VIVEKANANDA COLLEGE
THAKURPUKUR
KOLKATA-700063

NAAC ACCREDITED ‘A’ GRADE

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Name of the Teacher:	Mrs. Rinku Halder Sahu
Name of the Department:	Botany (Morning)

TOTAL YIELD OF ATP FROM COMPLETE OXIDATION OF GLUCOSE

The number of ATP molecules generated from the catabolism of glucose varies.

- For example, the number of hydrogen ions that the electron transport chain complexes can pump through the membrane varies between species.
- Another source of variance stems from the **shuttle of electrons across the membranes of the mitochondria**. Two types of shuttles are known which are located in the mitochondrial membrane of human beings. They are as follows:

1.Glycerol -3-phosphate shuttle **(in muscle and brain)**

- ➢ The NADH generated from glycolysis cannot easily enter mitochondria.
- ➢ In this case 3PGA acts as an electron carrier.
- ➢ First cytosolic NADH transfers its electron to DHAP in cytosol as a result of which DHAP is reduced to G3P and NADH is oxidised to NAD+.
- ➢ Now, membrane is permeable to G3P.
- ➢ After getting inside, G3P is reoxidised to DHAP on the outer surface of the inner mitochondrial membrane.
- ➢ Thus, electrons are picked up on the inside of mitochondria by either NAD^+ or FAD^+. When a pair of electrons is transferred to FAD as an electron acceptor , FADH2 is reoxidised in ETC , resulting in formation of 2ATP.

➢ Therefore, in glycerol phosphate shuttle one NADH + H+ forms 2 ATP, and 36 ATP are formed per glucose molecule.

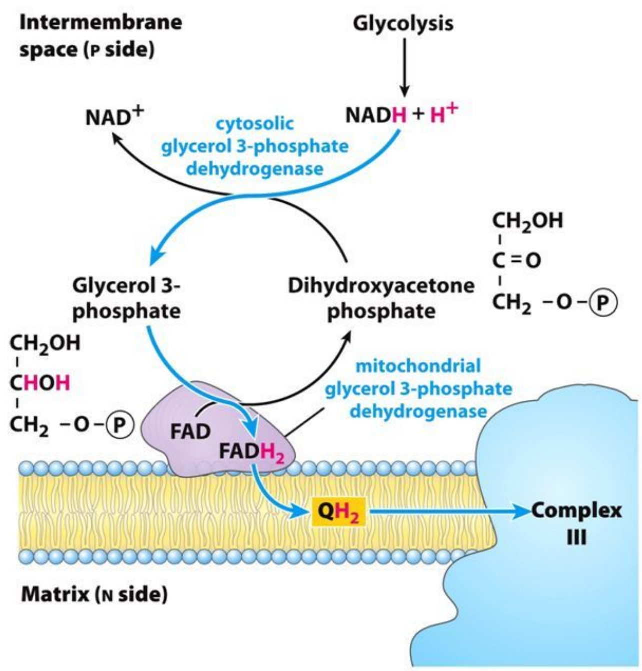


Figure 19-32
Lehninger Principles of Biochemistry, Sixth Edition

The glycerol 3-phosphate shuttle carries NADH into the matrix (skeletal muscle, brain)

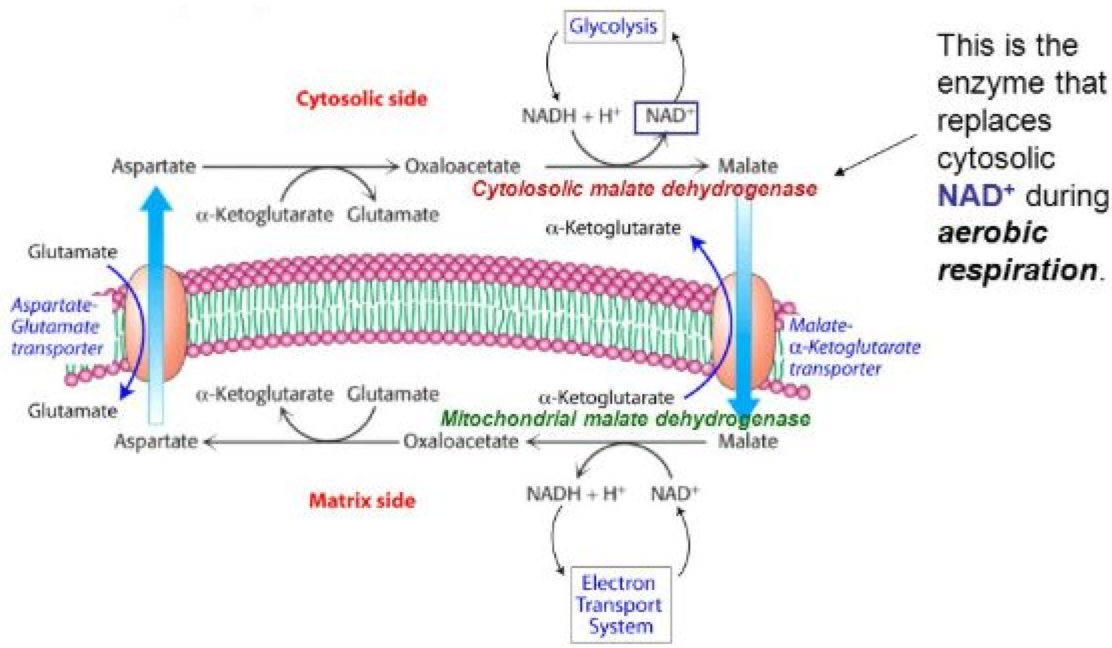
2. Malate-Aspartate Shuttle (in liver and heart):

➢ This shuttle enables transfer of NADH electrons into the mitochondrial matrix as NADH is unable to cross the mitochondrial membrane.

➢ In this process electrons from NADH are transferred to oxaloacetate forming malate.

➢ A transporter binds the malate and carries it across the membrane into the matrix, where malate dehydrogenase oxidizes malate back to oxaloacetate.

- Inside mitochondrial matrix electrons are transferred to NAD^+ regenerating NADH for use in electron transport to synthesise ATP.
- It produces 3 ATP molecules from one NADH + H+.
- Thus there is no loss of any ATP and net ATP production remains to be 38 per glucose molecule.



- Another factor that affects the yield of ATP molecules generated from glucose is the fact that intermediate compounds in these pathways are used for other purposes.

1. Glucose catabolism connects with the pathways that build or break down all other biochemical compounds in cells, and the result is somewhat messier than the ideal situations described thus far. For example, sugars other than glucose are fed into the glycolytic pathway for energy extraction. Moreover, the five-carbon sugars that form nucleic acids are made from intermediates in glycolysis.

2. Certain nonessential amino acids can be made from intermediates of both glycolysis and the citric acid cycle.
3. Lipids, such as cholesterol and triglycerides, are also made from intermediates in these pathways, and both amino acids and triglycerides are broken down for energy through these pathways.

Overall, in living systems, these pathways of glucose catabolism extract about 34 percent of the energy contained in glucose.

Summary of total energy yield of complete oxidation of one glucose molecule

- During **glycolysis**, a total **4 ATPs are formed out of which 2 are consumed**. However, the **2 molecules of NADH + H+** are produced per glucose, which will **yield 06 ATP in the ETC.**

In the cytoplasm		
Glycolysis:	2 ATP	⟶ 2 ATP
In the mitochondria		
From glycolysis:	2 NADH ⟶ 6 ATP	⟶ 6 ATP*

- During **link reaction i.e conversion of pyruvic acid to acetyl coA , 2 molecules of NADH2 are produced (1 per pyruvate) , which will yield 06 ATP in the ETC.**

In the mitochondria

From respiration:		
Pyruvic acid ⟶ acetyl CoA:	1 NADH ⟶ 3 ATP	(× 2) ⟶ 6 ATP

- The **Krebs cycle** produces **two molecules of ATP for every molecule of** glucose. The Krebs cycle also produces **six molecules of NADH** and **two molecules of FADH2 per molecule of glucose**. As **each molecule of NADH is equivalent to three ATPs** and **each FADH2 is equal to two ATPs**, we get 2+6×3 + 2×2 =24 ATPs from Krebs cycle.

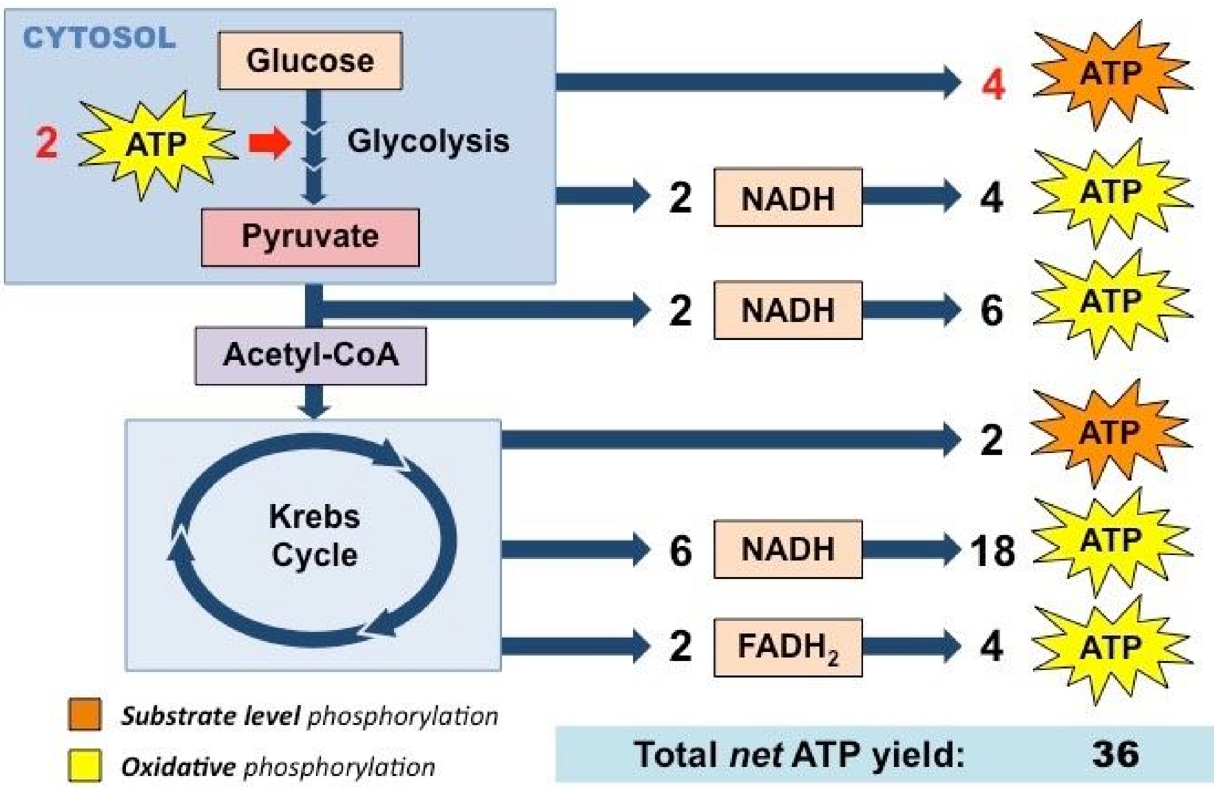
Krebs cycle:

$$\left.\begin{array}{r} 1\ ATP \\ 3\ NADH \longrightarrow 9\ ATP \\ 1\ FADH_2 \longrightarrow 2\ ATP \end{array}\right\} \quad (\times 2) \longrightarrow 24\ ATP$$

Source	Carbon Flow	Molecules of Reduced Coenzymes Produced	Net ATP Molecules Made by Substrate-Level Phosphory-lation	Net ATP Molecules Made by Oxidative Phosphory-lation	Theoretical Maximum Yield of ATP Molecules
Glycolysis (EMP)	Glucose (6C) ⟶ 2 pyruvates (2C)	2 NADH	2 ATP	6 ATP from 2 NADH	8
Transition reaction	2 pyruvates (3C) ⟶ 2 acetyl (2C) + 2 CO_2	2 NADH		6 ATP from 2 NADH	6
Krebs cycle	2 acetyl (2C) ⟶ 4 CO_2	6 NADH 2 $FADH_2$	2 ATP	18 ATP from 6 NADH 4 ATP from 2 $FADH_2$	24
Total:	glucose (6C) ⟶ 6 CO_2	10 NADH 2 $FADH_2$	4 ATP	34 ATP	38 ATP

ATP yield calculated with an assumed P/O ratio of 3.0 for NADH and 2.0 for FADH2

However, there are some eukaryotic cells , 2 ATP is required to transport NADH + H+ formed by glycolysis from the cytoplasm through the inner mitochondrial membrane. Since 2 ATP are used, **therefore only 36 ATP are produced instead of 38 ATP**.



As the shuttle system is absent in prokaryotes 38 ATP are formed from per molecule of glucose oxidation.

ATP yield during aerobic respiration is not 36-38, but only about 30-32 ATP molecules / 1 molecule of glucose .

According to some of newer sources the ATP yield during aerobic respiration is not 36–38, but only about 30–32 ATP molecules / 1 molecule of glucose ,because:

ATP : NADH + H^+ and ATP : $FADH_2$ ratios during the oxidative phosphorylation appear to be not 3 and 2, but 2.5 and 1.5 respectively. Unlike in the substrate-level phosphorylation, the stoichiometry here is difficult to establish.

ATP synthase produces 1 ATP / 3 H+. However the exchange of matrix ATP for cytosolic ADP and Pi (antiport with OH– or symport with H+) mediated by ATP–ADP translocase and phosphate carrier consumes 1 H+ / 1 ATP as a result of regeneration of the transmembrane potential changed during this transfer, so the net ratio is 1 ATP : 4 H+.

The mitochondrial electron transport chain proton pump transfers across the inner membrane 10H^+ /1NADH + H^+ (4+2+4)or 6H+ / 1$FADH_2$ (2+4).

So the final stoichiometry is

1 NADH + H^+ : 10 H+ : 10/4 ATP = 1 NADH + H+ : 2.5 ATP

1 $FADH_2$: 6 H+ : 6/4 ATP = 1 FADH2 : 1.5 ATP

ATP : NADH +H^+ coming from glycolysis ratio during the oxidative phosphorylation is

1.5, as for $FADH_2$, if hydrogen atoms ($2H^+$ + $2e^-$) are transferred from cytosolic NADH + H^+ to mitochondrial FAD by the **glycerol phosphate shuttle** located in the inner mitochondrial membrane.

2.5 in case of **malate-aspartate shuttle** transferring hydrogen atoms from cytosolic NADH + H^+ to mitochondrial NAD+

So finally we have, per molecule of glucose

- ***Substrate-level phosphorylation:***

2 ATP from glycolysis + 2 ATP (directly GTP) from Krebs cycle

- ***Oxidative phosphorylation:***

2 NADH + H^+ from glycolysis:

2 × 1.5 ATP (if glycerol phosphate shuttle transfers hydrogen atoms) or

2 × 2.5 ATP (malate-aspartate shuttle)

2 NADH + H^+ from the oxidative decarboxylation of pyruvate and 6 from Krebs cycle:

8 × 2.5 ATP

2 FADH2 from the Krebs cycle:

2 × 1.5 ATP

Altogether this gives 4 + 3 (or 5) + 20 + 3 = 30 (or 32) ATP per molecule of glucose

The total ATP yield in ethanol or lactic acid fermentation is only 2 molecules coming from glycolysis, because pyruvate is not transferred to the mitochondrion and finally oxidized to the carbon dioxide (CO_2), but reduced to ethanol or lactic acid in the cytoplasm.

A SUMMARY OF ATP YIELD IS GIVEN BELOW(ACCORDING TO NEW CONCEPT):

Yield of ATP from Glucose Oxidation				
	ATP Yield per Glucose			
Pathway	Glycerol–Phosphate Shuttle	Malate–Aspartate Shuttle	NADH	$FADH_2$
Glycolysis: glucose to pyruvate (cytosol)				
Phosphorylation of glucose	−1	−1		
Phosphorylation of fructose-6-phosphate	−1	−1		
Dephosphorylation of 2 molecules of 1,3-BPG	+2	+2		
Dephosphorylation of 2 molecules of PEP	+2	+2		
Oxidation of 2 molecules of glyceraldehyde-3-phosphate yields 2 NADH			+2	
Pyruvate conversion to acetyl-CoA (mitochondria)				
2 NADH produced			+2	
Citric acid cycle (mitochondria)				
2 molecules of GTP from 2 molecules of succinyl-CoA	+2	+2		
Oxidation of 2 molecules each of isocitrate, α-ketoglutarate, and malate yields 6 NADH			+6	
Oxidation of 2 molecules of succinate yields 2 $FADH_2$				+2
Oxidative phosphorylation (mitochondria)				
2 NADH from glycolysis yield 1.5 ATP each if NADH is oxidized by glycerol–phosphate shuttle; 2.5 ATP by malate–aspartate shuttle	+3	+5	−2	
Oxidative decarboxylation of 2 pyruvate to 2 acetyl-CoA: 2 NADH produce 2.5 ATP each	+5	+5	−2	
2 $FADH_2$ from each citric acid cycle produce 1.5 ATP each	+3	+3		−2
6 NADH from citric acid cycle produce 2.5 ATP each	+15	+15	−6	
Net Yield	+30	+32	0	0

These P/O ratios of 2.5 and 1.5 for mitochondrial oxidation of NADH and FADH2 are consensus values. Since they may not reflect the actual values since these ratios may change depending on metabolic conditions, these estimates of ATP yield from glucose oxidation are approximata.

P/O ratio:

The relationship between oxygen consumption (respiration) and ATP synthesis (phosphorylation)

The P:O Ratio

$$\text{P: O Ratio} = \frac{\text{molecules of ADP phosphorylated}}{\text{atoms of oxygen reduced}}$$

- Translocation of 3 H^+ are required by ATP synthase for each ATP produced
- 1 H^+ is needed for transport of P_i, ADP and ATP
- **NET: 4 H^+ transported for each ATP synthesized and transported**

Calculation of the P:O ratio

	Complex	I	III	IV
#H^+ translocated/2e^-		4	4	2

Recall that two species supplied 2 e^- each for proton translocation:

NADH and succinate ($FADH_2$)

For **NADH**: 10 H^+ translocated/O (2 e^-)

P/O = (10 H^+/4 H^+) = **2.5 ATP/O**

For **succinate**: ($FADH_2$ → QH_2) substrate = 6 H^+/O (2 e^-)

P/O = (6 H^+/4 H^+) = **1.5 ATP/O**