

Mitochondria Structure and the Intra-Mitochondrial ATP Formation Process

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Abstract: *There are two systems of energy formation in the body, namely anaerobic energy system and aerobic energy system. Anaerobic energy systems include ATP-PC (phosphagen) and anaerobic glycolysis (lactic acid). While the aerobic energy system includes the krebs cycle and the electron transport system. The process of the aerobic energy system (krebs cycle and electron transport system) is in the mitochondria and the anaerobic energy system (ATP-PC and LA) occurs outside the mitochondria, namely in sarcoplasm. Mitochondria are one of the cell organelles. The size of mitochondria is about 0.2-1 μm in diameter. The filamentous mitochondria vary in length up to 10 μm . The main role of mitochondria is as a cell energy plant that produces energy in the form of ATP. Energy produced in mitochondria through aerobic processes. Carbohydrate metabolism will end in mitochondria when pyruvic acid is transported and oxidized by O₂ to CO₂ and water. The mitochondrial structure consists of four main parts, namely the outer membrane (outer membrane), the inner membrane (inner membrane), the space between the membranes (inter membrane), and the matrix located on the inside of the membrane. The formation of ATP in the mitochondria results from the breakdown of glucose or fatty acids (glycerol) aerobically to pyruvic acid. There are two pathways for intra-mitochondrial ATP formation, namely the Krebs cycle and electron transport system. But before heading into the Krebs cycle and the electron transport system the initial stage of metabolism converts glucose to energy to synthesize ATP and pyruvic acid will take place through a process called glycolysis (Glycolysis). After pyruvic acid is formed from the glycolysis process, then it enters into mitochondria to the cellular respiration process which is divided into 3 main stages, namely Acetyl-CoA production, Acetyl-CoA oxidation process in the citric acid cycle (Citric-Acid Cycle) and Electron Transport Chain (Electron Chain Transfer / Oxidative Phosphorylation). In the aerobic formation process of Adenosine Triphosphate (ATP) in mitochondria 36 ATP is produced while the anaerobic process will only produce 2 ATP.*

Keywords: Atp-Pc, Mitochondria

1. Introduction

Every human being needs motion, because moving is an activity that is very important in everyday life. The importance of motion can be felt that every need we have in life always requires our physical to move so that the nature of healthy life is achieved. In carrying out daily activities, whatever form the body must require energy. Energy is the ability to do work. According to David R Lamb (1984), and Edward. L. Fox, et al. (1989) energy is the capacity to do a work / activity. Work / work is the result of multiplication of force and distance obtained. Therefore energy and work cannot be separated.

The body's energy needs will increase along with increasing body activity in exercise and exercise (Foss, 1998; Newssholme, 1993; Hickson, et al, 1884; Philips and Zuiraitis, 2003; Morgan, et al, 2003). The greatest energy is produced in mitochondria through an aerobic process (Guyton, 1999). With 36 ATP produced in the metabolic processes in mitochondria (intra-mitochondria), mitochondria are more often referred to as energy plants in the body (Ganong, 1999).

In line with the increasing energy needs of the body, which are caused by various human activities, it is necessary for us to discuss and explore more deeply the process of forming Adenosine Triphosphate (ATP) in our body. Especially the role of mitochondria, as the biggest energy producer in the body.

The supply of energy in the body can be fulfilled by the following systems: ATP-PC (phosphagen) system, anaerobic glycolysis system (lactic acid), and aerobic system (Joseph. H. and Aip S, 1996: 113). Likewise according to Fox (1984),

energy in the body is produced through 3 energy-forming systems namely the phosphagen system (ATP-PC), the glycolysis system, and the aerobic system (aerobic glycolysis, krebs cycle, and electron transport system). These three systems produce Adenosine Triphosphate (ATP) which the muscle needs to contract. As explained that there are two classifications of energy formation systems in the body and one in the two systems the process takes place within the mitochondria namely the aerobic energy system (krebs cycle and electron transport system), while the anaerobic energy system (ATP-PC and LA) processes occur outside mitochondria is sarcoplasm.

Based on the explanation above, it will be discussed in the next chapter, namely "Mitochondrial Structure and Intra-Mitochondrial ATP Formation Process".

2. Discussion

1) Mitochondria

Mitochondria are one of the cell organelles. Mitochondria appeared more than a million years ago when a bacterium, closely related to a proteobacteria, entered an eukaryotic cell. This endosymbiosis benefits both parties, both bacteria and eukaryotic cells. This symbiosis continues and now mitochondria are something that is essential for eukaryotic cells (Page & Holmes, 1998). For more details, below will be trapped about what mitochondria include:

- a) According to Fox and Bower (1993: 127) Mitochondria are units of cell units that are located in muscle cells that have a role as a place of processing of energy.
- b) In the research journal Suyanto Hadi (Professor of medical faculties at Diponegoro University, internal rheumatology specialist explains Mitochondrion (plural mitochondria: comes from English, mitochondrion,

Volume 7 Issue 9, September 2018

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mitochondria) which means part of the cell (compartment) or organelle where the system changes (conversion) energy in the form of ATP (adenosine triphosphate) molecules which are needed by various body cell activity activities (http://www.kalbefarma.com/cdk).

- c) Mitochondria are derived from the Greek word mito which means thread, and chondrion which means like granules (granules), can be interpreted as organelles that have DNA with a series of grains arranged like threads. (Explanation of Prof. Xavier Leverage at the 2nd Annual Scientific Meeting of Occupational Medicine Specialists (PERDOKI) February 19, 2005 at FKUI (http://www.kalbefarma.com).
- d) In his book Kus Irianto (2004) mitochondria is the place where respiratory cells occur and energy formation.

2) Mitochondrial structure

Anatomically mitochondria in skeletal muscle cells are located in the cytoplasm (Vander, 2001). Basically mitochondria are structures that can multiply themselves, which means that one mitochondria can form the second, third mitochondria and so on, this is needed by cells to increase the amount of ATP (Guyton, 1996).

The size and shape of mitochondria turns out to be different, some of which are only a few hundred millimicrons in diameter, and globular in shape, while others can reach 1 micron to 7 microns in diameter and form filaments (Guyton, 1996). Although mitochondrial morphology varies from cell to cell, each mitochondria basically has a structure that resembles a sausage. Mitochondria have an outer membrane and a deep and folded membrane forming a shelf called cristae. The space between the two membranes is called the intra-crista or inter membrane space and the space on the inner side of the inner membrane is called the matrix space (Ganong, 1999).

In the replication process, most proteins and lipids that have been formed in the cytoplasm will join in the mitochondria as they enlarge and then form new mitochondria (Guyton, 1996).

Mitochondria are also referred to as power plants in cells (Guyton, 1996). This means that without mitochondria, the cells are unable to tap the large amount of energy from food eaten and oxygen, and as a result the important functions of the cell will stop.

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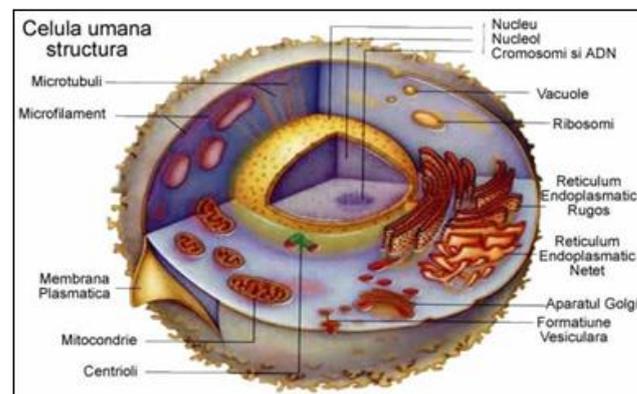


Figure 1: Cell Structure

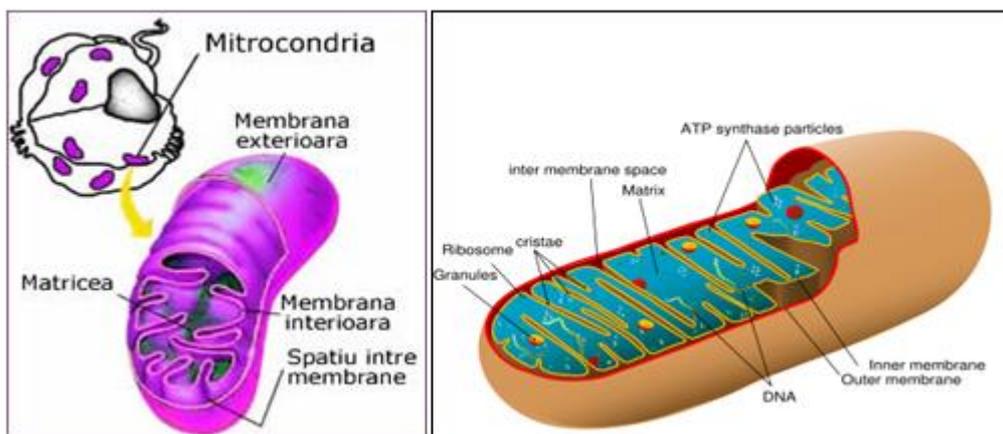


Figure 2: Mitochondrial structure

a) Outer membrane

The mitochondrial outer membrane contains enzymes related to biological oxidation, providing raw material for the reaction in mitochondria. The outer membrane contains a transport protein called porin. Porin forms relatively larger channels in the double layer of outer membrane lipids; so that the outer membrane can be considered as a filter that

allows the escape of 5 kDa or less ions or small molecules, including small proteins. These molecules are free to enter the space between the membranes, but most do not pass through an impermeable inner membrane. This means that in terms of the content of small molecules, in the space between the membranes is equivalent to the cytosol whereas in the matrix space is different. Proteins located on the outer

membrane include various enzymes involved in mitochondrial lipid biosynthesis and enzymes that convert lipid substrates into other forms to be further metabolized in the mitochondrial matrix.

b) Inner membrane

At this deep bed there is an enzyme that converts the products of carbohydrates, proteins and water located in the inner membrane of the mitochondria (Ganong, 1999). The matrix space and the space between the membrane and the outer membrane and inner membrane contain various enzymes.

c) Space between membranes

The space between the membranes is the space between the outer membrane and the inner membrane of the mitochondria. This space contains about 6% of the total mitochondrial protein and several enzymes that work using

ATP (adenosine triphosphate) which is passing through this space to phosphorylate other nucleotides.

d) Matrix

The matrix contains a number of enzymes found in the Krebs cycle (Tricarboxylat acyd Cycle, or TCA cycle) and sugar and water (Sheeler & Bianchi, 1996). Most (about 67%) mitochondrial protein is found in the matrix. The enzymes needed to process pyruvate, fatty acids and to run the tricarboxylic acid cycle are found in this matrix.

e) Respiration chain

The chain of respiration and inhibitors can be seen in the table below, which is also a summary of the mitochondrial metabolic pathways. All of these complexes are in the inner membrane and they can be reached by the substrate both on the membrane and on the matrix. It is also known that various respiration chain inhibitors and their clinical effects can be considered as initial knowledge of mitochondrial medicine.

Table 1: Complex mitochondrial respiration enzymes, subunits synthesized by mitochondria and respiration chain inhibitors

Activity complex	Enzyme	Number of Polypeptides (synthesized by mitochondria)	Redox Center	Inhibitor
I	NADH-coQ reductase	>45 [7;ND1 -4,4L,5,6]	8FeS (3pusat)	Retenon Pieridine Amytal
II	Succinate-coQ reductase	4[tidak ada]	2C2Cytochrome b Cytochrome c1 2 FeS (1pusat)	Malonate
III	CoQH2 Cytochrome c	7-8 [1;cytochrome b]	Cytochrome a Cytochrome a3	Antimycin A
IV	Reductase Cytochrome c	10 [3; CO I, COII, COIII]	2 Cu	CO CN
V	Oxidase ATP syntase	10-16 [2;ATP6, ATP8]	Tidak relevan	Oligomycin

Description: NADH: nicotinamide adenine dinucleotide; CoQ: coenzyme Q; ATP: adenosine triphosphate

3) Mitochondrial Function

In general, mitochondria function is as an energy generator in cells. Oxidative enzymes in the inner membrane and citric acid cycle enzymes in the mitochondrial matrix together oxidize acetyl residues to form carbon dioxide and water. Energy released from this oxidation will be used to synthesize very high-energy ingredients, namely adenosine triphosphate (ATP). This ATP, then, is removed from mitochondria into the cytosol for use by cells as a source of energy for various activities (Guyton, 1996; Murray et al., 1997; Wallace, 1999).

4) Intra-Mitochondrial ATP Formation Process

In general, the formation of ATP in the mitochondria results from the breakdown of glucose or fatty acids (glyserol) aerobically to pyruvic acid until the final process is in the form of transport electrons (figure 5). Before going any further in the discussion it is necessary to know about the following chemical terms: Acetyl, Acetyl-CoA, NAD +, NADH, FAD +, and FADH2. Acetyl is a collection of two carbon molecules. For example in the breakdown of carbohydrates, pyruvic acid loses CO2 to acetyl which combines with co-enzyme A to form acetyl-CoA before entering the krebs cycle. Likewise, in fatty acid metabolism, two acetyl groups are needed in the beta-oxidation process and then enter the krebs cycle. Meanwhile, the metabolism of amino acids is even more complex because only a few of the amino acid breakdown acids can enter the krebs cycle. NAD +, (nicotinamide adenine dinucleotide) and FAD + (flavin adenine dinucleotide) are hydrogen receptors and transport them. Whereas NADH and FADH were derived from NAD + and FAD + which functioned to carry electrons to the electron transport system (Fox and Bowers, 1993).

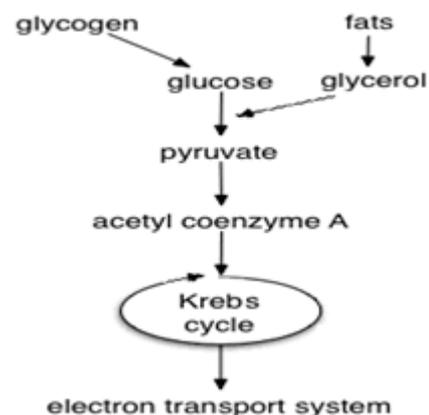


Figure 4: Metabolic Process in Mitochondria

Basically there are several reactions of aerobic systems that occur in mitochondria, namely: (1) Aerobic glycolysis, (2) The Krebs Cycle, and (3) Electron Transport System (ETS) (Foss, 1998; Fox and Bowers, 1993; Armstrong, 1995; Harper, 1996; Guyton, 1999; Ganong, 1999)

a) Aerobic Glycolysis

The first reaction is the breakdown of glycogen to CO2 and H2O is called glycolysis. Basically, there is only one difference between the process of anaerobic glycolysis with aerobics, ie in aerobic glycolysis there is no accumulation of lactic acid (Coyle, 1984). In other words, the presence of oxygen inhibits the formation of lactic acid, but no ATP re-formation process occurs. In glycolysis, the result is two molecules of pyruvic acid, two ATP and 4H. Briefly can be written in the following chemical formula:

Glucose + 2 ADP + 2P₀₄ → 2 Pyruvic acid + 2 ATP + 2ATP and 4H

Pyruvic acid that is formed is then converted into acetyl CoA (acetyl CoA) molecules. In this conversion process, ATP is not formed, but the 4 hydrogen atoms released will form 6 ATP molecules if the four hydrogen atoms are oxidized, as will be discussed in the citric acid cycle or the Krebs cycle.

b) Cycle of Citric Acid or Krebs Cycle

The next stage in the degradation of glucose molecules in mitochondria is called the citric acid cycle (also referred to as the tricarboxylic acid cycle or the krebs cycle) (Foss, 1998; Fox and Bowers, 1993; Armstrong, 1995; Harper, 1996; Guyton, 1999; Ganong, 1999). Called the citric acid cycle because the first compound formed is citric acid. Called the tricarboxylic acid cycle (-COOH) because almost in the beginning the cycle of the compound is composed of tricarboxylic acid. Called the krebs cycle, because the one who found was Mr. Hans Krebs. The main function of the Krebs cycle is the final oxidation pathway for Carbohydrates, Lipids and Proteins. Carbohydrates, fats and proteins will all be metabolized to acetyl-CoA.

So if we consume carbohydrates in the mouth it will be digested so that maltose (by ptyalin) and the end result is glucose in the duodenum it will enter the cell experiencing glycolysis, which eventually results in pyruvic acid when the atmosphere of the cytoplasm where pyruvic acid is aerobic, so mitochondria sure to be full of oxygen, pyruvic acid will continue the process of conversion to acetyl Co.A in the Pre-Cycle Krebs (oxidative decarboxylation). as well as lipids which then become fatty acids and glycerol. Fatty acids are broken down as acetyl Co.A, experiencing a process called lipolysis. The protein is converted to aminocytic acid and then becomes acetyl Co.A at the beginning of the krebs cycle.

The krebs cycle reaction in addition to having the main function, there are also two functions that are almost similar to the main function. The first function is the conservation of additional energy formed in the three stages of the reaction section. The three reactions are the change from succinyl-CoA to succinic to form ATP, the change from succinate to

fumarate which produces FADH₂, and the oxidation of malate to oxaloacetate which produces NADH. The second function is regeneration that produces oxaloacetate.

From the diagram below, the very strategic formation of Acetyl Coa has a major role in gluconeogenesis (glycogen formation), transamination, deamination (decomposition of proteins / amino groups) and lipogenesis (fat formation)

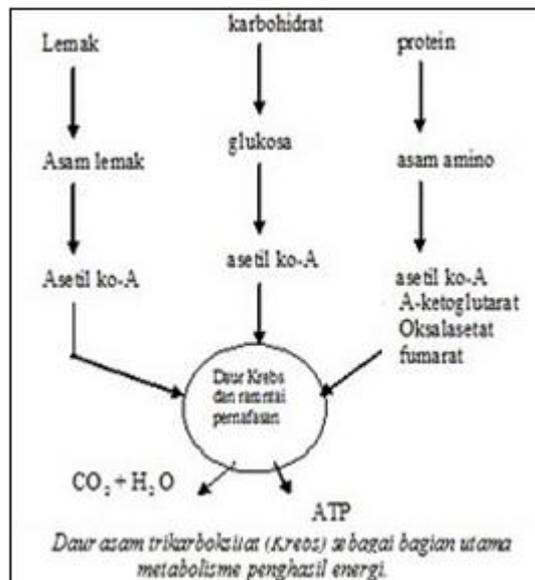
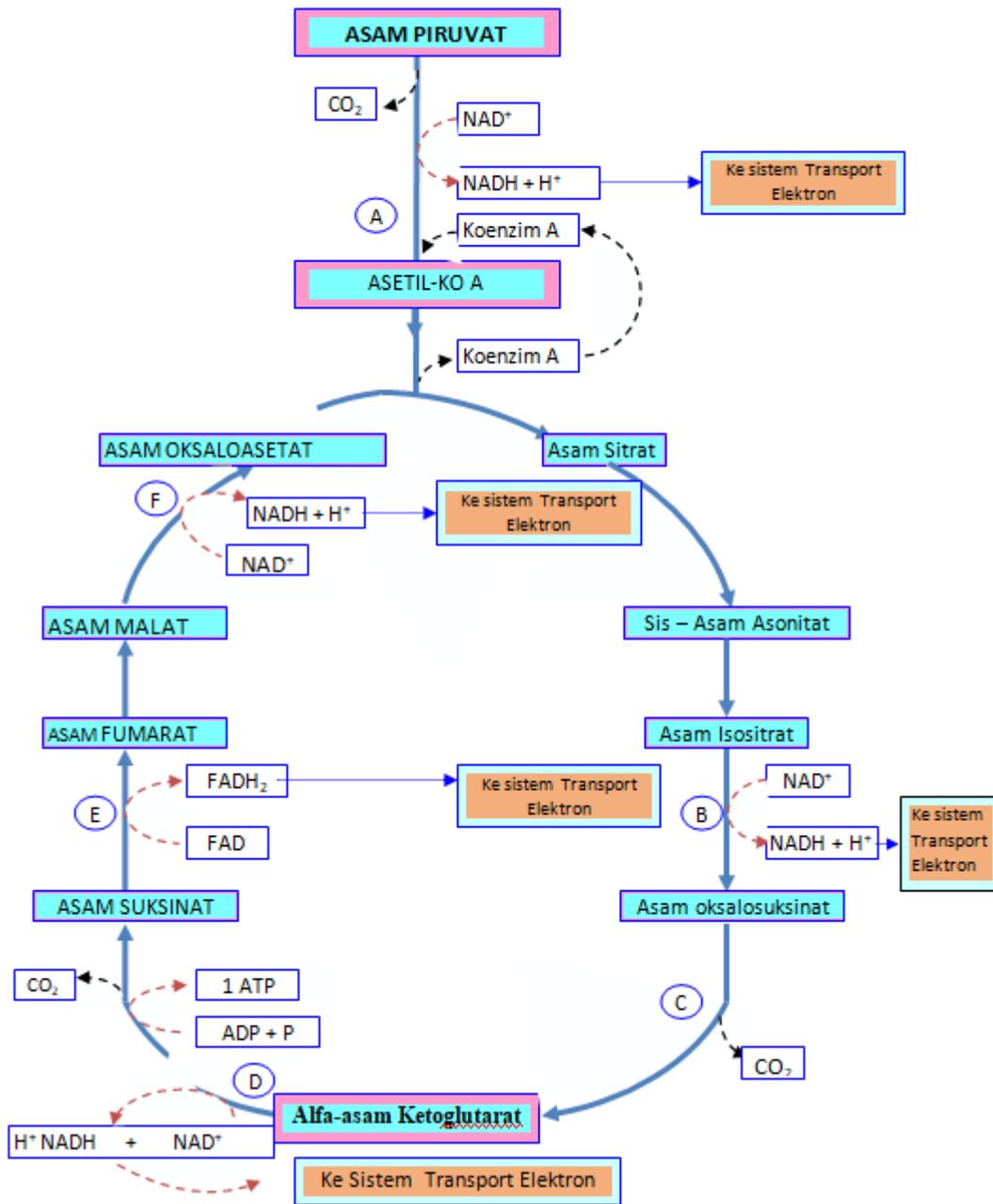


Figure 5: End Path of Oxidation of Carbohydrates, Lipids and Proteins

In short, the Krebs cycle consists of eight stages of reaction catalyzed by enzymes. The reaction starts from condensation of acetyl-CoA with oxaloacetate to citric acid. The group of acetate compounds is then degraded to form two molecules of carbon dioxide. The cycle includes four oxidation reactions, which results in three stages of NADH and one stage of FADH. One ATP molecule will be formed through substrate level phosphorylation. Finally, oxaloacetate is reshaped. Oxaloacetate will play a role in capturing other acetyl-CoA, so the Krebs Cycle will always take place. The figure below shows the sequence of reactions of citric acid / krebs cycle.

Krebs Cycle



The explanation of the series of chemical processes above is as follows:

Ecahan Solving pyruvic acid to CO_2 and H_2O in mitochondria using O_2 .

- 1) Each pyruvic acid molecule loses a carbon atom and 2 oxygen atoms as CO_2 . At the same time each pyruvate acid molecule is oxidized in the presence of NAD^+ , and loses 2 electrons and 2 H. electron electrons are very important for ATP production. The two carbon molecules remaining after each pyruvate acid molecule loses CO_2 , electrons and hydrogen ions are called acetyl groups and then join another group called "Co enzyme A (Co A) to form acetyl Co A. (reaction" A "). Each acetyl Co A molecule then enters the cycle circuit reaction called "kreb cycle".
- 2) In the picture it can be seen that Acetyl Co A joins oxaloacetic acid and loses the molecule of coenzyme A. The results of the reaction are the molecules of citric acid. Citric acid is then converted to sis-acetic acid and then converted to isocitric acid. E
- 3) Isocitric Acid "B" reaction (with the help of electron transport, NAD^+) to oxalosuccinic acid.
- 4) In the "C" reaction oxalosuccinic acid releases the CO_2 molecule and becomes alpha-ketoglutaric acid.
- 5) In the "D" reaction carbon is released again when the alpha-ketoglutaric acid oxidizes with NAD^+ and loses CO_2 when producing 1 ATP.

- 6) In the "E" reaction the electron carrier is FAD (Flavin Adenine Denukleotide)
- 7) In the "F" reaction, oxaloacetic acid regenerates and can start with a new one.
- 8) To produce a greater amount of ATP through aerobic breakdown of pyruvic acid, electrons and hydrogen ions are released to NAD and FAD electron devices and must be transported to oxygen via the electron transport system (Armstrong, 1995; Guyton, 1999; Ganong, 1999).
- 9) According to Armstrong, 1995; Guyton, 1999; and Ganong, 1999, the explanation of the above series of reactions as follows:
- 10) In the hydrogen ion electron transport system and electrons are transferred from one compound to the next compound.
- 11) In mitochondria chemical energy is released in 3 steps (A, D, G) to provide energy in ATP formation from ADP and phosphate groups.
- 12) The loss of electrons (oxidation) when subjected to various compounds is responsible for binding phosphate (phosphorylation) to ADP to form ATP in mitochondria associated with the sequential molecular oxidation of two in the electron transport system known as "oxidation phosphorylation". This process provides the greatest amount of ATP for muscle contraction.

Aksi The reaction "A" occurs with oxidation of NADH and in the reaction "B" is Flavoprotein H₂ which experiences a reaction in A, is now undergoing oxidation. From here until step H only electrons are transferred between compounds, while 2 hydrogen ions (H⁺) that have been bound to flavoprotein H₂ now enter the solution and can be used again in H, in oxidation-reduction reactions.

Igen Oxygen from the blood receives 2 electrons from the compound "G" (cytochrome oxidase) and joins the solution of Hydrogen ion (H⁺) to form water (H₂O).

Based on the description of the intra-mitochondrial aerobic ATP formation process above, it can be simplified about the amount of ATP produced by each Reaksi, as follows:

Table 2: Intra-mitochondrial aerobic ATP results

Step	coenzyme yield	ATP yield	Source of ATP
Glycolysis preparatory phase		-2	Phosphorylation of glucose and fructose 6-phosphate uses two ATP from the cytoplasm.
Glycolysis pay-off phase		4	Substrate-level phosphorylation
	2 NADH	4	Oxidative phosphorylation. Only 2 ATP per NADH since the coenzyme must feed into the electron transport chain from the cytoplasm rather than the mitochondrial matrix.
Oxidative	2 NADH	6	Oxidative phosphorylation

Krebs cycle	decarboxylation	I		
			2	Substrate-level phosphorylation
		6 NADH	18	Oxidative phosphorylation
	2 FADH ₂	4	Oxidative phosphorylation	

3. Conclusion

To maintain its survival, humans must move, which is an activity that is very important in daily life. In carrying out daily activities, whatever form the body must require energy. Anaerobically the process occurs in the cytosol, the energy system that works is the ATP-PC energy system, and Alactid Glycolytic.

Mitochondria are one of the cell organelles. mitochondria basically have a sausage-like structure, which has an outer membrane (outer membrane) and inner membrane (inner membrane) and which folds into a shelf called a cristae. The space between the two membranes is called intra crista or inter membrane space and the space contained inside the inner membrane is called matrix space.

The function of mitochondria is to produce energy (ATP), which can later be used to carry out activities by humans. Aerobic ATP formation in mitochondria will be obtained through three chemical processes, namely (1) Aerobic glycolysis, (2) The Krebs Cycle, and (3) Electron Transport System (ETS). While the highest amount of ATP produced comes from the aerobic energy system that occurs in the micondria which is 36 ATP.

Theoretical studies of "Mitochondrial Structures and the Intra-Mitochondrial ATP Formation Process", is one of the many theoretical studies relating to Sports Physical Sciences, this theory can be developed back into a more perfect theoretical study.

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