CHAPTER 20
BIOCHEMISTRY

This chapter provides a basic introduction to the very complex branch of biological sciences that studies the chemical substances and vital processes occurring in living organisms. A knowledge of biochemistry enables healthcare professionals to have more understanding of the reasoning behind some diagnostic medical investigations and procedures, and the actions and interactions of medications.

20.1 Understanding matter

Everything in the universe including the human body is made of **matter** – material that takes up space, has mass and therefore can be weighed (➔ Box 20.1). Matter is composed of particles – atoms and molecules – and can be an element, compound or mixture.

Box 20.1 Mass is the amount of matter in an object and does not change. Weight is a measure of gravity's effect on something, e.g. a person weighs less at the top of a mountain or in space than at ground level.

20.1.1 States of matter

Matter can exist as a solid, liquid or gas, e.g. water is liquid which, when heated, becomes a gas (water vapour; steam), and when frozen becomes solid (ice). Although the human body feels solid, it is mostly made of water which is a liquid (➔ Box 20.2).

Box 20.2 Plasma matter is a fourth state of matter. It is gas that has been heated to a very high temperature so that most of its atoms and molecules are broken down into free electrons and positive ions (➔ 20.2.1).

Particles in a solid:

- are tightly packed and held in rigid positions by chemical bonds that are difficult to break apart
- vibrate but generally do not move from place to place. The solid state is found at lower temperatures. As the temperature rises, the rate of vibration increases and the spacings between the particles get larger. When melting point is reached, the solid becomes liquid.

Particles in a liquid:

- are close together with no regular arrangement
- vibrate and move about randomly as they slide past each other, which allows a liquid to flow and take the shape of the container it is in, e.g. bodily fluids (➔ Box 20.3)
- form a film on the surface of the liquid which is caused by the cohesive properties (stickiness) of its particles – known as **surface tension**.

Box 20.3 In healthcare practice, liquids are often called **fluids**. Examples of body fluids are tissue fluid, blood, urine, sweat, tears, cerebrospinal fluid and breast milk.

Particles in a gas:

- are well separated with no regular arrangement and quickly fill the container that they are in
- vibrate, move freely and spread out (diffuse) randomly at high speeds, the speed of diffusion increasing with temperature
- have spaces between the particles, which allows the gas to be compressed, e.g. when oxygen (a gas) is compressed to a liquid for storage in a cylinder (➔ Box 20.4).

Box 20.4 The **gas laws** describe some properties of gases and are named after the people who discovered them; e.g. Boyle's law states 'When a gas is compressed, the force applied to the walls of the container increases'. This is because the gas has less space to move and particles will collide with the wall more frequently (as long as temperature remains constant).

20.2 Atoms

Matter consists of **atoms** – tiny particles that are so small they can only be seen with an electron microscope. Each type of atom has its own characteristics based on the subatomic particles it contains.

20.2.1 Structure of atoms

Atoms contain three types of **subatomic particle** – protons, neutrons and electrons:

- a **proton** has one unit of positive electric charge (→ Box 20.5) and one unit of atomic mass (see below)
- a **neutron** has no electrical charge and one unit of atomic mass
- an **electron** carries one unit of negative electrical charge and its mass is so small that it can be disregarded (→ Fig. 20.1).

Box 20.5 An electric charge is a force which is either positive or negative. **Positively charged particles** are repelled by each other but attracted to negatively charged substances. Similarly, **negatively charged particles** are repelled by each other and attracted to positive charges.

The protons and neutrons are densely packed in the **nucleus** at the centre of the atom and give it mass. The **electrons** are arranged in energy levels (shells) around the nucleus and orbit around the nucleus, usually in pairs, and can move to higher or lower energy levels (**shells**) but they cannot exist in between them. An orbit is the definite path of an electron as it moves around the nucleus in an atom.

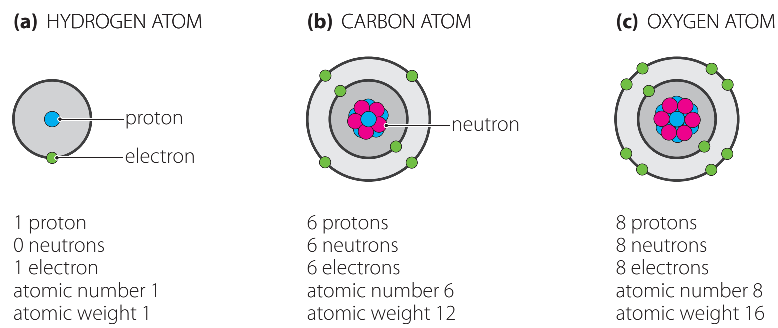

Fig. 20.1 Elements are made of atoms which are depicted with protons and neutrons located in the nucleus and electrons orbiting around the nucleus: (**a**) hydrogen; (**b**) carbon; (**c**) oxygen.

Points to note

Atomic number (proton number) of an atom is the number of protons in the nucleus of the atom, which is unique to each element. The higher the atomic number, the heavier the atom.

Atomic mass (atomic weight). The mass of an atom equals the combined number of protons and neutrons in its nucleus.

Box 20.6 The atomic mass of carbon is C 12, the isotope of carbon has an extra neutron and an atomic mass C 13, and C 14 has two extra neutrons.

Isotopes are atoms that have the same number of protons and electrons but different numbers of neutrons and therefore have different physical properties (→ Box 20.6).

Ions are electrically charged particles, meaning that they can conduct electricity. Each ion is an atom or group of atoms in which the number of electrons does not equal the number of protons.

Box 20.7 The periodic table is a chart of the chemical elements displayed in **horizontal rows** in order of increasing atomic number, and arranged so that **vertical columns** contain elements with similar physical and chemical properties.

20.3 Chemical elements

A **chemical element**, usually referred to as an ‘element’, is a pure chemical substance consisting of atoms of the same type which cannot be split by chemical means into simpler substances (→ Box 20.7). Ten of the

28 elements make up 99% of the human body (➔ Box 20.8). The rest are present in very small or minute amounts but they are all needed if the body is to stay alive and be healthy.

Chemical symbols

Each element also has its own **chemical symbol** – an internationally agreed code for that element, e.g. the symbol for oxygen is O. These are used as a form of shorthand to name the elements and the accompanying number refers to the number of atoms present, e.g.:

- oxygen **gas** (O_2) contains two oxygen atoms
- water (H_2O) contains two hydrogen atoms and one oxygen atom
- glucose ($C_6H_{12}O_6$) contains six carbon atoms, twelve hydrogen atoms and six oxygen atoms.

20.3.1 Hydrogen

Hydrogen (H) is the most abundant element in the world. It **reacts** with carbon to form a very wide range of combustible hydrocarbons, e.g. methane, propane, butane. Hydrogen gas (H_2) is highly flammable and reacts explosively with other elements. Hydrogen is also the main element in water (H_2O) and carbohydrates ($C_nH_{2n}O_n$) and is contained in saturated fats. The pH scale is a measure of the concentration of hydrogen ions in a solution (➔ 20.8.3).

20.3.2 Oxygen

Oxygen (O) exists in the air as a colourless and odourless gas with the chemical formula O_2. It readily **reacts** (undergoes chemical changes) with other elements to form part of water (H_2O), carbon dioxide (CO_2), carbohydrates, amino acids, fatty acids and other biologically important substances. The body requires a continuous supply of oxygen in the form of O_2 for respiration to convert food into energy, but oxygen gas in the air is not very soluble in water. For this reason, oxygen in the body is transported in blood as oxyhaemoglobin.

20.3.3 Carbon

The different forms of **carbon (C)** include very soft materials like graphite and the hardest known substance which is diamond. Carbon also combines with other elements in millions of different ways to form **organic compounds** (➔ Box 20.9). These can be as diverse as carbon dioxide – a colourless gas, the organic matter in soil, fossil fuels, and the very large, complex compounds – macronutrients – carbohydrates, proteins and fats (➔ Box 20.10).

20.3.4 Nitrogen

Nitrogen (N) in the molecular form of N_2 is the most abundant component in air. It is an essential requirement for the body and is obtained not from the air, but from protein foods (➔ Box 20.11). Protein in the diet is digested (broken down) into amino acids which are used as building blocks for the many types of proteins needed to build the various tissues. It is also needed for nucleic acids (DNA and RNA). Nitrogen is needed to make nitric oxide (NO) which has a wide variety of functions in the body.

Box 20.8 The 28 elements in the human body are shown below, each with its chemical symbol and the percentage present.

Main elements

Oxygen (O)	65%
Carbon (C)	18%
Hydrogen (H)	10%
Nitrogen (N)	3%
Calcium (Ca)	1.5%
Phosphorus (P)	1.0%
Potassium (K)	0.35%
Sulphur (S)	0.25%
Sodium (Na)	0.15%
Magnesium (Mg)	0.05%

Elements in very small amounts

Iron (Fe)	Copper (Cu)
Zinc (Zn)	Selenium (Se)
Molybdenum (Mo)	Fluorine (F)
Chlorine (Cl)	Iodine (I)
Manganese (Mn)	Cobalt (Co)

Trace elements – those in minute amounts

Lithium (Li)	Strontium (Sr)
Aluminium (Al)	Silicon (Si)
Lead (Pb)	Vanadium (V)
Arsenic (As)	Bromine (Br)

Box 20.9 Compounds which contain carbon are called organic compounds; the study of **organic chemistry** is the branch of chemistry devoted to them.

Box 20.10 The **carbon cycle** is the pathway taken by carbon in various forms as it circulates continuously between the air, oceans, plants, animals and soil. It becomes involved in processes that include photosynthesis, respiration and decomposition.

Box 20.11 Although the **air** which is breathed in and out of the body contains about 78% nitrogen, the body cannot use this tasteless, odourless, invisible gas. The body is unable to store nitrogen and if more protein is eaten than can be used, the excess is excreted in urine, e.g. urea and ammonia.

20.3.5 Calcium

Calcium (Ca) is the most abundant mineral in the human body; the average adult contains about 1 kg (➔ Box 20.12). Over 99% is found in bones and teeth where it is used as a reserve that can be released into the blood as required for functions that include the transmission of nerve impulses (➔ Fig. 9.11), contraction of muscle cells (➔ Fig. 4.22) and the clotting of blood (➔ Fig. 5.7).

Box 20.12 Bones play an important role in the homeostasis of blood **calcium** levels. The movement of calcium into and out of bones enables the level to be maintained within a narrow limit for optimum health. An excess of blood calcium is called **hypercalcaemia** and a deficiency of blood calcium is called **hypocalcaemia**.

20.3.6 Other important elements in the body

Phosphorus (P) is a component of DNA and other nucleic acids and is present in ATP (adenosine triphosphate) – the body's energy currency. It also combines with calcium in bones and teeth, and with lipids to form phospholipids that provide the basic structure of the plasma membrane (➔ 2.2.1).

Potassium (K) is an important intracellular electrolyte essential for the maintenance of the resting potential of nerve and muscle cells (➔ Box 20.13).

Box 20.13 The level of **potassium** in the blood is normally maintained within narrow limits; too much is called **hyperkalaemia** while having too little is **hypokalaemia**. Potassium can be lost through vomiting and diarrhoea, while some disorders, e.g. Crohn's disease (➔ 7.9.1) and some diuretic drugs can contribute to a deficiency.

Sulphur (S) is a part of some of the amino acids in the body and is necessary for protein synthesis, several enzyme reactions and the production of collagen. It forms part of keratin, giving strength to hair, skin and nails.

Sodium (Na) is present in blood and other extracellular fluids and helps in maintaining **fluid balance** – the correct amount of fluid in the body – and hence blood pressure. It also plays a key role in nerve and muscle function.

Magnesium (Mg) is a cofactor in many enzyme reactions and is necessary for the proper functioning of nerve and muscle tissue.

Chloride (Cl) is a negatively charged ion that is distributed through the extracellular fluids of the human body in association with sodium. It is an important constituent of gastric juice and plays a key role in acid–base homeostasis.

Iron (Fe) is an essential element in virtually all organisms because it is required for living processes including DNA synthesis, oxygen carriage by haemoglobin and electron transport in mitochondria.

20.4 Molecules

Most atoms do not exist on their own but bond together to form molecules. A **molecule** is defined as two or more atoms linked together by chemical bonds.

20.4.1 Chemical bonds and energy changes

A **chemical bond** is the force of attraction that holds atoms together in a molecule. Chemical bonds are involved in chemical reactions (chemical changes) when electrons are either:

- **shared** to form either strong or weak bonds; as there are no free electrons, these bonds do not conduct electricity
- **transferred**, i.e. relocated from one atom or molecule to another, as happens when electrons are transferred in the citric acid cycle (➔ 20.14).

Strong bonds

A strong bond is a attraction between atoms, ions or molecules that is strong enough to hold them together to form a chemical compound, and can be covalent or ionic.

Covalent bonds are bonds in which atoms share electrons (→ Fig. 20.2). Only the electrons in the outer energy level (valence shell) are involved in bond formation. A covalent bond can be:

- **polar.** A polar bond between two atoms occurs when the electrons forming the bond are unequally placed. This causes the molecule to have one end that is slightly positive (+) and the other that is slightly negative (–), e.g. water molecules (→ Fig. 20.2)
- **nonpolar.** A nonpolar bond is one in which the electrons are symmetrical and the charges all cancel out each other.

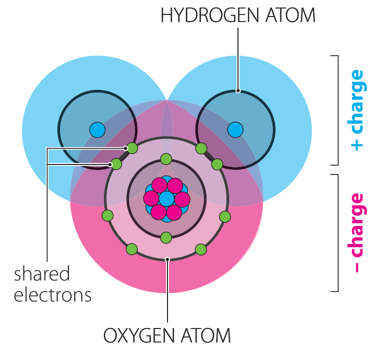

Fig. 20.2 Polar bonding in a water molecule (H_2O) – the two pairs of shared electrons are unequally placed.

Ionic bonds occur between positive and negative ions (→ 20.6.1), which attract each other and bind together to form ionic lattices. The lattice is held together by the strong attraction between oppositely charged ions, e.g. NaCl (table salt). When salt dissolves in water, the bonds break and the molecules dissociate into Na^+ and Cl^- (→ Fig. 20.3).

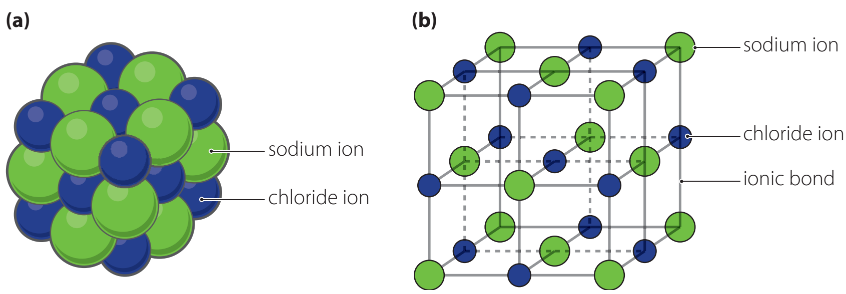

Fig. 20.3 (**a**) Salt molecule; (**b**) ionic bonding between sodium and chlorine atoms showing the lattice structure.

Weak bonds

Although indiviual bonds may be weak, the presence of many weak bonds in large macromolecules provides stability for the structure and gives these molecules their shape, e.g. in DNA and protein molecules.

20.5 Chemical compounds

A **chemical compound**, usually just referred to as a ‘compound’, is a molecule composed of two or more atoms combined together by chemical bonds. A compound often has quite different characteristics from the elements it contains. For example:

- liquid water (H_2O) is formed from two gases – hydrogen and oxygen
- glucose ($C_6H_{12}O_6$) is formed from carbon (a solid) and two gases – hydrogen and oxygen
- **sodium** (Na) is a soft, silvery-white metal and chlorine (Cl) is a greenish-yellow poisonous gas; together, they form sodium chloride (NaCl), which is common table salt (solid).

20.5.1 Organic and inorganic compounds

Organic compounds are a broad class of substances containing **carbon**. Many will frequently contain hydrogen, e.g. carbohydrates and hydrocarbons, and may also contain other elements, e.g. oxygen, nitrogen, sulphur and phosphorus. The body is dependent on organic compounds:

- carbohydrates, lipids and protein in the diet supply energy and building materials for the cells
- flavours and tastes of foods depend on the organic compounds detected by the nasal epithelium and taste buds
- many common drugs such as antibiotics and aspirin are derived from organic compounds.

Inorganic compounds lack carbon atoms, or when present are strongly bound to other atoms. The essential inorganic compound in the human body is water (H_2O). Other inorganic compounds are sodium chloride (NaCl) which is an essential electrolyte, nitric oxide (NO) which dilates blood vessels, ammonia (NH_3) which is a waste product, and minerals which are often metals.

Box 20.14 Water is unique in its molecular structure and for its importance in physiological systems. It covers 75% of the earth, exists in three states of matter – solid ice, liquid water and gaseous water vapour – and is a major component of cells. The special properties of water arise because water molecules are attracted to each other by hydrogen bonds.

Box 20.15 All life originated in the seas many millennia ago and the composition of body fluids is remarkably similar to that of seawater. **Homeostasis of body fluids** is maintained by hormones from the hypothalamus, kidneys and adrenal glands. They maintain the composition and concentration of body fluids ('internal sea') within narrow limits of the normal range.

20.6 Water

Water (H_2O) is a tasteless, colourless and odourless liquid that can exist as a solid, liquid or gas (→ Box 20.14). In its pure state, water has a neutral pH of 7, which means it is neither acidic nor basic (alkaline), although the pH changes when substances are dissolved in it.

Water is uniquely different from other substances and is vital for life.

- **It is a good solvent** (fluid in which a substance dissolves).
- **It provides a liquid medium** in which chemical reactions can take place within cells (→ Box 20.15).
- **It transports substances** from one place to another in blood and other fluids, and waste substance can be excreted in urine.
- **It allows diffusion to take place**; most movement of dissolved substances into and out of cells occurs by diffusion across cell membranes.
- **It has a high surface tension** because water molecules are attracted to each other, forming a film which is adhesive and elastic. The high surface tension enables water droplets to form and blood to move through the capillaries.
- **It is used in hydrolysis reactions** to form new compounds with other substances.
- **It is a good heat carrier**, distributing heat around the body in the circulating fluids. Because water has a high specific heat, it can absorb large amounts of heat energy and then release it as the water cools, which helps to maintain body temperature at an even level.
- When the body overheats, the excess heat is removed in the **evaporation** of sweat.

20.6.1 Water in the body

The adult body is about 65% water, which is present in the body's fluids as:

- **plasma** in blood vessels
- **lymph** in the lymph vessels
- **intracellular fluid** (ICF) inside the cells

- **interstitial fluid** (tissue fluid) that surrounds the tissue cells. Solutes dissolved in the water include electrolytes, sugars, salts, acids, hormones, neurotransmitters and cell waste
- **transcellular fluids** – a small but important group of fluids derived from plasma including saliva, cerebrospinal fluid, synovial fluid, urine, sweat, amniotic fluid and breast milk. These fluids are secreted by epithelium.

20.6.2 Water homeostasis

Homeostasis of water content is known as **osmoregulation** (→ Box 20.16). When the water content in the body is maintained within normal limits, the physiological processes can function correctly, allowing the:

- blood to circulate normally through the blood vessels
- cells to work at their optimum level because the enzymes and the substrates on which they act all need to be dissolved in water.

Box 20.16 Cells can be regarded as small sacs containing water with a high concentration of electrolytes in solution that are kept in balance by **osmoregulation**.

If cells were surrounded by pure water, the water would diffuse into the cells by osmosis, making them swell up and burst – a process called **lysis**.

If, however, cells were bathed by a solution containing a higher concentration of dissolved substances, reverse osmosis would occur and water would exit from the cells, causing them to shrink – a process known as **crenation** (→ Fig. 20.4).

20.7 Movement of particles

A **particle** is a very tiny object such as an atom or molecule. It will have volume, mass and chemical properties, and can move by diffusion.

20.7.1 Diffusion

Diffusion is the net movement of particles from an area of high concentration to one of low concentration. This difference in the concentration of particles across a space is called the **concentration gradient**. The rate of diffusion depends on the:

- **size and type** of particles involved – smaller particles diffuse faster than large particles
- **area** through which diffusion can take place
- **distance** to be crossed or the thickness of any membranes that must be crossed
- **temperature** – particles diffuse faster at higher temperatures than at lower temperatures. When heat is applied to them, particles move faster, and when they lose heat they move at a slower speed.

20.7.2 Osmosis

Osmosis is a special form of diffusion that enables water molecules to move across a **selectively permeable membrane** between different fluid compartments from an area of high concentration to an area of low concentration. Net movement of molecules depends on whether an environment is:

- **isotonic** – this refers to solutions with equal osmotic pressures
- **hypertonic** – this refers to a solution which has a higher osmotic pressure than another. This means that there is a greater number of solute particles in the solution (or a cell)
- **hypotonic** – this refers to a solution that has a lower osmotic pressure than another solution (or a cell) (→ Fig. 20.4).

Maintaining water balance

Water balance exists when the output of water from the body equals the amount taken into the body in food and drinks plus the small amount of water produced in cell respiration. Most water is lost from the body

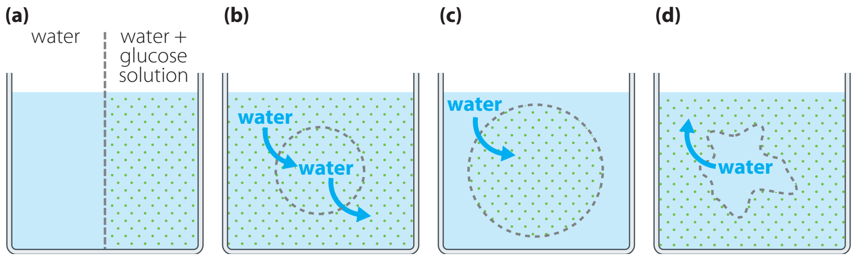

Fig. 20.4 Effect of osmosis on a model cell immersed in solutions; (**a**) two solutions with different concentrations of solute separated by a semipermeable membrane; (**b**) in isotonic solutions the net transfer of solvent molecules is at equilibrium, so the movement of water out of the cell is balanced by the movement of water into the cell; (**c**) hypotonic solution outside the cell and hypertonic solution inside the cell leads to a net inward movement of water that makes the cell swell and dilutes its contents; (**d**) hypertonic solution outside the cell and hypotonic solution inside the cell makes the cell shrink and its contents more concentrated – a situation known as **crenation** (➔ Box 20.17).

Box 20.17 Intravenous fluids are frequently used in acute hospital settings when patients are unable to drink enough to maintain adequate hydration. They are given as drips because their osmotic concentration is similar to plasma, which minimises the difference between the extracellular and intracellular fluids.

in urine but in abnormal conditions, increased volumes are lost, e.g. in excessive sweating, hyperventilation, haemorrhage, vomiting and diarrhoea (➔ Box 20.18).

Box 20.18 Water lost from the body in urine and sweat, vomitus and diarrhoea must be replaced by homeostatic mechanisms that increase secretion of antidiuretic hormone (ADH), resulting in greater reabsorption of water by the kidneys, reduced urine output and thirst, which stimulates drinking of fluids. If these responses do not happen, the body becomes dehydrated (**hypovolaemia**), which triggers a more intense range of cardiovascular and renal compensatory mechanisms; if these are not sufficient, then shock may develop (➔ 16.5.1).

Osmoregulation

Osmoregulation is the homeostatic process that keeps the concentration of water and electrolytes in balance inside cells. The hypothalamus plays an essential role in this process. When **negative water balance** arises (e.g. hypovolaemia or dehydration), a group of neurons in the hypothalamus are stimulated to release ADH – a hormone that makes the kidneys reabsorb more water, reduces urine output and induces feelings of thirst and the desire to drink. When ingestion of water replaces the water which was lost, the normal osmotic balance is restored. **Positive water balance** can arise when people ingest large volumes of water. The additional fluid load inhibits the secretion of ADH so kidneys reabsorb less water and the urine output increases.

20.7.3 Movement of particles through ion channels

Ion channels are small pores in the proteins in the plasma membrane of cells that allow ions to flow across the membrane. The channels can be non-gated or gated (➔ Fig. 20.5).

Non-gated channels are always open and allow particles to diffuse along a concentration gradient from high to low; if there is no gradient, then the particles do not flow.

Gated channels are protein channels that open in response to mechanical, electrical or chemical signals:

- **Mechanically-gated channels** open in response to touch or pressure.
- **Voltage-gated channels** are opened by an electrical signal and are responsible for processes that alter membrane potential such as heart-beat, muscle contraction, hormone secretion, vision, olfaction, pain and much else.
- **Ligand-gated channels** are opened by a chemical signal (➔ 18.8.2). These channels open to allow ions such as Na^+, K^+, Ca^{2+}, or Cl^- to pass rapidly through the membrane after binding to a ligand such as a neurotransmitter, e.g. molecule of acetylcholine, noradrenaline or a drug. The rate of ion transport through the channel is rapid – often 100 ions per second or more.

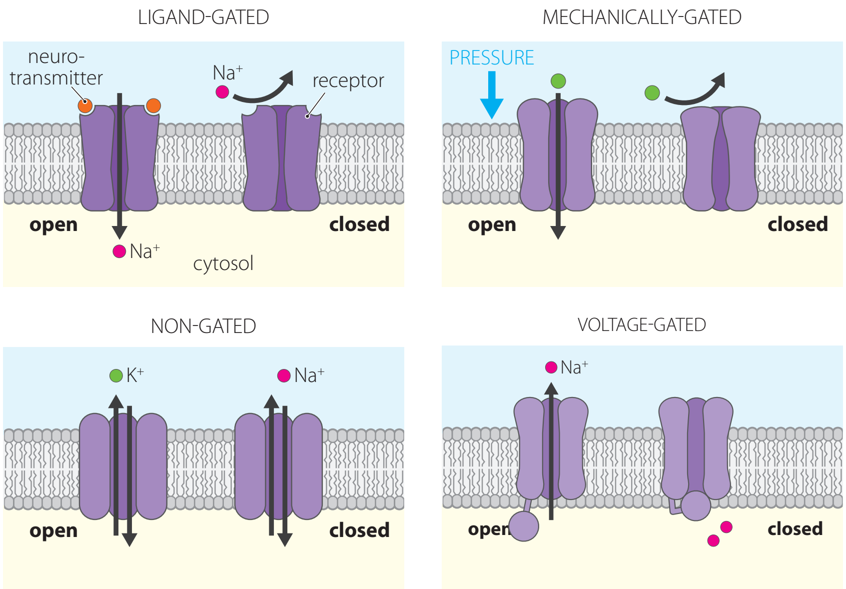

Fig. 20.5 Gated and non-gated ion channels.

20.8 Ions and electrolytes

Ions are electrically charged particles, and electrolytes are substances – liquid or gel – that contain them.

20.8.1 Ions

Ions are electrically charged particles, meaning that they can conduct electricity (→ Box 20.19). Each ion is an atom in which the number of electrons does not equal the number of protons, giving the particle either a positive charge (cations) or a negative charge (anions).

- A **cation** is an atom that has more protons than electrons and therefore has a positive charge, e.g. sodium (Na^+) and iron (Fe^+).
- An **anion** is an atom that has more electrons than protons and therefore has a negative charge, e.g. chloride ion (Cl^-) and iodide (I^-).

20.8.2 Electrolytes

Electrolytes are solutions (or gels) that contain ions (anions and cations) dissolved in water. Ions in blood and other body fluids include:

- **calcium** (Ca^{2+}) is a second messenger in signal transduction (→11.2.1), is essential for muscle contraction (→ Fig. 4.22) and is needed for neurotransmitter release from neurons (→ Fig. 9.13)
- **sodium** (Na^+) is mostly located outside cells and plays a key role in normal nerve and muscle function (→ Box 20.20)
- **chloride** (Cl^-) is essential for maintaining electrical balance across cell membranes and for regulating the movement of fluid in and out of cells
- **potassium** (K^+) is vital for the functioning of all cells.

Electrolytes form a large group of compounds that includes acids, bases and salts. When dissolved in water:

- a **base (alkali)** yields hydroxyl ions (OH^-)
- an **acid** yields hydrogen ions (H^+) (→ Box 20.21)

Box 20.19 The human body depends on **electrical activity**. In every cell of the body there is a slight electrical potential difference between the inside and the outside of the plasma membrane. It arises because of the unequal distribution of the ions across the plasma membrane.

Box 20.20 During strenuous exercise, the body loses electrolytes in sweat, particularly sodium and potassium. **Oral rehydration** is a type of fluid rehydration which uses preparations of electrolytes that can be dissolved in water and contains glucose which helps the absorption of sodium by the intestinal epithelium. Oral rehydration is especially indicated in children with diarrhoea.

Box 20.21 Common acids in the body are:
DNA – genetic material in the nucleus
amino acids – group of acids that form the basic building blocks for proteins
ascorbic acid – vitamin C
fatty acids – essential for plasma membranes, for making some hormones, and as an energy source
lactic acid – a waste product of anaerobic respiration.

Box 20.22 Fluid and electrolyte therapy uses water containing electrolytes (salts) to correct the water balance and restore electrolyte losses of sodium, potassium or calcium. It is used for patients following severe dehydration caused by vomiting, diarrhoea, haemorrhage, heat shock or burns.

- a **salt** yields both positive ions and negative ions. Sodium chloride (NaCl) is an example of a salt; it dissolves readily in water into positively charged sodium ions (Na^+) and negatively charged chloride ions (Cl^-) (→ Box 20.22).

Strong acids or bases are those that dissociate completely in water, e.g. hydrochloric acid and nitric acid. **Weak acids or bases** only partly dissociate, e.g. lactic acid and citric acid. Mixing acids and bases can cancel out – neutralise – their effects. **Neutral substances** are neither acids or bases.

20.8.3 Hydrogen ions

Hydrogen ions form part of metabolic acid that accumulates in the body as a result of metabolic processes, e.g. lactic acid, carbonic acid, or keto-acid (ketones). When these molecules are in solution, the hydrogen ions take on a positive charge and become electrolytes called **hydrogen ions** or **protons** and written as $\mathbf{H^+}$.

Example A function of the gastric (stomach) lining is to make hydrochloric acid (HCl) a part of the body's first line of defence (→ Fig. 14.2). In the lumen of the stomach, the acid dissociates to hydrogen ions (H^+) and chloride ions (Cl^-), thus forming a strong acid environment that can kill most bacteria.

pH scale

The **pH scale** (0 to 14) measures the concentration of hydrogen ions in a substance to find out how acidic or alkaline it is (→ Fig. 20.6).

- pH 7 is neutral. Pure water is neutral; when chemicals are mixed with the water, the mixture can become either acidic or basic (alkaline).
- pH less than 7 is acidic. The greater the number of hydrogen ions, the greater the acidity and the lower the reading on the pH scale.
- pH greater than 7 is basic. The smaller the number of hydrogen ions, the greater the alkalinity and the higher the reading on the pH scale (→ Box 20.23).

Box 20.23 The pH scale is logarithmic, with the result that each whole pH value below 7 is ten times more acidic, e.g. pH 4 is ten times more acidic than pH 5. The same applies to pH values above 7, e.g. pH 10 is ten times more basic (alkaline) than pH 9.

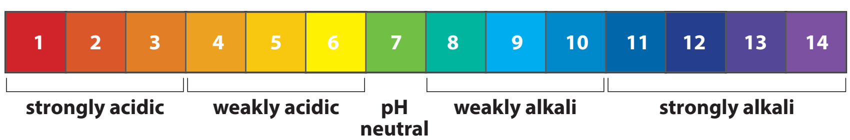

Fig. 20.6 The pH scale.

20.8.4 Acid–base balance

The acid–base balance in the body is the state of equilibrium between the amount of carbonic acid (H_2CO_3) and bicarbonate (HCO_3^-) in the blood. **Acid–base homeostasis** keeps the arterial blood pH at 7.35–7.45 and allows the cellular enzymes to function normally. Even a slight alteration in the pH causes acidosis or alkalosis (→ 20.8.5).

Acid–base balance is regulated by:

- the **lungs** – changing the respiratory rate alters the concentration of CO_2 in the blood, which in turn alters the pH, and is a rapid response
- the **kidneys** – by excreting excess acids or bases, a slow process that generally takes several days
- **buffers**.

A **buffer** is a solution that can resist a change of pH by the addition of either acidic or basic components as necessary. The major buffer in the blood is the **bicarbonate system** – the system that transports carbon dioxide from the tissues to the lungs. In this system, carbon dioxide (CO_2) combines with water (H_2O) to form carbonic acid (H_2CO_3), which in turn rapidly dissociates to form hydrogen ions (H^+) and bicarbonate (HCO_3^-) (→ Fig. 6.13). The process can be summed up in the equation:

$$H_2O + CO_2 \rightleftharpoons H_2CO_3 \rightleftharpoons \mathbf{HCO_3^-} + \mathbf{H^+}$$

20.8.5 Acidosis and alkalosis

These two conditions arise when the acid–base equilibrium in the body is disrupted due to failure of the mechanisms that maintain the balance between the acids (hydrogen ions) and bases (bicarbonate) in arterial blood. The pH of body fluids is then either above or below the normal range of pH 7.35–7.45 as measured in arterial blood (→ Box 1.2).

Acidosis

This condition occurs when there is too much acid in the blood and other body tissues; in other words, there is an increased hydrogen ion concentration.

Respiratory acidosis can occur when breathing is obstructed, e.g. by choking or emphysema, causing increased levels of CO_2 in the blood.

Metabolic acidosis occurs when the kidneys cannot eliminate enough hydrogen ions or when they excrete too many hydroxyl ions. **Diabetic ketoacidosis** (**DKA**) is an example of metabolic acidosis which occurs when the body is unable to use blood glucose (sugar) for energy due to a shortage of insulin. Fat is then used as an alternative source of fuel, which causes the build-up of a waste product called **keto-acid** (**ketones**).

Alkalosis

Alkalosis refers to a condition when the body fluids are too alkaline.

Respiratory alkalosis is related to decreased blood CO_2 levels and can be acute or chronic.

Acute respiratory alkalosis can result from **hyperventilation** (excessive deep breathing) and the excretion of too much CO_2:
- **during physical exercise**, resulting in muscle weakness, cramps and fainting
- **due to psychological distress** (anxiety and panic). When a low blood CO_2 level disrupts the calcium ion balance it causes hypocalcaemia (an abnormally low level of calcium in the blood) and results in cramp and fainting.

Metabolic alkalosis is caused by chemical reactions inside cells which raise the pH of tissue above 7.45. This results from either:
- **decreased hydrogen ion** concentration, often due to loss of chloride ions by vomiting or excretion via the kidneys
- **increased bicarbonate ions**, for which there are many contributing causes.

20.9 Chemical reactions

A **chemical reaction** (chemical change) is the rearrangement of atoms to form different substances, e.g.:

- when the gases oxygen and hydrogen react together they produce water – which is a liquid

$$2H_2 + O_2 \longrightarrow 2H_2O$$

- photosynthesis is a series of chemical reactions that use the energy of light to combine six molecules of carbon dioxide and six of water to produce one molecule of glucose and six molecules of oxygen:

$$6CO_2 + 6H_2O \longrightarrow C_6H_{12}O_6 + 6O_2$$

20.9.1 Types of reaction

A **spontaneous reaction** does not require an external source of energy, but occurs when the reactants come into contact with each other. The conditions necessary for the reaction might depend on temperature, an acid or basic environment, the presence or absence of oxygen, the presence or absence of catalyst, or other factors (→ Box 20.24).

Box 20.24 Most biochemical reactions that take place in the body's cells are spontaneous, but they would not proceed without the presence of **enzymes** (biological catalysts) to speed up the reactions (→ 20.12.1).

Some spontaneous reactions take place rapidly, e.g.:

- explosions
- table salt or glucose dissolving in water
- ice melting in lukewarm water
- a smell diffusing in a room.

Other spontaneous reactions may take many years, e.g.:

- iron rusting
- the formation of stalagmites or stalactites in a cave.

A **reversible reaction** is a chemical reaction that can occur in both the forward and reverse direction. An example is the combination of oxygen with haemoglobin in the lungs and its release in the tissues. In the lungs, each molecule of haemoglobin bonds with four molecules of oxygen and becomes oxyhaemoglobin, with a colour change from the deep red/purple of haemoglobin to the bright red colour of oxyhaemoglobin. The reverse reaction occurs as the blood circulates through the tissues and oxygen is released to the cells (→ Boxes 20.25 and 20.26).

$$\mathbf{Hb + 4O_2 \rightleftharpoons Hb.4O_2}$$

Box 20.25 Like all reversible reactions, those in the body are affected by environmental conditions, e.g. when the body is hot and lactic acid is being produced during exercise, the rate of unloading of oxygen from **haemoglobin** occurs more rapidly.

Box 20.26 Two arrows in a chemical equation indicate that the chemical change is **reversible**.

In a **irreversible reaction**, the reactants form products, which cannot change back into the reactants. An example is combustion – when substances burn they cannot return to their original state (→ Box 20.27).

Box 20.27 A **combustion reaction** always includes a hydrocarbon and oxygen as the reactants, produces carbon dioxide and water as products, and is irreversible.

Metabolic pathways

A **metabolic pathway** is a series of chemical reactions that is regulated by enzymes. These reactions take place inside cells, e.g. the citric acid cycle that releases stored energy from sugar (→ 20.13).

20.10 Mixtures

A **mixture** contains two or more substances that are mixed together, with each retaining its own chemical identity, e.g. air, blood, food and urine. The substances in a mixture can be separated by physical processes that include evaporation, as happens when water evaporates from sweat leaving the salt behind on the skin (→ 3.4), and in the fractionation of blood (→ Box 20.28).

Box 20.28 Blood fractionation refers to the process of separating the various components of blood – red cells, white cells, platelets, plasma and plasma proteins (→ 5.8.1).

Different types of mixture

A **solution** is a mixture of two or more substances in which one or more of these substances (solutes) is dissolved in another substance such as water or another liquid (the solvent), and they can be separated again, e.g. when water evaporates from a salt solution, crystals of salt remain.

A **suspension** contains substances that are not completely dissolved in the solution and may settle at the bottom of the container, e.g. blood cells and platelets settle into layers when blood is allowed to stand. Medicines in the form of a suspension need to be shaken before use.

A **colloid** is a type of mixture in which one substance is split up into tiny particles and spread throughout another substance. Unlike a suspension, the substances in a colloid do not separate if allowed to settle, e.g. the proteins remain dispersed in plasma.

20.11 Metabolism

Metabolism is the term used to sum up the enormous number of **metabolic reactions** (biochemical changes) that occur in each living cell. Chemical changes involve **energy** in the form of **adenosine triphosphate (ATP)** (➔ Box 20.29). The production of ATP depends on the presence of oxygen – a gas that is not stored in the body, but which is needed continually to release energy from nutrients. Metabolic reactions either build up (anabolic) or break down (catabolic):

- **anabolic reactions** use ATP to synthesise (build up) macromolecules from smaller ones (➔ Fig. 20.7(a))
- **catabolic reactions** release ATP when macromolecules are broken down into smaller ones (➔ Fig. 20.7(b)).

Box 20.29 When at rest or asleep, the need for **ATP** is relatively small, thus energy requirements and the need for oxygen are minimal. Whenever the level of activity increases, e.g. during exercise or fever, the demand for energy – and hence oxygen – also increases. To satisfy the increased demand for oxygen, ventilation and cardiac output increase accordingly.

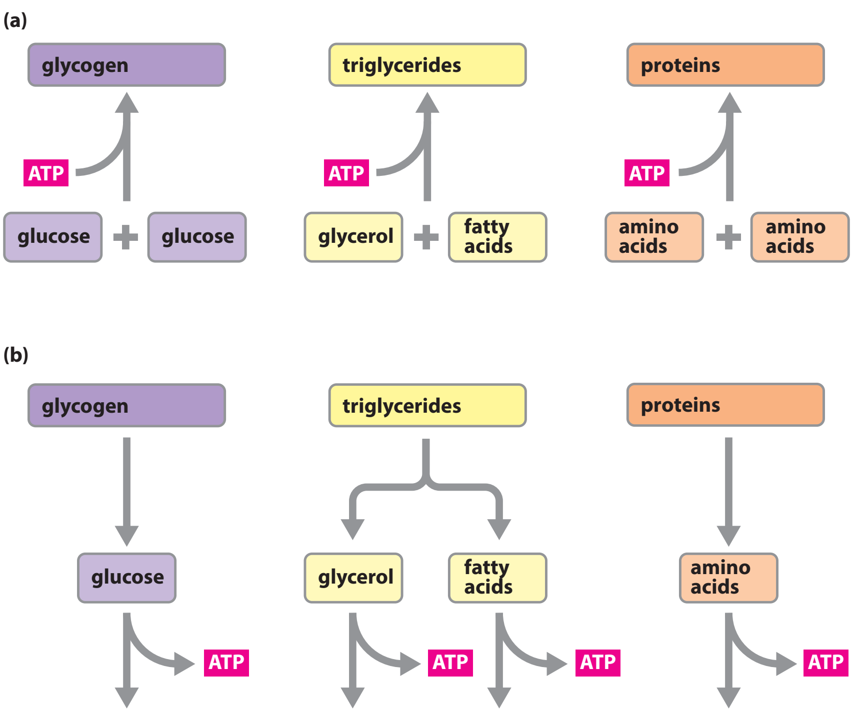

Fig. 20.7 (**a**) Anabolism; (**b**) catabolism.

20.12 Enzymes

Enzymes are specialised molecules of protein made inside living cells and their function is to speed up chemical reactions involved in metabolism. The body requires thousands of different enzymes for all the different chemical reactions needed to keep it alive, e.g. cell respiration and energy production. Many enzymes are intracellular, which means that they work inside the cells in which they were made. Extracellular enzymes are secreted from the cells in which they were made and have an effect in cells elsewhere in the body. Examples include digestive enzymes (→ 7.2), renin (→ 8.7) and complement protein (→ 14.4.4).

- **Enzymes are catalysts** – they speed up the rate of chemical reactions but are not themselves changed, and they can be used repeatedly.
- **Enzymes are specific** and each acts on only one substance called the **substrate**, e.g. amylase (enzyme) acts on starch, pepsin on protein and lipase on fat. The **specificity** of any enzyme usually depends on the 3D shape of its molecule and its active site (→ Fig. 20.8).
- **Enzymes are affected by temperature**. Human enzymes work best at about 37°C, and are denatured (altered) by heating above 43°C.
- **Enzymes are sensitive to pH**. The optimum pH for most intracellular enzymes is pH 7–7.5. The extracellular enzymes vary, e.g. pepsin in the stomach works best in an acid medium of pH 2, and lipase in the duodenum works best in a weak alkaline solution around pH 8.
- **Names of enzymes often end in 'ase'** e.g. lactase, amylase and phosphatase. The name often indicates the reaction that the enzyme catalyses, e.g. alcohol dehydrogenase is the enzyme that speeds up the detoxification of alcohol (→ Box 20.30).

Box 20.30 Alcohol is toxic to the nervous system and high levels are dealt with by **alcohol dehydrogenase** – an enzyme that is present in the liver and stomach. This enzyme converts alcohol to acetaldehyde (an even more toxic molecule) which is then quickly converted into acetate and other molecules that are easily utilised by the body's cells including glucose. In this way, a potentially dangerous molecule – alcohol – is converted by the enzyme into a foodstuff. Alcohol dehydrogenase in the average liver can detoxify alcohol at a rate of one unit per hour.

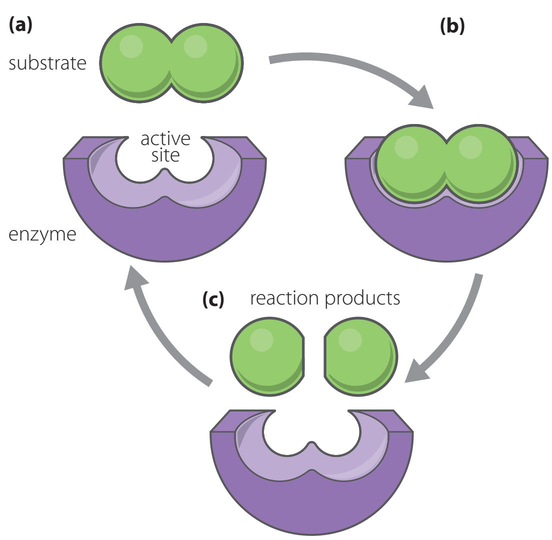

Fig. 20.8 The action of an enzyme on its substrate depends on the specific binding of the substrate to its active site: (**a**) enzymes are made of long chains of amino acids, folded to form the active site; (**b**) the substrate can bind to the enzyme to form an enzyme–substrate complex; (**c**) when the reaction is complete the products are released and the enzyme can be reused.

20.12.1 How enzymes work

An enzyme is a protein molecule formed from a long chain of amino acids that is coiled in a specific way to form an active site – a 3D shape into which a specific substrate can bind (→ Fig. 20.8a). The substrate binds to the active site in a lock-and-key manner and initiates a chemical reaction

(→ Fig. 20.8b). The products of the reaction are released and the active site can be reused (→ Fig. 20.8c).

Enzymes may also require:

- **enzyme activators** – they bind to enzymes to increase their activity by a process called phosphorylation and energy transfer from ATP.
- **cofactors** – substances that must be present in suitable amounts before certain enzymes can act. Water is a cofactor in all the chemical reactions that occur in the body. Other cofactors include minerals such as sodium, potassium or magnesium ions, also coenzymes.
- **coenzymes** – substances necessary for optimal function of enzymes because they enhance and improve enzyme performance. In many cases they do this by binding to the enzyme.

20.12.2 Homeostatic function of enzymes

Because their activity is tightly regulated, enzymes and enzyme inhibitors have a **homeostatic function** in the regulation of the cell's metabolism. For example, enzymes in a metabolic pathway can be inhibited by downstream products. This type of negative feedback, known as product inhibition, slows the production line when products begin to build up and is an important way to maintain homeostasis in a cell.

20.13 Energy

Energy is needed for the enormous number of chemical reactions that take place in a cell such as:

- **synthesis** (building) proteins, nucleic acid and other materials that the cell requires for growth and repair
- **transport** of materials within the cell
- **specialised functions** of some types of cell, e.g. contraction by muscle cells, transmission of nerve impulses by nerve cells, movement of cilia in ciliated cells and secretion by gland cells.

Cells need a continual supply of energy but the chemical energy stored in food, e.g. glucose, cannot be used until it has been transferred to ATP (adenosine triphosphate).

20.13.1 Glucose as fuel for cell functions

Energy is released aerobically when glucose and oxygen are metabolised to carbon dioxide and water, a process that can be summed up in the following chemical equation

$$\underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{oxygen}}{6O_2} \longrightarrow \underset{\text{carbon dioxide}}{6CO_2} + \underset{\text{water}}{6H_2O} + \underset{\text{ATP + heat}}{\text{energy}}$$

As the energy is released, it is used to build molecules of ATP (adenosine triphosphate) from ADP (adenosine diphosphate) and phosphate (PO_4), summed up in the equation

$$\underset{\text{molecule of ADP}}{\text{ADP}} + \underset{\text{phosphate group}}{PO_4} \longrightarrow \underset{\text{molecule of ATP}}{\text{ATP}}$$

The ATP molecule now contains energy that can be used in reversible chemical reactions in any part of the cell. The release of the energy is a gradual, continuous process during which ATP changes back to ADP and a phosphate group (PO_4)

$$\text{ATP} \longrightarrow \text{ADP} + PO_4 + \text{energy}$$

Box 20.31 Phosphorylation is the process that involves the addition of a phosphate group to a molecule, e.g. the phosphorylation of ADP to ATP (→ Fig. 20.9).

Box 20.32 Hydrolysis means splitting by water. When ATP is hydrolysed it separates into ADP and phosphate.

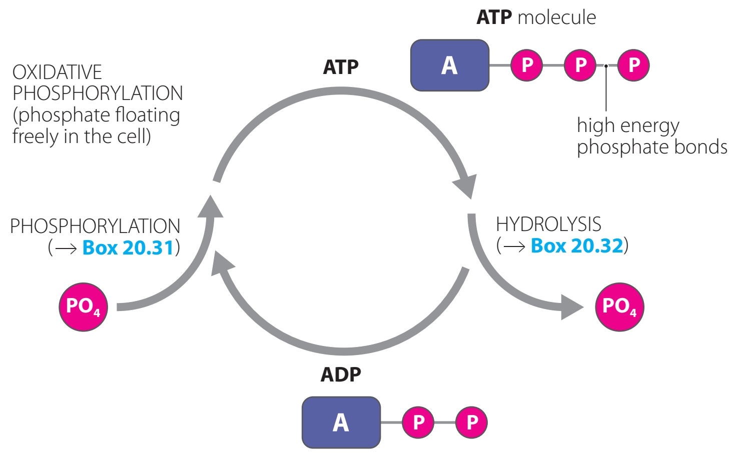

Fig. 20.9 ATP–ADP cycle.

ATP–ADP cycle

The ATP–ADP cycle is a continuous process during which energy is stored in ATP and then released, leaving ADP and a phosphate group free to be re-used to make more ATP (→ Fig. 20.10).

Glycogenolysis

When blood glucose levels are falling, more supplies of glucose are obtained from the breakdown of glycogen (**glycogenolysis**) stored in liver and muscle cells (→ Box 20.33). When this has been used up, fats can be used for energy and, last of all, protein in the muscles. When fat or protein are used to provide energy they must first be processed by the liver.

Box 20.33 Glycogenolysis is the production of glucose from glycogen. **Glycogen** is a storage carbohydrate; it is used to store glucose in liver and muscle cells. The hormone **glucagon** stimulates the breakdown of glycogen when plasma glucose levels are falling. **Adrenaline** can also stimulate release of glucose from glycogen to sustain fuel supplies to active muscles, and **cortisol** stimulates gluconeogenesis.

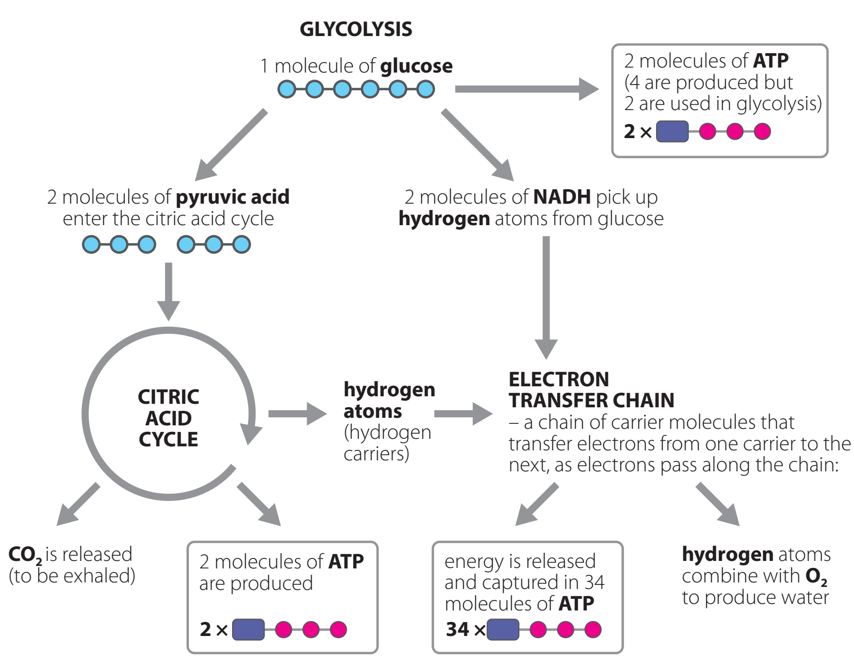

Fig. 20.10 Aerobic respiration is a complex process that yields ATP and includes glycolysis, the citric acid cycle and the electron transport chain.

Gluconeogenesis

Gluconeogenesis (making new glucose) is the term used to describe the complex metabolic processes in the liver (and sometimes kidneys) that result in creation of glucose molecules from:

- lactic acid, e.g. after intense exercise
- lipids, e.g. during fasting
- amino acids.

Gluconeogenesis is necessary to maintain glucose homeostasis and prevent **hypoglycaemia** that occurs when glucose is not directly available. The process of forming the new bonds between carbon atoms to produce glucose molecules is energy demanding, but shifts glucose to essential organs – brain and muscle – when it is needed.

20.14 Aerobic respiration

Aerobic respiration (cell respiration) takes place inside cells and requires oxygen for the release of energy from glucose. The process can be summed up in the equation

$$\underset{\text{(glucose)}}{C_6H_{12}O_6} + \underset{\text{(oxygen)}}{6O_2} \longrightarrow \underset{\text{(carbon dioxide)}}{6CO_2} + \underset{\text{(water)}}{6H_2O} + \underset{\text{(ATP and heat)}}{\text{energy}}$$

The method of obtaining energy can be divided into three stages; the first stage – glycolysis – takes place in the cytoplasm, and the next two stages – citric acid cycle and electron transfer chain – take place in the mitochondria.

Glycolysis

Glycolysis ('splitting sugar') is the first stage of respiration, during which a molecule of glucose is split by hydrolysis to produce:

- two molecules of pyruvic acid which enter the citric acid cycle
- four atoms of hydrogen which are transported to the electron transfer chain by the hydrogen carriers $NADH_2$ and $FADH_2$ (→ Box 20.34)
- two molecules of ATP which can be used as a quick source of energy.

Box 20.34 NAD (nicotinamide adenine dinucleotide) is a coenzyme found in all living cells. It acts as a hydrogen carrier and becomes $NADH_2$. **FAD** (flavin adenine dinucleotide) is a coenzyme derived from riboflavin (vitamin B2) and also acts as a hydrogen carrier – $FADH_2$.

Citric acid cycle

The **citric acid cycle** (Krebs cycle) is a series of biochemical reactions that act on a glucose molecule to produce:

- 2 molecules of ATP
- 6 molecules of CO_2 that will be exhaled
- 10 pairs of hydrogen atoms that go into the electron transfer chain.

Electron transfer chain

The **electron transfer chain** is a chain of carrier molecules that transfer the electrons from one carrier to the next to release energy in the form of 34 molecules of ATP. The hydrogen atoms are brought into the chain by $NADH_2$ and $FADH_2$. When the energy is transferred to ATP, inhaled oxygen serves as the final hydrogen acceptor, combining to form water.

20.14.1 Anaerobic respiration

Anaerobic respiration is a type of respiration that does not use oxygen (anaerobic means without air). It is not nearly as efficient as aerobic respiration, producing only a small amount of ATP because the glucose is partially, not completely, broken down. It can be summed up in the equation:

$$\underset{\text{glucose}}{C_6H_{12}O_6} \longrightarrow \underset{\text{lactic acid}}{2C_3H_6O_3} + \underset{\text{energy}}{2ATP}$$

20.14.2 Lactic acid

Lactic acid is produced continuously anaerobically in muscle tissue, both when the body is at rest and during moderate exercise. It is continuously removed by oxidation within the muscle fibres in which it was produced, or converted to pyruvate and then back to glucose to be used as a source of energy. Lactic acid accumulates in all tissues at times of oxygen deficit and the rate of production exceeds the rate of removal (→ Fig. 20.11), as happens:

- during strenuous exercise
- during acute illness
- when oxygen delivery to the tissues is not adequate despite an increased rate of breathing.

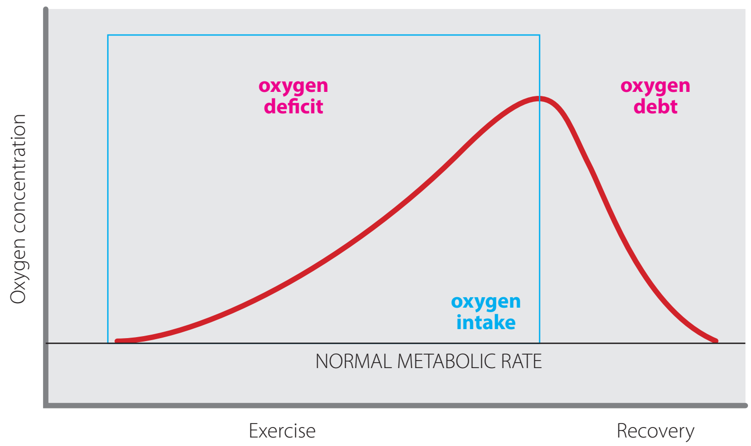

Fig. 20.11 Lactic acid accumulates when the body's demand for oxygen exceeds the supply.

The **oxygen debt** is the amount of oxygen needed to oxidise lactic acid to carbon dioxide and water after exertion has stopped. The debt is repaid by breathing quickly and deeply until the excess lactic acid has been oxidised.

Lactic acidosis

Lactic acidosis occurs when lactic acid accumulates in the bloodstream, the symptoms being deep and rapid breathing, vomiting and abdominal pain. Acidosis will tend to be experienced differently by people depending on their lactate threshold, which in turn depends on levels of training (exercise tolerance) and genetics (→ Box 20.35).

Box 20.35 Lactic acidosis, a form of metabolic acidosis (→20.8.5), occurs in people who are acutely unwell, e.g. in cases of infection or following trauma or in circulatory shock. In healthcare settings, it is usually assessed through arterial blood samples; however, venous blood sampling is an alternative.

20.14.3 ATP–PC system

The ATP–PC system produces energy more quickly than any other biochemical system and comes into action during the first 5–8 seconds of intense exercise. The action takes place in muscle tissue when **phosphocreatine (PC)** is used to produce **adenosine triphosphate (ATP)**. When activity continues beyond this time the body relies on aerobic respiration, then anaerobic respiration for energy.

Key points

1. Biochemistry is the branch of life sciences that seeks to understand the chemical building blocks of living organisms.
2. Everything in the universe is made of matter, and a relatively small number of atoms form bonds and make up all of the molecules important for life.
3. Knowledge of biochemistry can inform healthcare practice by helping to develop understanding of the nature of essential nutrients and gases and how they move between the environment and cells.
4. Biochemistry also seeks to understand how molecules – including nucleic acids, hormones and nutrients – interact in ways that enable cells, tissues and the body to function.
5. Cells depend on energy for their function, and biochemistry can help healthcare professionals to understand the diverse metabolic reactions that take place in the human body.
6. Biochemists and pharmacologists are also concerned with the effects of drugs and other ingested substances on biochemical pathways in the body.