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Metabolism of Carbohydrates

- Glycolysis & the Oxidation of Pyruvate
- The Citric Acid Cycle: The Central Pathway of Carbohydrate, Lipid & Amino Acid Metabolism
- Metabolism of Glycogen
- Gluconeogenesis & the Control of Blood Glucose
- The Pentose Phosphate Pathway & Other Pathways of Hexose Metabolism
Glycolysis & the Oxidation of Pyruvate

- Describe the pathway of glycolysis and its control.

- Describe the reaction of pyruvate dehydrogenase and its regulation.

- Explain how inhibition of pyruvate metabolism leads to lactic acidosis
Glycolysis, the major pathway for glucose metabolism, occurs in the cytosol of all cells. It can function either aerobically or anaerobically, depending on the availability of oxygen and the electron transport chain.

Erythrocytes, which lack mitochondria, are completely reliant on glucose as their metabolic fuel, and metabolize it by anaerobic glycolysis.
Glycolysis is the principal route for carbohydrate metabolism.

The ability of glycolysis to provide ATP in the absence of oxygen is especially important, because this allows skeletal muscle to perform at very high levels of work output when oxygen supply is insufficient, and it allows tissues to survive anoxic episodes.
Summary of glycolysis

1. **Phosphorylation**
   - Glucose → 2 ATP, 2 ADP

2. **Lysis**
   - Hexose Biphosphate

3. **Oxidation**
   - 2 Triose Phosphate Molecules → 2 NAD⁺, 2 NADH + H⁺

4. **ATP Formation**
   - 2 Pyruvate Molecules → 4 ADP, 4 ATP
2 × 3 carbon sugar molecules per glucose

Pyruvate kinase

Enolase

Phosphoglyceromutase

Phosphoglycerate kinase

\[ \text{Pyruvate} \xrightarrow{\text{ATP}} \text{Phosphoenolpyruvate} \xleftrightarrow{\text{ADP}} \text{2-Phosphoglycerate} \xrightarrow{\text{ATP}} \text{3-Phosphoglycerate} \xrightarrow{\text{ADP}} \text{Bisphosphoglycerate} \]

\[ \text{H}_3\text{PO}_4 \xrightarrow{\text{Glyceraldehyde-3-phosphate dehydrogenase}} \text{NAD}^+ \xrightarrow{\text{NADH}} \]
The 2,3-Bisphosphoglycerate pathway in erythrocytes.
Regulation of Glycolysis

Major sites of regulation of glycolysis:

1- Hexokinase (Glucokinase)

2- Pophofructokinase

3- Pyruvate kinase
## Regulation of Glycolysis

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Activator</th>
<th>Inhibitor</th>
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<tbody>
<tr>
<td>Hexokinase (Step 1)</td>
<td></td>
<td>Glucose-6-phosphate ATP</td>
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<tr>
<td></td>
<td></td>
<td>ATP</td>
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<tr>
<td>PFK (Step 3)</td>
<td>Fructose-2,6-bisphosphate AMP</td>
<td>Citrate ATP</td>
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<tr>
<td></td>
<td></td>
<td>ATP</td>
</tr>
<tr>
<td>Pyruvate kinase (Step 10)</td>
<td>Fructose-1,6-bisphosphate AMP</td>
<td>Acetyl-CoA ATP</td>
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</tbody>
</table>

These enzymes are allosterically regulated
THE OXIDATION OF PYRUVATE

- Pyruvate, formed in the cytosol,

- is transported into the mitochondrion by a proton symporter.

- Inside the mitochondrion, it is oxidatively decarboxylated to acetyl-CoA by a multienzyme complex that is associated with the inner mitochondrial membrane.
Pyruvate is converted to acetyl-CoA through the process of pyruvate dehydrogenase (PDH). The conversion involves the coenzyme NAD+ and the formation of NADH and CO₂. The reaction can be represented as follows:

\[
\text{Pyruvate} \rightarrow \text{Acetyl-CoA} + \text{NAD}^+ + \text{NADH} + \text{CO}_2
\]
Oxidative decarboxylation of pyruvate by the pyruvate dehydrogenase complex
Regulation of pyruvate dehydrogenase (PDH).
CLINICAL ASPECTS

- Inhibition of Pyruvate Metabolism Leads to Lactic Acidosis.
  - Arsenite and mercuric ions inhibit pyruvate dehydrogenase.
  - Dietary deficiency of thiamin results in pyruvate to accumulate.
- Patients with inherited pyruvate dehydrogenase deficiency
Inherited aldolase A deficiency and pyruvate kinase deficiency in erythrocytes cause hemolytic anemia.
The Citric Acid Cycle

- Describe the reactions of the citric acid cycle
- Explain the importance of vitamins in the citric acid cycle
- Explain how the activity of the citric acid cycle is controlled
The citric acid cycle
(the Krebs or tricarboxylic acid cycle)

- A sequence of reactions in mitochondria that oxidizes acetyl-CoA to CO2

- reduces coenzymes that are reoxidized through the electron transport chain linked to the formation of ATP.
The citric acid cycle is the final common pathway for the oxidation of carbohydrate, lipid, and protein. It also has a central role in gluconeogenesis, lipogenesis, and interconversion of amino acids.

Many of these processes occur in most tissues, but liver is the only tissue in which all occur to a significant extent.
The citric acid cycle
the citric acid cycle
Biosynthetic roles of The citric acid cycle