**Respiration**

**Syllabus:** The importance of respiration in converting chemical energy in food to chemical energy in ATP. 
The sites of respiration – the sites of the various biochemical pathways of respiration; the structure of mitochondrion as shown in electron micrographs. (refer to topic ‘The cell --- organelles of cell’)
Glycolysis – an outline of glycolysis to show:
(1) the phosphorylation of glucose;
(2) the break down of hexose phosphate to triose phosphate;
(3) the conversion of triose phosphate to pyruvate with the production of reduced NAD and ATP.
Aerobic pathway – the conversion of pyruvate to acetyl-CoA; an outline of the Krebs cycle to show:
(1) the combination of acetyl-CoA with 4-C compound to form 6-C compound;
(2) that the 6C compound undergoes a series of reactions to regenerate the 4C compound with the release of carbon dioxide;
(3) the production of reduced NAD and ATP.
Lipids and proteins can be used to produce reduced NAD and ATP; the electron transport chain as a process of oxidative phosphorylation; the role of molecular oxygen as the final electron acceptor.
Anaerobic pathway – the fate of pyruvate under anaerobic condition; the formation of lactic acid in muscle; the oxygen debt; the formation of ethanol and carbon dioxide in yeast.
Energy yield: the comparison of the energy yield of aerobic and anaerobic respiration, without calculating the number of ATP produced.
Role of ATP – the role of ATP in energy transfer.

**Cellular respiration**

It is a process occurs in cytoplasm and mitochondria of living cells that liberate chemical energy when organic molecules are oxidized. All organisms get their energy by respiration. Respiration takes place in the cells with generally involves the breakdown of sugar. The equation below summarizes the process:

\[
C_6H_{12}O_6 + 6 O_2 \rightarrow 6 CO_2 + 6 H_2O + \text{energy}
\]

The oxidation of food yields energy, but it cannot be used directly by the body. The chemical energy is mostly carried by the adenosine triphosphate (ATP) molecules which give an instance source of energy for the metabolic processes in the cells.

Cellular respiration involves oxidation of a substrate to yield ATP. Organic compounds which are used as substrate in respiration are always carbohydrates.
Carbohydrates - these are usually the first choice of most cells.
- brain cells of mammals can use only glucose, this is the reason why coma occurs in the patient who has suffer from hypoglycaemia (extreme low of blood glucose)
- polysaccharides are hydrolysed to monosaccharides before they enter the respiratory pathway

**Sites of respiration:**
Cellular respiration can divided into three different phases:
(1) glycolysis (occurs in the cytoplasm of cell),
(2) Krebs cycle (occurs in the matrix of mitochondrion)
(3) electron transport chain (carried out by the enzyme on the cristae of the mitochondrion)
The biochemical pathways:

A. Glycolysis:
- Represents a series of reactions in which a 6C glucose is broken down into two molecules of triose phosphate (3C) then pyruvate (3C) with the production of reduced NAD and ATP.
- This process does not require the presence of oxygen (anaerobic process)
  (i) Phosphorylation of glucose into 6C compound:
    : glycolysis begins with the phosphorylation of a glucose
    : this step requires energy from ATP
    : this initial phosphorylation is extremely important because it raises the energy level of the glucose molecules (activation of the glucose)
  (ii) Splitting up of the 6C compound into two triose phosphate:
    : the 6C compound splits up to give two molecules of triose phosphate which are later converted to pyruvate (pyruvic acid)
    : in this conversion, two ATP and two hydrogen atoms per triose phosphate are released (total 4 ATP and 4 H released per glucose molecule)
- the hydrogen atom released from the glycolysis would be carried by NAD to form NADH₂ and carried into mitochondria to carry out oxidative phosphorylation to yield ATP
- the overall equation of glycolysis:
  \[
  \text{glucose} + 2 \text{ATP} \rightarrow 6\text{C compound} \\
  6\text{C compound} \rightarrow 2 \text{triose phosphate} \\
  2 \text{triose phosphate} \rightarrow 2 \text{pyruvic acid} + 4 \text{ATP} + 4 \text{H} \\
  2 \text{NAD} + 4 \text{H} \rightarrow 2 \text{NADH}_2 \\
  \text{glucose} + 2 \text{NAD} \rightarrow 2 \text{pyruvic acid} + 2 \text{NADH}_2 + 2 \text{ATP}
  \]
(iii) Biological significance of glycolysis:
: glycolysis neither require oxygen nor mitochondrial enzymes, it occurs in cytoplasm anaerobically
: it can provide a small amount of energy to maintain the cellular activities in emergency, i.e. yeast live anaerobically or muscle cells after prolonged vigorous activities

![Glycolysis in outline](image)

**B. Aerobic pathway** :-
- If there is oxygen, the pyruvate passes directly into the Krebs cycle which take place in the mitochondrion only
  (a) oxidation of pyruvate:
    : before entering the Krebs cycle, pyruvate is both oxidized and decarboxylated into a 2C acetyl group
    : a molecule of NADH is produced and the acetyl group is temporarily attached to coenzyme A (CoA)
    : acetyl-CoA is formed and act as the starting substrate for the Krebs cycle

\[
\text{pyruvic acid (3C)} + \text{coenzyme A} + \text{NAD} \rightarrow \text{acetyl-CoA (2C)} + \text{CO}_2 + \text{NADH}
\]

(b) In the matrix of mitochondrion (Krebs cycle):
: acetyl-CoA enters into the mitochondrion
: after the entry of mitochondrion, the acetyl-CoA combines with 4C compound to form 6C compound and liberates coenzyme A out of mitochondrion
: acetyl-CoA (2C) + oxaloacetic acid (4C) \rightarrow \text{citric acid (6C)} + \text{coenzyme A}
: the citric acid will go through a cyclic reaction, in the course of the cycle, decarboxylation occur to yield two molecules of carbon dioxide, and 4C compound is regenerated
: at the same time, dehydrogenation is also occur and NADH and FADH are formed and energy is released to form ATP
: for each molecule of acetyl-CoA entering the cycle, four pairs of hydrogen atoms (3 pairs are carried by NAD to form NADH, one pair are carried by FAD to form FADH), two molecules of CO$_2$ and one molecule of ATP are produced
Importance of Krebs cycle:
- It provides H atoms which ultimately yield the major part of the energy derived from the oxidation of a glucose molecule through the electron transport chain.
- It is a valuable source of intermediates which are used to manufacture other substances, e.g., fatty acid, amino acids, etc.

(c) Electron transport chain / oxidative phosphorylation:
- The hydrogen atoms produced in glycolysis and the Krebs cycle are carried by NAD or FAD as NADH$_2$ and FADH$_2$ respectively, they are at a high energy level.
- In the course of the electron transport chain / oxidative phosphorylation, hydrogen or electrons are passed ‘down hill’ to the oxygen (electron acceptor) to form water.
- And the energy released in the process is used to form ATP from ADP.
- Electron transport chain contains different carriers, but at the end the hydrogen will combine with O$_2$ to form water.
- As the hydrogen atoms / electrons are moved from one carrier to another, it is an oxidative process; since it also involves the synthesis of ATP, the whole process of electron transport is known as “oxidative phosphorylation.”
- One molecule of NADH$_2$ passes the electron transport chain yielding 3 ATP, while one molecule of FADH$_2$ only yield 2 ATP.
- The number of ATP produced in the cellular aerobic respiration from one molecule of glucose is calculated as below:

<table>
<thead>
<tr>
<th>Process</th>
<th>Intermediates / products</th>
</tr>
</thead>
<tbody>
<tr>
<td>glycolysis</td>
<td>2 ATPs 2 NADH$_2$</td>
</tr>
<tr>
<td>conversion of pyruvic acid to acetyl-CoA</td>
<td>2 NADH$_2$</td>
</tr>
<tr>
<td>aerobic Krebs cycle</td>
<td>2 ATPs 6 NADH$_2$ 2 FADH$_2$</td>
</tr>
<tr>
<td>amount of ATP produced</td>
<td>4 ATPs 10 x 3 ATPs 2 x 2 ATPs</td>
</tr>
<tr>
<td>amount of ATP produced from one glucose</td>
<td>Total = 38 ATPs</td>
</tr>
</tbody>
</table>
Exercise:
(91 I 4)
By means of a flow diagram, briefly outline the three main stages of aerobic respiration with a carbohydrate substrate. Annotate your diagram to show the essential features of each of the three main stages.
<N.B. Chemical formulae of individual compounds are NOT required.> [7 marks]

(94 II 2)
(a) Describe the three stages of cellular respiration for carbohydrate metabolism. [10 marks]
(b) Compare and contrast the products of the metabolic process in (a) in the presence and absence of free oxygen. [3 marks]

(d) Oxidation of other organic molecules:
: sugars are not the only material which can be oxidized by cells to release energy.
: both fats and protein may also be used as respiratory substrates.
Fats - they form the “first reserve” and are mainly used when carbohydrates reserves have been exhausted
- but in skeletal muscle cells, if glucose and fatty acids are available, these cells respire the acids in preference to glucose
Proteins - they have many other essential functions, they are only used when all carbohydrates and fat reserves have been used up, as during prolonged starvation

Fig. 14 Summary of respiratory pathway.
C. Anaerobic condition: -
- If there is no oxygen, the pyruvate convert to alcohol in yeast and plant cells, and lactic acid in animal cells (e.g. muscle cells in human)
- The lactic acid will return to the liver via bloodstream for the resynthesis of carbohydrates or oxidation to carbon dioxide and water

(a) Alcoholic fermentation:
- Carried out by yeast and some plant cells
- Only 2 ATP is gained in the glycolysis
- The pyruvic acid is reduced by the NADH₂ and produce alcohol (ethanol) and carbon dioxide which both are toxic to the cells
- It is occurred only when the cell is shortage of O₂

\[
\text{glucose} \longrightarrow 2 \text{pyruvic acid} \longrightarrow 2 \text{ethanol} + 2 \text{CO}_2
\]

(b) Lactic acid fermentation:
- Carried out by muscle cells in the animals in the absence of oxygen during vigorous activity
- Only 2 ATP is gained in glycolysis
- Lactic acid is produced and accumulated in the muscle cells
- This is what happens in mammalian cells when they have an “oxygen debt”
- Later it will diffuse into the blood and is carried to the liver where it is oxidised into carbon dioxide and water or rebuilt of glucose or glycogen in the presence of oxygen

\[
\text{glucose} \longrightarrow 2 \text{pyruvic acid} \longrightarrow 2 \text{lactic acid} \longrightarrow \text{resynthesis to glucose / oxidized to CO}_2 \text{ and H}_2\text{O}
\]

Oxygen debt:
- To satisfy the energy demands of the exercise aerobically, 3 dm³ of oxygen of oxygen per minute must be supplied (see graph below).
- This is not achieved until 6 minutes after exercise began. So the oxygen debt (the amount of oxygen that was needed, but not supplied from outside the body by breathing, region A) is built up.
- The debt (region B in the graph) is repaid by continued rapid and deep breathing when the period of exercise ends.
- The extra oxygen then absorbed by the blood corresponds to the oxygen debt and is used to oxidize the lactic acid produced in anaerobic respiration to CO₂ and H₂O or converted the lactic acid to glucose / glycogen in liver.

Fig. 15 Oxygen uptake during exercise and recovery. This shows the principle of oxygen debt.
Importance of anaerobic respiration to everyday life:

1. Alcoholic fermentation
   - Alcohol produced in yeast can be used to produce beer (substrate used is partially germinated barley grain) and wine (substrate used is grapes).
   - Production of carbon dioxide in yeast is used in bread making, to make dough rise.
   - In sewage treatment plant, anaerobes can be used to decompose the wastes, the ethanol produced can be collected to make gasohol (a kind of fuel can be used in car) or used directly as fuel.

2. Lactic acid fermentation
   - Lactic acid bacteria in milk break down lactose anaerobically.
   - This can be used to produce dairy products:
     - Yogurt = substrate: whole milk
     - Cheese = substrate: solid part of milk, known as curd
     - Butter = substrate: cream of fresh milk

[NOTE] Anaerobic respiration is not common in higher living organisms because:

1. The small amount of energy is not enough to meet the demand of the organisms, this is especially true in active animals.
2. The by-products from anaerobic respiration are toxic to the organisms if accumulated to high concentration, i.e. alcohol or lactic acid.

Exercise:

(90 I 1a) What is oxygen debt? Explain its physiological significance. [5 marks]

(96 I 8b) Name and describe the major physiological process that takes place at matrix of cytoplasm during prolonged vigorous exercise. [4½ marks]

Comparison of aerobic and anaerobic respiration:

A. Differences:

<table>
<thead>
<tr>
<th>Item</th>
<th>Aerobic respiration</th>
<th>Anaerobic respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen requirement</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Oxidation of substrate</td>
<td>Complete oxidation</td>
<td>Incomplete oxidation</td>
</tr>
<tr>
<td>End products</td>
<td>Carbon dioxide and water</td>
<td>Plant cell: CO₂ and alcohol</td>
</tr>
<tr>
<td>Energy released per glucose</td>
<td>More (38 ATPs)</td>
<td>Less (2 ATPs)</td>
</tr>
<tr>
<td>Occurrence</td>
<td>In most organisms</td>
<td>In lower organisms, e.g. yeast, bacteria and muscle cells after prolonged contraction</td>
</tr>
</tbody>
</table>

B. Similarity: (1) Both aerobic and anaerobic respiration yield ATP (energy);
(2) Both require complex organic compound as substrate;
(3) Both are oxidative process;
(4) Both have the same initial stage (glycolysis);
(5) Both take place in living cells.
Role of ATP :

A. Structure of ATP :-
- it is a nucleotide consisting of adenosine (adenine + ribose) and attach with three phosphate groups
- the two end phosphate bonds are often known as ‘high energy bond’ since energy is liberated when ATP is hydrolysed

```
Adenine          ribose
↓               ↓
phosphate        phosphate        phosphate
```

B. Liberation of energy from ATP:--
- when hydrolysis of the ‘high energy bond’ of ATP occurs, the free energy yield is about 30.6 KJ

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ATP + H₂O → ADP + H₃PO₄ + 30.6 KJ

ADP + H₂O → AMP + H₃PO₄ + 30.6 KJ

AMP + H₂O → Adenosine + H₃PO₄ + 13.8 KJ
```
- ADP may be ‘rephosphorylated’ to ATP by respiratory activity

```
AMP + 30.6 KJ → ADP + 30.6 KJ → ATP
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C. Importance of ATP :-
(a) As universal energy carrier :
- since all the chemical energy is in one form (ATP), the energy consuming processes need only one system that accept chemical energy from ATP
- found in all living cells and is an instant source of energy within the cell
- it transports chemical energy to energy consuming processes within the cell
- when the cell requires energy, hydrolysis of ATP is all that has to occur for the energy to be made available

Examples (1) Biosynthesis of protein from amino acids;
(2) Muscle contraction.
(3) Active transport.
(b) As an intermediate in the metabolic reaction :
- it is a common intermediate between respiration and energy requiring process, with phosphate being removed or replaces
- ATP can donate the phosphate group to activate substances to initiate the reaction, e.g. phosphorylation of glucose in glycolysis

Exercise : (97 II 1a)
Explain the role of ATP in cellular metabolism. [3½ marks]