15.1 Human nutrition

Essential idea: A balanced diet is essential to human health.

**Essential nutrients**

<table>
<thead>
<tr>
<th>essential nutrients</th>
<th>non-essential nutrients</th>
</tr>
</thead>
<tbody>
<tr>
<td>• some amino acids</td>
<td>carbohydrate (such as starch and glucose)</td>
</tr>
<tr>
<td>• some unsaturated fatty acids</td>
<td>as respiratory substrates; lipids are</td>
</tr>
<tr>
<td>• some minerals</td>
<td>alternatives</td>
</tr>
<tr>
<td>• vitamins</td>
<td></td>
</tr>
<tr>
<td>• water</td>
<td></td>
</tr>
</tbody>
</table>

Table 15.1 Essential and non-essential nutrients

**Dietary minerals**

Dietary minerals are required in the diet in relatively small quantities.

- major minerals, in the form of ions, include:
  - calcium (major constituents of structures such as bones and teeth)
  - iron (needed to form hemoglobin)
  - phosphate (needed to make DNA, cell membranes, etc.)
  - sodium and chloride ions (control of the composition of body fluids)
- micronutrients (trace elements), such as manganese; they are often co-factors in the functioning of particular enzymes.

About 15 mineral elements are known to be essential for a healthy body (Table 15.2).

They are obtained from food sources, where they are present in low concentrations.

<table>
<thead>
<tr>
<th>Major minerals</th>
<th>Daily intake</th>
<th>Trace elements</th>
<th>Daily intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>calcium</td>
<td>0.9 g</td>
<td>fluoride</td>
<td>1.82 mg</td>
</tr>
<tr>
<td>phosphorus</td>
<td>1.5 g</td>
<td>copper</td>
<td>1.63 mg</td>
</tr>
<tr>
<td>potassium</td>
<td>3.2 g</td>
<td>selenium</td>
<td>0.06 mg</td>
</tr>
<tr>
<td>sodium</td>
<td>3.4 g</td>
<td>iodine</td>
<td>0.024 mg</td>
</tr>
<tr>
<td>chloride</td>
<td>5.2 g</td>
<td>manganese</td>
<td>5.0 mg</td>
</tr>
<tr>
<td>magnesium</td>
<td>0.3 g</td>
<td>chromium</td>
<td>0.09 mg</td>
</tr>
<tr>
<td>iron</td>
<td>14.0 mg</td>
<td>cobalt</td>
<td>0.3 mg</td>
</tr>
<tr>
<td>zinc</td>
<td>11.4 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 15.2 The major minerals and trace elements required
15.1 Human nutrition

Many vitamins are essential constituents of the diet because most cannot be manufactured in the body. Their absence from the diet tends to have marked effects (deficiency diseases).

- Vitamins have complex chemical structures.
- They do not belong to a single group of chemical compounds, and so are put in groups: vitamin A, vitamins of the B group, etc.
- The functions of vitamins are as diverse as their structures, although several function as coenzymes in the body.
- Some of the vitamins are fat-soluble, while others are water-soluble (Table 15.3).

### Table 15.3 Vitamins in the human diet

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Source</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat-soluble vitamins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A (retinol)</td>
<td>fish liver oils, animal liver; made in the body from carotene</td>
<td>required for normal immune system function and for production of rhodopsin (for retinal rod cells)</td>
</tr>
<tr>
<td>D (calciferol)</td>
<td>fish liver oils, butter, egg yolk; made in body by action of sunlight</td>
<td>required for absorption of calcium</td>
</tr>
<tr>
<td>E (tocopherol)</td>
<td>plant oils</td>
<td>antioxidant</td>
</tr>
<tr>
<td>K (phyloquinone)</td>
<td>dark green leafy vegetables; made by bacteria of gut</td>
<td>blood-clotting factor</td>
</tr>
<tr>
<td>Water-soluble vitamins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B₁ (thiamine)</td>
<td>widely occurring</td>
<td>coenzyme in decarboxylation in respiration</td>
</tr>
<tr>
<td>B₂ (riboflavin)</td>
<td>widely occurring</td>
<td>coenzyme in electron transport in respiration</td>
</tr>
<tr>
<td>B₃ (niacin, nicotinic acid)</td>
<td>meat, yeast extract, potatoes; made from the amino acid tryptophan</td>
<td>precursor of enzymes NAD/NADP</td>
</tr>
<tr>
<td>B₅ (pantothenic acid)</td>
<td>widely occurring</td>
<td>component of coenzyme A</td>
</tr>
<tr>
<td>B₆ (pyridoxine)</td>
<td>meat, fish, eggs, some vegetables</td>
<td>coenzyme in amino acid formation by transamination from fatty acids</td>
</tr>
<tr>
<td>B₁₂ (in some cobalt-containing compounds)</td>
<td>liver, yeast; not in plants</td>
<td>part of cell-division enzyme, for nerve function</td>
</tr>
<tr>
<td>folic acid</td>
<td>liver, white fish, raw leaf vegetables</td>
<td>for enzyme in DNA replication</td>
</tr>
<tr>
<td>H (biotin)</td>
<td>liver, yeast, egg white; synthesized by gut bacteria</td>
<td>coenzyme in energy metabolism</td>
</tr>
<tr>
<td>C (ascorbic acid)</td>
<td>potatoes, green vegetables, fruits</td>
<td>antioxidant, coenzyme in protein metabolism; involved in iron absorption</td>
</tr>
</tbody>
</table>

### Essential fatty acids and amino acids

#### Essential fatty acids

Bodies can synthesize most fatty acids from carbohydrates, but not all of them. Omega-3 fatty acids are essential fatty acids that cannot be synthesized from carbohydrate.

- They are a group of naturally occurring polyunsaturated fatty acids.
- Omega-3 fatty acids are chemically special because they have between three and six double bonds in the hydrocarbon tail and, in particular, the first double bond is always positioned between the third and the fourth carbon atom from the opposite (omega) end of the hydrocarbon chain to the carboxyl group (Figure 15.1).
- A number of omega-3 fatty acids occur in plant and fish oils, and are thought to be particularly beneficial to health.
Essential amino acids

Proteins in the diet are first digested (i.e. broken down) by proteases to their constituent amino acids. These are then absorbed into the body, and there contribute to the pool of amino acids from which new proteins are built (Figure 15.2).

About 20 amino acids are necessary components of the range of protein molecules made in our bodies (Topic 2, pages 47–48).

Half of all amino acids cannot be synthesized in the body, at least at some stage of life, and are, therefore, essential amino acids (Table 15.4).

Protein deficiency malnutrition: when one or more essential amino acids is limited and so the body cannot make sufficient protein it requires.

### Table 15.4 Essential amino acids

<table>
<thead>
<tr>
<th>Essential at all times</th>
<th>histidine, isoleucine, leucine, lysine, methionine, phenylalanine, tryptophan and valine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential in the diet of infants</td>
<td>arginine</td>
</tr>
<tr>
<td>Essential if the amino acid phenylalanine is absent</td>
<td>threonine</td>
</tr>
</tbody>
</table>

**Essential amino acids:** cannot be synthesized
These must be present in the proteins eaten in sufficient amounts if malnutrition is to be avoided.

**Any excess amino acids cannot be stored – instead they are deaminated** and the NH$_2$ group is combined with CO$_2$ to form urea (excreted).

**Expert tip**

Alpha-linoleic acid (an omega-3 fatty acid) and linoleic acid (an omega-6 fatty acid) are needed throughout the body. The presence in our diet of omega-3 fatty acids may also help prevent heart disease by reducing the tendency of the blood to form clots, and by giving us healthy, well-functioning plasma membranes about cardiac muscle fibres.

**Key fact**

Some fatty acids and some amino acids are essential.

---

Figure 15.2 The supply of amino acids in human nutrition
Malnutrition

Malnutrition may be caused by a deficiency, an imbalance or an excess of nutrients in the diet.

A poor diet can take a number of forms, such as:

- low total protein content
- excess of fats and/or carbohydrates (i.e. an excess of calorie content)
- absence of essential fatty acids or amino acids
- absence of specific vitamins or minerals.

Protein deficiency and malnutrition

Some diets, although energy-rich, are protein deficient. Examples include diets largely based on the tropical crops

- cassava (a root crop)
- plantain (a type of banana)
- sweet potato.

A starvation diet is when food intake is too little to meet bodily needs. When this occurs, any protein eaten is largely used as an energy source and the amino acids obtained by digestion are respired.

Protein-deficient malnutrition can lead to a lack of blood plasma proteins, with the result that fluid is retained in tissues.

- This causes swelling, referred to as ‘edema’, that is typically seen in the abdomen.
- When children experience prolonged, extreme protein deficiency their mental and physical development suffers.
- The clinical symptoms of protein deficiency are evident in patients with conditions known as kwashiorkor and marasmus (Figure 15.3).

Key definition

Malnutrition – a serious condition that occurs when a person’s diet doesn’t contain the right amount of nutrients.

Key fact

Malnutrition may be caused by a deficiency, imbalance or excess of nutrients in the diet.

Expert tip

In a healthy diet, proteins can be obtained from plant sources, such as wholegrain rice or wheat, or from fish and meat sources (more expensive than plant sources but more concentrated).

Figure 15.3 Kwashiorkor and marasmus – the clinical signs
Case study: phenylketonuria
Phenylketonuria (PKU) is a genetic error of protein metabolism.
- PKU is caused by a mutation in a gene coding for a protein which forms the enzyme that converts the amino acid phenylalanine into the amino acid tyrosine.
- In people born with the mutation, the phenylalanine that is taken into the body as part of the normal diet, and not immediately used in the synthesis of new proteins, starts to build up in the blood.
- An excess of phenylalanine in the blood causes many unpleasant and dangerous side-effects. Symptoms include
  - vomiting
  - seizure
  - growth deficiency
  - severe mental retardation (in severe cases).
In many countries, babies are screened at birth for this disorder.
- Where PKU is detected, the symptoms can largely be avoided by restricting the diet to one supplying only the amount of phenylalanine that the body requires for protein synthesis.
- Unfortunately, the patient may still develop learning difficulties.

Starvation and the breakdown of body tissues
Diets that are consistently very low in energy-rich foods, including lipids, have major health risks.
- In the absence of dietary intake of energy sources, the body will first exhaust its glycogen stores.
- In the continuation of such a diet, the body respires the amino acids derived from protein digestion, rather than using them to build and maintain tissues.
- On a continuing low-energy diet, muscle proteins are broken down and the body wastes away. For the nutritionally deprived members of communities in less-developed countries, muscle wastage due to starvation is a common problem.

Breakdown of heart muscle due to anorexia
The condition known as anorexia nervosa:
- is the result of deliberate dieting, and sometimes deliberate vomiting, by people who have developed an obsessive fear of gaining weight or becoming fat; they see themselves as much fatter than they actually are
- is believed to be on the increase, particularly among young Caucasian females, although the condition is not exclusive to females
- leads to serious weight loss and even the loss of consecutive menstrual cycles in women
- can lead to the breakdown of heart muscle, with serious consequence for the individual.

Excess energy-rich foods
A healthy diet requires sufficient metabolic energy: this energy is normally supplied from carbohydrates and lipids.
The amounts of energy that major food substances might yield, as when they are completely respired, are:

- carbohydrates 1600–1760 kJ/100 g
- lipids (fats and oils) 3700–4000 kJ/100 g
- protein 1700–1720 kJ/100 g.

Weight for weight, lipids provide far more energy than carbohydrates, but an excess of either of these components causes health problems.

## Clinical obesity

Diets containing an excess of lipids and fatty acids provide more energy-rich items than the body requires.

- People eating such a diet are in danger of becoming overweight and then obese, due to the storage of excess fat in the adipose tissue, present around the body organs and under the skin.
- The condition of clinical obesity is defined as having a Body Mass Index (BMI) of 30 and over.

## Health consequences of obesity

Being overweight has unfavourable health consequences.

1. There is an enhanced likelihood of acquiring Type II diabetes (Figure 6.38, page 191).
   - The β cells of the islets of Langerhans in the pancreas typically produce insulin in quantities that ought to be sufficient.
   - In the obese, the insulin receptors on target cells are less sensitive.
   - The patient has a generally raised blood glucose level, but other symptoms of diabetes are only mildly experienced.
   - As with other forms of diabetes, there is a raised risk of circulatory disorders, renal failure, blindness, strokes, or heart attacks if the condition is not diagnosed and treated.

2. There is an enhanced likelihood of hypertension.

   **Blood pressure** is quoted as two values.
   - The higher pressure is produced by ventricular systole (systolic pressure) and this is followed by low pressure at the end of ventricular diastole (diastolic pressure).
   - Normally, systolic, and diastolic pressures are about 15.8 and 10.5 kPa respectively.
   - Obesity can persistently increase blood pressure.

Hypertension is known as a ‘silent killer’ because of the damage it does to the heart, blood vessels, brain, and kidneys without causing noticeable discomfort.

### Key definitions

**Hypertension** – a condition of persistently raised blood pressure

**Blood pressure** – the pressure of the blood flowing through the arteries.

### Key fact

Overweight individuals are more likely to suffer hypertension and type II diabetes.
Determination of the energy value of food

Energy content of food can be measured using the apparatus shown in Figure 15.4. Suitable foods to use are biscuits, crisps, pasta, or crispbread. Nuts should not be used, as some people are allergic to them.

![Figure 15.4 A simple experiment to determine the energy content of food](image)

Method

1. Two or more different types of food are chosen.
2. A small sample of the first food to be measured is taken and its mass measured (g).
3. 20 cm³ of water is placed in a boiling tube, supported using a clamp stand.
4. The temperature (°C) of the water is measured and recorded.
5. The food is held using some heatproof tongs, or on the end of a mounted needle or spatula. The food is placed in a Bunsen flame until it catches fire (this may take 30 seconds or so).
6. As soon as the food is alight, the burning food is held directly under the boiling tube of water, so that the heat from the flame is transferred to the water. The boiling tube and burning food are positioned over a heatproof mat.
7. If the food goes out, it can be quickly relit. The equipment continues to trap the heat from the flame until no more food is left to burn.
8. The temperature is measured at the end of the experiment.

4.2 joules of energy are needed to raise the temperature of 1 g of water by 1°C. In this experiment, 20 g of water has been heated. (1 cm³ of water has a mass of 1 g, so 20 cm³ has a mass of 20 g.) This means 20 × 4.2 joules of energy are needed to raise the temperature of 20 g of water by 1°C.

9. The number of joules of energy given out by the food sample, per gram, can be calculated using this equation:

\[
\text{energy content of food (J/g)} = \frac{\text{mass of water heated (g)} \times \text{temperature rise (°C)} \times 4.2}{\text{mass of food sample (g)}}
\]

10. The experiment can be repeated using samples of the same food type. The average energy content per gram for this food type can be calculated.

11. The investigation can then be repeated using samples of a different food type. The average energy content per gram of the second food can be measured and compared with the first food.

A more accurate way of determining energy content is by using a bomb calorimeter (Figure 15.5). The energy available is released as heat, which raises the temperature of the water surrounding the combustion chamber.
The food sample is completely oxidized by burning it in oxygen.

The energy released is transferred to the water jacket.

The rise in temperature of the water is measured.

The energy value of the food is calculated using the fact that it takes 4.2 J of heat energy to raise 1 g of water by 1°C.

The energy values of foods are published in tables, and those of manufactured and packaged foods may be recorded on the wrapping.

Figure 15.5 A calorimeter for measuring the energy value of foods

The amount of energy in food is expressed as joules; 4.18 J of heat energy is needed to raise 1 g water through 1°C. On this basis, the energy provided by individual nutrients is:

- carbohydrate 16 kJ g⁻¹
- lipid 37 kJ g⁻¹
- protein 17 kJ g⁻¹.

The approximate energy value of individual food items can be calculated, provided the proportions of carbohydrate, lipid, and protein they contain are known.

Control of appetite

Appetite is controlled by a centre in the hypothalamus (Figure 15.6). This part of the brain operates by means of impulses sent to specific body organs and organ systems, via nerves and the spinal cord.

How the appetite control centre is kept informed

The appetite centre is chiefly stimulated by specific hormones sent from tissues and organs in the body.

There are three hormones involved in the control process.

- Leptin plays a part in the control of appetite (Topic 6, page 192).
- In adult life, the number of fat cells does not change significantly.
- If people overeat, fat cells fill up with lipids; when they are short of food, reserves are drawn upon and the fat cells empty.
- As the fat cells fill up, they secrete more leptin.
On reaching the appetite centre, leptin suppresses the sensation of hunger.

When fat cells empty and shrink, they secrete less leptin and the sensation of hunger is experienced in the brain.

Leptin is associated with long-term regulation of eating.

More immediately, control is influenced by additional hormones.

As the stomach empties, a hormone (ghrelin) is secreted.

Ghrelin stimulates the appetite control centre to create a wish to feed.

After eating, another hormone (PYY$_{3-36}$) is released.

- The hormone PYY$_{3-36}$ is released from the upper intestines and pancreas.
- This gut hormone is present in the blood from early in the digestion processes and, on reaching the appetite centre, suppresses the hunger sensation.
- The drive of hunger and the urge to feed is temporarily overcome.

**Key fact**

Appetite is controlled by a centre in the hypothalamus.
Vitamin deficiencies

**APPLICATIONS**

**CASE STUDY: VITAMIN C**

- Vitamin C (ascorbic acid) is an essential vitamin for only a limited number of vertebrate species, namely humans and other primates, the guinea pig, bats, some birds, and fishes.
- Other mammals synthesize this molecule without difficulty.

Ascorbic acid occurs mainly in foods of plant origin (fruits such as blackcurrants, rosehips, strawberries, oranges, and lemons) and in vegetables (green vegetables such as sprouts, cabbage, cauliflower, and watercress and in potatoes). There is a very small amount in cow's milk (reduced by pasteurization) but significantly more in human breast milk.

The importance of a vitamin is first recognized when it is absent from a diet. The vitamin C deficiency signs are:
- an increased susceptibility of the mouth and gums to infection
- a slowing down in the rate at which wounds and tissue damage heals
- eventually, a condition known as scurvy, in which
  - hemorrhages occur under the skin and other tissues
  - the gums become swollen and spongy
  - teeth loosen and fall out.

**Metabolic roles of vitamin C**

Ascorbic acid is involved in the synthesis of collagen.

- Collagen is the key structural protein in connective tissues.
- It makes up about 30% of the total of protein in the body.
- It is in the synthesis of the amino acid hydroxyproline from the amino acid proline that vitamin C is involved; hydroxyproline makes up about 15% of collagen.

Vitamin C is involved in the synthesis of lipoproteins, by which lipids are made soluble for transport in the blood plasma. Lack of this vitamin is linked with iron deficiency and to anaemia (due to low blood hemoglobin levels).

The cells involved in the formation of bone, enamel, and dentine fail to function properly without adequate vitamin C.

**The discovery of vitamin C**

**NATURE OF SCIENCE**

Falsification of theories with one theory being superseded by another – scurvy was thought to be specific to humans, because attempts to induce the symptoms in laboratory rats and mice were entirely unsuccessful.

- By 1753, a sea captain reported that scurvy could be avoided, or the symptoms cured, by supplementing the diet with oranges and lemons.
- Up to 1907, the disease of scurvy was thought to be specific to humans, for attempts to induce the symptoms in laboratory rats and mice were entirely unsuccessful.
- It was then discovered that the guinea pig was another animal which was unable to manufacture ascorbic acid.
- Guinea pigs, fed on diets free of this vitamin, displayed symptoms of the disease (Figure 15.7A).
- By using this animal model, it was proved conclusively that scurvy was a disease due to deficiency of vitamin C and that it was not a disease entirely specific to humans.

**Key fact**

Ascorbic acid is produced by some animals, but others can't so they need a source in their dietary supply.
The chemical, ascorbic acid, was isolated and named in 1932.

Much later, an investigation using human volunteers confirmed the role of vitamin C – this experiment might be viewed as unethical today (Figure 15.7B).

The guinea pig (Cavia porcellus) was an inspired choice for experiments on the importance of vitamin C – it is one of only very few animals unable to synthesize the vitamin.

**A Working with the guinea pig**

Fed guinea pigs a diet of bread baked from different grains

Scurvy-like symptoms developed

Diet supplemented with fresh cabbage or lemon juice

Full health returned

Published their results in 1907

Scientific uproar resulted – the concept of nutritional deficiencies was unknown

**B Working with human volunteers (1942–1944)**

<table>
<thead>
<tr>
<th>Pattern of experimental treatments</th>
<th>32 week – experimental treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 week – preliminary treatment</td>
<td></td>
</tr>
<tr>
<td>All volunteers given diet including 70 mg vitamin C per day</td>
<td>Group A: 3 volunteers kept on the diet with 70 mg per day</td>
</tr>
<tr>
<td>Group B: 7 volunteers had their diet adjusted to supply only 10 mg per day</td>
<td></td>
</tr>
<tr>
<td>Group C: 7 volunteers had their diet adjusted to provide no vitamin C*</td>
<td>All developed scurvy</td>
</tr>
</tbody>
</table>

* When the symptoms of scurvy were evident, these volunteers were subjected to superficial cuts of length 3 cm in the skin of their thighs. These were then surgically stitched up and kept under observation. The wounds failed to heal.

Figure 15.7 The experimental evidence for the role of vitamin C

**APPLICATIONS**

**CASE STUDY: VITAMIN D**

Vitamin D is found almost exclusively in foods of animal origin, but there are few really rich food sources of this vitamin (Table 15.5).

<table>
<thead>
<tr>
<th>Foods in which vitamin D occurs (μg/100g)</th>
<th>Halibut liver oil</th>
<th>Cod liver oil</th>
<th>Herring/sardines</th>
<th>Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 10000</td>
<td>200–750</td>
<td>5–45</td>
<td>4–30</td>
<td></td>
</tr>
<tr>
<td>Low-fat spread</td>
<td>Butter</td>
<td>Eggs</td>
<td>Cheese</td>
<td></td>
</tr>
<tr>
<td>7.5</td>
<td>Up to 2</td>
<td>1–1.5</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>

Table 15.5 Foods in which vitamin D occurs (μg/100g)

The majority of vitamin D comes from the action of sunlight on a precursor chemical which occurs in the skin.

- **Problems of supply normally only arise for people who are exposed to relatively little sunlight (e.g. in people who are housebound).**
- **Children and expectant or lactating mothers have especially high requirements, so these groups also need food containing sufficient vitamin D.**
Vitamin D is involved with the absorption of calcium and phosphorus by the body:

- In the absence of sufficient vitamin D, calcium and phosphorus instead pass out with the faeces.
- Lack of vitamin D or calcium can affect bone mineralization.

Infants who are deprived of vitamin D or calcium develop rickets and have deformed bones (Figure 15.8).

- In the elderly, deficiency in vitamin D or calcium leads to a disease, osteomalacia, in which the bones soften.

This patient experienced prolonged vitamin D deficiency as a child and has developed rickets – the weak bones have bent permanently under normal body weight.

Lack of vitamin D or calcium can affect bone mineralization and cause rickets or osteomalacia.

APPLICATIONS

Blood cholesterol as an indicator of risk of coronary heart disease

Cholesterol, a steroid (Figure 1.12, page 17), is a lipid of a different chemical structure from that of the fatty acids. Cholesterol is required for normal, healthy metabolism:

- Cholesterol is a component in the plasma membranes of all cells.
- In mammals, cholesterol is needed to produce the sex hormones (progesterone, estrogen, and testosterone).
- Bile salts, compounds involved in lipid transport in the blood plasma, are synthesized from cholesterol.

Lipids are insoluble in water, and so are transported about the body in association with proteins, in components which are either low-density lipoproteins (LDLs) or high-density lipoproteins (HDLs) according to the relative proportions of protein and lipid.

Diseases of the blood vessels are mainly due to a condition called atherosclerosis (Topic 6, pages 167–168). This develops after strands of low-density lipoproteins ('bad cholesterol') are deposited under the endothelium of arteries.

<table>
<thead>
<tr>
<th>LDL cholesterol level</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 200 mg dm$^{-3}$</td>
<td>desirable</td>
</tr>
<tr>
<td>200–239 mg dm$^{-3}$</td>
<td>borderline high</td>
</tr>
<tr>
<td>above 240 mg dm$^{-3}$</td>
<td>high</td>
</tr>
</tbody>
</table>

Table 15.6 Total blood cholesterol

Key fact
Cholesterol in blood is an indicator of the risk of coronary heart disease.
Databases of nutritional content of foods

A balanced diet is essential to human health. A listing of the amounts of nutrients in a wide variety of raw and cooked foods – is shown in:


This resource gives insight into the composition of a 100 g of edible portions of a variety of items common to daily diets.

An online database can be used to analyse a diet (i.e. food eaten on a daily basis), and to find out whether it contains sufficient quantities of the essential nutrients. Free software to do this is available from the US Department of Agriculture:

https://www.supertracker.usda.gov/default.aspx

This facility can compare consumption in a diet to the recommended intake.

15.2 Digestion

**Essential idea:** Digestion is controlled by nervous and hormonal mechanisms.

The control of secretion of ‘digestive juices’

Digestive juice is not secreted continuously, but is coordinated with the presence of food in a particular part of the gut. This coordination is regulated by nervous and hormonal mechanisms, ensuring that digestive juice is secreted:

- when and where it is required
- in the volume and composition appropriate to the food substance.

![The gut wall and location of exocrine glands](image)

**Figure 15.9 The gut wall and location of exocrine glands**

**Key fact**

Nervous and hormonal mechanisms control the secretion of digestive juices.

**Key fact**

Exocrine glands secrete to the surface of the body or the lumen of the gut (Figure 15.9).
Digestion in the stomach

Millions of gastric glands are present in the wall of the stomach (Figure 15.10), secreting the components of gastric juice. This juice includes:

- hydrochloric acid – creates an environment of pH 1.5–2.0 (optimum pH for protein digestion)
- protease enzymes, e.g. pepsin.

Hydrochloric acid activates protease, and also kills any bacteria that are present in the in-coming food.

The whole stomach lining is supplied with goblet cells that secrete mucus.

- Mucus bathes the interior lining of the stomach.
- Mucus forms an effective barrier to both the hydrochloric acid and the proteases of the gastric juices, preventing autolysis (self-digestion) of the stomach wall.

As the food is mixed with gastric juice and churned by muscle action, it becomes a semi-liquid called chyme. The churning action of the stomach is an important part of the mechanical digestion process.

Mechanism of secretion control

The volume and content of gastric secretions are controlled by nervous and hormonal mechanisms. There are three components to the control of the secretion of gastric juice during the 4 hours that food spends in the stomach (Figure 15.11).

1. The sight or smell of food initiates secretion of gastric juice.
2. When food arrives in the stomach, the stomach wall is stretched. This mechanical stimulation triggers further secretion of gastric juice by reflex action.
3. Cells in the stomach lining are stimulated to secrete a hormone, gastrin, into the bloodstream, in response to protein in the meal.
   a. On reaching the gastric glands, via the blood, further secretion of gastric juice is stimulated.
   b. Food intake in which protein is absent (or in very low concentration) triggers less additional secretion of gastric juice. In this way, the volume of gastric secretion is hormone controlled.

Key fact

The volume and content of gastric secretions are controlled by nervous and hormonal mechanisms.
4 When the pH of the stomach contents falls to 3.5, gastrin secretion slows and, once the pH has fallen to 1.5, it stops.
   a The protein present in food acts as a buffer to stomach acid.
   b When a protein-rich meal is present, the pH of the stomach content falls more slowly and gastric juice secretion persists for longer.
5 Partially digested chyme starts to enter the duodenum.
   a Chyme is still rich in partially digested protein, and so stimulates the lining of the duodenum to secrete an ‘intestinal’ gastrin.
   b Gastrin circulates in the bloodstream and triggers further gastric juice secretion.
   c Protein digestion in the stomach is maintained and enhanced.
6 When chyme containing fatty acids and glucose, but low in protein, starts to enter the duodenum, the gut wall here secretes two hormones, secretin and cholecystokinin.
   a The effect of these two hormones on the stomach wall is to decrease gastric juice secretion.
   b The emptying of the chyme into the duodenum now proceeds.
Hormones continue to regulate secretion in the subsequent stages of digestion. In the duodenum – the first part of the small intestine – the pancreatic juice and bile are regulated by hormones (secretin and cholecystokinin) produced by cells in the wall of this part of the gut.

The discovery of the role of gastric secretions

**NATURE OF SCIENCE**

Serendipity and scientific discoveries – the role of gastric acid in digestion was established by William Beaumont while observing the process of digestion in an open wound caused by gunshot.

Gastric activity was first studied in 1822:

- A Canadian fur trapper was injured by an accidental gunshot to the stomach.
- The gunshot produced a permanent opening from the stomach interior to the outside of the body (called a gastric fistula – Figure 15.12).
- William Beaumont, a surgeon in the United States Army, treated the fur trapper and then studied the activities of the stomach.
- The activities of the stomach could be observed through the gastric fistula.
- Gastric juice secretions were collected and their effect on food samples observed.
- How the rate of digestion and the composition of the gastric juice changed with different foods was recorded.

Figure 15.12 A gastric fistula – an accidental result of a gunshot wound

**Acid conditions in the stomach**

Acid conditions in the stomach favour hydrolysis reactions, and help to control pathogens ingested with the food.

- If the pH of the stomach contents falls too low, the stomach wall could be endangered.
- If pH falls too low, two additional hormones, secretin and somatostatin, inhibit the secretion of gastrin, decreasing acid secretion.
- Where stomach acidity is persistently too low, inhibitory drugs may be prescribed.

**Key fact**

Acid conditions in the stomach favour some hydrolysis reactions and help to control pathogens in ingested food.
APPLICATIONS

Reduction of stomach acid secretion by proton pump inhibitor drugs

The cells responsible for the hydrochloric acid in gastric juice are the parietal cells of the gastric glands (Figure 15.10), which pump out hydrogen ions. This proton pump:

- is powered by ATP
- transports $H^+$ ions out and $K^+$ ions in (and is known as an $H^+/K^+$ ATPase pump).

The hydrogen ions are joined by chloride ions, transported via a separate, specific membrane channel protein in the cell’s plasma membrane (Topic 1, pages 15–16).

Proton-pump inhibitor drugs are used to treat gastroesophageal diseases with symptoms of low stomach pH.

- The use of these drugs suppresses gastric acid production by inhibiting the activity of the proton pumps.
- Inhibition of the proton pumps raises the pH of the stomach contents.

Expert tip
Proton-pump inhibitor drugs may encourage the growth of gut microflora. They may increase the patient’s susceptibility to bacterial colonizations there.

APPLICATIONS

Helicobacter pylori infection as a cause of stomach ulcers

Despite the strong acidity of the stomach contents, a spiral-shaped bacterium, $H. \text{ pylori}$, is able to survive there. It was discovered first in certain patients, associated with their stomach ulcers.

- $H. \text{ pylori}$ does not invade cells, but survives by attaching to receptors on the plasma membrane of the cells of the stomach mucosa, underneath the mucus lining.
- It is largely protected by the mucus layer that lines the inner surface throughout the entire gut.
- Any hydrogen ions that penetrate to the bacterium are neutralized by hydrogen-carbonate ions and ammonium ions that the bacterium produces by the action of the enzyme urease on urea.

The persistent presence of $H. \text{ pylori}$ causes the body’s immune system to become sensitized.

- Antibodies are produced in the vicinity of the infection, and killer cells of the immune system accumulate there.
- Because the killer cells cannot reach the invading cells on the exterior of the plasma membrane, they are ineffective.
- An inflammation reaction occurs at the site of infection – a condition known as gastritis.
- A further outcome may be the progressive failure of goblet cells in the infected area.
  - If this occurs, cells of the stomach lining become exposed to the protease and hydrochloric acid of the gastric juice.
  - The result may be an unpleasant stomach ulcer (gastric ulcer).

Key fact
The reduction of stomach acid secretion by proton pump inhibitor drugs.
**Location, structure, and function of exocrine glands of the gut**

Different digestive juices are secreted onto food at several points as it is moved along the gut (Table 5.7).

<table>
<thead>
<tr>
<th>Secretion and gland</th>
<th>Site of action</th>
<th>pH</th>
<th>Enzymes and non-enzyme components</th>
<th>Substrate and effect</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>saliva – salivary glands</td>
<td>mouth</td>
<td>6.5–7.5</td>
<td>amylase</td>
<td>starch (polysaccharide)</td>
<td>maltose (disaccharide)</td>
</tr>
<tr>
<td>gastric juice – gastric glands in wall of stomach</td>
<td>stomach</td>
<td>2.0</td>
<td>pepsin, rennin (young mammals only), hydrochloric acid</td>
<td>proteins</td>
<td>polypeptides</td>
</tr>
<tr>
<td>pancreatic juice – pancreas</td>
<td>small intestine</td>
<td>7.0</td>
<td>amylase, proteases (trypsin and chymotrypsin), peptidases, lipases, nucleases</td>
<td>starch, proteins, polypeptides, triglycerides, nucleotides</td>
<td>maltose, polypeptides, peptides and amino acids, fatty acids and glycerol, pentose sugars, P, and bases</td>
</tr>
</tbody>
</table>

Table 15.7 Digestive secretions, sites, and actions

The basic structure of an exocrine gland is seen in salivary glands (Figure 15.13A).

- The role of saliva includes lubricating the mouth, throat and the bolus of food as it is swallowed.
- Amylase in the saliva initiates the digestion of starch.

The pancreas is situated beside the duodenum.

- Pancreatic juices are transported onto the food by the pancreatic duct, which enters the intestine in the duodenum (the first part of the intestine after the stomach).
- The structure of the enzyme-secreting glands of the pancreas and their ducts is shown in Figure 15.13B, and the ultrastructure of the secretory cells is shown in the electron micrograph in Figure 15.14.
- The pancreas is a rich source of hydrolytic enzymes (Table 15.7).
A salivary glands

Figure 15.13 Exocrine glands of the digestive system

■ The identification of exocrine cells, observed by electron microscopy

Interpretation of electron micrographs – a skill to develop
Make a representative drawing of an exocrine cell showing key organelles recognized, including:
• mitochondria
• nucleus
• rough endoplasmic reticulum
• lysosomes
• plasma membrane

Figure 15.14 The exocrine glands of the pancreas. Parts of six gland cells are shown, arranged around a central space that leads into a duct, down which pancreatic juice flows
The secretory cells have a distinctive structure.

- The cytosol is packed with rough endoplasmic reticulum (RER). Here, the attached ribosomes are the sites of the synthesis of proteins to be packaged for export from the cells (in the secretory vesicles).
- Many mitochondria are present – the source of the ATP necessary for the protein synthesis.

Absorption in the small intestine

- **The structure of the small intestine and its villi**
  - The small intestine is about 5–6 metres long in total.
  - The wall of the small intestine contains involuntary muscle tissue.
  - The innermost surface is lined with an epithelium layer, called a mucosa, which contains many goblet cells.
  - The goblet cells of the mucosa secrete mucus, a lubricating secretion that:
    - adheres to the cells lining the gut
    - protects the gut from mechanical damage and helps resist self-digestion.

In the small intestine, the inner layers of the gut wall are shaped into finger-like projections called villi.

- The epithelium of villi contains many goblet cells.
- The wall of the small intestine and the villi it supports are shown in Figure 15.15.

---

**Figure 15.15** The small intestine – the absorption surface

Expert tip

You need to be able to identify exocrine gland cells that secrete digestive juices from electron micrographs.
Adaptations of the villi include:

- microvilli
  - foldings of the cell surface facing the lumen of the gut
  - greatly increase the surface area in contact with material to be absorbed
- mitochondria
  - present in large numbers
  - use to provide a significant demand for ATP in these cells
- pinocytotic vesicles
  - the site of pinocytosis
  - fluid is taken up or released in tiny vesicles across the plasma membrane of a cell
- basal channels between epithelium cells, below the tight junctions
- tight junctions
  - bind together the individual epithelial cells
  - the only way into the tissues of the body is through the epithelium.

**Ultrastructure of villus epithelium cells**

The structure of cells of the epithelium of the villi is adapted to the absorption of food.

The electron micrograph of a villus epithelium cell (Figure 15.16) shows the structural features that play vital roles in the absorption of the products of digestion.

![Electron micrograph of an epithelium cell of a villus of the small intestine (×8000)](cell_surface_membrane_microvilli.png)

**What other organelles do you recognize?**

**Figure 15.16** Electron micrograph of an epithelium cell of a villus of the small intestine (x8000)

Features that can be seen in the electron micrograph that indicate the adaptations of the villus for absorption:

- microvilli
- abundant mitochondria
- tight connections between adjacent cells (‘tight junctions’ – see above).
The rate of transit and fate of undigested matter in the large intestine

Remaining undigested material passes on into the large intestine by waves of contraction of the muscle layers in the gut wall (peristalsis). By this stage, most of the useful products of digestion have been absorbed. Remaining material includes:

- mineral ions
- water.

Minerals and water are absorbed in the large intestine.

Egestion and the role of dietary fibre

The materials that are not absorbed are egested as faeces. Faeces contain insoluble fibre, largely consisting of cellulose and lignin from plant matter.

- Cellulose makes up the dietary fibre (roughage) that is a necessary component of the human diet.
- Humans, along with all other mammals, do not have cellulase enzymes and so are not able to digest cellulose.
- The value of dietary fibre is as bulk that stimulates movement of the chyme through the gut.
- The presence of dietary fibre may slow the absorption of glucose, so reducing the risk of developing type II diabetes.
- The risks of various diseases of the large intestine, including bowel cancer, are reduced by a consistently high fibre diet.

APPLICATIONS

Cholera and the danger of dehydration

Cholera is caused by the Gram-negative, curved rod bacterium *Vibrio cholerae*.

- Cholera is acquired almost exclusively from drinking water that is heavily contaminated by the faeces of patients (or carriers) of the pathogen.
- A large number of cholera bacteria must normally be ingested for the disease to develop; less than $10^8–10^9$ organisms is ineffective.
- If the bacteria survive the stomach acid and reach the intestine, then the pathogen increases in numbers and attaches itself to the epithelium membrane. The release of enterotoxin follows.
- The effect of the enterotoxin is to trigger a loss of ions from these cells. Outflow of water follows.
- The patient loses a massive amount of body fluid; 15–20 litres may drain from the body as watery diarrhoea.
- Death may easily result from this dehydration, for the severely reduced level of body fluid causes the blood circulation to collapse.
How cholera toxin works

The cholera enterotoxin consists of a ‘two-protein’ complex.

- The B part is the binding protein, which attaches the toxin complex to a particular binding site – a glycolipid on the plasma membranes of intestine epithelial cells.

- The A part is an enzyme that activates the enzyme systems of the plasma membrane of the epithelium cell to which it is attached, causing secretion of chloride ions into the gut lumen and inhibiting any uptake of sodium ions.

- Hypersecretion of chloride ions results, and is followed by water loss (Figure 15.17).

The treatment of cholera

Properly treated, few people, less than 1%, are likely to die from this disease.

- A cholera patient requires immediate oral administration of a dilute solution of electrolytes (oral rehydration salts – ORS).

- ORS make good the fluid and ions lost from the body.

- In places where cholera is endemic, correctly treating cholera may be problematic:
  - many who contract the disease are weakened by shortage of food
  - drinking water may have to be carried some distance
  - boiling water to make it safe to use in the rehydration fluid requires scarce fuel.

For prevention of the spread of cholera, the boiling of drinking water is critical.
15.3 Functions of the liver

Essential idea: The chemical composition of the blood is regulated by the liver.

APPLICATIONS

Blood supply to the liver

Blood arrives in the liver from:

- the hepatic artery
  - brings oxygen-rich blood to the liver
  - is formed from a branch of the aorta, which brings blood directly from the heart.

- the hepatic portal vein
  - carries most of the blood circulating in the liver
  - brings blood from the stomach and small intestine, containing nutrients from digested food
  - has an oxygen content that is lower than the hepatic artery, because the blood has already travelled through other organs.

Sinusoids within the liver are formed from subdivisions of the hepatic portal vein (Figure 15.18).

- Sinusoids are blood-filled channels.
- Arterial blood mixes with blood from the hepatic portal vein as it flows through the sinusoids.
- Blood flowing through the sinusoids comes into contact with liver cells (hepatocytes), and allows proteins (e.g. albumen) to enter or leave the blood.
- The sinusoids merge with venules as they leave the liver, leading to the hepatic vein.
- The hepatic vein carries blood away from the liver to the vena cava.
Within the liver the hepatic portal vein branches into sinusoids where the blood comes into close contact with the liver cells. The hepatic artery divides into arterioles lined by phagocytic cells. Arterioles eventually join with the sinusoids. Blood exits the liver by a branch of the hepatic vein.

**Figure 15.18 Liver cells and their dual blood supply**

The sinusoids differ from the capillaries:
- Sinusoids are wider than capillaries
- Sinusoids are without walls separating blood from the liver cells.
- In the sinusoids, blood and liver cells are in direct contact.
- Many phagocytic cells line the sinusoids.

Between two rows of liver cells is a bile channel, which is isolated from the blood supply.
- Bile from the liver cells flows into these channels.
- The bile channels merge into bile ducts, carrying the bile to the gall bladder.
The roles of the liver

- **Detoxification**
  The liver removes toxins from the blood and detoxifies them.
  - Alcohol (ethanol) is oxidized to acetaldehyde (ethanal) by the action of the enzyme alcohol dehydrogenase.
  - Acetaldehyde is further oxidized to acetic acid (ethanoic acid) by acetaldehyde dehydrogenase.
  - Acetic acid becomes part of the pool of metabolites that are oxidized to carbon dioxide and water by various biochemical pathways.
  - The liver acts on drugs and toxins that have entered the bloodstream, converting them to less harmful forms for excretion in the kidneys.

- **The breakdown of red blood cells**
  Liver cells break down redundant red cells (erythrocytes).
  - Red cells are formed in bone marrow and lose their nucleus on formation.
  - Red blood cells remain functional for only a limited time before they are broken down and replaced.

  The process of breakdown of red blood cells:
  - Worn-out cells are taken up by phagocytosis by macrophage cells.
    - This occurs in phagocytes called Kupffer cells.
    - Kupffer cells are attached to the walls of the sinusoids.
  - The globin (protein) and heme (non-protein part containing iron ions) of hemoglobin are split apart.
  - The globin is hydrolysed by proteases to amino acids.
  - Iron in the form of iron III ions (Fe\(^{3+}\)) is formed from the breakdown of the heme.
  - Fe\(^{3+}\) is removed and attached to a carrier protein.
  - Iron is stored in the liver cells and eventually exported via the blood plasma to the bone marrow, where it may be stored before reuse to make new red blood cells.
  - The remainder of the heme part is converted into bile pigments in the liver cells, and these are then secreted into the bile channels, between the sinusoids, as a component of the bile formed by the liver (Figure 15.19).

![Figure 15.19 Red blood cell breakdown, iron storage and bile formation](image)
Production of bile salts

Most of the cholesterol required by the body on a daily basis is manufactured in the liver; the remainder is taken in as part of the diet.

- Some surplus cholesterol is converted into **bile salts**.
- Bile, containing bile salts, is transported to the gall bladder.
- In the gall bladder, bile is concentrated and stored.
- Bile is subsequently used to break down fats into multiple microscopic droplets that disperse in aqueous solutions for effective breakdown by digestive enzymes in the duodenum (emulsification – Topic 6, page 158).

Production of plasma proteins

- The level of amino acids is also adjusted by the liver cells as the blood passes along the liver sinusoids.
- A pool of amino acids is maintained in the plasma, in the liver and in other tissues that are undergoing rapid protein synthesis.

Synthesis of blood plasma proteins includes globulins, albumin, prothrombin, and fibrinogen. These are examples of proteins that are produced for ‘export’ from the liver cells.

- These proteins are formed at ribosomes of the RER.
- They are then transferred to the Golgi apparatus.
- At the Golgi body they are packaged in vesicles for discharge across the plasma membrane by exocytosis.

Most proteins are short lived and are again broken down, contributing to the amino acid pool from which the new proteins are made. However, the body cannot store amino acids, should there be an excess.

- Excess amino acids are deaminated in the liver.

- In deamination
  - the organic acid part of each amino acid is removed and respired, or converted to fat or carbohydrate
  - the \(-\text{NH}_2\) (amine) group(s) of each amino acid are converted to ammonia and combined with carbon dioxide to form urea:
    \[2\text{NH}_2 + \text{CO}_2 \rightarrow (\text{NH}_2)_2\text{C}=\text{O} + \text{H}_2\text{O}\]

Regulation of nutrient levels in the blood

- Glucose, amino acids, and short-chain fatty acids first reach the liver via the hepatic portal vein, after absorption via the villi.
- In the liver, their concentrations of glucose, amino acids, and short-chain fatty acids in the plasma are regulated.
- If concentrations were not regulated, the composition of the blood would vary dangerously at different times of the day.
- Some nutrients in excess can be stored in the liver.

The normal level of blood glucose in humans is about 90 mg per 100 cm\(^3\) (90 mg 100 cm\(^{-3}\)). The concentration varies between:

- 70 mg – when the body has been without food for a prolonged period
- 150 mg – in the hepatic portal vein after a carbohydrate-rich meal has been digested and absorbed.

On arrival in the liver sinusoids, excess glucose is withdrawn from the plasma solution and used in metabolism or stored as glycogen (Topic 6, page 190).
Respiring tissues of the body receive glucose supplies from the blood circulation. As the level of blood glucose falls due to respiration in tissues, glycogen reserves in the liver are converted back to glucose to maintain the normal plasma concentration (Figure 15.20). Insulin and glucagon control blood glucose levels (Topic 6, page 190).

**Key fact**

The liver intercepts blood from the gut to regulate nutrient levels.

**Key fact**

Some nutrients in excess can be stored in the liver.

**Expert tip**

As well as storage in the liver, glycogen reserves are also stored elsewhere in the body, particularly in the skeletal muscles.

---

**Nutrients in excess are stored**

Liver cells are sites of nutrient storage, including:

- iron
- carbohydrate (glycogen)
- fats
- vitamins
  - vitamin A – as retinal
  - vitamin B12
  - vitamin D – as calciferol
  - vitamin E
  - vitamin K.

**Expert tip**

Vitamins stored in the liver, with the exception of B12, are all fat-soluble. They are released from the liver when needed elsewhere in the body.

**Key fact**

Some nutrients in excess can be stored in the liver.
‘Good’ and ‘bad’ cholesterol

**NATURE OF SCIENCE**

Educating the public on scientific claims – scientific studies have shown that high-density lipoprotein could be considered ‘good’ cholesterol.

- Lipids must be transported about the body – they are required as respiratory substrates in muscle tissue and other body tissues, for example.
- Cholesterol is used in the production of steroid hormones and the maintenance and repair of cell membranes.
- Since they are insoluble in water, lipids are carried in association with proteins, in components which are either low- or high-density lipoproteins (LDLs or HDLs) according to the relative proportions of protein and lipid (Table 15.8).

<table>
<thead>
<tr>
<th>Protein (raises density)</th>
<th>Lipid (reduces density)</th>
<th>Particle size</th>
<th>Known as</th>
</tr>
</thead>
<tbody>
<tr>
<td>low-density lipoprotein (LDL)</td>
<td>10–27%</td>
<td>5–61%</td>
<td>20–90 nm*</td>
</tr>
<tr>
<td>high-density lipoprotein (HDL)</td>
<td>50%</td>
<td>3%</td>
<td>7–10 nm*</td>
</tr>
</tbody>
</table>

*A nanometre is an SI-derived unit of length, and is \(10^{-9}\) of a metre.

**Table 15.8 Low- and high-density lipoproteins**

- Most cholesterol is transported as LDLs.
- An excess of LDLs in the bloodstream can block up receptor points in the cell membranes of cells that metabolize or store lipid, leaving even higher quantities of LDLs circulating in the blood plasma.
- The excess of LDLs is deposited under the endothelium of artery walls, beginning or enhancing plaque formations.
- Monosaturated fats help to remove the LDLs. Polyunsaturated fats are even more beneficial; these fats further increase the efficiency of the receptor sites at removal of ‘bad cholesterol’ from the blood.

**APPLICATIONS**

Jaundice – causes and consequences

The immediate cause of jaundice is the presence of the bile pigment bilirubin, which is formed in the liver from the heme part of hemoglobin after the iron has been removed. Possible causes of this condition are:

- the breakdown of red blood cells at an abnormal (accelerated) rate
- damage or disease of the liver, e.g. by alcohol-induced cirrhosis or due to malaria
- a blocked bile duct.

The symptoms of jaundice will disappear naturally, provided the underlying cause can be corrected.

Newborn babies may suffer from jaundice briefly.

- The hemoglobin of the fetus, produced during its time in the uterus, is different from the hemoglobin our body forms after birth and for the rest of life.
- Immediately after birth, the breakdown of fetal hemoglobin occurs at an accelerated rate, and bilirubin is formed more quickly than it can be broken down.
- The problem self-corrects quickly.

**Expert tip**

The difference between LDLs and HDLs is technical and, therefore, difficult to communicate correctly to the public. HDLs are ‘good’ but while people should avoid a diet that is too rich in saturated fats and cholesterol, this lipid is an essential body metabolite which is manufactured in the liver in the absence of absorbed dietary cholesterol.

**Key definition**

Jaundice – condition in which the skin develops a yellowish tinge along with the whites of the eye (sclera).
15.4 The heart

Essential idea: Internal and external factors influence heart function.

Cardiac muscle cells

Cardiac muscle has similarities with skeletal muscle (Topic 11, pages 293–294).

- Like skeletal muscle fibres, cardiac muscle fibres are surrounded and enclosed by a membrane, the sarcolemma, from which transverse tubules (T tubules) tunnel in and around the sarcomeres.
- Also in common is the sarcoplasmic reticulum – a modified form of endoplasmic reticulum.
- Like skeletal muscle fibres, cardiac muscle fibres are striated in appearance, and have a similar arrangement of actin and myosin filaments.
- All muscle tissue consists of fibres that are able to shorten by a half to a third of their length.

Unlike skeletal muscle, cardiac muscle is unique to the heart.

Cardiac muscle cells (Figure 15.21):

- are much shorter and wider than skeletal muscle (15 μm in diameter and 100 μm long)
- have a single nucleus, rather than being multicellular like skeletal muscle.
- are branching (Y-shaped) and joined end to end in a complex three-dimensional network that allows contractions in three dimensions
- have many mitochondria, which make up a larger proportion of the cell volume than in skeletal muscle
- have a transverse tubular system that consists of wider invaginations of the cell surface than skeletal muscle fibres and their branching sarcoplasmic reticulum is more abundant
- contract even in the absence of stimulation by a nerve, and throughout their life, but their contraction is not under voluntary control (as in the case of skeletal muscle).
Structure of cardiac muscle cells allows propagation of stimuli throughout the heart wall

- **Intercalated discs** are present at the junctions between cardiac muscle cells.
- The direct electrical coupling between cells allows waves of depolarization to pass through the entire network, synchronizing contraction of the muscle, as if in a single cell.
- Cardiac muscle fibres form an interconnected network.

The network system of the walls of the atria is entirely separate from that of the ventricles. This ensures a transmission delay of electrical signal between atria and ventricles.

The cardiac cycle

The heart beats at a rate of about 75 times per minute, so each **cardiac cycle** (Figure 15.22) is ca. 0.8 seconds long. This period of ‘heartbeat’ is divided into two stages: **systole** and **diastole**.

- When the muscular walls of the chambers of the heart contract, the volume of the chambers is decreased.

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**Key definition**

**Intercalated disc** – a double membrane with gap junctions, through which are cytoplasmic connections between adjacent cardiac cells.

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**Key fact**

Structure of cardiac muscle cells allows propagation of stimuli through the heart wall.

---

**Key definitions**

**Cardiac cycle** – the sequence of events of a heartbeat, by which blood is pumped around the body.

- **Systole** – contraction of heart muscle.
- **Diastole** – Relaxation of heart muscle.
The heart beats rhythmically throughout life, without needing to be stimulated by an external nerve: this is myogenic activity.

A network of specialized, self-excitable cardiac muscle fibres triggers heartbeats.

These fibres are located in the right atrial wall, close to the points where the vena cavae empty into the heart.

This network of fibres is known as the sinoatrial (SA) node or ‘pacemaker’ (Figure 15.23).
Each electrical charge is simultaneously propagated through the entire network of muscle fibres in the walls of both atria, via the gap junctions in the intercalated discs.

In response to each electrical charge, the muscle of both atrial walls contracts simultaneously (atrial systole).

**Key fact**
Although cardiac muscle fibres form an interconnected network, the network system of the walls of the atria is entirely separate from that of the ventricles. This ensures a transmission delay between atria and ventricles.

**The atrioventricular node**

- The signal originating from the SAN, while causing contraction of the entire atrial walls, cannot pass directly from the atria to the ventricles.
- Instead, the stimulus is picked up by the atrioventricular (AV) node, situated at the base of the right atrium (Figure 15.23).

There is a delay between the arrival and passing on of a stimulus at the AV node. This delay is the product of:

- the cells of the atrioventricular node taking longer to become excited than those of the SA node
- the smaller diameter of the AV cells, compared with those of the SA node, slowing conduction results
- fewer sodium ion channels in the membranes of AV cells, and a more negative resting potential (Topic 6, page 184) than develops in the cells of the SA node
- fewer gap junctions in the intercalated discs of the cells of the AV node than in the SA node.

The result of this delay in transmission (of about 100ms) gives time for the atria to contract fully, adding to the volume of blood delivered to the ventricles. The delay also prevents the atria and ventricles from contracting simultaneously.

**Figure 15.23 Control of heart rate**

**Key fact**
Signals from the sinoatrial node that cause contraction cannot pass directly from atria to ventricles.

**Key facts**
- There is a delay between the arrival and passing on of a stimulus at the atrioventricular node.
- This delay allows time for atrial systole before the atrioventricular valves close.
Contraction of the ventricle wall

From the atrioventricular node, a bundle of fibres (the AV bundle) conducts the signal into the ventricles to a point where it splits into right and left branches.

- Separate bundles deliver the signal to the base of each ventricle via conducting fibres, known as the Purkinje fibres (Figure 15.23).

- These conducting fibres ensure the coordinated contraction of the entire ventricle walls, starting from the base of the heart upwards (ventricular systole).

Conduction at this point is fast because the fibres:

- are of large diameter
- have numerous voltage-gated sodium ion channels
- are well supplied with mitochondria and have a glycogen store
- the glycogen store provides a direct source of glucose for respiration.

Expert tip

After every contraction, cardiac muscle has a period of insensitivity to stimulation, the refractory period (a period of enforced non-contraction – diastole). In this phase, the heart passively begins to refill with blood. This recovery period is a relatively long one in heart muscle, and it enables the heart to beat throughout life.

APPLICATIONS

Use of artificial pacemakers to regulate the heart rate

If the SA node becomes diseased or damaged, normal heart rhythm can be restored by the surgical implantation of an artificial pacemaker.

- The pacemaker delivers electrical impulses via electrodes to the heart wall.

- It is fitted to patients
  - where the heart does not beat fast enough
  - where the system of fibres that conducts the signals within and between atria and ventricles is faulty.

- The pacemaker may be designed to deliver a regular signal, or only when a normal heartbeat is missed.

Heart sounds

- The valves of the heart close whenever there is a tendency for blood to flow in the reverse direction.

- The relative pressures in the atria, ventricles, and arteries determine the opening and closing of valves, since blood always flows from a region of high pressure to a region of lower pressure.

The sounds of the valves of the heart closing can be heard by using a stethoscope (Figure 15.24).

- The first sound is due to the simultaneous closure of the atrioventricular valves. This the ‘lub’ sound.

- The second heart sound is due to the closure of the semilunar valves in ventricular diastole. This is the ‘dub’ sound.

Key fact

Conducting strands ensure coordinated contraction of the entire ventricle wall.

Key fact

Conducting fibres ensure coordinated contraction of the entire ventricle wall.
As the heart pumps, the repeated sequence ‘lub dub (pause) lub dub’ is heard.

**Invention of the stethoscope**

**NATURE OF SCIENCE**

Developments in scientific research followed improvements in apparatus or instrumentation – the invention of the stethoscope led to improved knowledge of the workings of the heart.

The first stethoscope was invented by René Laennec in 1819. The invention of the stethoscope changed approaches to internal disease in the nineteenth century.

- The stethoscope gave access for the first time to body noises, such as the sound of breathing and the working of the heart valves.
- Investigations could be conducted on living people.

By learning normal and abnormal breathing sounds, Laennec developed skills for the diagnosis of pulmonary ailments such as bronchitis, pneumonia, and tuberculosis. The invention of the stethoscope led to vastly improved knowledge of the workings of the chest.

**Key fact**

Normal heart sounds are caused by the atrioventricular valves and semilunar valves closing causing changes in blood flow.

---

**Measurement and interpretation of heart rate under different conditions**

Heartbeat is controlled by the SA node, but nervous, hormonal, and other factors can override this basic rhythm, according to the needs of the body.

- The body’s demands on the circulatory system change and, as a consequence, the heart rate is constantly adjusted.
The heart may beat between 50 and 200 times a minute. Ventricular contractions force a wave of blood through the arteries.

- The expansion of the arteries can be felt as a pulse.
- It can be particularly felt where the artery is near the skin surface and passes over a bone.
- The pulse is traditionally taken above the wrist (Figure 15.25).

![Figure 15.25 Taking the pulse](image)

### Designing an investigation

When working with a human as an experimental subject in a heart rate experiment, make certain that:

- the subject is reasonably fit
- everyone understands and is confident about the procedures
- a risk assessment has been undertaken
- no one experiences prolonged discomfort
- no medical or genetic ‘diagnosis’ is made as a result of the experiment.

Working in groups of two (or more), one person should be the experimental subject – the one whose pulse is taken:

- after 5–20 minutes of quiet rest
- after standing very upright (as if to attention) for 5 minutes
- immediately after an agreed exercise task (e.g. stepping up and down from a stepping stool for a fixed number of minutes)
- at short intervals subsequently until the pulse has returned to normal.

The changes in pulse rate from resting to strong exercise, and the profile of recovery to ‘resting’ state can be presented as a table and in graph form.

Cardiovascular efficiency can be calculated. If the ‘3-minute step test’ is used (see Expert tip box), then:

\[
\text{cardiovascular efficiency} = \frac{\text{duration of exercise} \times 100}{\text{recovery pulse} \times 5.6}
\]

Cardiovascular efficiency is assessed as:

- 0–27 = very poor
- 28–38 = poor
- 39–48 = fair
- 49–59 = good
- 60–70 = very good
- 71–100 = excellent

### Expert tip

A useful procedure for investigating the effect of exercise on heart rate is the ‘three-minute step test’. This involves:

- stepping rate 24 steps per minute
- step height 45 cm
- duration of exercise 3 minutes
Interpretation of systolic and diastolic blood pressure measurements

The pascal (Pa) and its multiple the kilopascal (kPa) are generally used by scientists to measure pressure, but in medicine the older unit of pressure, ‘millimetre of mercury’ (mmHg) is still used (1 mmHg = 0.13 kPa).

<table>
<thead>
<tr>
<th>Systolic</th>
<th>Diastolic</th>
<th>Condition</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>80</td>
<td>optimum</td>
<td></td>
</tr>
<tr>
<td>&lt;130</td>
<td>&lt;85</td>
<td>normal</td>
<td>biennial checks</td>
</tr>
<tr>
<td>130–139</td>
<td>85–89</td>
<td>high–normal</td>
<td>annual checks</td>
</tr>
<tr>
<td>140–159</td>
<td>90–99</td>
<td>stage 1 hypertension</td>
<td>check every 2 months</td>
</tr>
<tr>
<td>160–179</td>
<td>100–109</td>
<td>moderate (stage 2) hypertension</td>
<td>treatment is essential if these conditions persist</td>
</tr>
<tr>
<td>180–209</td>
<td>110–119</td>
<td>severe (stage 3) hypertension</td>
<td></td>
</tr>
<tr>
<td>&gt;210</td>
<td>&gt;120</td>
<td>very severe (stage 4) hypertension</td>
<td></td>
</tr>
</tbody>
</table>

Table 15.9 Interpretation of systolic and diastolic blood pressure measurements

APPLICATIONS

Cause and consequences of hypertension

A blood pressure of 120/80 is normal and preferable in an adult. Hypertension is defined as systolic pressure greater than 140 mmHg and diastolic pressure greater than 90 mmHg.

The causes of hypertension are:

1. The deposition of fat in arteries and the formation of fibrous tissue:
   - blood flow is impeded
   - the thickening of the artery wall also leads to loss of elasticity, further contributing to raised blood pressure.

2. High salt content in the diet:
   - leads to greater retention of water in the body
   - as volume of blood increase, blood pressure increases.

3. Smoking:
   - nicotine is a vasoconstricting drug
   - when arterioles constrict, blood pressure is temporarily elevated.

4. Obesity and lack of exercise:
   - particularly a problem in the abdominal obesity
   - the direct effect on blood pressure of being overweight is not clear, but blood pressures fall again when weight is lost.
5 Excessive alcohol consumption:
- the direct relationship between high alcohol consumption and hypertension is not clear, but a reversal of an alcohol drinking habit leads to lowered blood pressure.

The consequences of hypertension are that it:
- damages the heart, blood vessels, brain, and kidneys, without causing noticeable discomfort
- accelerates onset of atherosclerosis
- increases the workload of the heart and makes a brain hemorrhage more likely.

Hypertension is a condition that, once detected (Table 15.9), can be successfully treated with drugs.

APPLICATIONS

Causes and consequences of thrombosis

The cause of thrombosis is the diseases of blood vessels known as atherosclerosis – the progressive degeneration of the artery walls. The steps to atherosclerosis in arteries are:

1. Damage to the artery walls – this is due to strands of yellow fat being deposited under the endothelium.
   - Fat builds up from low-density lipoproteins (LDLs – ‘bad cholesterol’) circulating in the blood.
   - Fibrous tissue is laid down with the fatty streaks.

2. Raised blood pressure:
   - fatty deposits and the formation of fibrous tissue start to impede blood flow.

3. Inflammation and plaque formation at the site of fat deposit:
   - inflammation causes smooth lining of the artery to break down
   - the circulating blood is exposed to the fatty, fibrous deposits, causing atherosclerotic plaques to form
   - further deposition occurs as cholesterol accumulates, and smooth muscle fibres and collagen fibres proliferate in the plaque
   - blood platelets tend to collect at the exposed roughened surface, and these platelets release factors that trigger a defensive inflammatory response. This includes blood clotting leads to the formation of a thrombus.

The consequences of a thrombosis that leads to a free-circulating embolism are:

1. A ‘heart attack’ (myocardial infarction):
   - occurs when an embolus may be swept into a coronary artery
   - immediately, the blood supply to the tissue downstream of the blockage is deprived of oxygen – and without oxygen tissues die
   - when sufficient heart muscle dies, the heart may cease to be an effective pump

2. A stroke:
   - occurs when an embolus blocks an artery in the brain
   - neurons of the brain depend on a continuous supply of blood for oxygen and glucose, within a few minutes of the blood supply being lost, the affected neurons will die
   - neurons cannot be replaced, so the result of the blockage is a loss of some body functions controlled by that region of the brain.
Electrocardiography

■ Mapping of the cardiac cycle to a normal electrocardiogram (ECG) trace

The impulses (action potentials) that originate in the SA node (pacemaker) of the heart during the cardiac cycle produce electrical currents.

■ These electrical currents are conducted through the fluids of the body as a whole.

■ The electrical currents can be detected at the body surface by electrocardiography.

Electrodes are attached to the patient’s chest and the electrical activity is displayed as an electrocardiogram (ECG) by means of a chart recorder (Figure 15.27). Changes in the ECG trace are related to events in the cardiac cycle.

Electrocardiography has clinical applications:

■ It is an aid in the diagnosis of cardiovascular disease (CVD).

■ Some heart conditions that can be detected via ECG analysis are listed in Table 15.10.

### normal electrocardiogram (ECG), analysed

[Diagram showing various waveforms and intervals]

**Key**
- atrial contraction (atrial systole)
- ventricular contraction (systole)
- P wave: atrial depolarization – leads to atrial contraction
- P–R interval: time for impulse to be conducted from SA node to ventricles, via AV node
- QRS complex: onset of ventricular depolarization – leads to ventricular contraction
- T wave: ventricular repolarization – relaxation phase
- S–T segment: ST abnormality (elevation or depression) may indicate a heart attack

### abnormal traces showing

1. **tachycardia**
   - heart rate is over 100 beats/minute

2. **ventricular fibrillation**
   - uncontrolled contraction of the ventricles – little blood is pumped

3. **heart block**
   - ventricles not always stimulated

Figure 15.27 Electrocardiography
Arrhythmia is a condition of irregularity in heart rhythm due to a defect in the conduction system of the heart. It may be due to:

- drugs, such as nicotine or alcohol
- anxiety, hypothyroidism, or potassium deficiency

Ventricular fibrillation
Asynchronous contraction of the ventricle muscle fibres results in a failure of the heart to pump sufficient blood, because some muscle fibres are contracting while others are relaxing.

Tachycardia
A normal adult heart beats between 60 and 100 times a minute, whereas a heart rate over 100 beats a minute is called tachycardia. Tachycardia may be relatively harmless and need no treatment, but other forms can be life threatening.

Heart block
The most common site of obstruction of the electrical impulse is at the atrioventricular node.

**Table 15.10 Heart conditions detected by ECG analysis**

**APPLICATIONS**

**Use of defibrillation to treat life-threatening cardiac conditions**

Table 15.10 lists cardiac conditions that are potentially life threatening. They can be successfully treated by defibrillation.

- Defibrillation involves delivering a therapeutic dose of electrical energy to the heart with a device called a defibrillator.
- The electrical energy terminates the faulty rhythmical electrical activity and then re-establishes the normal pacemaker activity.

The major breakthrough came with the development of automated portable defibrillators (Figure 15.28). These analyse the existing heart rhythm, diagnose whether the condition is treatable and, if so, administer the correct electric shock. Inexperienced people can use this type of machine without clinical skills.

![Figure 15.28 Automated external defibrillator](image)
15.5 Hormones and metabolism (AHL)

Essential idea: Hormones are not secreted at a uniform rate and exert their effect at low concentrations.

Endocrine glands secrete hormones directly into the bloodstream

Hormones are chemical messengers that are produced and secreted from the cells of the ductless or endocrine glands (Figure 6.35, page 189).

- Hormones are secreted directly into the bloodstream.
- They are transported around the body, but only act at specific sites (target organs).
- Although present in small quantities, hormones are extremely effective in the control and coordination of several body activities.
- Hormone circulation in the bloodstream is only brief – molecules that do not reach a target organ are removed and broken down in the liver. Breakdown products that are no longer of use to the body are excreted in the kidneys.

Key definitions

Endocrine glands – secrete hormones directly into the bloodstream.

Target organ – specific site where a hormone has an effect.

QUICK CHECK QUESTIONS

1. Draw and label a diagram of the heart as seen in LS. Show positions of the sinoatrial (SA) node and atrioventricular (AV) node within the right atrium.

2. A causal relationship is suggested by statistical studies of deaths from coronary heart disease (CHD) per 1000 of the population each year, plotted against the levels of cholesterol and LDLs measured in blood serum (Figure 15.29). The establishment of the role of LDLs in triggering CHD was provided by experimental laboratory and clinical evidence that destructive plaques are created as a result of these raised levels of blood serum LDLs.

Figure 15.29 The relationship between deaths from CHD and blood serum cholesterol levels

- a. Explain to what extent the data in Figure 15.29 support the hypothesis that high blood cholesterol is a causal factor in CHD.
- b. During vigorous activity, the heart beats more quickly. Explain what causes this raised heart rate, and how is it brought about.

3. Outline the cause and consequences of hypertension.
Long-acting hormones must be secreted continuously into the bloodstream to be effective.

**Expert tip**

Hormone control of body function is different from nervous control:

- Nervous coordination is concerned with quick, precise communication.
- Hormones can work by causing specific changes in metabolism and development, often over an extended period of time.

Nervous system and hormones work together. Both systems are coordinated by the brain.

The structure of endocrine glands (ductless glands) can be contrasted with exocrine (ducted) glands (Table 15.11).

### Table 15.11 Endocrine and exocrine glands compared

<table>
<thead>
<tr>
<th>Endocrine glands</th>
<th>Exocrine glands</th>
</tr>
</thead>
<tbody>
<tr>
<td>These secrete hormones directly into the bloodstream. At target organs, hormones typically work by triggering changes to specific metabolic reactions.</td>
<td>These deliver their secretions via ducts, typically into the lumen of the gut or onto the body surface.</td>
</tr>
<tr>
<td><strong>Examples</strong></td>
<td></td>
</tr>
<tr>
<td>Islets of Langerhans — secrete insulin (Figure 6.36, page 190), targeted at muscle and other tissues.</td>
<td>sweat glands — secrete sweat onto the skin’s surface.</td>
</tr>
<tr>
<td>Posterior pituitary gland — secretes anti-diuretic hormone (ADH, Figure 11.23, page 306), targeted at collecting ducts of kidney tubules.</td>
<td>salivary glands — secrete saliva into the mouth (Figure 15.13A).</td>
</tr>
<tr>
<td>Gonads — secrete sex hormones (Topic 6, pages 193–197), targeted at the gonads and other body tissues.</td>
<td>gastric glands — secrete gastric juice into the stomach (Figure 15.10).</td>
</tr>
<tr>
<td>Pineal gland — secretes melatonin, targeted at tissues and organs that respond to our ‘body clock’ (Figure 6.39, page 193).</td>
<td>exocrine glands in pancreas — secrete digestive juice (of several digestive enzymes) into the duodenum (Figure 15.13B).</td>
</tr>
</tbody>
</table>

### Two modes of hormone action

**Expert tip**

Hormones can affect the metabolism of target cells in two ways, depending on whether they are a lipid-soluble steroid hormone or a water-soluble hormone, e.g. a peptide.

- **Steroid hormones**

  Steroid hormones are lipid soluble:
  
  - They diffuse from the bloodstream, through the lipid bilayer of plasma membranes and into the cytoplasm of cells (Figure 15.30).
  - If the cell is a target cell, the hormone binds to a receptor molecule which may be present in the cytoplasm or may be within the nucleus.
  - The receptor molecule is activated and alters the expression of particular genes.
Transcription of a gene may be switched on or switched off, depending on a hormone's mode of action.

- If a gene has been activated, new RNA is formed, leaves the nucleus, and then directs the formation of new proteins (most likely an enzyme) at ribosomes.
- New proteins or enzymes will bring about a structural or functional change in the cell.
- If a gene is switched off by hormone action, some cell process will be interrupted or terminated.

**Peptide hormones**

- Peptide hormones are hydrophilic, so they cannot pass through the membrane directly (Figure 15.31).
- Peptide hormones bind to receptors in the plasma membrane of a target cell.

The binding of a single molecule of hormone triggers the formation of 10,000 (10^4) molecules of cAMP which then activate a cascade of enzymes that further amplify the hormone signal. This is a three-stage process of cell signalling.

**The role of the second messenger**

The impact of the hormone on cell activity or structure comes from a series of reactions following the binding of a hormone to the cell membrane.

Binding of hormones to membrane receptors activates a cascade mediated by a second messenger inside the cell.

- The binding of the hormone causes the activation of an enzyme in the membrane, called adenylate cyclase.
- Adenylate cyclase converts ATP into cyclic AMP (cAMP) in the cytoplasm of the cell.
- cAMP (the second messenger) activates one or more protein kinase enzymes, present in the cytoplasm or attached to a membrane.
The action of protein kinase is to add a phosphate group (from a molecule of ATP) to one or more enzymes:

- sometimes this activates an enzyme
- sometimes it inactivates the normal action of an enzyme.

After a brief period, cAMP is inactivated by another enzyme, and the impact of the hormone on the cell is terminated, unless new hormone continues to bind to the plasma membrane receptors.

**Key fact**

Binding of hormones to membrane receptors activates a cascade mediated by a second messenger inside the cell.

---

**The hypothalamus controls hormone secretion by the pituitary gland**

**The role of the hypothalamus**

The hypothalamus has a key role in the control of many aspects of body function. The hypothalamus is exceptionally well supplied with blood vessels and is a part of the brain that has a major endocrine function.

- It constantly monitors blood composition as it circulates through the capillary networks of the hypothalamus.
- Data from the blood, and from receptors in key organs in the body via nerves, enable the hypothalamus to regulate many body activities concerned with maintenance of a constant internal environment – homeostasis.

The pituitary gland:

- is situated below the hypothalamus, and is connected to it
- consists of two parts: the anterior pituitary and the posterior pituitary lobes.

---

**Figure 15.31 The mechanism of action of a peptide hormone**

- **peptide hormone**
- **binds to receptor in plasma membrane**
- **hormone does not enter cell**
- **cyclic AMP**
- **ATP**
- **protein kinase**
- **activated (or inactivated) enzyme(s)**
- **structure/ function of cell altered**
- **phosphorylated enzyme catalyses reactions that produce a physiological or biochemical change in cell**
- **enzyme 1-P**
- **ADP**
- **enzyme 2-P**
- **phosphorylated enzyme no longer able to catalyse a reaction that triggers a physiological or biochemical reaction in cell**
- **cAMP**
- **cAMP eventually inactivated**
- **activated protein kinase**
- **ATP and/or ADP**
- **enzyme 2**
- **and/or ATP**
- **enzyme 1**

---

*Binding of hormones to membrane receptors activates a cascade mediated by a second messenger inside the cell.*
The hypothalamus controls the endocrine activity of the pituitary gland. The hypothalamus does this by releasing a number of hormones from its special **neurosecretory cells** (Figure 15.32) into the portal vein running between hypothalamus and anterior lobe (Figure 15.33), as well as by nerve impulses via other neurons that connect with the pituitary.

**Key definition**

**Neurosecretory cell** – a special type of neuron that secretes chemical messengers which travel round the body via the blood circulation.

---

**Figure 15.32 A working neurosecretory cell of the hypothalamus**

---

**Figure 15.33 The hypothalamus and pituitary gland**

The hypothalamus is the site of production of several hormones (Table 15.12).

- Hormones produced by the hypothalamus largely control the secretion of other hormones by the anterior and posterior pituitary glands, either by stimulating release of specific hormones or inhibiting release of specific hormones.

**Key fact**

The hypothalamus controls hormone secretion by the anterior and posterior lobes of the pituitary gland.
Hormones secreted by the pituitary gland control growth, developmental changes in the body's tissues and organs, reproduction, and homeostasis.

The posterior pituitary does not synthesize hormones but stores and releases two hormones produced in the hypothalamus (oxytocin and antidiuretic hormone – ADH).

### Hypothalamus

<table>
<thead>
<tr>
<th>Hormones</th>
<th>Roles</th>
</tr>
</thead>
<tbody>
<tr>
<td>thyrotropin-releasing hormone</td>
<td>stimulates anterior pituitary to release thyroid-stimulating hormone</td>
</tr>
<tr>
<td>dopamine</td>
<td>inhibits release of prolactin by the anterior pituitary</td>
</tr>
<tr>
<td>growth hormone-releasing hormone</td>
<td>stimulates growth hormone release from anterior pituitary</td>
</tr>
<tr>
<td>somatostatin</td>
<td>inhibits release of growth hormone and thyroid-stimulating hormone by the anterior pituitary</td>
</tr>
<tr>
<td>gonadotropin-releasing hormone</td>
<td>secreted at onset of puberty and then triggers sexual development</td>
</tr>
<tr>
<td>corticotropin-releasing hormone</td>
<td>stimulates release of adrenocorticotropic hormone from anterior pituitary</td>
</tr>
</tbody>
</table>

Oxytocin and anti-diuretic hormones are also produced here but are stored in the posterior pituitary for later release.

### Anterior pituitary gland

<table>
<thead>
<tr>
<th>Hormones</th>
<th>Roles</th>
</tr>
</thead>
<tbody>
<tr>
<td>thyroid-stimulating hormone</td>
<td>stimulates thyroid gland to secrete thyroxin</td>
</tr>
<tr>
<td>adreno-corticotropic hormone</td>
<td>stimulate secretion of cortisol by adrenal cortex</td>
</tr>
<tr>
<td>follicle-stimulating hormone</td>
<td>in females, initiates development of oocytes and secretion of estrogen by ovaries; in males, sperm production by testes</td>
</tr>
<tr>
<td>luteinizing hormone</td>
<td>in females, stimulates secretion of estrogen and progesterone, ovulation, and formation of the corpus luteum; in males, stimulates interstitial cells of testes to form and secrete testosterone</td>
</tr>
<tr>
<td>prolactin</td>
<td>together with other hormones, initiates and maintains milk secretion by the mammary glands</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hormones</th>
<th>Roles</th>
</tr>
</thead>
<tbody>
<tr>
<td>oxytocin (stored here)</td>
<td>after birth, enhances contraction of smooth muscle cells of uterus and release of milk from mammary glands</td>
</tr>
<tr>
<td>anti-diuretic hormone (stored here)</td>
<td>decreases urine production by causing collecting ducts of nephrons to return more water to the blood circulation</td>
</tr>
</tbody>
</table>

### Table 15.12 Hormones of the hypothalamus and pituitary glands

#### APPLICATIONS

**Control of milk secretion – a case study in hormone interaction**

Hormones are involved in lactation.

- Prolactin, secreted by the anterior pituitary, promotes milk secretion.
  - During pregnancy, the concentration of prolactin starts to build up, but progesterone inhibits its effects on the mammary glands.
  - Immediately after birth of the baby, the estrogen and progesterone levels in the blood fall. The inhibition of prolactin now ends.
  - The stimulus of the sucking action of the baby on the mother’s nipples maintains prolactin secretion for as long as breastfeeding continues.

---

**Key fact**

Hormones secreted by the pituitary control growth, developmental changes, reproduction, and homeostasis.

**Expert tip**

You need to know how milk secretion is controlled by oxytocin and prolactin.

**Key definition**

**Lactation** – the production and secretion of milk by the mammary glands after birth.
Oxytocin, secreted from the posterior pituitary, causes release of milk into the mammary ducts, from where it can be sucked out by the baby.

- Stimulation of touch receptors in the nipple initiates sensory nerve impulses that are relayed via sensory neurons and the spinal cord to the hypothalamus.
- As a result of nerve impulses, release of oxytocin increases.

Iodine for the thyroid hormone - thyroxin

**NATURE OF SCIENCE**

Cooperation and collaboration between groups of scientists – the International Council for the Control of Iodine Deficiency Disorders includes a number of scientists who work to eliminate the harm done by iodine deficiency.

The thyroid is an endocrine gland at the base of the neck (Figure 6.35, page 189).

- Thyroid hormones affect all body cells.
- Thyroxin, produced by the thyroid, is made from the amino acid tyrosine with the addition of the mineral iodine.
- Thyroxine causes an increase in the metabolic rate.

Iodine deficiency is common in many countries. Drinking water sometimes provides a natural dietary source of iodine, when present as the iodide and iodate ions. However, in some areas, the soil and rocks contain little of this element and, as a result, the water is deficient too.

- If iodine is not added in the diet, people develop a distinctly swollen thyroid gland, which causes goitre.
- One method of combating iodine deficiency is the addition of iodine (as the iodate ion) to table and cooking salt.
- Currently, collaboration between groups of scientists from many countries is seeking to eliminate the harm done by iodine deficiency. The work of this group of scientists is the province of the International Council for the Control of Iodine Deficiency Disorders.

**APPLICATIONS**

Growth hormones as aids to athletes

The naturally occurring sex hormones, testosterone and estrogen, influence the release of growth hormone, stimulating muscle growth and increased bone strength.

Some athletes take hormones, such as testosterone, as ‘performance-improving’ drugs to build their muscles.

- Testosterone has androgenic effects, leading to the ‘masculinizing’ of the body.
- Facial hair growth increases and the voice deepens – all unfortunate consequences – for female athletes who choose to use the hormone.
- Testosterone has to be administered by injection and, even then, is short lived in effects – it is rapidly broken down in the body and excreted.

A laboratory synthesized form of testosterone, nandrolone, can be made, with only minor changes to the molecule's structure. The effects of this on the body are almost identical to those of testosterone.

- The use of this ‘hormone’ is banned by the International Olympic Committee.
- The sale of such hormones is a criminal offence in some countries.

**Expert tip**

Sea foods are about the only good source of iodine; most foods are naturally deficient in this mineral.
However, it is alleged that, among sales of illegal substances, sales of anabolic
steroids are second only to sales of cannabis. Those who sell ‘banned’ drugs to users
(including some gym users who are keen to increase muscle size and ‘improve’ their
appearance) are able to import from countries where their sale is legal.

The ethics of using performance-enhancing drugs
The widespread use and abuse of performance-enhancing drugs (doping) raises
many ethical issues. In Table 15.13 some of these issues are raised.

<table>
<thead>
<tr>
<th>Why drugs attract some competitors</th>
<th>Why drug taking should be banned</th>
</tr>
</thead>
<tbody>
<tr>
<td>allows exceptional development of skeletal muscles</td>
<td>not fair; rather the user is cheating by gaining an unfair advantage</td>
</tr>
<tr>
<td>enables competitors to train harder</td>
<td>health risks and a danger of death</td>
</tr>
<tr>
<td>increases aggression and competitiveness</td>
<td>dangerous role model for young fans</td>
</tr>
<tr>
<td>drugs are reading obtained and, if use is monitored, health risks can be avoided</td>
<td>drug development should focus on disease prevention and curing patients</td>
</tr>
<tr>
<td>suppresses fears of not ‘making it’, given the high expectations of peers, press, etc.</td>
<td>gives technologically developed countries an unfair advantage</td>
</tr>
</tbody>
</table>

Table 15.13 Ethical issues with the use of drugs, such as anabolic steroids
The widespread use of performance-enhancing drugs raises medical and
health issues. The complex interaction of hormones in the working of the
body means that side-effects may be experienced many years ahead, if not
immediately.

QUICK CHECK QUESTIONS
1 Explain how the effects of hormones are restricted to particular cells or
tissues.
2 Explain how the binding of hormones to membrane receptors activates a
cascade mediated by a second messenger inside the cell.
3 Explain how hormones control milk secretion.

15.6 Transport of respiratory gases (AHL)

Essential idea: Red blood cells are vital in the transport of respiratory gases.

Transport of oxygen

The pressure of a specific gas in a mixture of gases is called its partial pressure.
The symbol for partial pressure is \( p \), so \( pO_2 \) denotes the partial pressure of oxygen.

Partial pressure is defined as the fraction of the total gas pressure that is exerted by
a particular constituent gas.

- The unit of pressure is the pascal (Pa) and its multiple the kilopascal (kPa).
- At sea level, the atmospheric pressure is typically about 101.3 kPa, and the
  partial pressure of oxygen is 21.2 kPa.

The significance of atmospheric \( pO_2 \) is reflected in the properties of the respiratory
pigment hemoglobin that transports oxygen in the blood.
The role of hemoglobin

Hemoglobin occurs in the red blood cells (erythrocytes).

- The hemoglobin molecule is built of four interlocking subunits (Figure 15.34).
- Hemoglobin subunits are composed of a large globular protein with a non-protein heme group attached, containing iron.
- One molecule of oxygen combines with each heme group, at the concentration of oxygen that occurs in our lungs.
- Each hemoglobin molecule is able to transport four molecules of oxygen:

\[
\text{hemoglobin} + \text{oxygen} \rightarrow \text{oxyhemoglobin}
\]

\[
\text{Hb} + 4\text{O}_2 \rightarrow \text{HbO}_8
\]

Figure 15.34 The structure of hemoglobin and its affinity for oxygen

The affinity of hemoglobin for oxygen is measured experimentally by finding the percentage saturation with oxygen of blood exposed to air mixtures that contain different partial pressures of oxygen. The result is called an oxygen dissociation curve (Figure 15.34).

- The oxygen dissociation curve is S-shaped.
- The amount of oxygen held by hemoglobin depends on the partial pressure of oxygen.
- In the hemoglobin molecule
  - the first oxygen molecule attaches with difficulty
  - once first oxygen molecule has attached, the second combines more easily, and so on until all four are attached and the molecule is saturated.

In the body, the amount of oxygen held by hemoglobin also depends on the partial pressure. In the lungs, air is saturated with water vapour and so the partial pressure of the component gases is different from that outside, in dry air (Table 15.14).

<table>
<thead>
<tr>
<th>Component gases</th>
<th>% Composition</th>
<th>Partial pressure/kPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>nitrogen</td>
<td>75.5</td>
<td>76.4</td>
</tr>
<tr>
<td>oxygen</td>
<td>13.1</td>
<td>13.3</td>
</tr>
<tr>
<td>carbon dioxide</td>
<td>5.2</td>
<td>5.3</td>
</tr>
<tr>
<td>water vapour</td>
<td>6.2</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Table 15.14 Partial pressures of the components of air in the alveoli

Expert tip

You need to be able to analyse the dissociation curve for hemoglobin.

Key fact

Oxygen dissociation curves show the affinity of hemoglobin for oxygen.
The oxygen dissociation curve shows that
- the hemoglobin in red cells in the capillaries around the alveoli in the lungs will be about 95% saturated
- in respiring tissues, the oxygen partial pressure is much lower due to aerobic respiration there
- the oxygen partial pressure in actively respiring tissues may be 0.0–4.0 kPa:
  - at these partial pressures, oxyhemoglobin breaks down
  - oxygen is released in solution and this rapidly diffuses into the surrounding tissues.

The structure and chemistry of hemoglobin makes it a very efficient for oxygen transport molecule, given the partial pressure of oxygen in respiring tissue compared with that in the lungs.

The effect of carbon dioxide on oxygen transport – the Bohr shift

The blood circulation also transports carbon dioxide from respiring tissues (where it is at relatively high partial pressures) to the lungs.

In respiring cells, the concentration of carbon dioxide is approximately 9.3 kPa, whereas in the lungs it is 5.3 kPa (Table 15.14). The effects of these partial pressures of carbon dioxide on the oxygen dissociation curve of hemoglobin are significant (Figure 15.35).

The effect of carbon dioxide on oxygen transport:
- There is an increase in carbon dioxide concentration shifts the oxygen dissociation curve to the right.
- Where the carbon dioxide concentration is high (in actively respiring cells), oxygen is released from oxyhemoglobin even more readily.
- This is known as the Bohr effect.

![Figure 15.35 How carbon dioxide favours release of oxygen in respiring tissues](image)

Key fact

The Bohr shift explains the increased release of oxygen by hemoglobin in respiring tissues.
Myoglobin

Myoglobin is a respiratory pigment

- It consists of a single heme–globin unit, similar to the four units in hemoglobin.
- It is only found in skeletal muscle cells, where it acts as a reserve of oxygen.
- The reserve of oxygen stored in myoglobin is drawn on during intense muscle contraction, when the oxygen supply would otherwise be insufficient.

Myoglobin has a much higher affinity for oxygen than hemoglobin (Figure 15.36A).

- In normal conditions in muscle, the myoglobin is saturated with oxygen.
- It functions as an oxygen store.
- When muscle is very active for a prolonged period, the oxygen concentration in the muscle tissue may fall below 0.5 kPa.
  - When this happens, oxymyoglobin will dissociate and supply oxygen, allowing aerobic respiration to continue.

If muscle contraction continues and all the myoglobin has yielded its oxygen, then muscle tissue switches to anaerobic respiration by lactic fermentation (Topic 2, page 67) and muscle contraction can continue for longer.

Fetal hemoglobin and oxyhemoglobin

The fetus obtains oxygen from its mother’s blood through the placenta, where the maternal and fetal circulations come very close together, but do not mix.

The hemoglobin of the adult mammal and the hemoglobin in the fetal circulation differ slightly in their chemistry.

- Fetal haemoglobin has the higher affinity for oxygen (Figure 15.36B).
- The hemoglobin present in the circulation of the fetus therefore combines with oxygen more readily than maternal hemoglobin does at the same partial pressure.
- It is advantageous for fetal hemoglobin to have this property:
  - The only access to an oxygen supply is via the placenta.
  - If fetal haemoglobin had a lower affinity than maternal hemoglobin, oxygen would pass from the fetus to the mother.

![Figure 15.36](image-url) The oxygen dissociation curves of A myoglobin and B fetal hemoglobin

**Expert tip**

You need to be able to analyse the dissociation curve for myoglobin.

**Expert tip**

Fetal hemoglobin is different from adult haemoglobin, allowing the transfer of oxygen in the placenta onto the fetal haemoglobin.
The transport of carbon dioxide in the blood

Carbon dioxide is transported from the respiring tissues to the lungs in the blood. The bulk of it in one of three forms:

1. A little carbon dioxide dissolves in the plasma. About 7% travels in this way.
2. More carbon dioxide combines with hemoglobin. The product is a compound, carbaminohemoglobin (HbCO₂). About 23% travels in this way.
3. The bulk of the carbon dioxide is transported as hydrogencarbonate ions.
   - Red cells contain the enzyme carbonic anhydrase which greatly accelerates the formation of hydrogencarbonate ions from carbon dioxide and water.
   - About 70% of the carbon dioxide is transported by this mechanism.

\[
\text{carbonic anhydrase} \quad \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{HCO}_3^- + \text{H}^+
\]

- The hydrogen ions are buffered by the plasma proteins and hemoglobin, preventing the blood from becoming acidic.

The pumping action of the heart causes the deoxygenated blood in the respiring tissues, loaded with hydrogencarbonate ions and carbaminohemoglobin, to return to the lungs. In the capillaries of the lungs, these ‘loading’ processes are reversed, and carbon dioxide diffuses into the lungs.

Figure 15.37 The transport of respiratory gases between respiring tissues and lungs

Key fact
Carbon dioxide is carried in solution and bound to hemoglobin in the blood.

Key fact
Carbon dioxide is transformed in red blood cells into hydrogencarbonate ions.
The control of breathing – the ventilation of the lungs

- The respiratory centre, situated in the medulla oblongata of the hindbrain, controls the rate at which we breathe.
- Two adjacent and interacting groups of nerve cells (neurons), known as the inspiratory centre and the expiratory centre respectively, bring about ventilation movements by reflex action.

Breathing occurs automatically (involuntarily).
- The inspiratory centre sends impulses to increase rate and depth of breathing.
- The expiratory centre sends impulses to inhibit the inspiratory centre and stimulate expiration.
- Alternating impulses from these two centres cause rhythmic breathing.

Breathing rates may also be adjusted without conscious thought.
- This occurs during increased physical activity, when voluntary muscles use much more oxygen and more carbon dioxide is produced and transported in the blood.
- The main stimulus that affects breathing is the concentration of carbon dioxide in the blood.
- Blood carbon dioxide level is detected by the chemoreceptors present in the carotid arteries and aorta (Figure 15.38).

When carbon dioxide level increases, as during strenuous physical activity:
- chemoreceptors that are hydrogen ion detectors (CO₂ is an acid gas, in solution) send impulses to the inspiratory centre
- the inspiratory centre sends additional impulses to the intercostal muscles and diaphragm, causing an increase in their contraction rates. (To a lesser extent, lowered oxygen concentration is also detected.)

An increase in the CO₂ concentration of the blood is detected by chemoreceptors in the medulla, the aorta, and in the carotid bodies.

**Figure 15.38 The control of ventilation rate**

**Expert tip**

The breathing rate is continually adjusted.
- On average, our normal rate of breathing is about 15 breaths per minute.
- It is possible to consciously override the breathing rate with messages sent from the cerebral hemispheres, e.g. when playing a wind instrument that needs breathing to be controlled.

**Expert tip**

The tidal volume is typically 400 cm³, and so the volume of air taken into the lungs in one minute (ventilation rate), given an average breathing rate of 15 breaths per minute, is about 6 litres.

**Key fact**

The rate of ventilation is controlled by the respiratory control centre in the medulla oblongata.

**Key fact**

Chemoreceptors are sensitive to changes in blood pH.
After strenuous exercise stops, the concentration of carbon dioxide in the blood falls (and the concentration of oxygen rises). These changes are detected and the ventilation rate is regulated accordingly.

**APPLICATIONS**

**pH of the blood – how it is regulated**

The pH of the blood is regulated to stay within the narrow range of 7.35 to 7.45 (it is slightly basic).

- The presence of buffers ensures the pH of blood is relatively constant.
- A buffer solution acts to resist pH change if a little acid or alkali is added.
- In the body of the mammal, the blood is very powerfully buffered by the presence of hydrogen carbonate ions, and blood amino acids and proteins.

Amino acids and proteins act as ‘buffers’.

- In solution, amino acids ionize; both the amino group and the carboxyl group do this.
- The carboxyl group can produce H\(^+\) ions and so it acts as an acid:
  \[-\text{COOH} \rightleftharpoons -\text{COO}^- + \text{H}^+\]
  The amino group can remove H\(^+\) ions from solution, so it acts as a base
  \[-\text{NH}_2 + \text{H}^+ \rightleftharpoons -\text{NH}_3^+\]
- In neutral solution both the amino group and the carboxyl groups are ionized.
  - In an acid solution (low pH), the amino acid picks up H\(^+\) ions and becomes positively charged.
  - In alkaline solution (high pH) the amino acid donates H\(^+\) to the medium and becomes negatively charged.

Amino acids tend to stabilize the pH of a solution, because they remove excess H\(^+\) or excess OH\(^-\) ions, forming water. They are acting as buffers, owing to the amino and carboxyl groups they support.

Hydrogen carbonate ions in the blood also function as an efficient buffer because of the way carbonic acid dissociates:

\[\text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+\]

**The effect of smoking**

**NATURE OF SCIENCE**

Scientists have a role in informing the public – scientific research has led to a change in public perception of smoking.

Scientists have a role in informing the public on issues such as the danger to health of smoking. Scientific research has led to changes in public perception of smoking.

- Bold and aggressive advertising campaigns, persuasive product placement in films, and the generous sponsorship of sporting and cultural events by cigarette manufacturers all encouraged greater smoking by men, and persuaded women to take it up, too.
- Very slowly, the dangers of smoking became known, but many people doubted the evidence.
- In the 1950s people started to recognize the dangers of cigarette smoking and inhalation of cigarette smoke, initially due to the pioneering research of Dr Richard Doll and other scientists.
Cigarette smoke reaches the smoker’s lungs when it is drawn down the cigarette and inhaled. The diseases that are directly induced by cigarette smoke are lung cancer, cardiovascular disease and chronic obstructive pulmonary disease, including emphysema.

### APPLICATIONS

> **Causes and treatments of emphysema**

Emphysema is a disease in which the walls of the alveoli lose their elasticity.

- The loss of elasticity and destruction of the lung tissue with time occurs due to the accumulation of large numbers of phagocytic white blood cell from the blood.
- Phagocytic cells release high levels of hydrolytic enzymes that break down the elastic fibres of the alveolar walls (Figure 6.28, page 182), and also far too little of the natural inhibitor of this enzyme.
- With failing elastic fibres, alveoli fail to recoil and expire air properly, so these air sacs are left overinflated and air becomes trapped in them.
- Small holes develop in the walls of the alveoli; these begin to merge, forming huge air spaces with drastically lowered surface area for gas exchange (Figure 15.39).

A patient with emphysema becomes permanently breathless. The destruction of air sacs can be halted by stopping smoking, but any damage done to the lungs cannot be reversed.

![Figure 15.39 Scanning electron micrograph of A healthy human lung tissue, and B lung tissue showing advanced emphysema](image)

## ATT protein and emphysema

Transgenic sheep have been successfully engineered to yield rare and expensive human proteins in their milk that may be useful as medicines. One example of this type of genetic engineering is the production of a special human blood protein, known as AAT.

- Production of AAT enables people to maintain their vital lung elasticity.
- Patients with a rare genetic disease are unable to manufacture AAT at all and they develop emphysema.

The human gene for AAT production has been identified and isolated.

- The gene has been cloned into sheep together with a promoter gene (a sheep’s milk protein promoter) attached to it.
- The sheep’s mammary glands produce the human protein and secrete it in their milk during lactation.
- AAT is, in this way, made available for use with patients.
APPLICATIONS

Consequences of high altitude for gas exchange

More than 40 million people live and work at altitudes of 3000–5500m, mainly in the Andes and Himalayas. The problems of gaseous exchange at high altitude arise because the partial pressure of oxygen falls there (Table 15.15).

<table>
<thead>
<tr>
<th>Altitude/m above sea level</th>
<th>Atmospheric pressure/kPa</th>
<th>Oxygen content/%</th>
<th>Partial pressure of oxygen/kPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>101.3</td>
<td>20.9</td>
<td>21.2</td>
</tr>
<tr>
<td>2500</td>
<td>74.7</td>
<td>20.9</td>
<td>15.7</td>
</tr>
<tr>
<td>5000</td>
<td>54.0</td>
<td>20.9</td>
<td>11.3</td>
</tr>
<tr>
<td>7000</td>
<td>38.5</td>
<td>20.9</td>
<td>8.1</td>
</tr>
<tr>
<td>10000</td>
<td>26.4</td>
<td>20.9</td>
<td>5.5</td>
</tr>
</tbody>
</table>

Table 15.15 Change in partial pressure of oxygen at altitude

The result of these changes is

- as altitude increases, it becomes increasingly difficult for hemoglobin in red blood cells in the lungs to load oxygen
- once the percentage saturation of hemoglobin with oxygen is lowered, this is detected by chemoreceptors
- the respiratory centre responds by stimulating the lungs to take extra-deep breaths
- as a result of deeper breaths, more carbon dioxide is lost from the body, which causes a small but significant rise in the pH of the blood
- the chemoreceptors become ineffective and ventilation regulation is hampered.

The body cannot adapt to high altitude immediately; sudden, prolonged exposure at these altitudes by unacclimatized people can be fatal. However, progressively the following changes take place.

- A more alkaline urine is secreted by the kidney tubules via the collecting ducts, and the pH of the blood returns to normal; as a result, the carbon dioxide chemoreceptors become sensitive again and normal ventilation is maintained.
- Bone marrow tissue, the site of red blood cell formation, is produced and releases more red cells, thereby enhancing the oxygen-carrying capacity of the blood (Table 15.16).

<table>
<thead>
<tr>
<th>Altitude/m above sea level</th>
<th>Red cell count/10¹⁵ dm⁻³</th>
</tr>
</thead>
<tbody>
<tr>
<td>human</td>
<td></td>
</tr>
<tr>
<td>0 (sea level)</td>
<td>5.00</td>
</tr>
<tr>
<td>5000+ as a temporary visitor</td>
<td>5.95</td>
</tr>
<tr>
<td>5000+ as a resident</td>
<td>7.37</td>
</tr>
<tr>
<td>rabbit</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4.55</td>
</tr>
<tr>
<td>5000+</td>
<td>7.00</td>
</tr>
<tr>
<td>sheep</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10.5</td>
</tr>
<tr>
<td>5000+</td>
<td>12.05</td>
</tr>
</tbody>
</table>

Table 15.16 Acclimatization and adaptation of mammals to breathing at high altitude
Animals that have evolved at high altitude have a form of hemoglobin in their red blood cells that loads more easily at lower partial pressures of oxygen, as shown by an oxygen saturation curve obtained with samples of their blood (Figure 15.40). So, for example, a llama from high in the Andes mountains of South America has a much lower loading partial pressure for its hemoglobin than a similar mammal from the lowlands of South America.

![Dissociation curve of hemoglobin of llama from mountains in South America](image)

**Figure 15.40** Dissociation curve of hemoglobin of llama from mountains in South America

### QUICK CHECK QUESTIONS

1. Explain the significance of the S-shaped curve dissociation curve of human hemoglobin.

2. Examine the light micrograph and electron micrographs in thin sections of lung tissue, shown in Figure 15.41. List the distinguishing structural features of pneumocytes, capillary endothelium cells, and blood cells by which they may be identified in light micrographs and electron micrographs of thin sections of alveoli.

**A Light micrograph of thin sections of alveoli**

- type I pneumocytes in the alveolar wall (only 0.15 µm thick)
- type II pneumocyte in alveolar wall (secrete a solution containing surfactant)
- phagocyte
- tiny blood capillary in section between adjacent alveoli – with wall of very thin cells (red blood cells in capillary are less than 0.5 µm from air in the alveoli)
- arteriole of pulmonary circulation, containing many red cells – (surrounded by connective tissue)

**B Electron micrograph of thin sections of alveoli**

**Figure 15.41** Light micrograph and electron micrograph of thin sections of alveoli

**Expert tip**

Gaseous exchange occurs in the air sacs (alveoli) of the lungs. The structure of alveoli is shown in Figures 6.24 and 6.25 (pages 179 and 180).
3 With reference to Figure 15.42, deduce the difference in carrying capacity of hemoglobin and myoglobin at a $p\text{O}_2$ of (a) 1 kPa and (b) 5 kPa. Explain the significance of these differences in relation to the requirements of muscle tissue for oxygen.

4 Training camps for athletes are frequently located at high altitude because it is believed this puts the athletes at an advantage when they return to lower ground for competition. Explain the science behind this training system.