Electron Transport chain & Oxidative Phosphorylation

Electron Transport chain:

It is present in inner mitochondrial membrane. It consists of four redox compounds which are referred as

Complex I,
Complex II,
Complex III and
Complex IV

Their composition is as follows:

Complex I:

It is also known as NADH-dehydrogenase or NADH coenzyme Q-reductase. Its prosthetic groups are FMN & Fe-S centre. It is responsible for oxidation of NADH which is present in mitochondrial matrix. It transfers e^- to Ubiquinone (UQ) or coenzyme Q.

Complex II:

It is also known as succinate dehydrogenase or succinate cytochrome Q-reductase.

It is responsible for oxidation of succinate.

Its prosthetic groups are FAD, Fe-S & haem (of cytochrome $_{b560}$)

It transfers e^- to UQ.

UQ is responsible for oxidizing complex I as well as complex II.

UQ transfers e^- to complex III.

Complex III:

It is also known as cytochrome bc_1 complex. It is responsible for oxidation of reduced UQ.

Its prosthetic groups are haem (of cytochrome c & cytochrome c1) and Fe-S centres

It is oxidized by cytochrome c

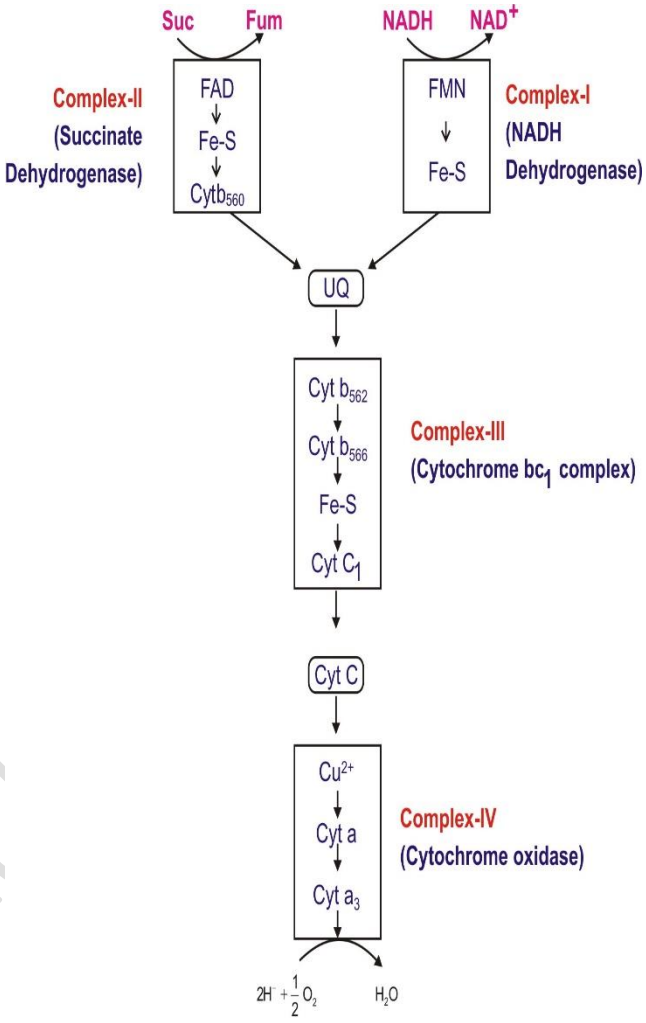
Complex IV:

It is also known as Cytochrome oxidase.

It is responsible for oxidation of reduced cytochrome c.

Its prosthetic groups are Cu^{2+} and haem (Cytochrome a and a_3)

It transfers electron to oxygen. The final product is H_2O.



ETC (Electron transport Chain)

Oxidative Phosphorylation

Oxidative of respiratory substrates with the help of various reaction sequences generate reduced coenzyme – NADH & $FADH_2$.The amount of reduced coenzymes in cell is highly limited. They must be regenerated, so that they could act as e^- acceptor during oxidation of the respiratory substrate. They are regenerated by oxidizing them. They are oxidized by electron transport chain (ETC). Electrons released during oxidation of NADH or $FADH_2$ are passed through a series of redox compounds which constitute electron transport chain. Finally, the electron is accepted by oxygen (O_2).

Flow of electrons through redox compounds is spontaneous because these compounds are arranged in increasing order of their redox potential (E_o').A redox compound having lower E_o' has higher e^- pressure and lower affinity for e^- compared to redox compound of higher E_o'. The flow of electrons from redox compounds to oxygen is spontaneous and exergonic in which free energy is released. Free energy being released is conserved with approximately 40% efficiency by synthesizing ATP.

Oxidation driven phosphorylation of ADP into ATP is called oxidative phosphorylation.

ADP + Pi $\rightarrow$ ATP

Mechanism of ATP formation:

ATP is formed by phosphorylating ADP with the help of energy.

Chemi-osmatic hypothesis explains ATP formation.

Chemi-osmotic hypothesis/Mitchel's hypothesis:

A number of evidences are available in favour of this hypothesis. On that basis, it is almost a theory now.

It is one of unifying hypotheses in biology, because it explains oxidative phosphorylation as well as photophosphoryalation.

According to this hypothesis, the electron flow from reduced coenzymes to oxygen is neither responsible for generation of high energy coupling factor nor for high energy conformation. Rather, it is responsible for generation of high energy state.

Free energy released during electron flow is conserved by generating a transmembrane proton gradient across mitochondrial membrane, which takes the form of proton motive force.

Proton gradient across the inner mitochondrial membrane gives rise to pH gradient, and electrical gradient which together represent electrochemical gradient.

The gradient of proton motive force is responsible for causing flow of proton from higher electrochemical potential to lower electrochemical potential. Protons move passively through proton pore in F_0-F_1 particles, present in cristae.

The passive flow of protons provides energy for phosphorylation of ADP into ATP.

When NADH present in mitochondrial matrix is oxidized, $2e^-$ are transported through electron transport chain. During this electron flow, $6H^+$ are pumped from mitochondrial matrix to inter membrane space. Now, it has been found that its oxidation is responsible for transport of $10H^+$ across the inner mitochondrial membrane.

Oxidation of succinate in ETC with the help of complex is coupled with pumping of $6H^+$ across the inner mitochondrial membrane. According to old concept $4H^+$ are pumped.

Oxidation of NADH in mitochondrial matrix yields 3ATP, while that of $FADH_2$ yields (oxidation of succinate) 2 ATP.

According to new concept oxidation of NADH in mitochondrial matrix yields 2.5 ATP, while that of succinate yields 1.5 ATP.

Oxidation of cytosolic NADH:

During glycolysis, NAD^+ is reduced into NADH. This NADH should be oxidized to generate NAD^+, so that it could continue to act as e^- acceptor during oxidation of respiratory substrates.

NADH dehydrogenase complex of ETC is responsible for oxidation of NADH which is present in mitochondrial matrix.

Cytosolic NADH fails to arrive in the matrix because inner mitochondrial membrane is not permeable for it. So, there should be provision to oxidize it outside the matrix.

There are 3-strategies for its oxidation

A: **Oxidation of cytosolic NADH with the help of external NADH dehydrogenase:**

In plant mitochondria, outer face of inner mitochondrial membrane has another NADH dehydrogenase which is called external NADH dehydrogenase.

Cytosolic NADH can arrive inter membrane space due to permeability of outer membrane.

Here (at inter membrane space), cytosolic NADH is oxidized, with help of external NADH dehydrogenase.

2ATP are formed after oxidation of cytosolic NADH by external NADH dehydrogenase.

B: Oxidation of cytosolic NADH by MALATE ASPARTATE SHUTTLE:

Malate aspartate shuttle operates in the cells of heart, kidney & liver.

Oxidation of one cytosolic NADH with help of malate –aspartate shuttle yields 3ATP.

C. **Oxidation of cytosolic NADH with the help of Glycerol Phosphate Shuttle**: It operates in muscle fibers and cells of brain. Oxidation of one cytosolic NADH with help of glycerol (P) shuttle yields 2ATP.

ATP yield after complete oxidation of one molecule of Glucose:

	Step	Reduced coenzyme	No. of ATP generated	
A	Glycolysis 2(p)glyceraldehydes→ 1,3 bis(P) glycerate	2NADH	2×2=4* or 2×3=6#	8* ATP 10# ATP
	2(1,3 bis (P) glycerate →3 (P) glycerate)	2 [NADH] ATP	2×1=2	
	2(PEP →Pyruvate)	2[NADH] ATP	2×1=2	
B.	Intermediate step 2(Pyruvate →Acetyl CoA)	2NADH	2×3=6	[6ATP]
C.	Krebs cycle 2(Isocitrate →α-Ketoglutarate)	2NADH	2×3=6	24ATP
	2(α-Ketoglutarate →Succinyl CoA	2NADH	2×3=6	
	2(Succinyl CoA →Succinate)	2 [NADH] ATP	2×1=2	
	2 (Succinate→ Fumarate)	2$FADH_2$	2×2=4	
	2(Malate →Oxaloacetate)	2NADH	*38ATP # 40 ATP	

- *** Oxidation of cytosolic NADH with the help of external NADH dehydrogenase or Oxidation of cytosolic NADH with the help of Glycerol Phosphate Shuttle**
- **# Oxidation of cytosolic NADH by MALATE ASPARTATE SHUTTLE**