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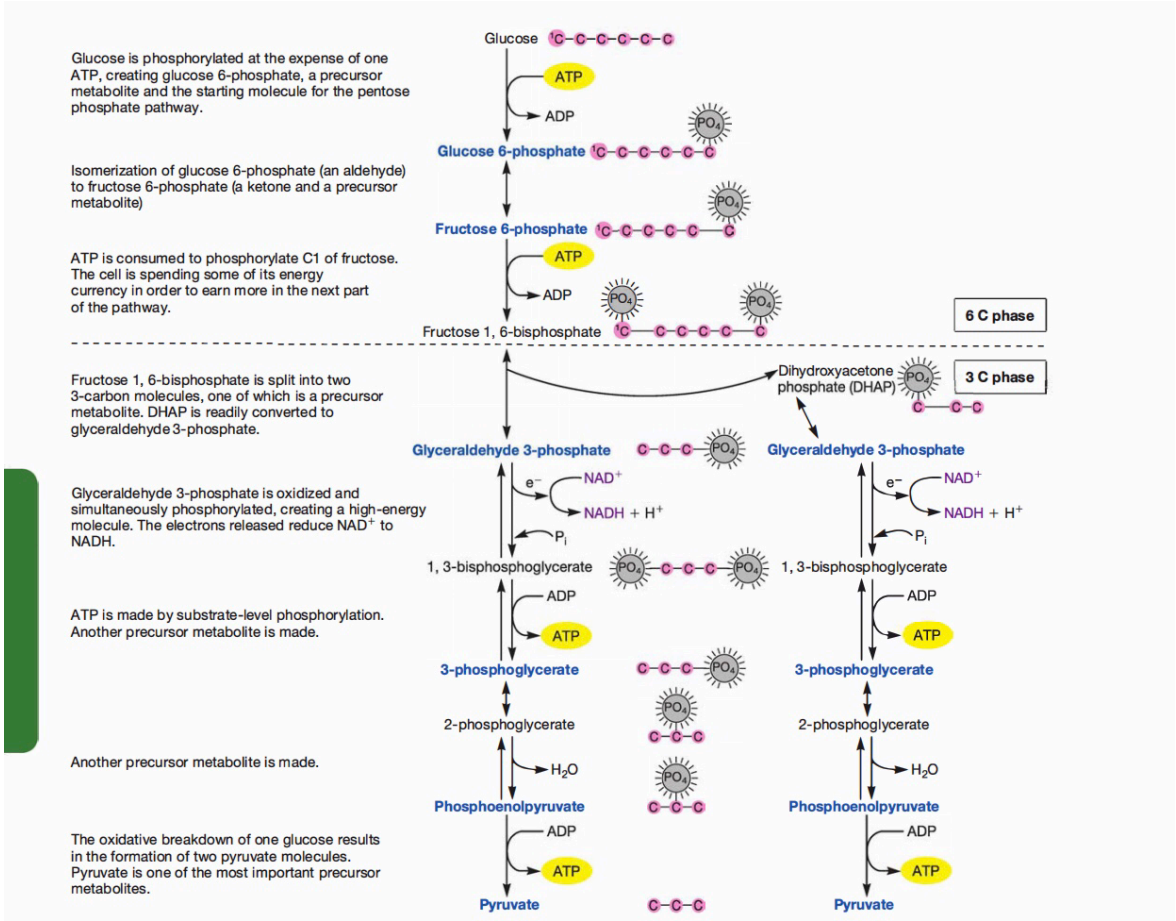
General microbiology
MCB 202

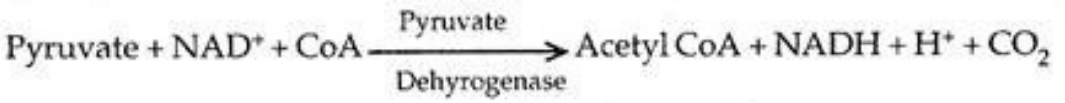
Question
Describe the mechanism in aerobic respiration .

Aerobic respiration is an enzymatically controlled release of energy in a stepwise catabolic process of complete oxidation of organic food into carbon dioxide and water with oxygen acting as terminal oxidant. It is also a process that can completely catabolize a reduced organic energy source to C02 using the glycolytic pathways and TCA cycle with 02 as the terminal electron acceptor for an electron transport chain. The common mechanism of aerobic respiration is also called common pathway because its first step, called glycolysis, is common to both aerobic and anaerobic modes of respiration. The common aerobic respiration consists of three steps—glycolysis, Krebs cycle and terminal oxidation.

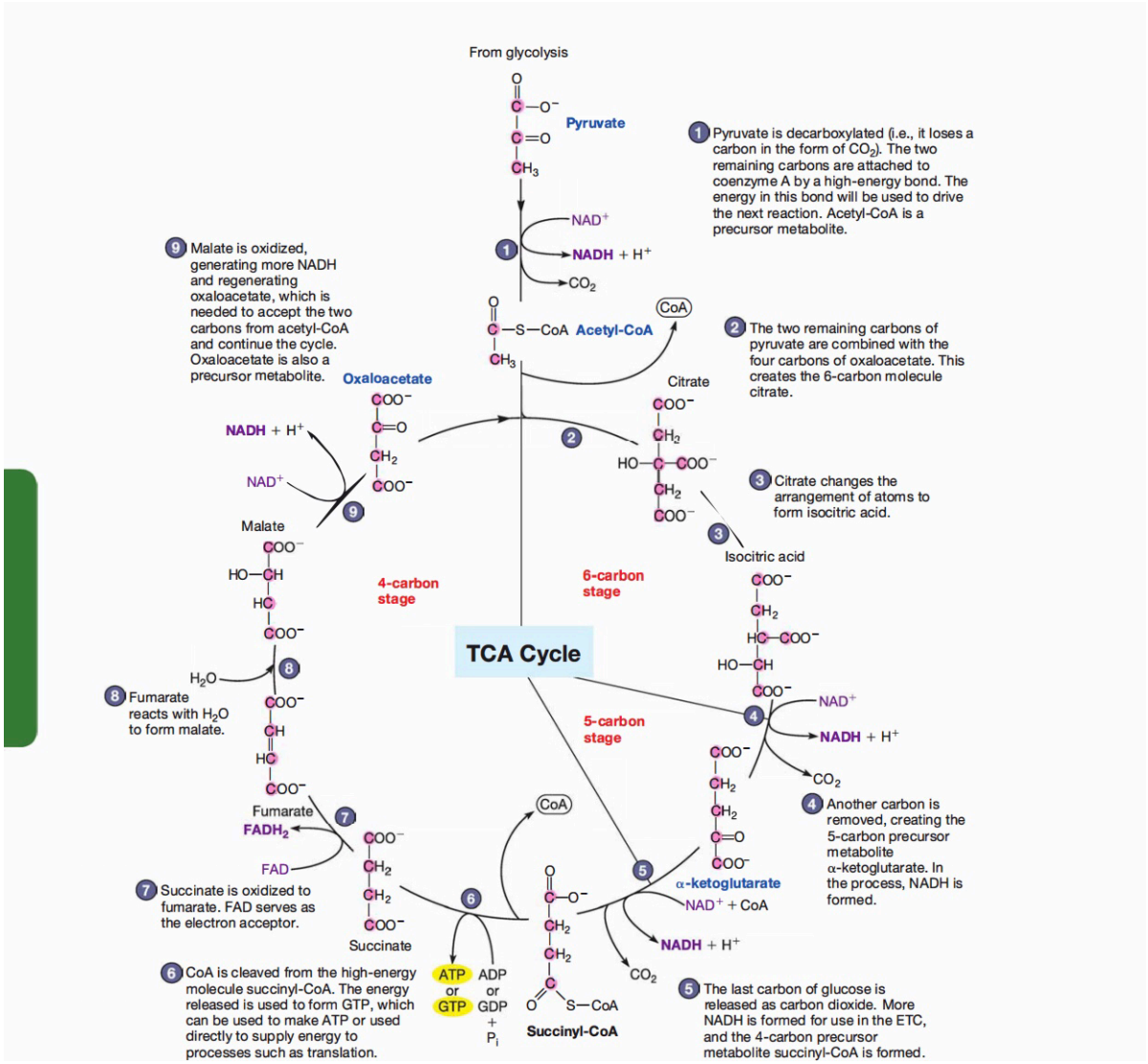
Glycolysis:
Microorganisms employ several metabolic pathways to catabolize glucose to pyruvate, including (1) the Embden-Meyerhof Parnas pathway, (2) the Entner-Doudoroff pathway, and (3) the pentose phosphate pathway.
Glycolysis is the process of breakdown of glucose or similar hexose sugar to molecules of pyruvic acid through a series of enzyme mediated reactions releasing some energy (as ATP) and reducing power (as NADH2). It occurs in the cytoplasm. It takes place as follows;



Krebs Cycle:
The cycle was discovered by Hans Krebs (1937, 1940, Nobel Prize 1953). It occurs inside mitochondria. The cycle is also named as citric acid cycle or tricarboxylic acid (TCA) cycle after the initial product. Krebs cycle is stepwise oxidative and cyclic degradation of activated acetate derived from pyruvate.
Oxidation of Pyruvate to Acetyl-CoA:
Pyruvate enters mitochondria. It is decarboxylated oxidatively to produce CO2 and NADH. The product combines with sulphur containing coenzyme A to form acetyl CoA or activated acetate. The reaction occurs in the presence of an enzyme complex pyruvate dehydrogenase (made up of a decarboxylase, lipoic acid, TPP, transacetylase and Mg2+).



Acetyl CoA functions as substrate entrant for Krebs cycle. The acceptor molecule of Krebs cycle is a 4-carbon compound oxaloacetate. Kerbs cycle involves two decarboxylations and four dehydroge- nations. The various components of Krebs cycle are as follows.

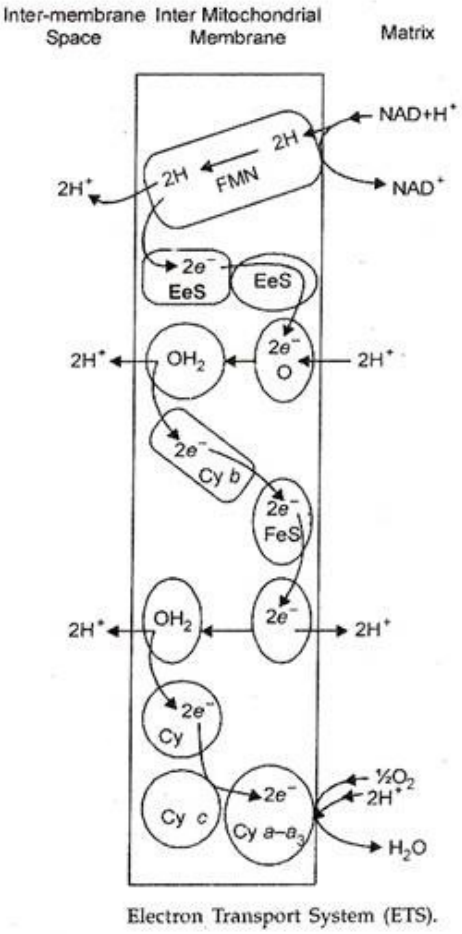


Terminal Oxidation:
It is the name of oxidation found in aerobic respiration that occurs towards the end of catabolic process and involves the passage of both electrons and protons of reduced coenzymes to oxygen.

$$FADH_2 \rightleftharpoons FAD + 2H^+ + 2e^-$$
$$\tfrac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$$

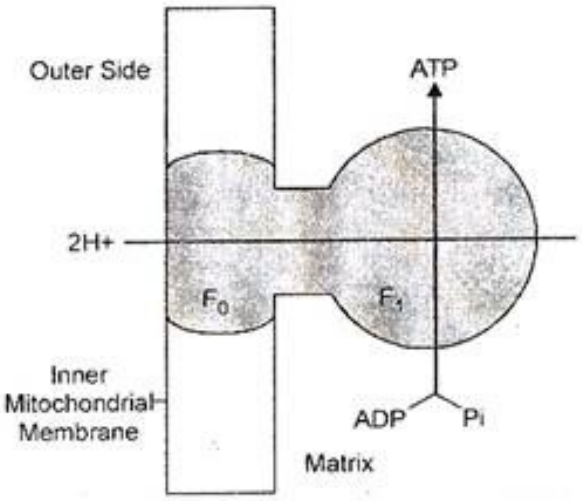
Terminal oxidation consists of two processes-electron transport and oxidative phosphorylation.

Electron Transport Chain:
Inner mitochondrial membrane contains groups of electron and proton transporting enzymes. In each group the enzymes are arranged in a specific series called electron transport chain (ETC) or mitochondrial respiratory chain or electron transport system (ETS).
An electron transport chain or system is a series of coenzymes and cytochromes that take part in the passage of electrons from a chemical to its ultimate acceptor. The passage of electrons from one enzyme or cytochrome to the next is a downhill journey with a loss of energy at each step. At each step the electron carriers include flavins, iron sulphur complexes, quinones and cytochromes.
Most of them are prosthetic groups of proteins. Quinones are highly mobile electron carriers. Four enzymes are involved in electron transport—(i) NADH-Q reductase or NADH- dehydrogenase (ii) Succinate Q-reductase complex (iii) QH2-cytochrome c reductase complex (iv) Cytochrome c oxidase complex. NADH-Q reductase (or NADH- dehydrogenase) has two prosthetic groups, flavin mononucleotide (FMN) and iron sulphur (Fe-S) complexes. Both electrons and protons pass from NADH2 to FMN. The latter is reduced.



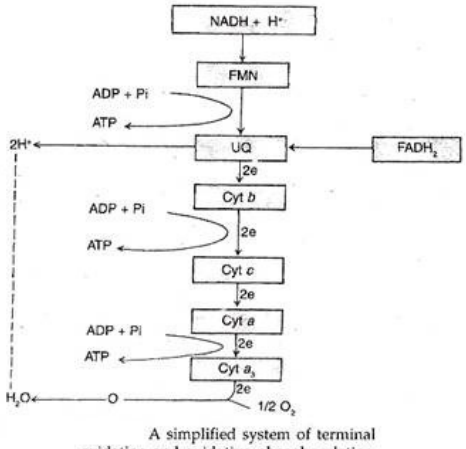
Electron Transport System (ETS).

NADH + H+ + FMN——> FMNH2 +NAD+
Electron now moves to the FeS complex and from there to a quinone. The common quinone is co-enzyme Q, also called ubiquinone (UQ).
FMNH2 + 2Fe3+ S——>FMN + 2Fe2+ S + 2H+
2Fe2+ S + Q + 2H+——>2Fe3+ S + QH2
FADH2 produced during reduction of succinate also hands over its electrons and protons to co-enzyme Q through FeS complex. The enzyme is succinate-Q reductase complex.
FADH2 + 2Fe3+ S——> 2Fe2+ S + 2H+ + FAD
2Fe2+ S + Q + 2H+——> 2Fe3+ S + QH2
QH2-cytochrome c reductase complex has three components—cytochrome b, FeS complex and cytochrome c1. Coenzyme Q may also be involved between FeS complex and cytochrome c1.
QH2 + 2Fe3 + cyt.b ——> Q + 2H+ + 2Fe2+cyt.b
2Fe2 + cyt.b + 2Fe3+ S ——> 2Fe3 + cyt.b + 2Fe2 + S
2Fe2 + S + Q + 2H+——> 2Fe3 + S + QH2 (?)
QH2 + 2Fe3 + cyt.c1 ——> Q + 2H+ + 2Fe2+cyt.c1
Cytochrome c1 hands over its electron to cytochrome c. Like co-enzyme Q, cytochrome c is also mobile carrier of electrons.
2Fe2 + cyt.c1 + 2Fe3+ cyt.c ——> 2Fe3 cyt.c1 + 2Fe2+ cyt.c
Cytochrome c oxidase complex comprises cytochrome a and cytochrome a3. Cytochrome a3 also possesses copper. The latter helps in transfer of electron to oxygen.
2Fe2 + cyt.c + 2Fe3+ cyt.a ——> 2Fe3 + cyt.c + 2Fe2+ Cyt.a
2Fe2 + cyt.a + 2Fe3+ cyt.a3 Cu2+ ——> 2Fe3+ cyt.a + 2Fe2+ cyt.a3 Cu2+
2Fe2 cyt.a3 Cu2+ ——> 2Fe3 cyt.c3 Cu1+
2Fe3 cyt.a3 Cu1+ + [O] ——> 2Fe3+ cyt.a3 Cu2++ [O]
Oxygen is the ultimate acceptor of electrons. It becomes reactive and combines with protons to form metabolic water.
2H+ + O”——– > 2H2O
Energy released during passage of electrons from one carrier to the next is made available to specific transmembrane complexes, which pump protons ((H+) from the matrix side of the inner mitochondrial membrane to the outer chamber. There are three such sites corresponding to three enzymes present in the electron transport chain (NADH-Q reductase, QH2-cytcxhrome c reductase and cytochrome c-oxidase).
This increases proton concentration in the outer chamber or outer surface of the inner mitochondrial membrane. The difference in the proton concentration on the outer and inner sides of the inner mitochondrial membrane is known as proton gradient.



Diagramatic presentation of ATP synthesis in mitochondria.

Oxidative Phosphorylation:
Oxidative phosphorylation is the synthesis of energy rich ATP molecules with the help of energy liberated during oxidation of reduced co-enzymes (NADH2, FADH2) produced in respiration. The enzyme required for this synthesis is called ATP synthetase.
It is located in F1 or head piece of F0-F1 or elementary particles present in the inner mitochondrial membrane. ATP-synthetase becomes active in ATP formation only where there is a proton gradient having higher concentration of H+ or protons on the F0 side as compared to F1 side (chemiosmotic hypothesis of Peter Mitchel, 1961).
Increased proton concentration is produced in the outer chamber or outer surface of inner mitochondrial membrane by the pushing of protons with the help of energy liberated, by passage of electrons from one carrier to another.
Transport of the electrons from nadh2 over ETC helps in pushing three pairs of protons to the outer chamber while two pairs of protons are sent outwardly during electron flow from fadh2 (as the latter donates its electrons further down to the ETC).
Higher proton concentration in the outer chamber causes the protons to pass inwardly into matrix or inner chamber through the inner membrane. The latter possesses special proton channels in the region of FQ (base) of the F0—F1 particles.
The flow of protons through the F0 channel induces F, particles to function as ATP-synthetase.
The energy of the proton gradient is used in attaching a phosphate radicle to ADP by high energy bond. This produces ATP. Oxidation of one molecule of NADH2 produces 3 ATP molecules while a similar oxidation of FADH2 forms 2 ATP molecules.
2 ATP molecules are produced during glycolysis and 2 ATP (GTP) molecules during double Krebs cycle. Glycolysis also forms 2NADH2. Its reducing power is transferred to mitochondria for ATP synthesis. For this a shuttle system operates at the inner mitochondrion membrane. (i) NADH2 —> NAD -> NADH2. (ii) NADH2 -> FAD -> FADH2.
The former operates in liver, heart and kidney cells. No energy is spent. The second method occurs in muscle and nerve cells. It lowers the energy level of 2NADH2 by 2ATP molecules. A total of 10 NADH2 and 2FADH2 molecules are formed in aerobic respiration.
They help in formation of 34 ATP molecules. The net gain from complete oxidation of a molecule of glucose in muscle and nerve cells is 36 ATP molecules (10 NADH2 = 30 ATP, 2 FADH2 = 4 ATP, four formed by substrate level phosphorylation in glycolysis and Krebs cycle and two consumed in transport of theNADH2 molecules into mitochondria).
In procaryotes, heart, liver, and kidneys, 38 ATP molecules are produced per glucose molecules oxidised. Passage of ATP molecules from inside of mitochondria to cytoplasm is through facilitated diffusion.
Since, one ATP molecule stores 8.9 kcal/mole (7 kcal/mole according to early estimates) the total energy trapped per gm mole of glucose is 338.2 kcal (266 kcal) or an efficiency of 49.3% (38.8% according to older estimates). The rest of the energy is lost as heat.



A simplified system of terminal oxidation and oxidative phosphorylation.

Significance of Krebs Cycle:

1. Apart from serving as an energy-generating system, Krebs cycle yields several substances that figure as starting points for a number of biosynthetic reactions. Ordinarily Krebs cycle of respiration is considered catabolic in nature, but it provides a number of intermediates for anabolic pathways. Therefore Krebs cycle is amphibolic (both catabolic and anabolic). A few examples are cited below:

(a) The synthesis of sucrose by way of glyoxylytic acid cycle is an instance in point. A slightly modified Krebs cycle leads to the formation of glyoxylate, malate, oxaloacetate, phosphoenol pyruvate and then by a reversed glycolytic pathway, sucrose is formed.

(b) There are two keto acids in Krebs cycle and on amination they yield the respective amino acids- Pyruvic acid —> alanine; Oxaloacetic acid —> aspartic acid; and oc-ketoglutaric acid —> glutamic acid.

The last of these opens up new pathways leading to the synthesis of glutamine, ornithine, proline, hydroxyproline, citruiline and arginine.

(c) Succinyl-CoA is the starting point for the biosynthesis of several porphyrins.

2. Krebs cycle is a common pathway of oxidative breakdown of carbohydrates, fatty acids, and amino acids.