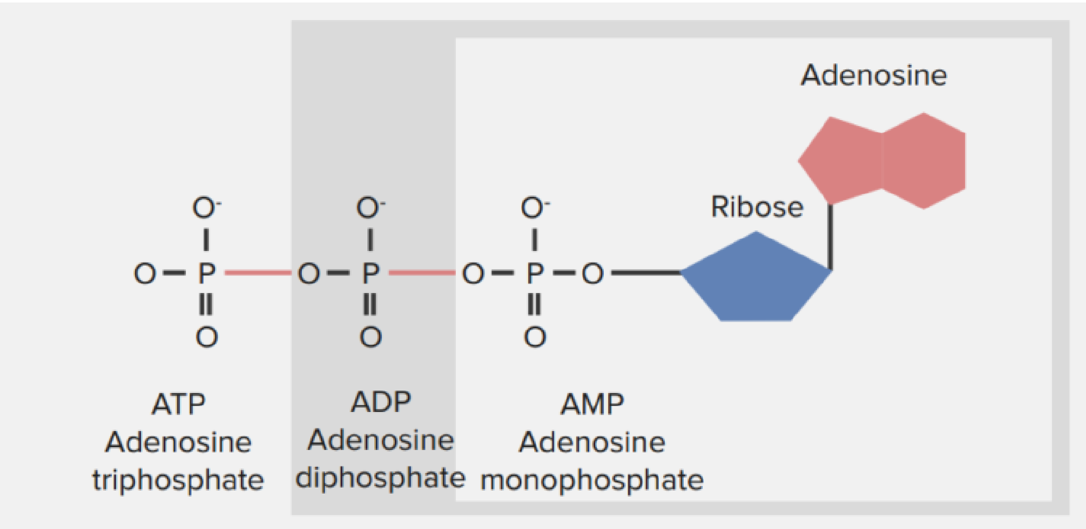
Adenosine Triphosphate (ATP): Chemical Properties and Synthesis

See online here

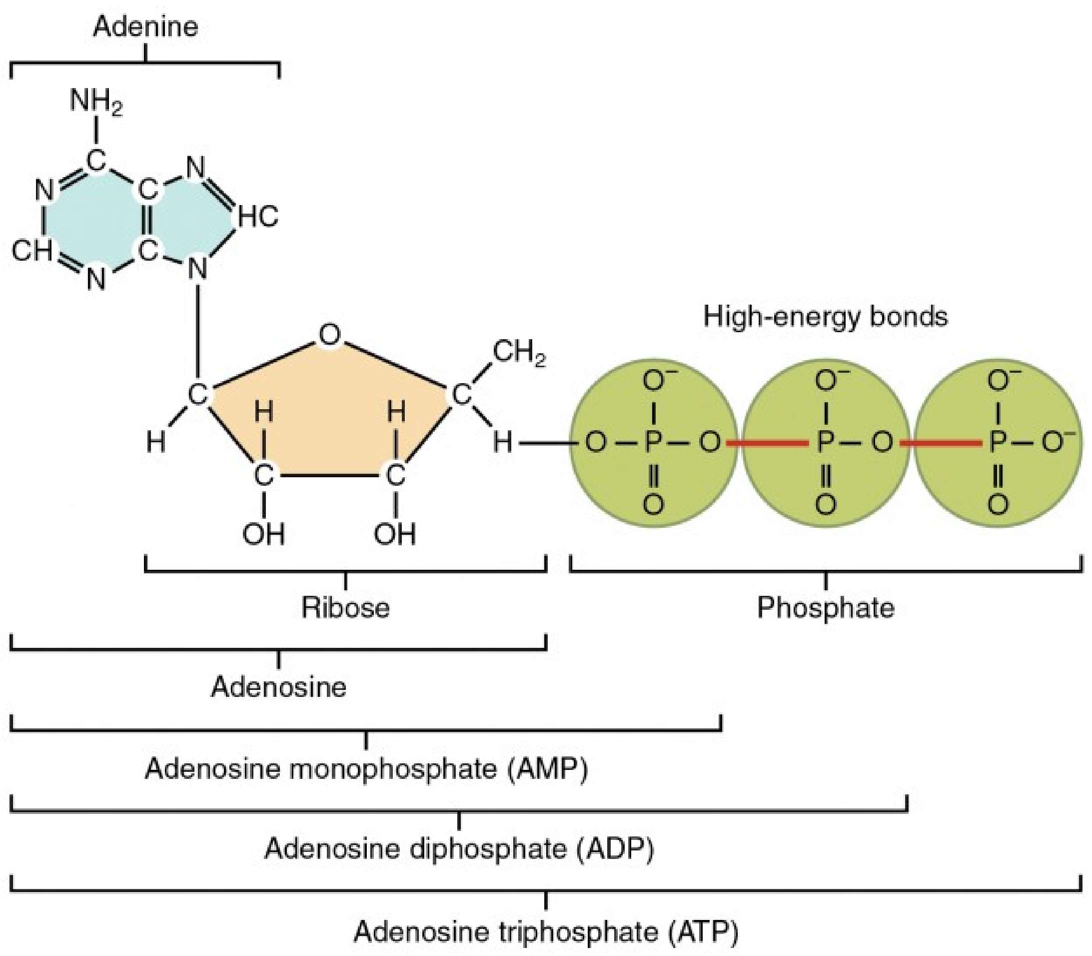
Adenosine triphosphate is a purine nucleotide with three phosphate groups connected to a carbon ring. It provides energy to all cells of the human body. It is derived from phosphorylation of ADP. ATP is needed as the storage form of energy needed for cellular respiration. Understanding how ATP can be synthesized, and how it is used by the body, forms a fundamental part of pre-med biochemistry.



Chemical Properties of ATP

Adenosine triphosphate is a purine nucleotide that has three phosphate groups connected to the 5'-carbon of the ribose ring. It is composed of the following parts:

- **Adenine: a purine base**
- **Ribose: a 5-carbon sugar ring**
- **Triphosphate: three phosphorous groups**



Adenine and ribose form together a nucleoside called adenosine. If they are connected to three phosphorous groups, the resulting structure is called adenosine triphosphate. The purine base is connected to the ribose’s 1’-carbon via an **N-glycosidic bond**. An **ester bond** connects the triphosphate group with the 5’-carbon of the ribose.

The ATP’s high energy content is contained in the anhydride bond of the triphosphate group. In the hydrolysis of ATP to adenosine diphosphate (ADP) at standard state, the anhydride bonds are cleaved and release approximately 30.5 kJ/mol. When ADP is further hydrolyzed to adenosine monophosphate (AMP), another anhydride bond is cleaved, and another 30.5 kJ/mol are released at standard state.

It is also possible to directly convert ATP to AMP by cleaving a pyrophosphate unit from ATP. Under the typical conditions in a human cell, however, the **energy release is approximately 50 kJ/mol!**

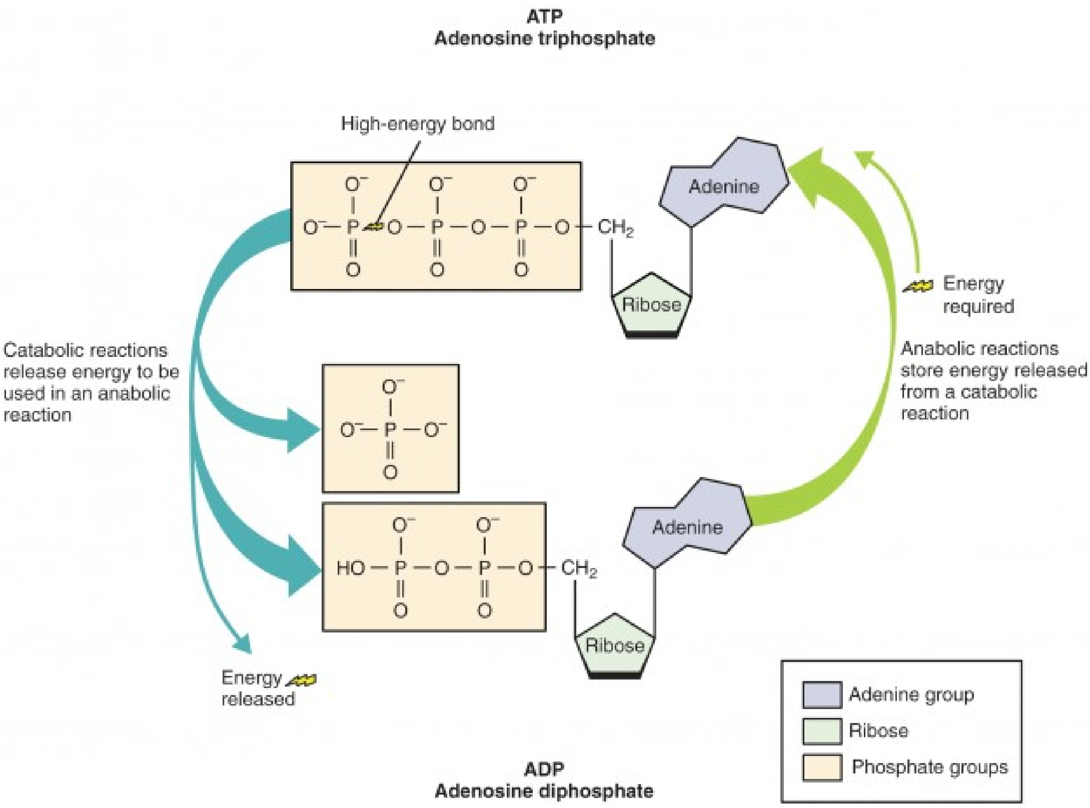


Image: “Structure of the ATP Molecule” by Phil Schatz. License: CC-BY 4.0

Synthesis of ATP

In the entire metabolic system, there are **four reactions that generate high-energy nucleoside triphosphates** (ATP or GTP = guanosine triphosphate). In **cellular respiration**, ATP is produced from ADP through **oxidative phosphorylation**. In **glycolysis** and the **citric acid cycle**, the phosphate is added to ADP through **substrate-level phosphorylation.**

Cellular respiration

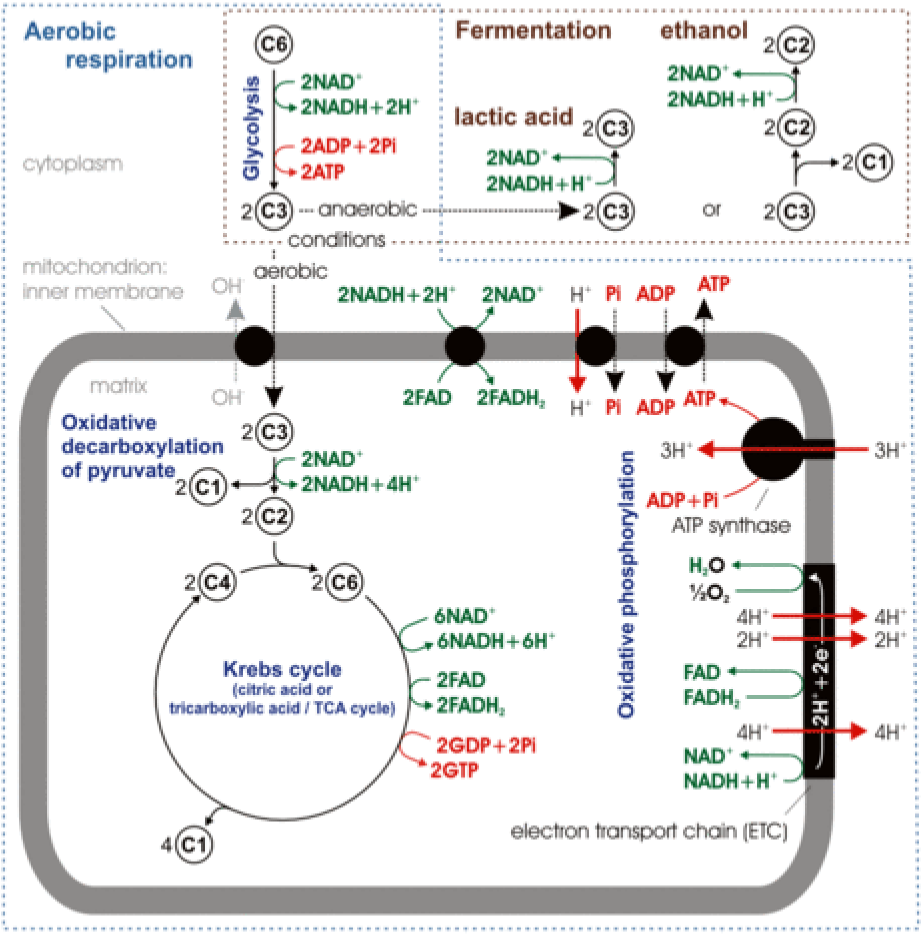


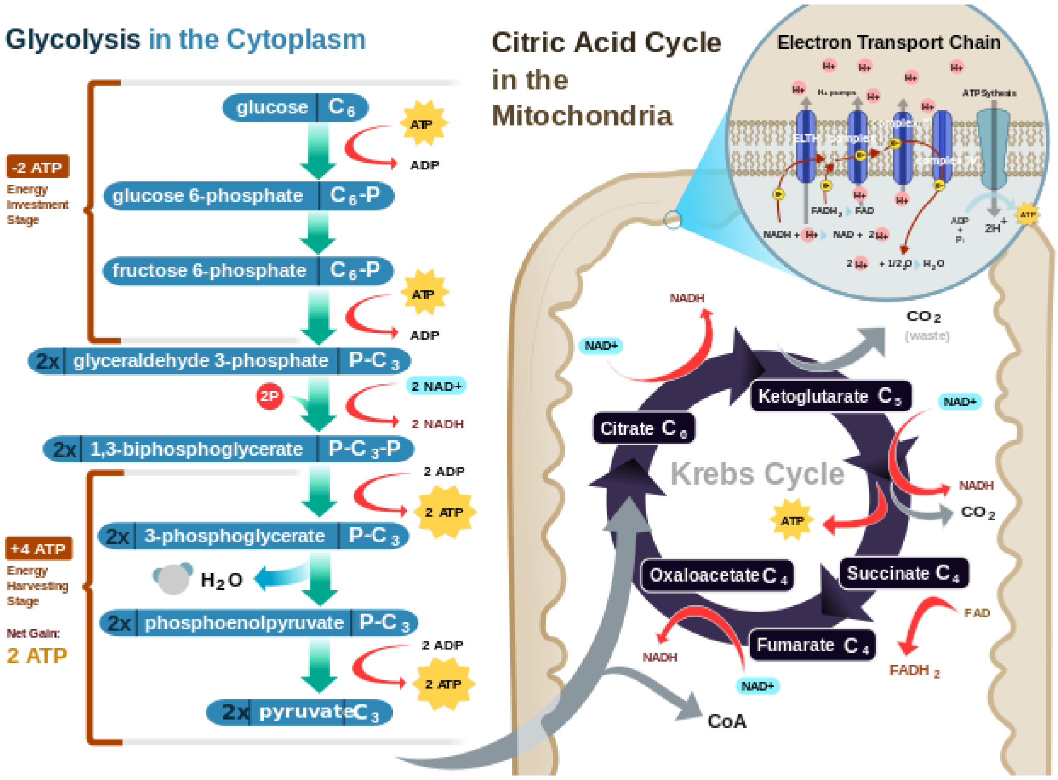
Image: "Comparison of aerobic respiration and most known fermentation types in eukaryotic cells." by Darekk2. License: CC BY-SA 3.0

The central functional component of cellular respiration is **ATP synthase**, an enzyme consisting of two parts: The catalytic head part (F1 portion) projects into the matrix of the mitochondrion and is connected to the F0 portion, which is a proton channel embedded on the **inside of the mitochondrial membrane**.

The **energy needed for the synthesis of ATP comes from a proton gradient** across the inner mitochondrial membrane, which is generated by the **four preceding respiratory chain complexes** (H^+ concentration in the intermembrane space > H^+ concentration in the matrix). Due to the gradient-directed passing of H^+ ions through the F0 portion of the ATPase, the catalytic center of the F1 portion experiences a change in conformation. Bound ADP is phosphorylated to ATP.

This entire process is called **oxidative phosphorylation** because the **energy** needed to generate the proton gradient **comes from the redox reactions of the four respiratory chain complexes**. For these redox reactions, **$NADH+H^+$ and $FADH_2$** are needed, which are provided by glycolysis and the citric acid cycle.

Substrate-level phosphorylation



[Image](https://): "A diagram of cellular respiration including glycolysis, Krebs cycle (AKA citric acid cycle) and the electron transport chain" by Regis Frey. License: CC BY-SA 3.0

The process of substrate-level phosphorylation occurs during glycolysis and the citric acid cycle. **Substrate-level phosphorylation** uses the energy released from reactions of a metabolic pathway (substrate level) to transfer an **inorganic phosphate group** from a substrate to ADP or GDP.

During **glycolysis**, the following reactions yield ATP from ADP:

- **1,3-bisphosphoglycerate + ADP + P_i → 3-phosphoglycerate + ATP**: This reaction is catalyzed by phosphoglycerate kinase.
- **Phosphoenolpyruvate + ADP + P_i → pyruvate + ATP:** This reaction is catalyzed by pyruvate kinase.

For more information, see: Glycolysis – Energy Metabolism

In the **citric acid cycle**, GTP is synthesized from GDP. GTP is similar to ATP regarding its energy content:

- **Succinyl-CoA + GDP + P_i → succinate + GTP + CoA**: This reaction is catalyzed by succinyl-CoA synthetase.

Energy balance

In sum, one can calculate how many ATP molecules can be generated from one mole of glucose. Such a calculation is based on the assumption that **one NADH yields 10 protons and one $FADH_2$ yield 6 protons for the creation of the proton gradient of cellular respiration**. **For the synthesis of 1 ATP from ADP + P_i, a flow of 4 protons across the inner mitochondrial membrane is needed**, meaning that one NADH can produce 2.5 ATP, and one $FADH_2$ can produce 1.5 ATP. This results in the following high-energy compounds generated from one mole of glucose:

- **Glycolysis: 2 ATP + 2 NADH → 7 ATP**

- **Pyruvate dehydrogenase: 2 NADH → 5 ATP**
- **Citric acid cycle: 6 NADH, 2 $FADH_2$, 2 GTP → 19 ATP**

Total: 31 ATP

However, since **1 ATP is used by the glycerophosphate shuttle**, which transports NADH from glycolysis to the cellular respiration of the mitochondria, **1 mole of glucose yields 30 moles of ATP!**

References

Rodwell, V. W., Bender, D. A., Botham, K. M., Kennelly, P. J., & Weil, P. A. (2015). *Harpers illustrated biochemistry*. New York: McGraw-Hill Education.

Sheriff, D. S. (2004). *Medical biochemistry*. New Delhi, India: Jaypee Brothers Medical (p).

Notes