

Stages of respiration

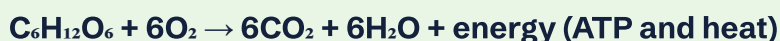
Revision notes · Glycolysis, the link reaction, the Krebs cycle and oxidative phosphorylation, plus anaerobic respiration and what happens to lactate.

For Pearson Edexcel International AS Biology XBI11 and International A Level Biology YBI11. **A Level only** is IA2 content (Units 4 to 6), not needed for the International AS.

Stages of respiration **Spec 7.1-7.5** **A Level only**

Aerobic respiration: the overall reaction **Spec 7.1**

Respiration transfers the chemical energy in a **respiratory substrate** (usually glucose) to ATP, the energy currency of the cell. Aerobic respiration needs oxygen. The overall reaction is shown below.



Two things happen to the substrate. Its carbon atoms are removed as carbon dioxide, which is a waste product (**decarboxylation**). Its hydrogen atoms are removed and picked up by the hydrogen carriers NAD and FAD, which become reduced NAD and reduced FAD (**dehydrogenation**). At the end of the process the hydrogen is reunited with atmospheric oxygen to make water, and this releases a large amount of energy that is used to make ATP.

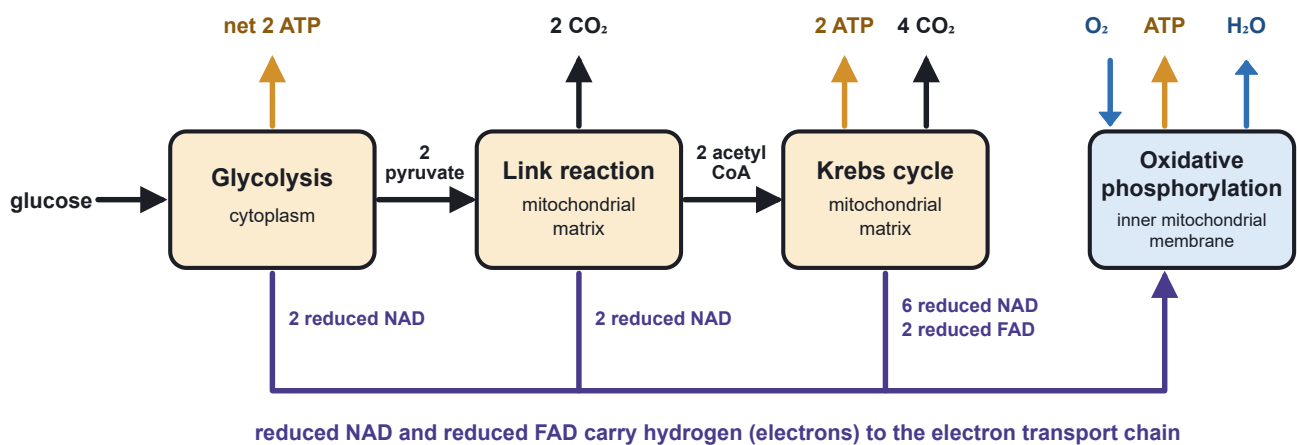
Respiratory substrate	An organic molecule, such as glucose, that is oxidised in respiration to release energy.
Decarboxylation	Removal of carbon dioxide from a substrate molecule.
Dehydrogenation	Removal of hydrogen atoms from a substrate molecule, usually by an enzyme with NAD or FAD as the hydrogen acceptor.

Why respiration is a stepped process

Respiration is not one reaction but a series of small steps. **Each step is controlled and catalysed by a specific intracellular enzyme**, so the names of the individual enzymes are not required.

- Energy is released in small, manageable amounts rather than one large burst.
- More of the energy can be captured in ATP, and less is lost as heat that could damage the cell.
- Each step can be controlled separately, so the cell can speed up or slow down respiration to match its needs.
- Intermediate compounds can be diverted into other metabolic pathways.

Common mistake: The carbon dioxide does not come from the oxygen you breathe in. It comes from the carbon in the substrate, removed by decarboxylation. Oxygen only accepts hydrogen at the end, forming water.



The four stages of aerobic respiration for one glucose molecule. Reduced NAD and reduced FAD carry hydrogen to the electron transport chain.

Glycolysis Spec 7.2

Glycolysis happens in the cytoplasm and does not need oxygen. It is the first stage of both aerobic and anaerobic respiration. Details of the intermediate stages and compounds are not required.

1. Phosphorylation: two ATP molecules each donate a phosphate to the hexose (glucose), making hexose biphosphate. This makes the sugar more reactive and traps it in the cell.
2. Lysis: the hexose biphosphate splits into two molecules of triose phosphate (3C).
3. Oxidation: each triose phosphate is dehydrogenated. The hydrogen is accepted by NAD, forming reduced NAD.
4. ATP formation: four ATP are made in total by substrate-level phosphorylation, and each triose phosphate is converted to a molecule of pyruvate (3C).

net yield per glucose = 2 ATP (4 made – 2 used) + 2 reduced NAD + 2 pyruvate

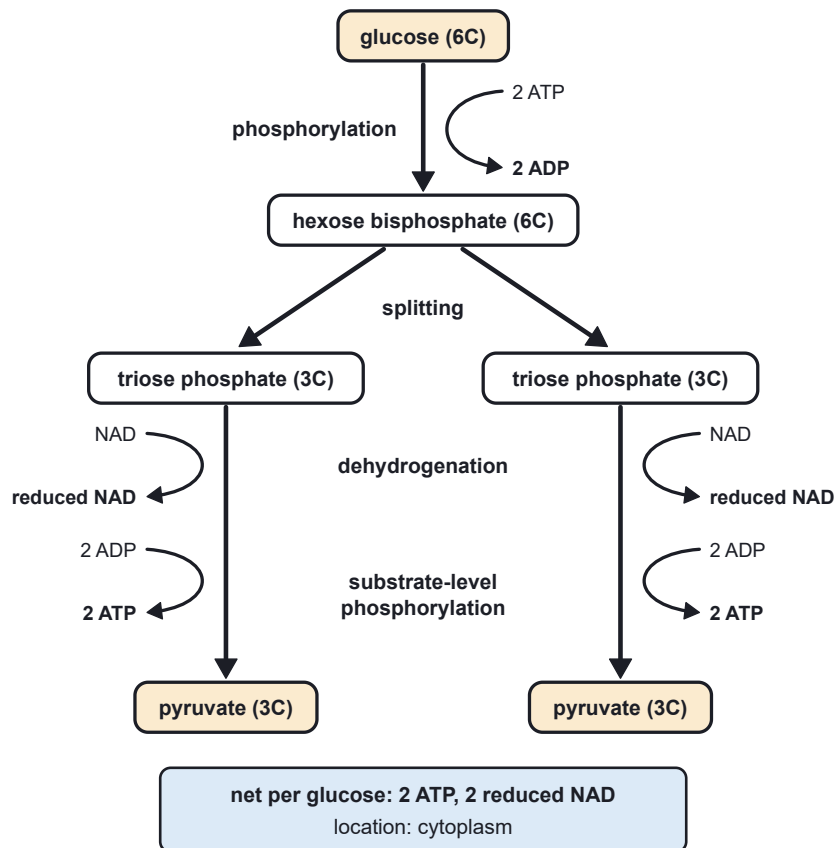
Substrate-level phosphorylation

Formation of ATP by the direct transfer of a phosphate group from a substrate molecule to ADP, without the electron transport chain.

Pyruvate

The 3C product of glycolysis. It enters the mitochondrion in aerobic respiration or is converted to lactate in anaerobic respiration in animals.

Exam tip: Always say net gain of 2 ATP. Four ATP are made, but two were used at the start. Marks are lost for writing 4 ATP.



Glycolysis in the cytoplasm: two ATP are used, four are made, so the **net gain is 2 ATP**.

The link reaction and the Krebs cycle Spec 7.3

Unlike glycolysis, which happens in the cytoplasm, the link reaction and the Krebs cycle take place in the **mitochondria** (the matrix). Pyruvate from glycolysis is actively transported into the matrix. Together they achieve the complete oxidation of glucose. Names of the other compounds are not required.

The link reaction

- Pyruvate (3C) is decarboxylated: one carbon is lost as CO_2 .
- It is also dehydrogenated: hydrogen is removed and passed to NAD, forming reduced NAD.
- The remaining 2C acetyl group combines with coenzyme A to form acetyl CoA, which carries it into the Krebs cycle.
- This happens twice per glucose, because glycolysis makes two pyruvate.

The Krebs cycle

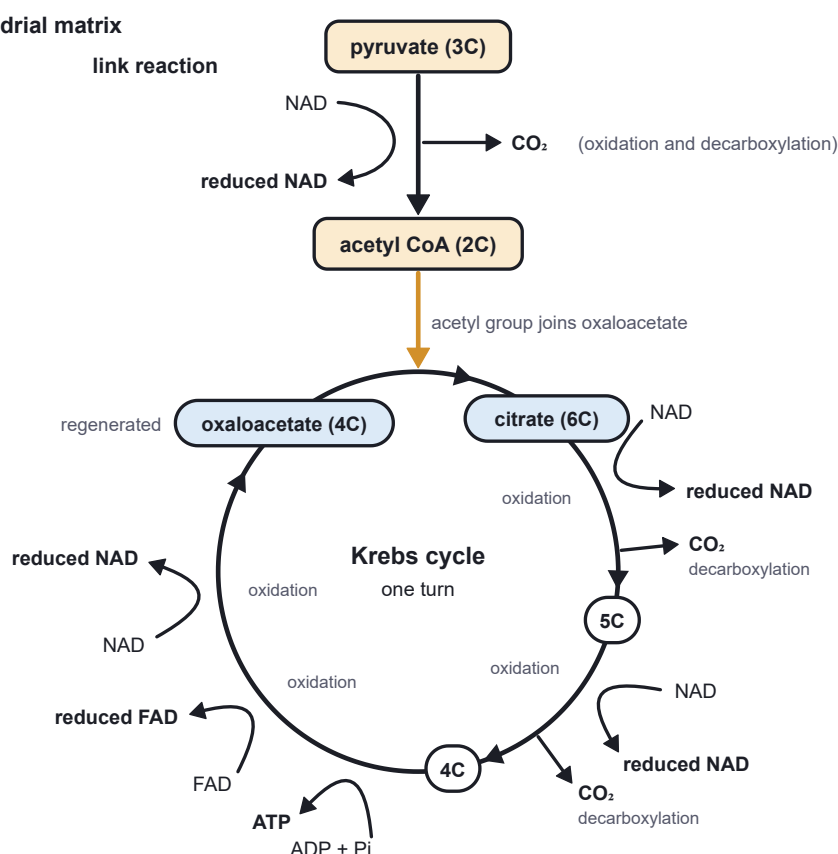
The acetyl group (2C) from acetyl CoA joins a 4C compound to form a 6C compound. The 6C compound is then converted back to the 4C compound in a series of enzyme-controlled steps, so the cycle can start again. In each turn:

- two carbon atoms are lost as CO_2 by **decarboxylation**;
- hydrogen is removed by **dehydrogenation** and accepted by NAD (3 reduced NAD) and by FAD (1 reduced FAD);
- one ATP is made by **substrate-level phosphorylation**.

The cycle turns twice for each glucose molecule, so the totals are doubled.

Products of the link reaction and Krebs cycle per glucose molecule				
Stage	CO ₂	Reduced NAD	Reduced FAD	ATP
Link reaction (2 pyruvate)	2	2	0	0
Krebs cycle (2 turns)	4	6	2	2
Total for both	6	8	2	2

Exam tip: Reduced NAD and reduced FAD are the main products: they carry hydrogen (electrons) to the electron transport chain, where most ATP is made. Only the cycle itself makes ATP directly.



The link reaction and Krebs cycle in the **mitochondrial matrix**, labelled by carbon number.

Oxidative phosphorylation Spec 7.4

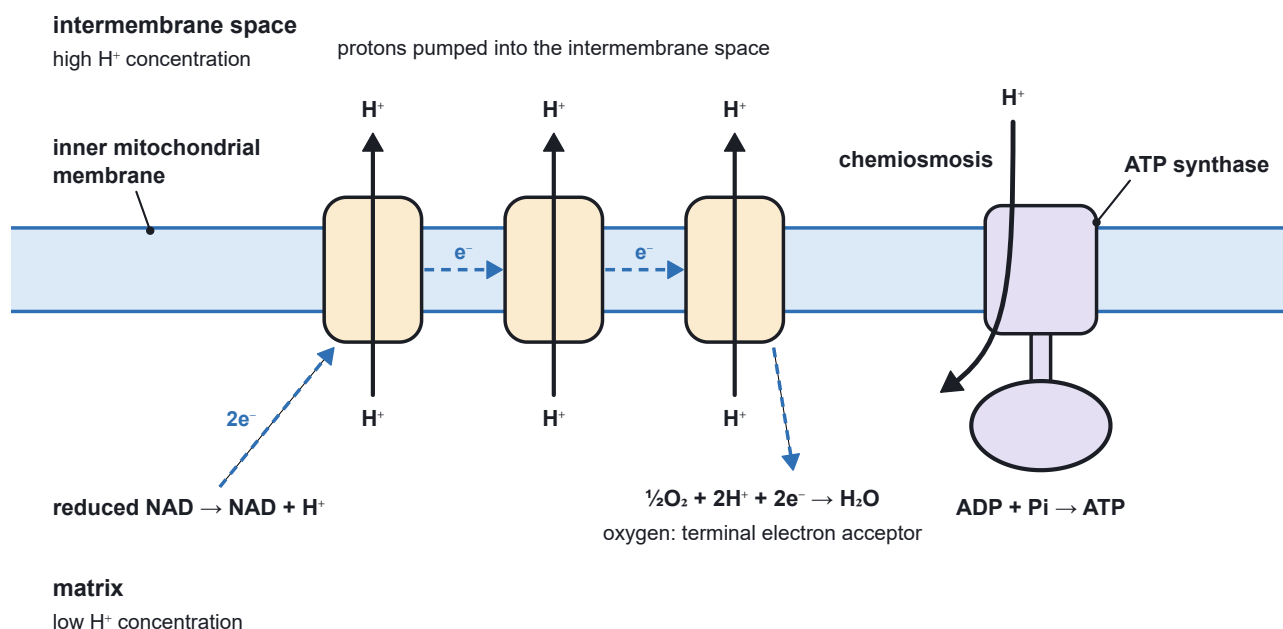
Most ATP is made by **oxidative phosphorylation**, which is linked to the electron transport chain on the inner mitochondrial membrane. The folded cristae give a large surface area for the carriers and ATP synthase.

1. Reduced NAD and reduced FAD deliver hydrogen to the chain. They are oxidised back to NAD and FAD, which can be used again in glycolysis, the link reaction and the Krebs cycle. The hydrogen splits into protons (H⁺) and electrons.
2. The electrons pass along a chain of electron carriers in a series of redox reactions. Each step releases a little energy.
3. This energy is used to pump protons from the matrix into the intermembrane space, building up a high concentration of H⁺ there: a proton gradient across the inner membrane.
4. Protons diffuse back into the matrix down their gradient through channels in the enzyme **ATP synthase**. This flow of protons is called **chemiosmosis**, and it provides the energy to join ADP and inorganic phosphate (Pi) to form ATP.

5. At the end of the chain, oxygen is the final electron acceptor. It combines with electrons and protons to form water.

Summary of aerobic respiration for one glucose molecule				
Stage	Site	ATP made directly	Reduced NAD	Reduced FAD
Glycolysis	Cytoplasm	2 (net)	2	0
Link reaction	Matrix	0	2	0
Krebs cycle	Matrix	2	6	2
Oxidative phosphorylation	Inner membrane	Most of the ATP (from reduced NAD and FAD)	Oxidised	Oxidised

Exam tip: Without oxygen the chain stops. Reduced NAD and reduced FAD are not oxidised, so NAD and FAD run out, and the link reaction and Krebs cycle also stop.



Electrons passing along the chain pump protons across the membrane; protons flow back through **ATP synthase** (chemiosmosis).

Anaerobic respiration and lactate Spec 7.2, 7.5

When oxygen is in short supply, as in muscle during vigorous exercise, the electron transport chain cannot work. Reduced NAD cannot be oxidised, so there would be no NAD for glycolysis. Anaerobic respiration solves this.

- Glycolysis continues, giving a net gain of 2 ATP per glucose.
- Pyruvate accepts hydrogen from reduced NAD and is converted to **lactate**.
- This reforms NAD, so glycolysis can carry on making ATP, although only a small amount compared with aerobic respiration.

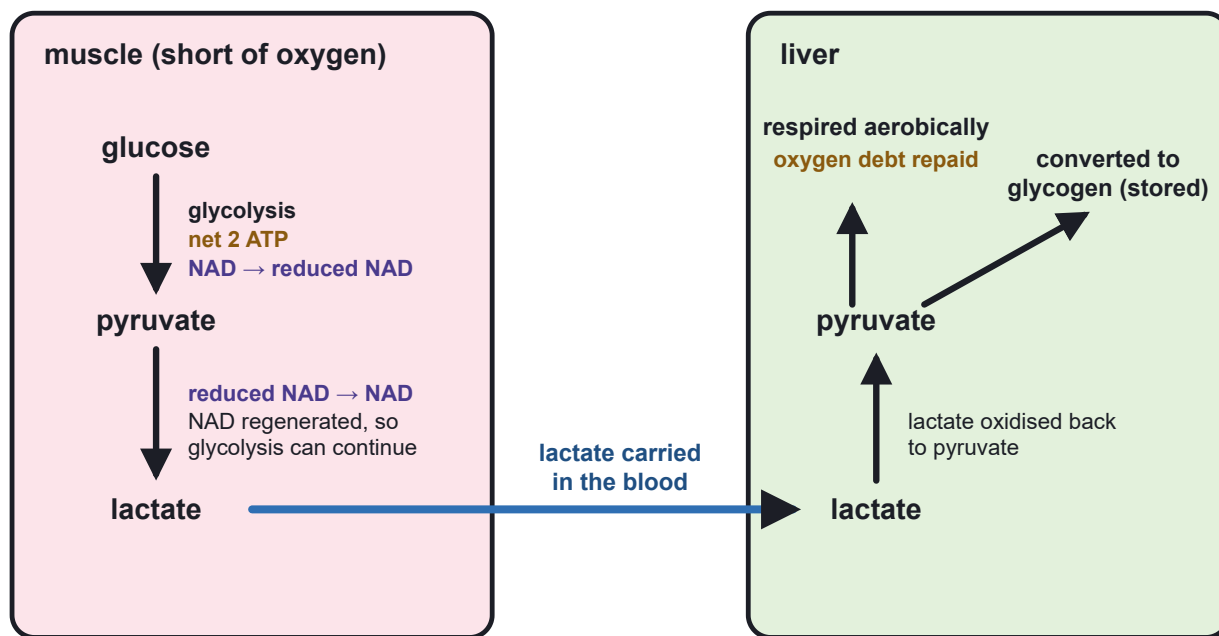
Lactate lowers the pH of the muscle cells, which interferes with enzyme action and contributes to muscle fatigue.

What happens to lactate

- Lactate diffuses out of the muscle cells into the blood and is carried to the liver.

2. When enough oxygen is available again, in the liver the lactate is oxidised back to pyruvate.
3. Some pyruvate enters aerobic respiration (link reaction, Krebs cycle and oxidative phosphorylation) to release ATP; the rest is converted to glucose and then glycogen for storage.
4. Extra oxygen is taken in for some time after the exercise. This is why breathing stays fast and deep: the **oxygen debt** is being repaid.

Common mistake: Lactate does not build up because there is 'no oxygen' in the cell. It forms because pyruvate has to accept hydrogen so that NAD is regenerated. Say that glycolysis would stop without it.



Lactate formed in muscle is carried to the **liver** for removal.

Quick check

1. In which part of the cell does glycolysis take place?
2. How many ATP molecules are made by glycolysis, net, per glucose molecule?
3. What are the products of the link reaction?
4. What is the role of oxygen in aerobic respiration?
5. Why does glycolysis stop if pyruvate cannot be converted to lactate in anaerobic conditions?

Quick check answers

Stages of respiration

1. In the cytoplasm.
2. Two (four are made, two are used).
3. Acetyl CoA, carbon dioxide and reduced NAD.
4. It is the final electron acceptor, combining with electrons and protons to form water.
5. Reduced NAD would not be oxidised, so NAD would not be regenerated for glycolysis.