11 Mitochondria

The ***mitochondria*** are *thread-like or granular cytoplasmic organelles* (Gr.***mito*** = thread, ***chondrion*** = granule). They contain many enzymes and coenzymes which are responsible for energy metabolism. They are described as the ***power plants*** or ***power houses*** of cells. The mitochondria play main roles in ***cellular respiration*** and ***energy production.***

The mitochondria were first observed by ***Flemming*** and ***Kolliker*** in 1882. These organelles were first called ***bioblasts*** by ***Altmann.*** Later, the term ***mitochondria*** was introduced by ***Benda*** in 1898.

Mitochondria are found both in plant and animal cells. But they are absent from ***prokaryotes.***

The mitochondria may be ***filamentous*** or ***granular*** in shape. The shape of mitochondria may change from one to another depending upon the physiological conditions of the cell. They may be rod-shaped, club-shaped, ring-shaped, rounded or vesicular.

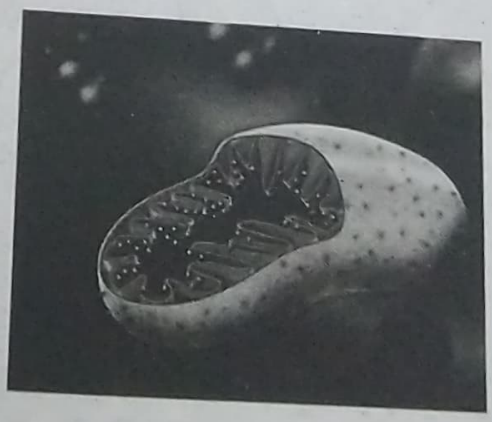

Fig.11.1 : Mitochondria.

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The size of the mitochondria is highly variable. In most cells, their length varies from 3 to 10 microns and their width from 0.2 to 1.0 micron. The smallest mitochondrion is seen in yeast. The largest mitochondria are found in the ***oocytes*** of amphibia.

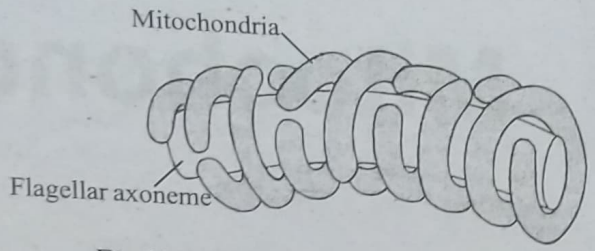

Fig.11.2: Mitochondria in sperm tail.

The number is particularly related to the functional state of the cell. If the metabolic activity is high, the number of mitochondria is also high. A small number indicates cells of low metabolic activity. Thus, they are found to be more abundant in liver and kidney cells. The giant *Amoeba* ***(Chaos chaos)*** contains 50,000 mitochondria whereas the egg of sea urchin contains 1,40,000-1,50,000 mitochondria.

In most cells, the mitochondria are distributed uniformly throughout the cytoplasm. But in some cases, they are aggregated around the nucleus. In *Paramecium*, they are located just beneath the surface of the cell. In the cells of ***kidney tubules,*** they occur in the folds of basal regions near plasma membrane. In ***neurons,*** they are located in the transmitting region of impulse. During cell-division, they are concentrated around the spindle. Generally, they are concentrated in the region of ***higher activity.***

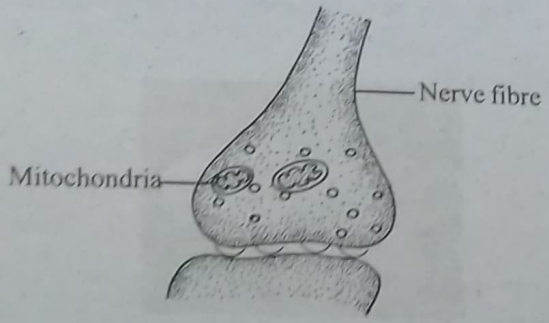

Fig.11.3: Mitochondria(in neurons).

The mitochondria are covered by two ***unit membranes,*** namely an ***outer*** and an ***inner mitochondrial membranes,*** each measuring about 60A° in thickness. The two membranes are separated by a space of 80 to 100A°. The space between the outer and inner mitochondrial membranes is called ***outer chamber*** or ***perimitochondrial space.*** This chamber is filled with a fluid of low viscosity and density.

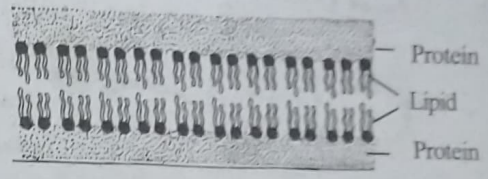

Fig.11.4: Unit membrane model.

The central space of the mitochondria is called the ***inner chamber.*** The inner chamber is filled with ***mitochondrial matrix***. The matrix may contain filamentous materials or dense granules. The inner mitochondrial membrane produces ***finger-like*** projections known as ***cristae*** into the inner chamber.

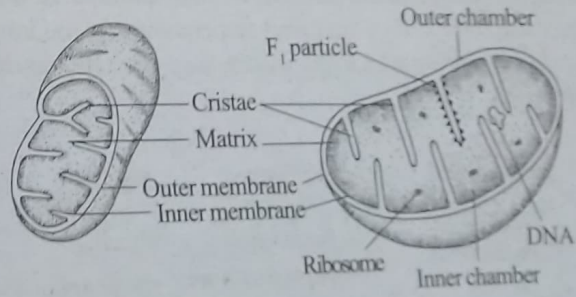

Fig.11.5: Structure of a typical mitochondrion.

The mitochondrial membrane contains small particles called ***elementary particles*** or ***F_1 particles*** or ***oxysomes*** or ***electron transport particles*** (ETP). The particles of the outer membrane are stalkless.

ETP particles of the inner membrane are stalked. Each stalked particle consists of a ***base,*** a ***stalk*** and a ***head***. They are regularly placed at a distance of 100A°.

Cristae are the ***finger-like*** projections found inside the mitochondria. They develop as inpushings projecting into the central space from the inner membrane. They form incomplete septa. They are present inside the inner chamber of mitochondria.

The cristae are covered with small particles called ***elementary particles*** or ***F_1 particles.*** Each F_1 particle has ***a base, a stalk*** and ***a head.*** The head is 80-100A° in diameter and the stalk is about 30-40A° in diameter.

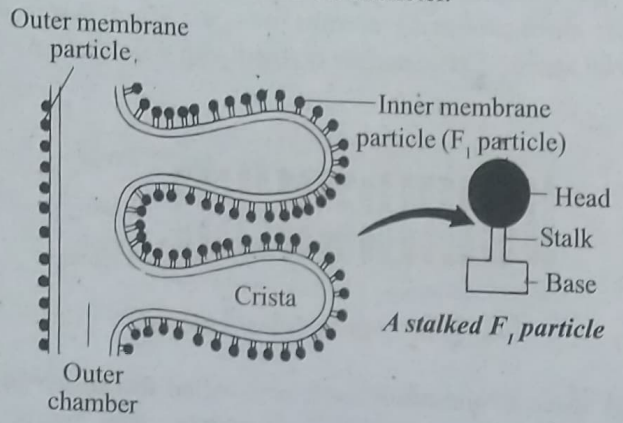

Fig.11.6: Cristae showing F_1 particles.

The cristae are variously arranged. In frogs, they are ***longitudinal*** and the cristae are arranged parallel to the long axis of mitochondria. In the adrenal cortex, the cristae are ***transverse*** as they are found perpendicular to the long axis. They are ***network-like*** in the WBC of man. In plant cells, the cristae are tubular and are called ***tubuli*** or ***microvilli.***

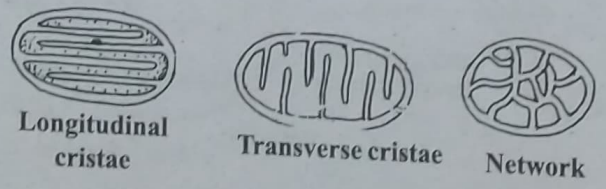

Fig.11.7: Mitochondria showing various arrangements of cristae.

The mitochondria contain 65 to 75% protein, 25 to 30% lipid, 0.5% RNA and small amount of DNA. The lipid part of mitochondria is composed of 90% phospholipids, 5% cholesterol and 5% free fatty acids. Small amount of sulphur, iron, copper and some vitamins are present. There are more than 70 enzymes and coenzymes in mitochondria. These enzymes are distributed in the matrix and in the membranes.

Mitochondria contain several vitamins and enzymes concerned with cellular respiration and energy productions.

Mitochondria contain one or more DNA called ***mitochondrial DNA (mDNA).*** It is ***circular*** in shape like bacterial DNA. It is double stranded. It can self-replicate. It can also produce RNAs like that of nuclear DNA. The mDNA is associated with ***cytoplasmic inheritance.***

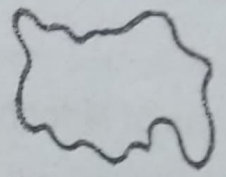

Fig.11.8: Mitochondrial DNA.

Origin of Mitochondria

The following hypotheses have been postulated for the origin of mitochondria :

1. Division of Pre-Existing Mitochondria: The new mitochondria originate by the division of the pre-existing mitochondria. Sometimes the mitochondria become elongated and broken into small pieces. Each piece forms a new mitochondrion in later stages.

2. Origin from the E.R. or Plasma membrane: The mitochondria may be formed from the growth and influx of membranes from the plasma membrane as well as from the endoplasmic reticulum.

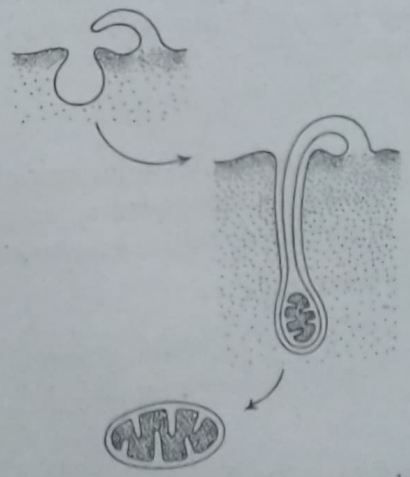

Fig.11.9: Origin of mitochondria from plasma membrane.

3. De Novo Origin: The mitochondria may be synthesized from non-mitochondrial fragment. But there is no direct evidence for this hypothesis.

4. Prokaryotic Origin: According to ***Altmann*** and ***Schnimper*** (1890), the mitochondria might have originated from prokaryotic cells like bacteria. The bacteria entered the cells as parasites. In the course of time, they maintained a ***symbiotic relationship*** with the eukaryotic cells. These form the mitochondria.

Functions of Mitochondria

Mitochondria perform the following functions:

1. *Thermogenesis*
2. *Protein synthesis*
3. *Synthesis of steroid hormones*
4. *Urea cycle*
5. *Calcium accumulation*
6. *Energy supply*
7. *Cellular respiration*

1. Thermogenesis

In young mammals and hibernating mammals such as bats, there is a special tissue in the chest region. It is called ***brown fat.*** It consists of extensive vascularization and numerous mitochondria. It functions as an ***automatic furnace*** and generates enormous heat. Here mitochondria are concerned with the release of heat energy rather than synthesizing ATP.

2. Protein Synthesis

Mitochondria contain DNA. About 5 to 10% of proteins of mitochondria are synthesized by the mitochondrial genes. Mitochondria synthesize sub-units of ***ATPase,*** portions of ***reductase*** and three sub-units of ***cytochrome oxidase.***

3. Synthesis of Steroid Hormones

The early steps in the conversion of cholesterol to steroid hormones in the adrenal cortex, are catalyzed by mitochondrial enzymes.

4. Urea Cycle

In urea cycle, urea is synthesized. The first step of the urea cycle, that is the conversion of ***ornithine*** to ***citrulline*** occurs in the mitochondria.

5. Calcium Accumulation

One of the important functions of mitochondria is the accumulation of ***cations,*** such as calcium. Calcium can be accumulated in mitochondria several hundred times than the normal values. Phosphate can also enter along with calcium. This process usually occurs in the ***osteoblast*** during the formation of bone.

6. Energy Supply

Mitochondria are the energy plants of the cell. Mitochondria synthesize the energy rich compound, ATP. It is stored inside the mitochondria. When a site is in need of energy, mitochondria get collected around the site. The mitochondrial membrane contracts and squeezes out ATPs. Mitochondria are found in high concentrations at the sites of active transport where large amount of energy is needed. This happens in kidney cells.

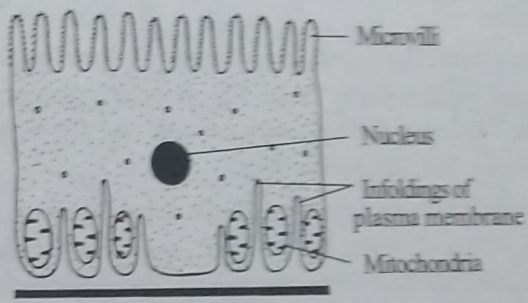

Fig.11.10: Mitochondria get collected in the region of active transport in a kidney cell.

7. Cell Respiration

Mitochondria are the ***respiratory centres*** of the cell. They bring about the oxidation of the various food stuffs such as carbohydrates, fats and proteins. During oxidation, the food stuffs are degraded to CO_2 and water with the release of energy. This energy is utilized by the mitochondria for the synthesis of energy rich compound called ***ATP***. As mitochondrion synthesizes the energy rich compounds, it is called the ***power house*** of the cell.

The cell respiration involves the following steps:

a. Glycolysis
b. Oxidative decarboxylation
c. Krebs' cycle
d. Electron transport system
e. Oxidative phosphorylation

a. Glycolysis: Glycolysis occurs inside the cytoplasm but outside the mitochondria. Mitochondrion has nothing to do with glycolysis. Glycolysis does not require oxygen and hence it is an ***anaerobic process.***

Glycolysis is a series of enzymatic reactions which convert ***glucose*** into ***pyruvic acid.*** The various steps involved in glycolysis were worked out by ***Embden*** and ***Meyerhof*** and hence it is also called ***Embden- Meyerhof pathway.***

During glycolysis, two hydrogen pairs are released. The hydrogen pairs enter the mitochondria and are processed by the electron transport system for the synthesis of ATP.

b. Oxidative Decarboxylation: The pyruvic acid produced during glycolysis enters the mitochondria. It is degraded to ***acetyl CoA*** by oxidation and decarboxylation. During ***oxidation,*** a pair of hydrogens (2H) is removed and during decarboxylation a CO_2 is removed. The H enters the electron transport system and is oxidised there.

c. Krebs' Cycle: The degradation of acetyl CoA into oxaloacetic acid through a series of steps is called ***Krebs' cycle.*** It is an aerobic process occurring inside the mitochondria. It releases four hydrogen pairs and one ATP molecule. The hydrogen pairs enter the electron transport system.

d. Electron Transport System: The hydrogen pairs released in glycolysis, oxidative decarboxylation and Krebs' cycle are oxidized in the electron transport system to produce H_2O with the release of ATP. The enzymes for electron transport system reside in the mitochondrial membrane.

e. Oxidative phosphorylation: The oxidative phosphorylation takes place in ETP particles in the mitochondrial membrane. The ETP particles contain cytochromes b, c, a and a_3, FAD and ubiquinone. All these compounds together constitute an ***electron transport system.*** During the oxidative phosphorylation, $NADH_2$ generated in glycolysis, Krebs' Cycle and oxidative decarboxylation is oxidized to produce ATPs with the release of H_2O. Hydrogen ions get oxidized by ½ O_2 into H_2O. Therefore, it is known as ***terminal oxidation.***

Oxidative Decarboxylation

It is a process of oxidation where pyruvic acid is converted into ***acetyl co-enzyme A (Acetyl Co-A)***. Pyruvic acid is formed from glucose through glycolysis. Glycolysis occurs inside the cytoplasm. The pyruvic acid produced in the cytoplasm enters the elementary particles located on the outer membrane of the mitochondria. These particles contain a complex enzyme called ***pyruvic acid dehydrogenase.*** With the help of this enzyme, pyruvic acid undergoes ***decarboxylation*** and ***oxidation.***

During decarboxylation CO_2 is removed and during oxidation two hydrogen atoms are removed from pyruvic acid. As a result, pyruvic acid is converted into ***acetyl CoA.***

$$\text{Pyruvic acid} + \text{CoA} \longrightarrow \text{Acetyl CoA} + CO_2 + H_2$$

During this process, two hydrogen atoms are released. The two hydrogen atoms are accepted by NAD and the NAD becomes reduced to $NADH_2$

$$\text{NAD} + H_2 \longrightarrow NADH_2$$

The $NADH_2$ enters the electron transport system and it is oxidized there to produce ATP.

Krebs' Cycle

The oxidation of pyruvic acid into CO_2 and water is called ***Krebs' cycle.*** This cycle is also called ***citric acid cycle,*** because the cycle begins with the formation of citric acid.

The citric acid is a carboxylic acid containing three COOH groups. Hence, this cycle is also called ***tricarboxylic acid cycle***. This cycle was first described by ***Krebs*** in 1936. This cycle occurs only in the presence of oxygen. Hence, it is an ***aerobic process.*** Krebs' cycle takes place mainly in the mitochondria. It involves the following steps:

1. *Formation of citric acid*
2. *Dehydration*
3. *Hydration*
4. *Dehydrogenation I*
5. *Decarboxylation*
6. *Oxidative-decarboxylation*
7. *Oxidation*
8. *Hydration*
9. *Dehydrogenation II*

1. Formation of citric acid: The acetyl-CoA combines with oxaloacetic acid to form citric acid. It contains 6 carbon atoms. This reaction is catalyzed by an enzyme called ***citric acid synthetase.***

2. Dehydration: The citric acid undergoes dehydration and forms ***cis-aconitic acid.*** This reaction is catalyzed by the enzyme ***aconitase.***

3. Hydration: The aconitic acid is hydrated and it forms ***isocitric acid.*** This reaction is catalyzed by the enzyme aconitase.

4. Dehydrogenation I: The isocitric acid undergoes dehydrogenation in the presence of ***isocitric acid dehydrogenase*** to form ***oxalosuccinic acid.*** In this reaction, two hydrogen atoms are released. They are accepted by NAD^+ to form NADH.

$$NAD^+ + 2H \longrightarrow NADH + H^+$$

5. Decarboxylation: The oxalosuccinic acid undergoes decarboxylation to form ***ketoglutaric acid.*** This reaction is catalyzed by ***decarboxylase***. In this reaction, one CO_2 is eliminated. Hence the ketoglutaric acid has only 5 carbon atoms.

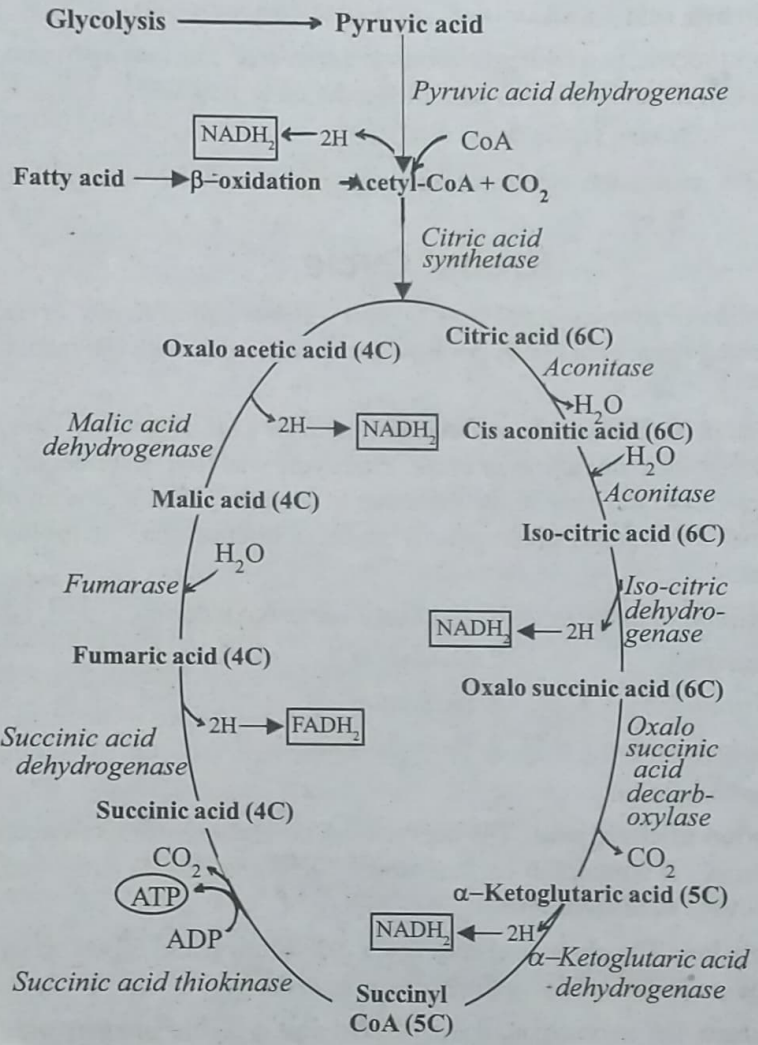

Fig.11.11: Krebs' cycle.

6. Oxidative Decarboxylation: During oxidative decarboxylation, a-keto glutaric acid is converted into ***succinyl CoA.*** This reaction is catalyzed by ***a - ketoglutaric acid dehydrogenase.*** Two hydrogen atoms are released and they are transferred to NAD. The NAD is converted into NADH.

In the next step, the succinyl CoA is decarboxylated to succinic acid. This step is catalyzed by ***succinic acid thiokinase.*** CoA is liberated.

7. Oxidation: The succinic acid is oxidized to ***fumaric acid*** by the removal of two hydrogen atoms. This reaction is catalyzed by ***succinic acid dehydrogenase.*** The hydrogen atoms are accepted by FAD and it forms $FADH_2$.

8. Hydration: The fumaric acid then undergoes hydration to form ***malic acid.*** This reaction is catalyzed by ***fumarase.***

9. Dehydrogenation II : It is the final step in Krebs' cycle. Oxaloacetic acid is regenerated from malic acid by a process of dehydrogenation. This reaction is catalyzed by ***malic acid dehydrogenase*** in the presence of NAD. The 2 hydrogens removed are accepted by NAD to become NADH.

The oxaloacetic acid formed in the above reaction condenses with the acetyl CoA to form citric acid again and thus the cycle is repeated.

Electron Transport System or Respiratory Chain

It is a system of enzymes and coenzymes, where the reduced coenzymes like FADH, NADH are oxidized (FAD, NAD) to release energy. The energy released in electron transport system is used for the synthesis of ATP. The synthesis of ATP is called ***oxidative phosphorylation.*** The electron transport system occurs in the inner membrane of the mitochondria. The electron transport system contains mainly six components arranged in the following sequence:

1. *NAD*
2. *FAD*
3. *NADH*
4. *FADH*
5. *Cytochrome a and*
6. *Cytochrome a_3*

The oxidation of FADH and NADH occurs by the following steps:

1. The initiation of electron transport system is the removal of hydrogen from the substrate (NADH or FADH) by the enzyme dehydrogenase. The hydrogen atom becomes ionized into protons (+) and electrons (-).

$$2H \longrightarrow 2H^+ \text{ (Proton)} + 2e^- \text{ (Electron)}$$

2. The hydrogen ion reduces the coenzyme NAD.

$$NAD + 2H^+ \longrightarrow NADH + H^+$$

3. The NADH is oxidized into NAD by transferring its hydrogen ion to FAD which acts as the hydrogen carrier.

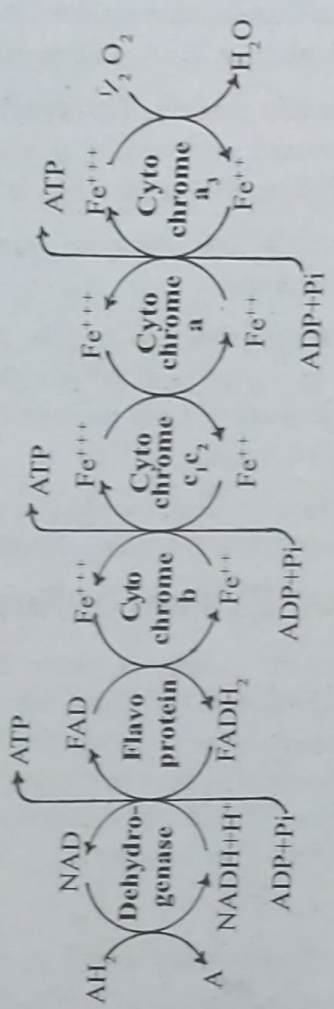

Fig.11.12: Electron transport system.

4. From FAD each hydrogen ion is discharged in the cell fluid and electrons are passed on to the cytochromes b,c,a and a_3.

5. From the cytochromes the electrons are given to the enzyme ***cytochrome oxidase.***

6. The cytochrome oxidase finally discharges electrons to oxygen. This oxygen unites with hydrogen ions forming water.

Oxidative Phosphorylation

In the respiratory chain, when a cytochrome transfers the electrons to another cytochrome, enormous amount of energy is released. This energy is trapped by ADP molecule to form one molecule of ATP.

$$ADP + Pi + Energy \longrightarrow ATP$$

The process of ATP formation occurring during the oxidative reactions of Krebs' cycle is known as ***oxidative phosphorylation.***

$$C_6H_{12}O_6 + 6O_2 + 6H_2O + 38\,ADP + 38\,pi \xrightarrow[enzymes]{Respiratory} 6CO_2 + 12H_2O + 38ATP$$

The ATP molecules are the intracellular energy carriers, having a readily utilizable source of energy. With the release of energy they are converted back to ADP.

Synthesis of ATP in Krebs' Cycle

In Krebs' cycle, only one molecule of ATP is synthesized directly. It is produced when succinyl CoA is converted into succinic acid.

Synthesis of ATP in Electron Transport System

The ETS oxidizes the NADH and FADH released during glycolysis, oxidative decarboxylation and Krebs' cycle. The NADH and FADH molecules produced during the metabolism of a glucose molecule are as follows:

1. Glycolysis	NADH = 2
2. Oxidative decarboxylation	NADH = 1
3. Krebs' cycle	NADH = 4
	FADH = 1

When one molecule of NADH molecule is oxidised in ETS, 3 molecules of ATP are synthesized. Similarly, when one molecule of FADH is oxidized in ETS, 2 molecules of ATP are synthesized.

Energetics of Mitochondria

The metabolism of a glucose molecule releases 40 molecules of ATP. But glycolysis utilizes 2 molecules of ATP. So the total number of ATP molecules in glucose metabolism is 40-2=38. The synthesis of ATP is given as follows:

1. Glycolysis

1. *Glucose* ⟶ *Fructose 1,6 diphosphate* = 2 ATP
2. *Triose P* ⟶ *2,3-phosphoglyceric* = +2 ATP
   acid + 2DPNH

3. *2 Phosphopyruvic acid* ⟶ *2 Pyruvic acid* = *+2 ATP*
4. *2NADH* ⟶ *2NAD + H⁺* = *+6 ATP*

Total = *8 ATP*

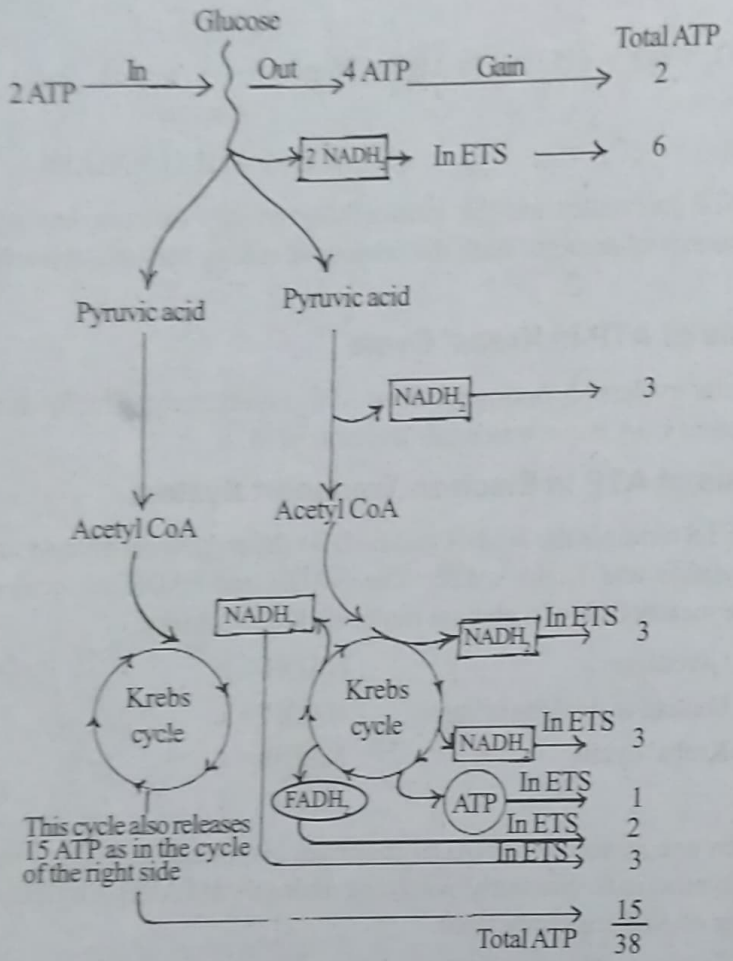

Fig.11.13 : Energy budget of a glucose molecule. One $NADH_2$ releases 3 ATP molecules; one $FADH_2$ releases 2ATP molecules.

2. Oxidative decarboxylation: 1 NADH = *3 ATP*

3. Krebs' cycle

1. *Oxidation of isocitric acid via NAD+* = *3 ATP*
   to oxalosuccinic acid
2. *Oxidation of ketoglutaric acid via NAD+* = *3 ATP*
   to succinyl CoA

3. *Oxidation of succinic acid via FAD to* = *2 ATP*
   fumaric acid
4. *Oxidation of malic acid via NAD+* = *3 ATP*
   to oxaloacetic acid
5. *Conversion of succinyl CoA to* = *1 ATP*
   succinic acid

Total ATP molecules produced for = *15 ATP*
*each **pyruvic acid***

Thus the oxidation of one pyruvic acid molecule yields 15 ATP molecules. Since two molecules of pyruvic acid are produced from each glucose molecule, the total number of ATP molecules produced during the oxidation of two molecules of pyruvic acid are 15 X 2 = 30.

Glycolysis yields 8 molecules of ATP. Thus the complete oxidation of one glucose molecule yields 30 + 8 = 38 molecules of ATP.