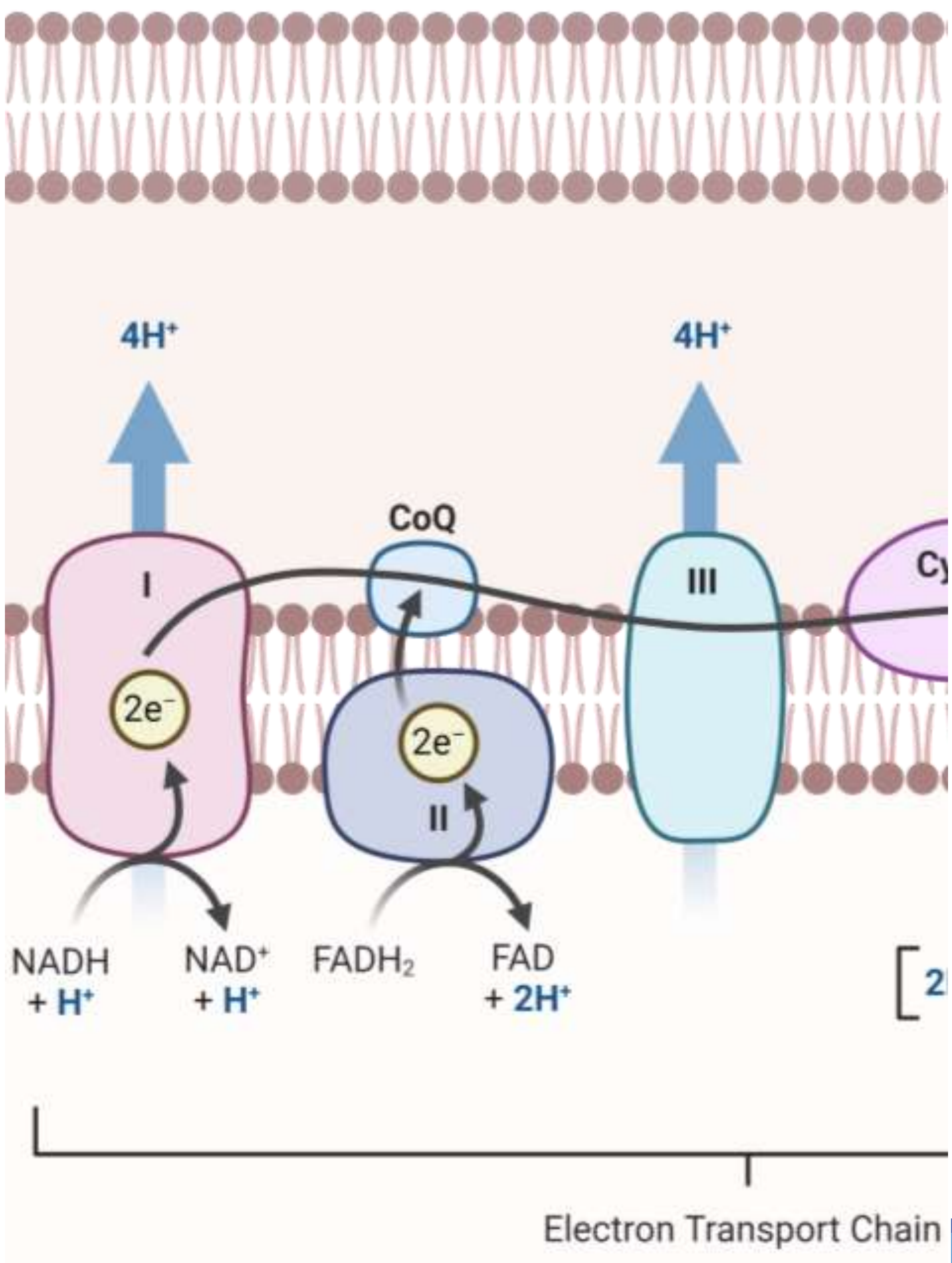
- The first step in oxidative phosphorylation **in the mitochondria** is to ionize the hydrogen atoms that have been removed from the food substrates.
- These hydrogen atoms are removed in pairs: one immediately becomes a hydrogen ion, (H+) the other combines with NAD+ to form reduced nicotinamide adenine dinucleotide (NADH).
- Then the other hydrogen atom(H+) removed from the NADH, and reconstitutes NAD+ that will be reused repeatedly.



CHEMIOSMOTIC MECHANISM OF THE MITOCHONDRIA TO FORM ATP

Stage (2): Ionization of Hydrogen, the Electron Transport Chain, and Formation of Water:

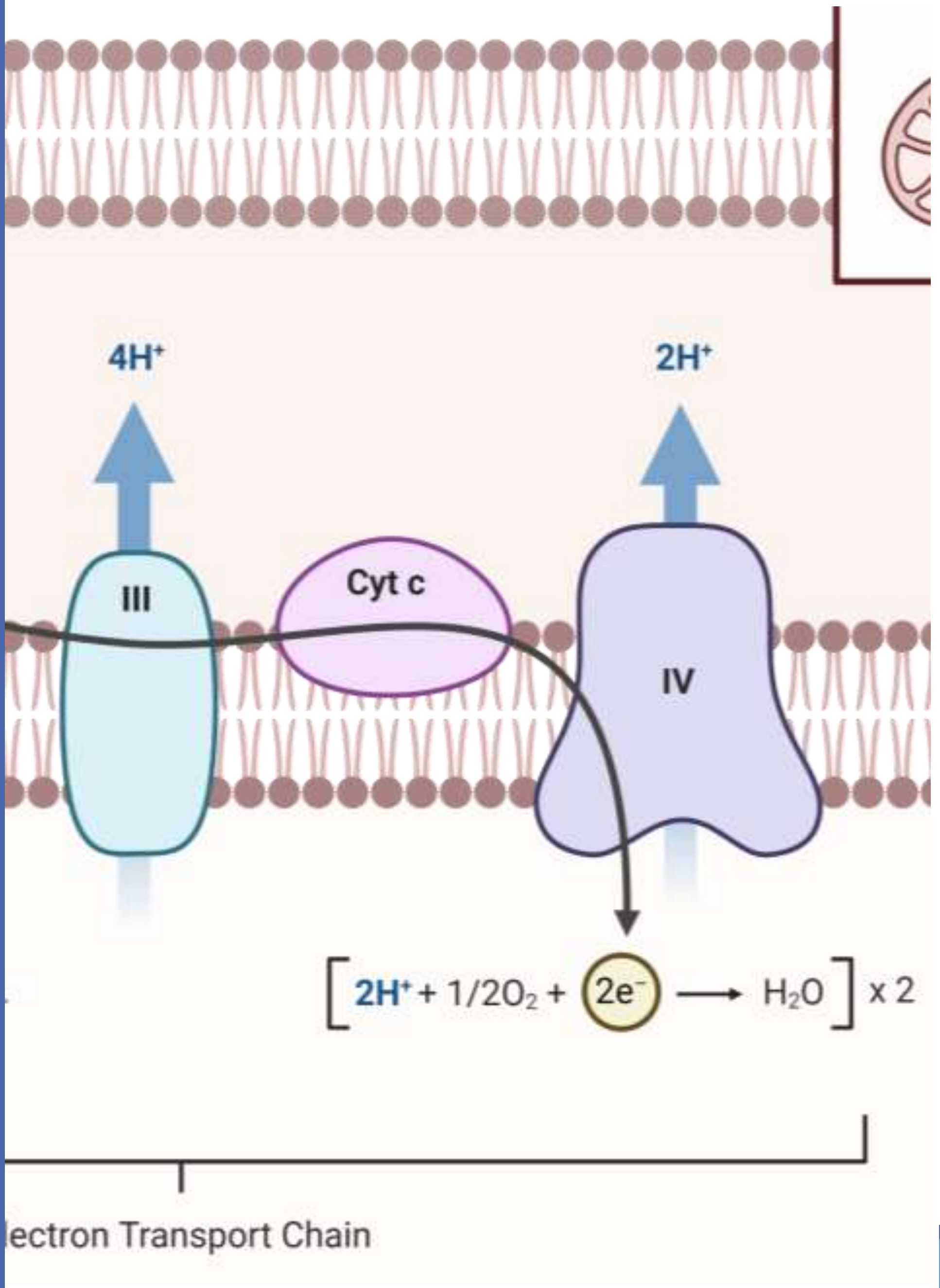
- The electrons that are removed from the hydrogen atoms to cause the hydrogen ionization immediately enter an electron transport chain of electron acceptors that are an integral part of the inner membrane of the mitochondrion.
- Each electron is shuttled from one of these acceptors to the next until the elemental oxygen reduced to form ionic oxygen, which then combines with hydrogen ions to form water.



CHEMIOSMOTIC MECHANISM OF THE MITOCHONDRIA TO FORM ATP

Stage (2): Ionization of Hydrogen, the Electron Transport Chain, and Formation of Water:

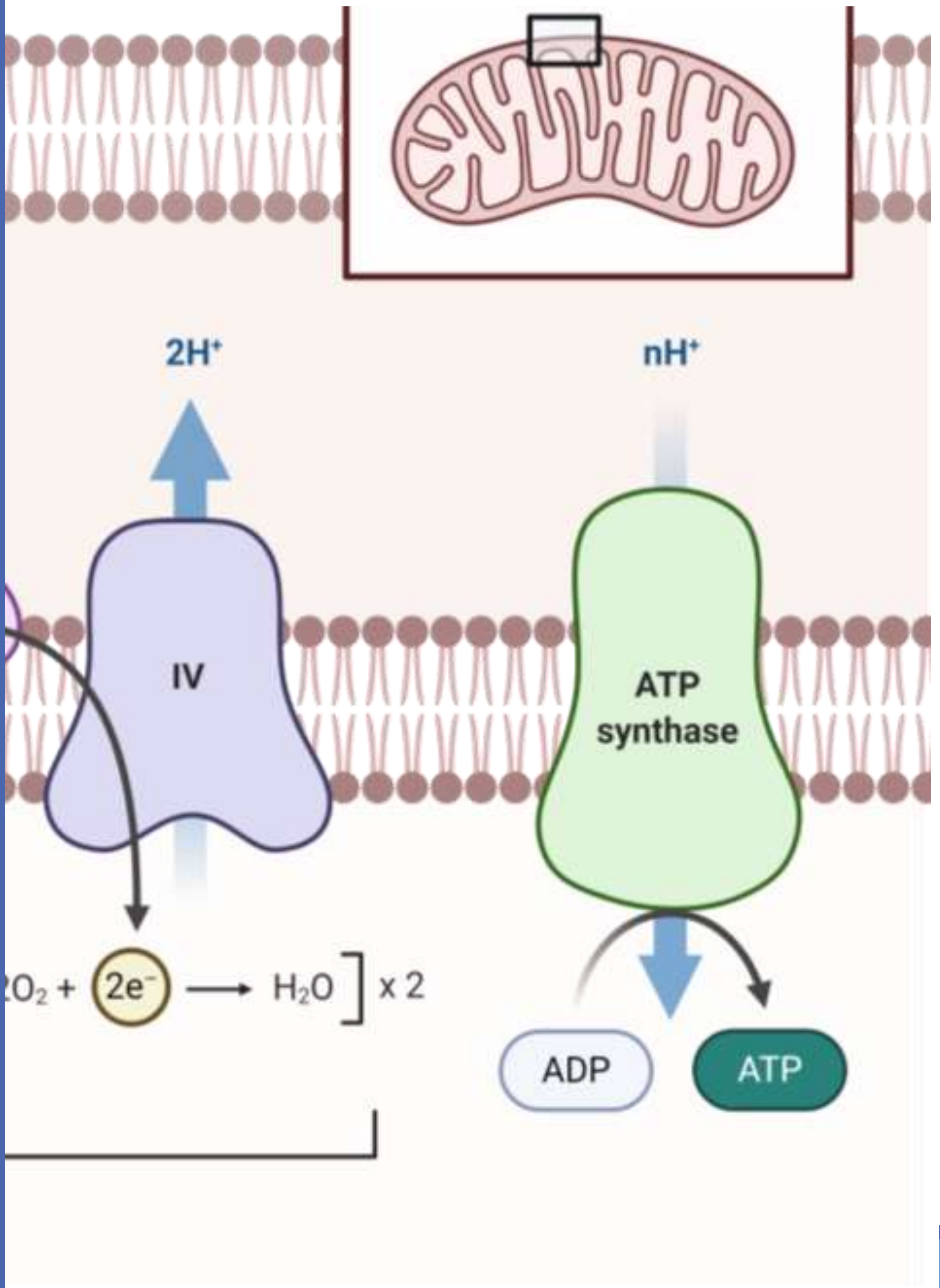
- Pumping of hydrogen ions into the outer chamber of the mitochondrion, caused by the electron transport chain and result in releasing large amounts of energy.
- This energy is used to pump hydrogen ions from the inner matrix of the mitochondrion into the outer chamber between the inner and outer mitochondrial membranes.
- This process creates a high concentration of positively charged hydrogen ions in this chamber; it also creates a strong negative electrical potential in the inner matrix.



CHEMIOSMOTIC MECHANISM OF THE MITOCHONDRIA TO FORM ATP

Stage (3): Formation of ATP.

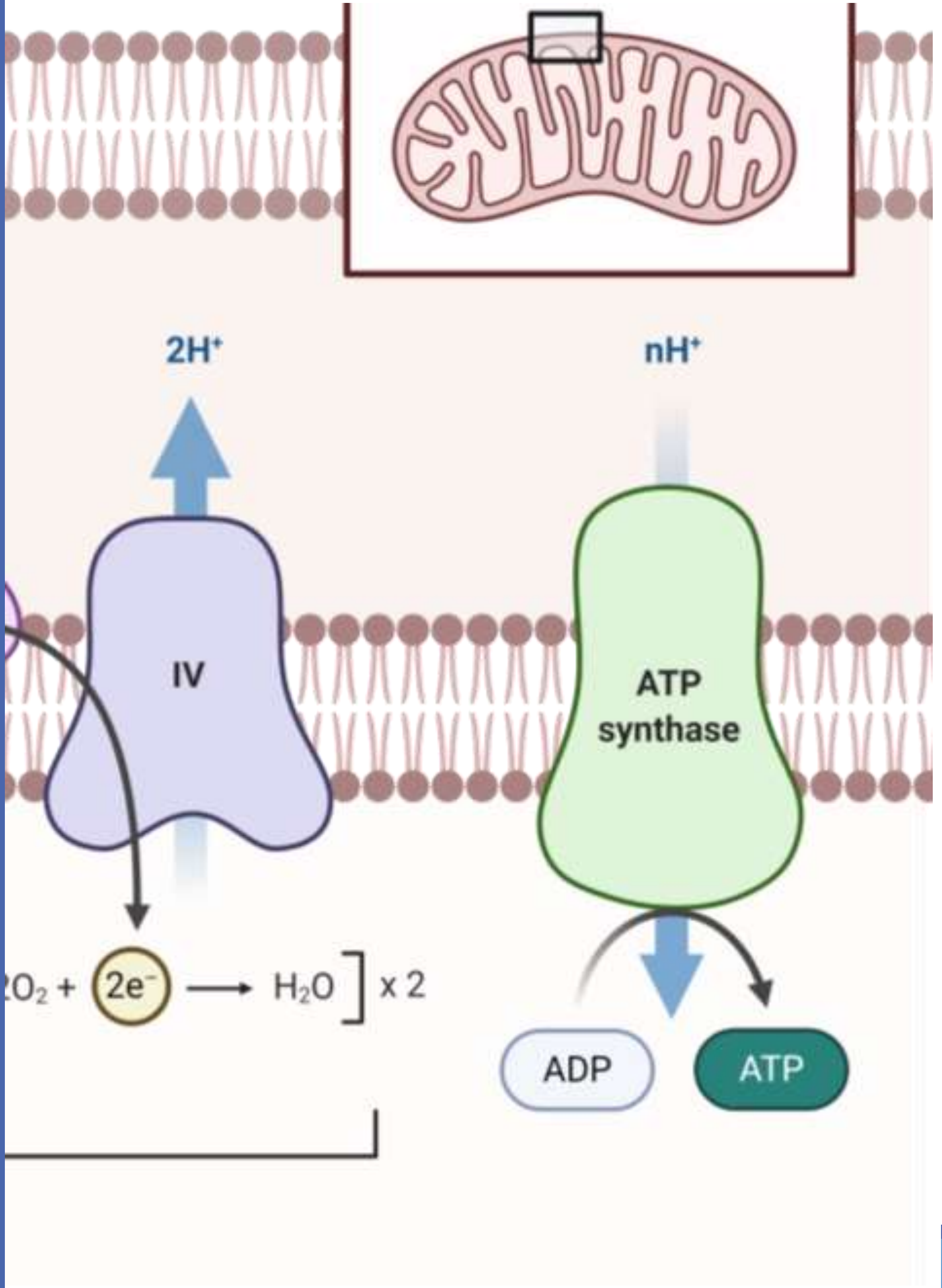
- The next step in oxidative phosphorylation is to convert ADP into ATP.
- This conversion occurs in conjunction with a large protein molecule that protrudes all the way through the inner mitochondrial membrane and projects with a knoblike head into the inner mitochondrial matrix.
- This molecule is an ATPase and it called ATP synthetase.



CHEMIOSMOTIC MECHANISM OF THE MITOCHONDRIA TO FORM ATP

Stage (3): Formation of ATP.

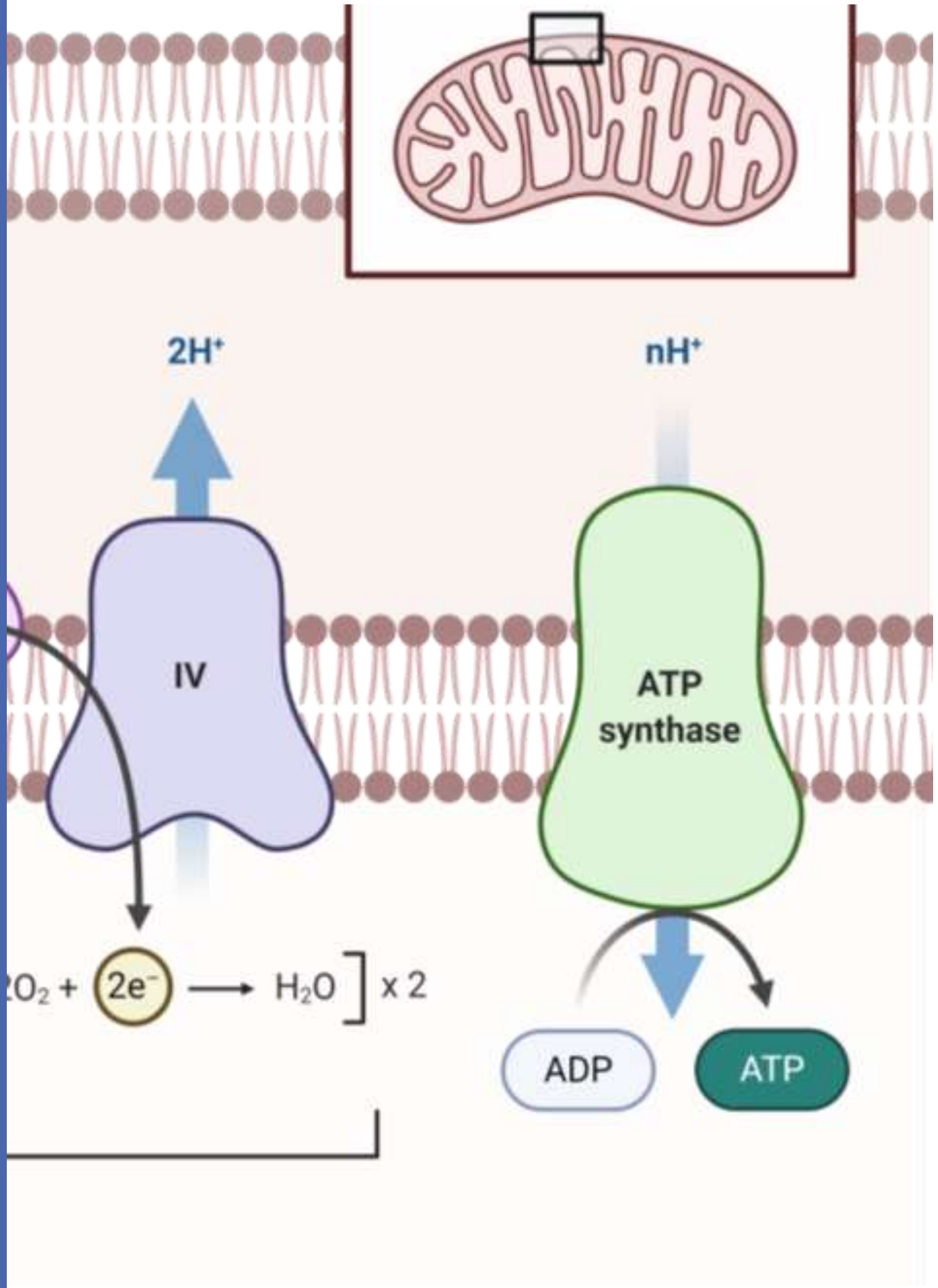
- The high concentration of positively charged hydrogen ions in the outer chamber and the large electrical potential difference across the inner membrane cause the hydrogen ions to flow into the inner mitochondrial matrix through the substance of the ATPase molecule.
- In doing so, energy derived from this hydrogen ion flow is used by ATPase to convert ADP into ATP by combining ADP with a free ionic phosphate radical (Pi), thus adding another high-energy phosphate bond to the molecule.



CHEMIOSMOTIC MECHANISM OF THE MITOCHONDRIA TO FORM ATP

Stage (3): Formation of ATP.

- For each two electrons that pass through the entire electron transport chain (representing the ionization of two hydrogen atoms), up to three ATP molecules are synthesized.

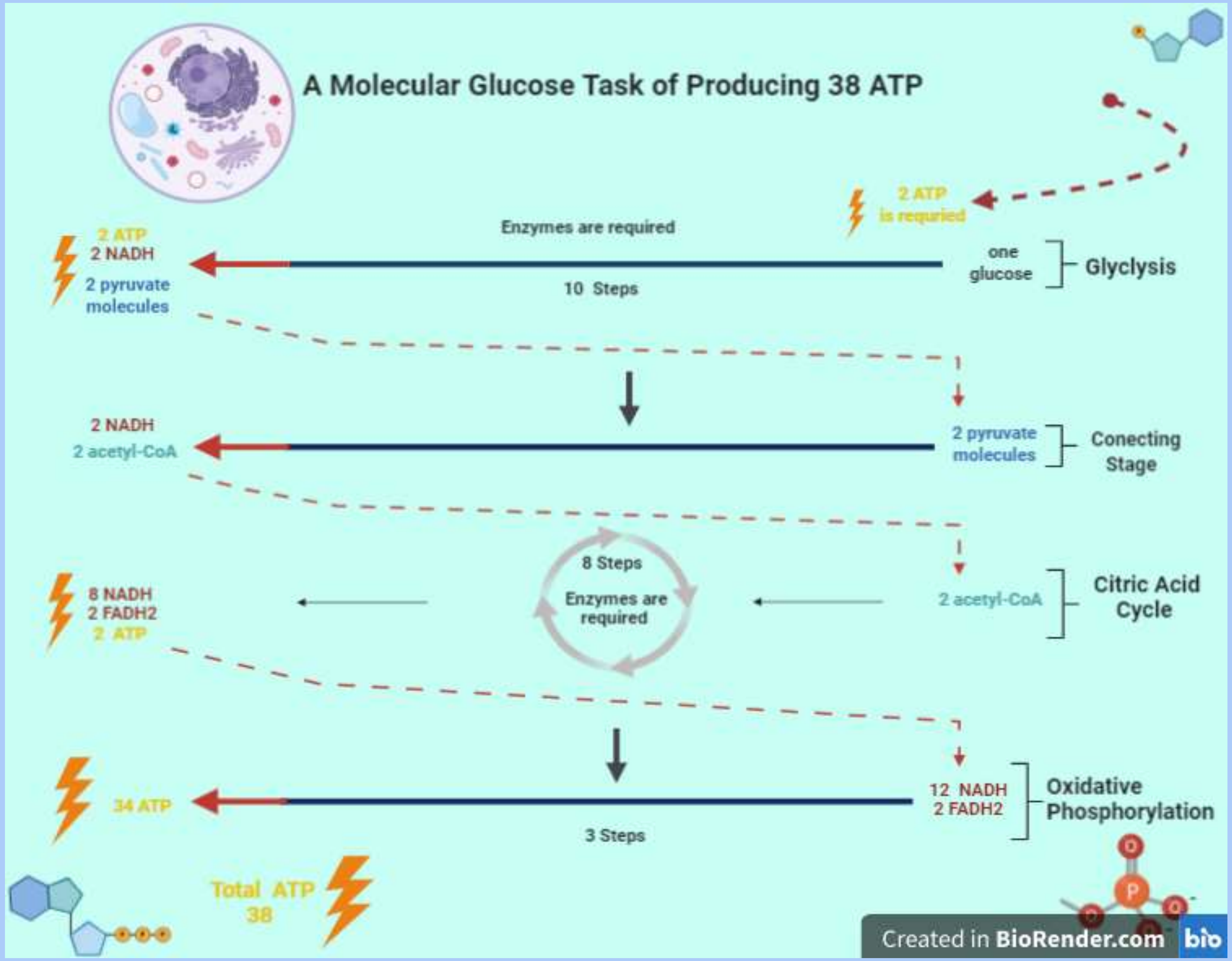


SUMMARY OF ATP FORMATION DURING THE BREAKDOWN OF GLUCOSE

Pathways	Sit	Main goal	ATP net	Other products
Glycolysis	Cytoplasm	Produce 2 pyruvate molecules	2	2 NADH 2 Pyruvate
Connected stage	Mitochondrial matrix	Conversion of Pyruvic Acid to Acetyl Coenzyme A(Acetyl-CoA)	0	2 CO_2 2 NADH 2 Acetyl-CoA
Citric Acid Cycle	Mitochondrial matrix	Produce high-energy electrons	2	8 NADH 2 $FADH_2$
Oxidative Phosphorylation	Mitochondria matrix and inner membrane	Produce high amount of ATP	34	6 O_2 12 H_2O 2 FAD 10 NAD^+

MIND MAP 1

Total ATP produced in main glucose metabolism pathways



EFFECT OF ATP AND ADP CELL CONCENTRATIONS IN CONTROLLING GLYCOLYSIS AND GLUCOSE OXIDATION

- Continual release of energy from glucose when the cells do not need energy would be an extremely wasteful process.

- Instead, glycolysis and the subsequent oxidation of hydrogen atoms are continually controlled **based on** the need of the cells for ATP.

- This control is *accomplished by* the effects of cell concentrations of both ADP and ATP.

EFFECT OF ATP AND ADP CELL CONCENTRATIONS IN CONTROLLING GLYCOLYSIS AND GLUCOSE OXIDATION

ATP role in control energy metabolism(glycolysis and glucose oxidation) :

1. **Inhibit** the enzyme **phosphofructokinase** (promotes the formation of fructose-1,6-diphosphate, one of the initial steps in the glycolysis).
2. Slow or stop glycolysis by the net effect of **excess** cellular **ATP**, which in turn stops most carbohydrate metabolism.

ADP (and AMP as well) role in control energy metabolism(glycolysis and glucose oxidation) :

1- **Increasing** enzyme **phosphofructokinase** activity.

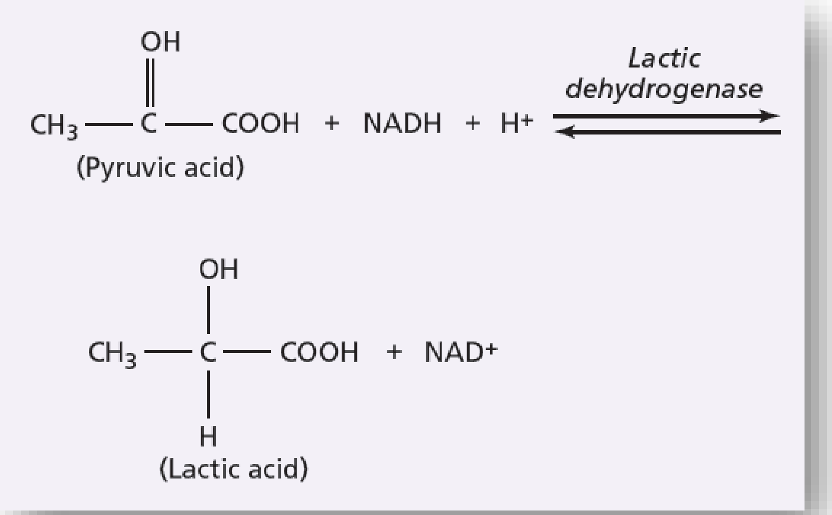
2- **Increase** glycolysis by the net effect of **excess** cellular **ADP**.

ANAEROBIC RELEASE OF ENERGY
(ANAEROBIC GLYCOLYSIS)

- When oxygen unavailable or insufficient, oxidative phosphorylation cannot take place. At these conditions, a small amount of energy can still be released to the cells by the glycolysis stage of carbohydrate degradation, because the chemical reactions for the breakdown of glucose to pyruvic acid do not require oxygen.
- Anaerobic glycolysis energy is the glycolytic energy releases to the cells as a result of carbohydrate glycolysis degradation without oxygen present
- it can be a lifesaving measure for up to a few minutes when oxygen becomes unavailable.

ANAEROBIC RELEASE OF ENERGY

(ANAEROBIC GLYCOLYSIS)



Formation of Lactic Acid During Anaerobic Glycolysis Allows Release of Extra Anaerobic Energy:

- The law of mass action : as the end products of a chemical reaction build up in a reacting medium, the rate of the reaction decreases, approaching zero.
- The two end products of the glycolytic reactions are (1) pyruvic acid and (2) hydrogen atoms combined with NAD+ to form NADH and H+.
- The buildup of either or both substances would stop the glycolytic process and prevent further formation of ATP. When their quantities begin to be excessive, these two end products react with each other to form lactic acid, in accordance with the equation.

ANAEROBIC RELEASE OF ENERGY (ANAEROBIC GLYCOLYSIS)

Formation of Lactic Acid During Anaerobic Glycolysis Allows Release of Extra Anaerobic Energy:

- As a result, under anaerobic conditions, the major portion of the pyruvic acid is converted into lactic acid, which diffuses readily out of the cells into the extracellular fluids and even into the intracellular fluids of other less active cells.
- For that reason, lactic acid represents a type of “sinkhole” into which the glycolytic end products can disappear, allowing glycolysis to proceed far longer than would otherwise be possible.
- Glycolysis can proceed for several minutes, supplying the body with considerable extra quantities of ATP, even in the absence of respiratory oxygen.

ANAEROBIC RELEASE OF ENERGY (ANAEROBIC GLYCOLYSIS)

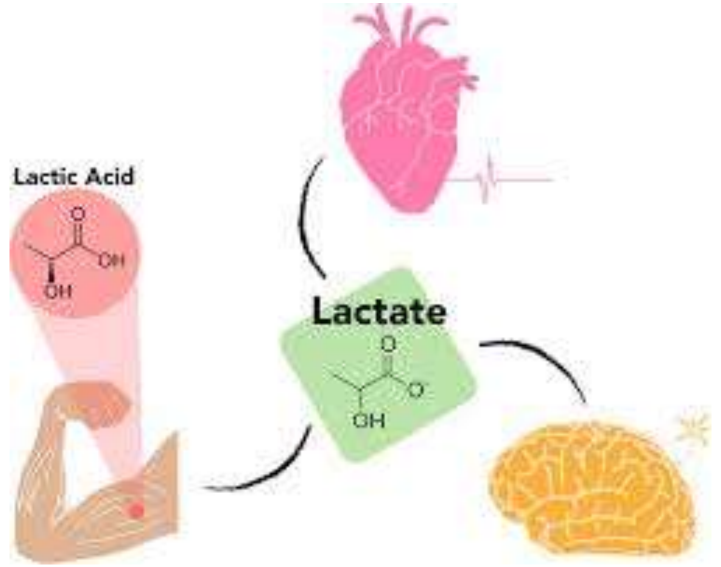
Reconversion of Lactic Acid to Pyruvic Acid When Oxygen Becomes Available Again:

- When a person begins to breathe oxygen again after a period of anaerobic metabolism:
- Lactic acid is reconverted to pyruvic acid and NADH plus H+.
- Large portions of these substances (pyruvic acid and NADH plus H+) are immediately oxidized to form large quantities of ATP.
- ATP then causes the remaining excess pyruvic acid to be converted back into glucose.
- As a result the large amount of lactic acid (forms during anaerobic glycolysis) can be either reconverted to glucose or used directly for energy.
- This reconversion occurs in the liver, but a small amount can also occur in other tissues.

ANAERBIC RELEASE OF ENERGY (ANAEROBIC GLYCOLYSIS)

Use of Lactic Acid by the Heart for Energy:

- Heart muscle is especially capable of converting lactic acid to pyruvic acid and then using the pyruvic acid for energy.
- This process occurs mostly during heavy exercise, when large amounts of lactic acid are released into the blood from the skeletal muscles and consumed as an extra energy source by the heart.

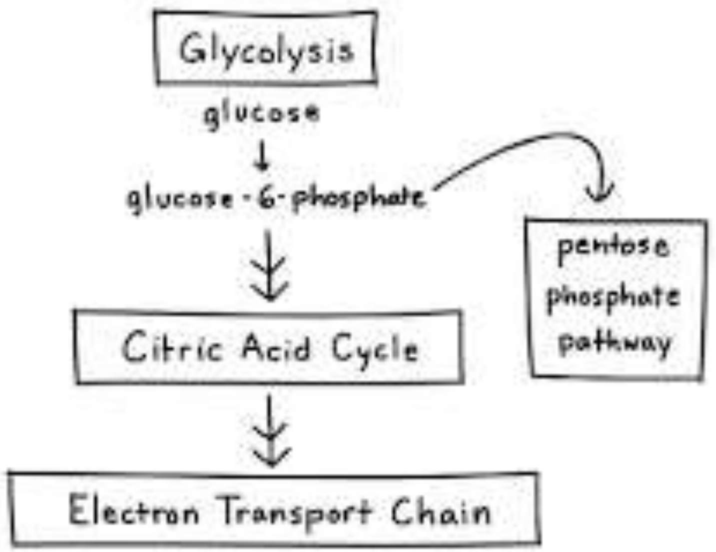


RELEASE OF ENERGY FROM GLUCOSE BY THE PENTOSE PHOSPHATE PATHWAY

- A second important mechanism for the breakdown and oxidation of glucose is called the **pentose phosphate pathway** (or phosphogluconate pathway), which is responsible for as much as 30 percent of the glucose breakdown in the liver and even more than this in fat cells.

Pentose phosphate pathway is important because:

- It can provide energy independently of all the enzymes of the citric acid cycle and therefore is an alternative pathway for energy metabolism when certain enzymatic abnormalities occur in cells.
- It has a special capacity for providing energy to multiple cellular synthetic processes.



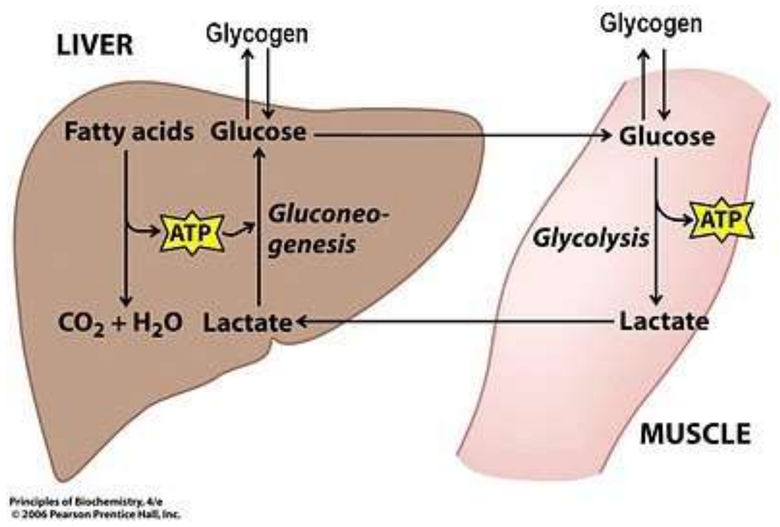
RELEASE OF ENERGY FROM GLUCOSE BY THE PENTOSE PHOSPHATE PATHWAY

- This is another way in which energy in the glucose molecule is used other than for the formation of ATP—in this instance, *for the formation and storage of fat in the body*.
- When the glycolytic pathway for using glucose becomes slowed because of cellular inactivity, the pentose phosphate pathway remains operative (mainly in the liver) to break down any excess glucose that continues to be transported into the cells, and NADPH becomes abundant to help convert acetyl-CoA -derived from glucose- into long fatty acid chains.

GLUCOSE CONVERSION TO GLYCOGEN OR FAT

- When glucose is not immediately required for energy, the extra glucose that continually enters the cells is either stored as glycogen or converted into fat.
- Glucose is stored as glycogen until the cells have stored as much glycogen as they can (an amount sufficient to supply the energy needs of the body for only 12 to 24 hours).
- When the glycogen-storing cells (primarily liver and muscle cells) approach saturation with glycogen, the additional glucose is converted into fat in liver and fat cells and is stored as fat in the fat cells.

FORMATION OF CARBOHYDRATES FROM PROTEINS AND FATS (GLUCONEOGENESIS)



Gluconeogenesis: Formation of glucose from **amino acid** and **glycerol** portion of fat.

Gluconeogenesis is important in:

Preventing reduction in the blood glucose concentration during fasting.

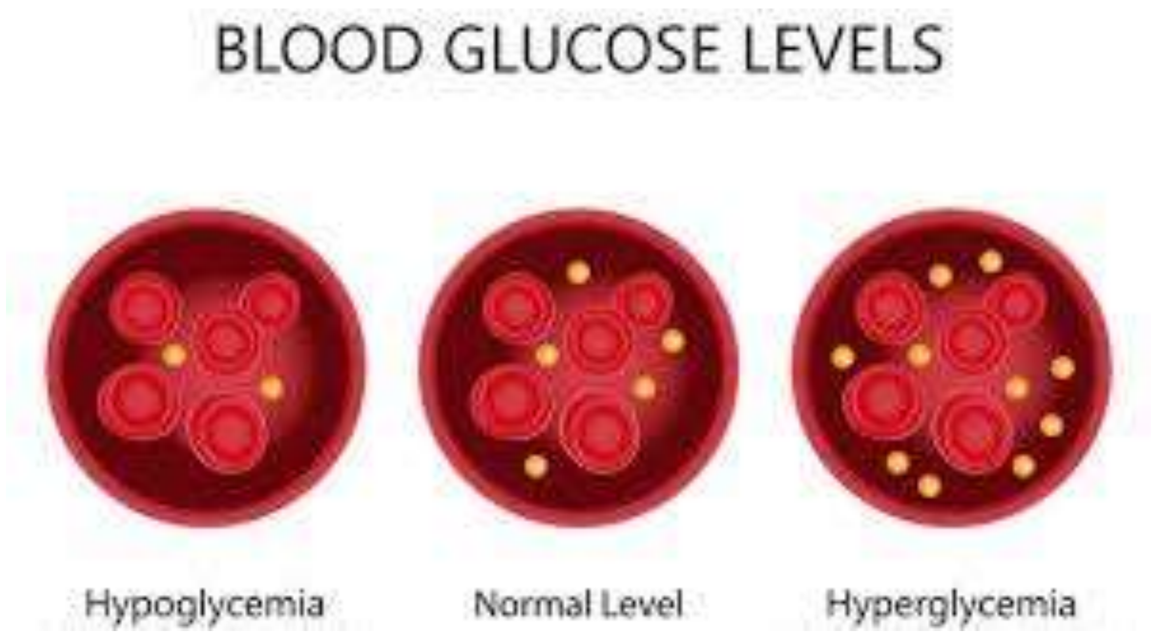
REGULATION OF GLUCONEOGENESIS

The basic stimuli that increase the rate of gluconeogenesis

1- Decreased carbohydrates in the cells.

2- Decreased blood sugar.

- Reduction of carbohydrates can directly reverse many of the glycolytic and phosphogluconate reactions, thus allowing the conversion of deaminated amino acids and glycerol into carbohydrates. Under the regulation of the *cortisol* hormone.

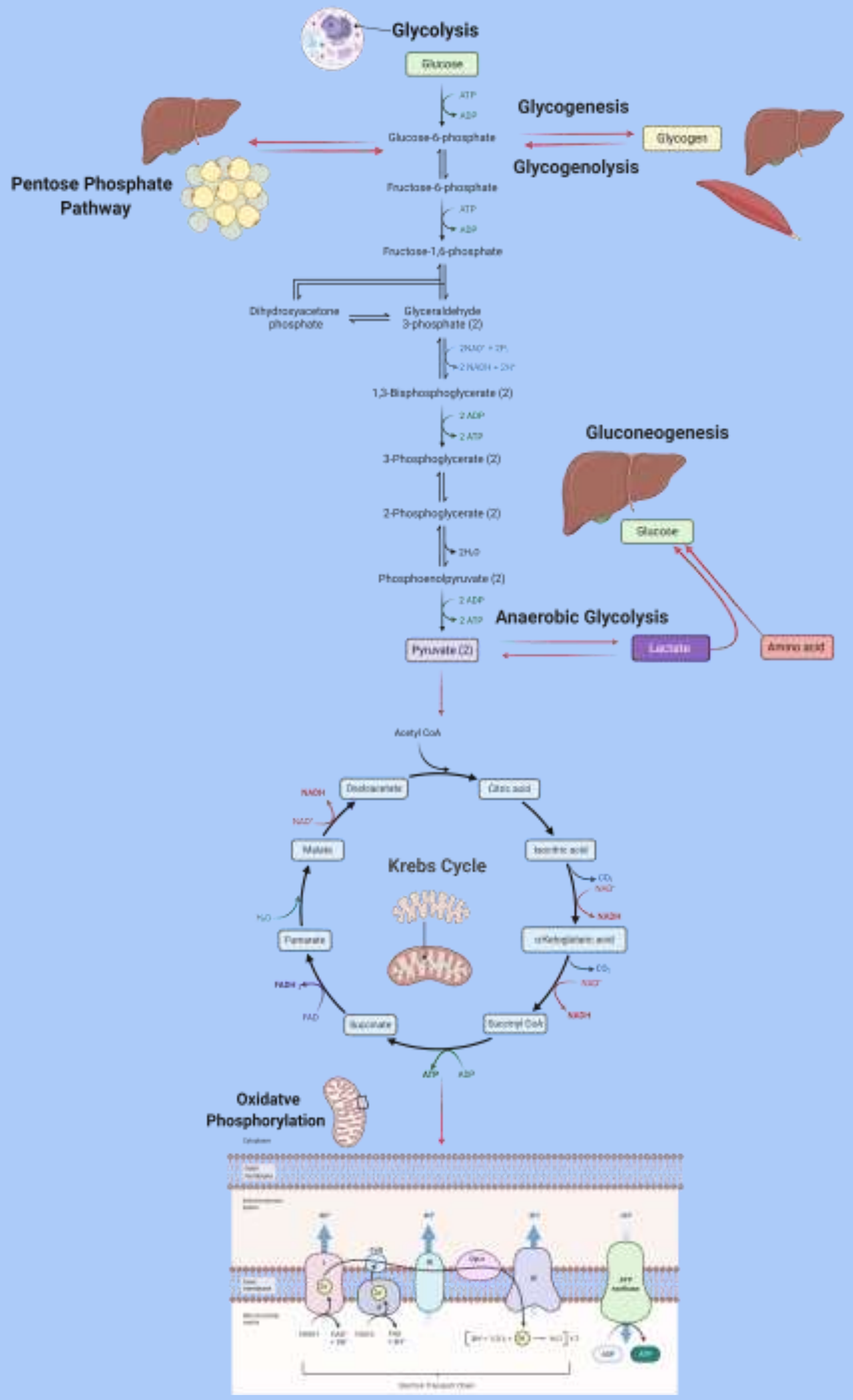


BLOOD GLUCOSE

- The normal blood glucose concentration in fasted (3 to 4 hours) is about 90 mg/dl. After a meal containing large amounts of carbohydrates, this level sires above 140 mg/dl unless the person has diabetes mellitus.
- The regulation of blood glucose concentration is intimately related to the pancreatic hormones insulin and glucagon.

MIND MAP 2

Summary of glucose metabolism pathways



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