Respiratory system

The cells of the body need energy for all their metabolic activities. Most of this energy is derived from chemical reactions, which can only take place in the presence of oxygen (O2). The main waste product of these reactions is carbon dioxide (CO2). The respiratory system provides the route by which the supply of oxygen present in the atmospheric air enters the body, and it provides the route of excretion for carbon dioxide.

The condition of the atmospheric air entering the body varies considerably according to the external environment, e.g. it may be dry or moist, warm or cold, and carry varying quantities of pollutants, dust or dirt. As the air breathed in moves through the air passages to reach the lungs, it is warmed or cooled to body temperature, saturated with water vapour and ‘cleaned’ as particles of dust stick to the mucus which coats the lining membrane. Blood provides the transport system for O2 and CO2 between the lungs and the cells of the body.

Exchange of gases between the blood and the lungs is called external respiration and that between the blood and the cells internal respiration. The organs of the respiratory system are:

- nose
- pharynx
- larynx
- trachea
- two bronchi (one bronchus to each lung)
- bronchioles and smaller air passages
- two lungs and their coverings, the pleura
- muscles of breathing – the intercostal muscles and the diaphragm.
Structures associated with the respiratory system.

Nose and nasal cavity

Position and structure
The nasal cavity is the main route of air entry, and consists of a large irregular cavity divided into two equal passages by a septum. The posterior bony part of the septum is formed by the perpendicular plate of the ethmoid bone and the vomer. Anteriorly, it consists of hyaline cartilage. The roof is formed by the cribriform plate of the ethmoid bone and the sphenoid bone, frontal bone and nasal bones.

Respiratory function of the nose
The nose is the first of the respiratory passages through which the inspired air passes. In the nasal cavity, air is warmed, moistened and filtered. The three projecting conchae increase the surface area and cause turbulence, spreading inspired air over the whole nasal surface. The large surface area maximises warming, humidification and filtering.

Warming: The immense vascularity of the mucosa permits rapid warming as the air flows past. This also explains the large blood loss when a nosebleed (epistaxis) occurs.

Filtering and cleaning: Hairs at the anterior nares trap larger particles. Smaller particles such as dust and bacteria settle and adhere to the mucus. Mucus protects the underlying epithelium from...
irritation and prevents drying. Synchronous beating of the cilia wafts the mucus towards the throat where it is swallowed or coughed up (expectorated).

**Humidification:** As air travels over the moist mucosa, it becomes saturated with water vapour. Irritation of the nasal mucosa results in sneezing, a reflex action that forcibly expels an irritant.

**The sense of smell**
The nose is the organ of the sense of smell (olfaction). Specialised receptors that detect smell are located in the roof of the nose in the area of the cribiform plate of the ethmoid bones and the superior conchae. These receptors are stimulated by airborne odours. The resultant nerve signals are carried by the olfactory nerves to the brain where the sensation of smell is perceived.

**Pharynx**

**Position**
The pharynx (throat) is a passageway about 12–14 cm long. It extends from the posterior nares, and runs behind the mouth and the larynx to the level of the 6th thoracic vertebra, where it becomes the oesophagus.

**The nasopharynx**
The nasal part of the pharynx lies behind the nose above the level of the soft palate. On its lateral walls are the two openings of the auditory tubes, one leading to each middle ear. On the posterior wall are the pharyngeal tonsils (adenoids), consisting of lymphoid tissue. They are most prominent in children up to approximately 7 years of age. Thereafter they gradually atrophy.

**The oropharynx**
The oral part of the pharynx lies behind the mouth, extending from below the level of the soft palate to the level of the upper part of the body of the 3rd cervical vertebra. The lateral walls of the pharynx blend with the soft palate to form two folds on each side. Between each pair of folds is a collection of lymphoid tissue called the palatine tonsil.

When swallowing, the soft palate and uvula are pushed upwards, sealing off the nasal cavity and preventing the entry of food and fluids.

**The laryngopharynx**
The laryngeal part of the pharynx extends from the oropharynx above and continues as the oesophagus below, with the larynx lying anteriorly.
Functions

Passageway for air and food
The pharynx is involved in both the respiratory and the digestive systems: air passes through the nasal and oral sections, and food through the oral and laryngeal sections.

Warming and humidifying
By the same methods as in the nose, the air is further warmed and moistened as it passes towards the lungs.

Hearing
The auditory tube, extending from the nasopharynx to each middle ear, allows air to enter the middle ear. This leads to air in the middle ear being at the same pressure as the outer ear, protecting the tympanic membrane from any changes in atmospheric pressure.

Protection
The lymphatic tissue of the pharyngeal and laryngeal tonsils produces antibodies in response to swallowed or inhaled antigens. The tonsils are larger in children and tend to atrophy in adults.

Speech
The pharynx functions in speech; by acting as a resonating chamber for sound ascending from the larynx, it helps (together with the sinuses) to give the voice its individual characteristics.

Larynx

Position
The larynx or ‘voice box’ links the laryngopharynx and the trachea. It lies in front of the laryngopharynx and the 3rd, 4th, 5th and 6th cervical vertebrae. Until puberty there is little difference in the size of the larynx between the sexes. Thereafter, it grows larger in the male, which explains the prominence of the ‘Adam’s apple’ and the generally deeper voice.

Structure

Cartilages
The larynx is composed of several irregularly shaped cartilages attached to each other by ligaments and membranes.

The main cartilages are:
- 1 thyroid cartilage
- 1 cricoid cartilage
- 2 arytenoid cartilages
Several ligaments attach the cartilages to each other and to the hyoid bone.

**The thyroid cartilage**

This is the most prominent of the laryngeal cartilages. Made of hyaline cartilage, it lies to the front of the neck. Its anterior wall projects into the soft tissues of the front of the throat, forming the laryngeal prominence or Adam’s apple, which is easily felt and often visible in adult males. The anterior wall is partially divided by the thyroid notch. The cartilage is incomplete posteriorly, and is bound with ligaments to the hyoid bone above and the cricoid cartilage below. The upper part of the thyroid cartilage is lined with stratified squamous epithelium like the larynx, and the lower part with ciliated columnar epithelium like the trachea. There are many muscles attached to its outer surface. The thyroid cartilage forms most of the anterior and lateral walls of the larynx.

**The cricoid cartilage**

This lies below the thyroid cartilage and is also composed of hyaline cartilage. It is shaped like a signet ring, completely encircling the larynx with the narrow part anteriorly and the broad part posteriorly. The broad posterior part articulates with the arytenoid cartilages and with the thyroid cartilage. It is lined with ciliated columnar epithelium and there are muscles and ligaments attached to its outer surface. The lower border of the cricoid cartilage marks the end of the upper respiratory tract.

**The arytenoid cartilages**

These are two roughly pyramid-shaped hyaline cartilages situated on top of the broad part of the cricoid cartilage forming part of the posterior wall of the larynx. They give attachment to the vocal cords and to muscles and are lined with ciliated columnar epithelium.

**The epiglottis**

This is a leaf shaped fibro-elastic cartilage attached on a flexible stalk of cartilage to the inner surface of the anterior wall of the thyroid cartilage immediately below the thyroid notch. It rises obliquely upwards behind the tongue and the body of the hyoid bone. It is covered with stratified squamous epithelium. If the larynx is likened to a box then the epiglottis acts as the lid; it closes off the larynx during swallowing, protecting the lungs from accidental inhalation of foreign objects.
Functions

Production of sound: Sound has the properties of pitch, volume and resonance.
- Pitch of the voice depends on the length and tightness of the cords. Shorter cords produce higher pitched sounds. At puberty, the male vocal cords begin to grow longer, hence the lower pitch of the adult male voice.
- Volume of the voice depends upon the force with which the cords vibrate. The greater the force of expired air, the more strongly the cords vibrates and the louder the sound emitted.
- Resonance, or tone, is dependent upon the shape of the mouth, the position of the tongue and the lips, the facial muscles and the air in the para-nasal sinuses.

Speech: This is produced when the sounds produced by the vocal cords are amplified and manipulated by the tongue, cheeks and lips.

Protection of the lower respiratory tract: During swallowing (p. 297) the larynx moves upwards, blocking the opening into it from the pharynx. In addition, the hinged epiglottis closes over the larynx. This ensures that food passes into the oesophagus and not into the trachea.

Passageway for air: The larynx links the pharynx above with the trachea below.

Humidifying, filtering and warming: These processes continue as inspired air travels through the larynx.

Trachea

Position
The trachea or windpipe is a continuation of the larynx and extends downwards to about the level of the 5th thoracic vertebra where it divides at the carina into the right and left primary bronchi, one bronchus going to each lung. It is approximately 10–11 cm long and lies mainly in the median plane in front of the oesophagus

Structure
The tracheal wall is composed of three layers of tissue, and is held open by between 16 and 20 incomplete (C-shaped) rings of hyaline cartilage lying one above the other. The rings are incomplete posteriorly where the trachea lies against the oesophagus. The cartilages are embedded in a sleeve of smooth muscle and connective tissue, which also forms the posterior wall where the rings are incomplete. Three layers of tissue ‘clothe’ the cartilages of the trachea.

- The outer layer contains fibrous and elastic tissue and encloses the cartilages.
The middle layer consists of cartilages and bands of smooth muscle that wind round the trachea in a helical arrangement. There is some areolar tissue, containing blood and lymph vessels and autonomic nerves. The free ends of the incomplete cartilages are connected by the trachealis muscle, which allows for adjustment of tracheal diameter.

The lining is ciliated columnar epithelium, containing mucus-secreting goblet cells (F

Functions

Support and patency: Tracheal cartilages hold the trachea permanently open (patent), but the soft tissue bands in between the cartilages allow flexibility so that the head and neck can move freely without obstructing or kinking the trachea. The absence of cartilage posteriorly permits the oesophagus to expand comfortably during swallowing. Contraction or relaxation of the trachealis muscle, which links the free ends of the C-shaped cartilages, helps to regulate the diameter of the trachea.

Mucociliary escalator: This is the synchronous and regular beating of the cilia of the mucous membrane lining that wafts mucus with adherent particles upwards towards the larynx where it is either swallowed or coughed up.

Cough reflex: Nerve endings in the larynx, trachea and bronchi are sensitive to irritation, which generates nerve impulses conducted by the vagus nerves to the respiratory centre in the brain stem. The reflex motor response is deep inspiration followed by closure of the glottis, i.e. closure of the vocal cords. The abdominal and respiratory muscles then contract causing a sudden and rapid increase of pressure in the lungs. Then the glottis opens, expelling air through the mouth, taking mucus and/or foreign material with it.

Warming, humidifying and filtering: These continue as in the nose, although air is normally saturated and at body temperature when it reaches the trachea.

Lungs

Position and gross structure

There are two lungs, one lying on each side of the midline in the thoracic cavity. They are cone-shaped and have an apex, a base, a tip, costal surface and medial surface.
The apex This is rounded and rises into the root of the neck, about 25 mm above the level of the middle third of the clavicle. It lies close to the first rib and the blood vessels and nerves in the root of the neck.

**The base**
This is concave and semilunar in shape, and lies on the upper (thoracic) surface of the diaphragm.

**The costal surface**
This is the broad outer surface of the lung that lies directly against the costal cartilages, the ribs and the intercostal muscles.

**The medial surface**
The medial surface of each lung faces the other directly across the space between the lungs, the mediastinum. Each is concave and has a roughly triangular-shaped area, called the hilum, at the level of the 5th, 6th and 7th thoracic vertebrae. The primary bronchus, the pulmonary artery supplying the lung and the two pulmonary veins draining it, the bronchial artery and veins, and the lymphatic and nerve supply enter and leave the lung at the hilum.

The mediastinum contains the heart, great vessels, trachea, right and left bronchi, oesophagus, lymph nodes, lymph vessels and nerves.

The right lung is divided into three distinct lobes: superior, middle and inferior. The left lung is smaller because the heart occupies space left of the midline. It is divided into only two lobes: superior and inferior. The divisions between the lobes are called fissures.

**Pleura and pleural cavity**
The pleura consist of a closed sac of serous membrane (one for each lung) which contains a small amount of serous fluid. The lung is pushed into this sac so that it forms two layers: one adheres to the lung and the other to the wall of the thoracic cavity.

**The visceral pleura**
This is adherent to the lung, covering each lobe and passing into the fissures that separate them.

**The parietal pleura**
This is adherent to the inside of the chest wall and the thoracic surface of the diaphragm. It is not attached to other structures in the mediastinum and is continuous with the visceral pleura round the edges of the hilum.

**The pleural cavity**
This is only a potential space and contains no air, so the pressure within is negative relative to atmospheric pressure. In health, the two layers of pleura are separated by a thin film of serous fluid (pleural fluid), which allows them to glide over each other, preventing friction between them during breathing. The pleural fluid is secreted by the epithelial cells of the membrane. The double membrane arrangement of the pleura is similar to the serous pericardium of the heart. The two layers of pleura, with pleural fluid between them, behave in the same way as two pieces of glass separated by a thin film of water. They glide over each other easily but can be pulled apart only with difficulty, because of the surface tension between the membranes and the fluid. This is essential for keeping the lung inflated against the inside of the chest wall. The airways and the alveoli of the lungs are embedded in elastic tissue, which constantly pull the lung tissues towards the hilum, but because pleural fluid holds the two pleura together, the lung remains expanded. If either layer of pleura is punctured, air is sucked into the pleural space and part or all of the entire underlying lung collapses.

**Interior of the lungs**
The lungs are composed of the bronchi and smaller air passages, alveoli, connective tissue, blood vessels, lymph vessels and nerves, all embedded in an elastic connective tissue matrix. Each lobe is made up of a large number of lobules.

Organs associated with the lungs.
The lobes of the lungs and vessels/airways of each hilum.

**Bronchi and bronchioles**

The two primary bronchi are formed when the trachea divides, at about the level of the 5th thoracic vertebra.

**The right bronchus:** This is wider, shorter and more vertical than the left bronchus and is therefore more likely to become obstructed by an inhaled foreign body. It is approximately 2.5 cm long. After entering the right lung at the hilum it divides into three branches, one to each lobe. Each branch then subdivides into numerous smaller branches.

**The left bronchus:** This is about 5 cm long and is narrower than the right. After entering the lung at the hilum it divides into two branches, one to each lobe. Each branch then subdivides into progressively smaller airways within the lung substance.

**Structure**

The bronchial walls contain the same three layers of tissue as the trachea, and are lined with ciliated columnar epithelium. The bronchi progressively subdivide into bronchioles, terminal bronchioles, respiratory bronchioles, alveolar ducts and finally, alveoli. The wider passages are called conducting airways because their function is to bring air into the lungs, and their walls are too thick to permit gas exchange.

**Structural changes in the bronchial passages**

As the bronchi divide and become progressively smaller, their structure changes to match their function.
Cartilage: Since rigid cartilage would interfere with expansion of lung tissue and the exchange of gases, it is present for support in the larger airways only. The bronchi contain cartilage rings like the trachea, but as the airways divide, these rings become much smaller plates, and at the bronchiolar level there is no cartilage present in the airway walls at all.

Smooth muscle: As the cartilage disappears from airway walls, it is replaced by smooth muscle. This allows the diameter of the airways to be increased or decreased through the influence of the autonomic nervous system, regulating airflow within each lung.

Epithelial lining: The ciliated epithelium is gradually replaced with non-ciliated epithelium, and goblet cells disappear.

Functions

Control of air entry: The diameter of the respiratory passages is altered by contraction or relaxation of the smooth muscle in their walls, regulating the speed and volume of airflow into and within the lungs. These changes are controlled by the autonomic nerve supply: parasympathetic stimulation causes constriction and sympathetic stimulation causes dilation.

The following functions continue as in the upper airways:
- warming and humidifying
- support and patency
- removal of particulate matter
- cough reflex.

Respiratory bronchioles and alveoli

Structure

Within each lobe, the lung tissue is further divided by fine sheets of connective tissue into lobules. Each lobule is supplied with air by a terminal bronchiole, which further subdivides into respiratory bronchioles, alveolar ducts and large numbers of alveoli (air sacs). There are about 150 million alveoli in the adult lung. It is in these structures that the process of gas exchange occurs. As airways progressively divide and become smaller and smaller, their walls gradually become thinner until muscle and connective tissue disappear, leaving a single layer of simple squamous epithelial cells in the alveolar ducts and alveoli. These distal respiratory passages are supported by a loose network of elastic connective tissue in which macrophages, fibroblasts, nerves and blood and lymph vessels are embedded. The alveoli are surrounded by a dense
network of capillaries. Exchange of gases in the lung (external respiration) takes place across a membrane made up of the alveolar wall and the capillary wall fused firmly together. This is called the respiratory membrane.

On microscopic examination, the extensive air spaces are clearly seen and healthy lung tissue has a honeycomb appearance.

Lying between the squamous cells are septal cells that secrete surfactant, a phospholipid fluid which prevents the alveoli from drying out and reduces surface tension preventing alveolar collapse during expiration. Secretion of surfactant into the distal air passages and alveoli begins about the 35th week of fetal life. Its presence in newborn babies permits expansion of the lungs and the establishment of respiration immediately after birth. It may not be present in sufficient amounts in the immature lungs of premature babies, causing serious breathing problems.

Functions

External respiration

Defence against infection: At this level, ciliated epithelium, goblet cells and mucus are no longer present, because their presence would impede gas exchange and encourage infection. By the time inspired air reaches the alveoli, it is usually clean. Defense relies on protective cells present within the lung tissue. These include lymphocytes and plasma cells, which produce
antibodies, and phagocytes, including alveolar macrophages. These cells are most active in the distal air passages where ciliated epithelium has been replaced by squamous (flattened) cells.

**Warming and humidifying:** These continue as in the upper airways. Inhalation of dry or inadequately humidified air over a period of time irritates the mucosa and encourages infection.
Mechanism of Respiration

The term respiration means the exchange of gases between body cells and the environment. This involves two main processes.

Breathing (pulmonary ventilation): This is movement of air into and out of the lungs.

Exchange of gases: This takes place:

- in the lungs: external respiration
- in the tissues: internal respiration.

Each of these will be considered later in this section.

Breathing

Breathing supplies oxygen to the alveoli, and eliminates carbon dioxide.

Muscles of breathing

Expansion of the chest during inspiration occurs as a result of muscular activity, partly voluntary and partly involuntary. The main muscles used in normal quiet breathing are the external intercostal muscles and the diaphragm.

Intercostal muscles

There are 11 pairs of intercostal muscles occupying the spaces between the 12 pairs of ribs. They are arranged in two layers, the external and internal intercostal muscles.

The external intercostal muscles: These extend downwards and forwards from the lower border of the rib above to the upper border of the rib below. They are involved in inspiration.

The internal intercostal muscles: These extend downwards and backwards from the lower border of the rib above to the upper border of the rib below, crossing the external intercostal muscle fibres at right angles. The internal intercostals are used when expiration becomes active, as in exercise.

The first rib is fixed. Therefore, when the external intercostal muscles contract they pull all the other ribs towards the first rib. The ribcage moves as a unit, upwards and outwards, enlarging the thoracic cavity. The intercostal muscles are stimulated to contract by the intercostal nerves.

Diaphragm

The diaphragm is a dome-shaped muscular structure separating the thoracic and abdominal cavities. It forms the floor of the thoracic cavity and the roof of the abdominal cavity and consists of a central tendon from which muscle fibres radiate to be attached to the lower ribs and sternum and to the vertebral column by two crura. When the diaphragm is relaxed, the central tendon is at the level of the 8th thoracic vertebra. When it contracts, its muscle fibres
shorten and the central tendon is pulled downwards to the level of the 9th thoracic vertebra, lengthening the thoracic cavity. This decreases pressure in the thoracic cavity and increases it in the abdominal and pelvic cavities. The diaphragm is supplied by the phrenic nerves. Quiet, restful breathing is sometimes called diaphragmatic breathing because 75% of the work is done by the diaphragm.

During inspiration, the external intercostal muscles and the diaphragm contract simultaneously, enlarging the thoracic cavity in all directions, that is from back to front, side to side and top to bottom.

**Accessory muscles of respiration**

When extra respiratory effort is required, additional muscles are used. Forced inspiration is assisted by the sternocleidomastoid muscles and the scalene muscles, which link the cervical vertebrae to the first two ribs, and increase ribcage expansion. Forced expiration is helped by the activity of the internal intercostal muscles and sometimes the abdominal muscles, which increase the pressure in the thorax by squeezing the abdominal contents.

**Cycle of breathing**

The average respiratory rate is 12–15 breaths per minute. Each breath consists of three phases: inspiration, expiration and pause.

The visceral pleura is adherent to the lungs and the parietal pleura to the inner wall of the thorax and to the diaphragm. Between them is a thin film of pleural fluid. Breathing depends upon changes in pressure and volume in the thoracic cavity. It follows the underlying physical principle that increasing the volume of a container decreases the pressure inside it, and that decreasing the volume of a container increases the pressure inside it. Since air flows from an area of high pressure to an area of low pressure, changing the pressure inside the lungs determines the direction of airflow.

**Inspiration**

Simultaneous contraction of the external intercostal muscles and the diaphragm expands the thorax. As the parietal pleura is firmly adhered to the diaphragm and the inside of the ribcage, it is pulled outward along with them. This pulls the visceral pleura outwards too, since the two pleura are held together by the thin film of pleural fluid. Because the visceral pleura is firmly adherent to the lung, the lung tissue is, therefore, also pulled up and out with the ribs, and downwards with the diaphragm. This expands the lungs, and the pressure within the alveoli and in the air passages falls, drawing air into the lungs in an attempt to equalise atmospheric and alveolar air pressures.
The process of inspiration is active, as it needs energy for muscle contraction. The negative pressure created in the thoracic cavity aids venous return to the heart and is known as the respiratory pump. At rest, inspiration lasts about 2 seconds.

Expiration
Relaxation of the external intercostal muscles and the diaphragm results in downward and inward movement of the ribcage and elastic recoil of the lungs. As this occurs, pressure inside the lungs rises and expels air from the respiratory tract. At the end of expiration, the lungs still contain some air, and are prevented from complete collapse by the intact pleura. This process is passive as it does not require the expenditure of energy.

At rest, expiration lasts about 3 seconds, and after expiration there is a pause before the next cycle begins.

Physiological variables affecting breathing
Elasticity: Elasticity is the ability of the lung to return to its normal shape after each breath. Loss of elasticity, e.g. in emphysema, of the connective tissue in the lungs necessitates forced expiration and increased effort on inspiration.

Compliance: This is the stretchability of the lungs, i.e. the effort required to inflate the alveoli. The healthy lung is very compliant, and inflates with very little effort. When compliance is low the effort needed to inflate the lungs is greater than normal, e.g. when insufficient surfactant is present. Note that compliance and elasticity are opposing forces.

Airway resistance: When this is increased, e.g. in bronchoconstriction, more respiratory effort is required to inflate the lungs.

Lung volumes and capacities
In normal quiet breathing there are about 15 complete respiratory cycles per minute. The lungs and the air passages are never empty and, as the exchange of gases takes place only across the walls of the alveolar ducts and alveoli, the remaining capacity of the respiratory passages is called the anatomical dead space (about 150 mL).

Tidal volume (TV): This is the amount of air passing into and out of the lungs during each cycle of breathing (about 500 mL at rest).

Inspiratory reserve volume (IRV): This is the extra volume of air that can be inhaled into the lungs during maximal inspiration, i.e. over and above normal TV.

Inspiratory capacity (IC): This is the amount of air that can be inspired with maximum effort. It consists of the tidal volume (500 ml) plus the inspiratory reserve volume.

Functional residual capacity (FRC): This is the amount of air remaining in the air passages and alveoli at the end of quiet expiration. Tidal air mixes with this air, causing relatively
small changes in the composition of alveolar air. As blood flows continuously through the pulmonary capillaries, this means that exchange of gases is not interrupted between breaths, preventing moment-to-moment changes in the concentration of blood gases. The functional residual volume also prevents collapse of the alveoli on expiration.

Expiratory reserve volume (ERV): This is the largest volume of air which can be expelled from the lungs during maximal expiration.

Residual volume (RV): This cannot be directly measured but is the volume of air remaining in the lungs after forced expiration.

Vital capacity (VC): This is the maximum volume of air which can be moved into and out of the lungs:

\[ VC = \text{Tidal volume} + \text{IRV} + \text{ERV} \]

Total lung capacity (TLC). This is the maximum amount of air the lungs can hold. In an adult of average build, it is normally around 6 litres. Total lung capacity represents the sum of the vital capacity and the residual volume. It cannot be directly measured in clinical tests because even after forced expiration, the residual volume of air still remains in the lungs.

Exchange of gases
Although breathing involves the alternating processes of inspiration and expiration, gas exchange at the respiratory membrane and in the tissues is a continuous and ongoing process. Diffusion of oxygen and carbon dioxide depends on pressure differences, e.g. between atmospheric air and the blood, or blood and the tissues.

Composition of air
Atmospheric pressure at sea level is 101.3 kilopascals (kPa) or 760 mmHg. With increasing height above sea level, atmospheric pressure is progressively reduced and at 5500 m, about two-thirds the height of Mount Everest (8850 m), it is about half that at sea level. Under water, pressure increases by approximately 1 atmosphere per 10 m below sea level.

Air is a mixture of gases: nitrogen, oxygen, carbon dioxide, water vapour and small quantities of inert gases. The percentage of each in inspired and expired air is listed in table below. Each gas in the mixture exerts a part of the total pressure proportional to its concentration, i.e. the partial pressure. This is denoted as, e.g. PO2, PCO2.
Alveolar air
The composition of alveolar air remains fairly constant and is different from atmospheric air. It is saturated with water vapour, and contains more carbon dioxide and less oxygen. Saturation with water vapour provides 6.3 kPa (47 mmHg) thus reducing the partial pressure of all the other gases present. Gaseous exchange between the alveoli and the bloodstream (external respiration) is a continuous process, as the alveoli are never empty, so it is independent of the respiratory cycle. During each inspiration only some of the alveolar gases are exchanged.

Diffusion of gases
Exchange of gases occurs when a difference in partial pressure exists across a semipermeable membrane. Gases move by diffusion from the higher concentration to the lower until equilibrium is established. Atmospheric nitrogen is not used by the body so its partial pressure remains unchanged and is the same in inspired and expired air, alveolar air and in the blood.

These principles govern the diffusion of gases in and out of the alveoli across the respiratory membrane (external respiration) and across capillary membranes in the tissues (internal respiration).

External respiration
This is exchange of gases by diffusion between the alveoli and the blood in the alveolar capillaries, across the respiratory membrane. Each alveolar wall is one cell thick and is surrounded by a network of tiny capillaries (the walls of which are also only one cell thick). The total area of respiratory membrane for gas exchange in the lungs is about equivalent to the area of a tennis court. Venous blood arriving at the lungs in the pulmonary artery has travelled from all the tissues of the body, and contains high levels of CO2 and low levels of O2. Carbon dioxide diffuses from venous blood down its concentration gradient into the
alveoli until equilibrium with alveolar air is reached. By the same process, oxygen diffuses from the alveoli into the blood. The relatively slow flow of blood through the capillaries increases the time available for gas exchange to occur. When blood leaves the alveolar capillaries, the oxygen and carbon dioxide concentrations are in equilibrium with those of alveolar air.

**Internal respiration**

This is exchange of gases by diffusion between blood in the capillaries and the body cells. Gas exchange does not occur across the walls of the arteries carrying blood from the heart to the tissues, because their walls are too thick. PO2 of blood arriving at the capillary bed is therefore the same as blood leaving the lungs. Blood arriving at the tissues has been cleansed of its CO2 and saturated with O2 during its passage through the lungs, and therefore has a higher PO2 and a lower PCO2 than the tissues. This creates concentration gradients between capillary blood and the tissues, and gas exchange therefore occurs. O2 diffuses from the bloodstream through the capillary wall into the tissues. CO2 diffuses from the cells into the extracellular fluid, then into the bloodstream towards the venous end of the capillary.

![Diagram of respiration](image)

*Figure 1 Respiration. A. External respiration. B. Internal respiration.*
Regulation of air and blood flow in the lung

During quiet breathing, only a small portion of the lung’s total capacity is ventilated with each breath. This means that only a fraction of the total alveolar numbers are being ventilated, usually in the upper lobes, and much of the remaining lung is temporarily collapsed. Airways supplying alveoli that are not being used are constricted, directing airflow into functioning alveoli. In addition, the pulmonary arterioles bringing blood into the ventilated alveoli are dilated, to maximise gas exchange, and blood flow (perfusion) past the non-functioning alveoli is reduced.

When respiratory requirements are increased, e.g. in exercise, the increased tidal volume expands additional alveoli, and the blood flow is redistributed to perfuse these too. In this way, air flow (ventilation) and blood flow (perfusion) are matched to maximise the opportunity for gas exchange.

Regulation and control of respiration

Effective control of respiration enables the body to regulate blood gas levels over a wide range of physiological, environmental and pathological conditions, and is normally involuntary. Voluntary control is exerted during activities such as speaking and singing but is overridden if blood CO2 rises (hypercapnia).

The respiratory centre

This is formed by groups of nerves in the medulla, the respiratory rhythmicity centre, which control the respiratory pattern, i.e. the rate and depth of breathing. Regular discharge of inspiratory neurones within this centre set the rate and depth of breathing.

Activity of the respiratory rhythmicity centre is adjusted by nerves in the pons (the pneumotaxic centre and the apneustic centre), in response to input from other parts of the brain.

Motor impulses leaving the respiratory centre pass in the phrenic and intercostal nerves to the diaphragm and intercostal muscles respectively to stimulate respiration.

Chemoreceptors

These are receptors that respond to changes in the partial pressures of oxygen and carbon dioxide in the blood and cerebrospinal fluid. They are located centrally and peripherally.

Central chemoreceptors: These are located on the surface of the medulla oblongata and are bathed in cerebrospinal fluid. When arterial PCO2 rises (hypercapnia), even slightly, the
central chemoreceptors respond by stimulating the respiratory centre, increasing ventilation of the lungs and reducing arterial PCO2. The sensitivity of the central chemoreceptors to raised arterial PCO2 is the most important factor in controlling normal blood gas levels. A small reduction in PO2 (hypoxaemia) has the same, but less pronounced effect, but a substantial reduction depresses breathing.

Peripheral chemoreceptors: These are situated in the arch of the aorta and in the carotid bodies. They respond to changes in blood CO2 and O2 levels, but are much more sensitive to carbon dioxide than oxygen. Even a slight rise in CO2 levels activates these receptors, triggering nerve impulses to the respiratory centre via the glossopharyngeal and vagus nerves. This stimulates an immediate rise in the rate and depth of respiration. An increase in blood acidity (decreased pH or raised [H+]) also stimulates the peripheral chemoreceptors, resulting in increased ventilation, increased CO2 excretion and increased blood pH. These chemoreceptors also help to regulate blood pressure.

Artificial respiration
Artificial respiration, (also called artificial ventilation) is means of assisting or stimulating respiration, a metabolic process referring to the overall exchange of gases in the body by pulmonary ventilation, external respiration, and internal respiration. It may take the form of manually providing air for a person who is not breathing or is not making sufficient respiratory effort, or it may be mechanical ventilation involving the use of a mechanical ventilator to move air in and out of the lungs when an individual is unable to breathe on their own, for example during surgery with general anesthesia or when an individual is in a coma.

Manual methods
Pulmonary ventilation (and hence external parts of respiration) is achieved through manual insufflation of the lungs either by the rescuer blowing into the patient's lungs (mouth-to-mouth resuscitation), or by using a mechanical device to do so. This method of insufflation has been proved more effective than methods which involve mechanical manipulation of the patient's chest or arms, such as the Silvester method.

Mouth-to-mouth resuscitation is also part of cardiopulmonary resuscitation (CPR) making it an essential skill for first aid. In some situations, mouth to mouth is also performed separately, for instance in near-drowning and opiate overdoses. The performance of mouth to
mouth in its own is now limited in most protocols to health professionals, whereas lay first
aiders are advised to undertake full CPR in any case where the patient is not breathing
sufficiently.

**Mechanical ventilation**

Mechanical ventilation is a method to mechanically assist or replace spontaneous breathing. This may involve a machine called a ventilator or the breathing may be assisted by a registered nurse, physician, physician assistant, respiratory therapist, paramedic, or other suitable person compressing a bag valve mask or set of bellows. Mechanical ventilation is termed "invasive" if it involves any instrument penetrating through the mouth (such as an endotracheal tube) or the skin (such as a tracheostomy tube). There are two main modes of mechanical ventilation within the two divisions: positive pressure ventilation, where air (or another gas mix) is pushed into the trachea, and negative pressure ventilation, where air is, in essence, sucked into the lungs. Tracheal intubation is often used for short-term mechanical ventilation. A tube is inserted through the nose (nasotracheal intubation) or mouth (orotracheal intubation) and advanced into the trachea. In most cases tubes with inflatable cuffs are used for protection against leakage and aspiration. Intubation with a cuffed tube is thought to provide the best protection against aspiration. Tracheal tubes inevitably cause pain and coughing. Therefore, unless a patient is unconscious or anesthetized for other reasons, sedative drugs are usually given to provide tolerance of the tube. Other disadvantages of tracheal intubation include damage to the mucosal lining of the nasopharynx or oropharynx and subglottic stenosis.

In an emergency a cricothyrotomy can be used by health care professionals, where an airway is inserted through a surgical opening in the cricothyroid membrane. This is similar to a tracheostomy but a cricothyrotomy is reserved for emergency access. This is usually only used when there is a complete blockage of the pharynx or there is massive maxillofacial injury, preventing other adjuncts being used.

**Resuscitation Methods**

It is also known as cardiopulmonary resuscitation (CPR). It is an emergency procedure that combines chest compressions often with artificial ventilation in an effort to manually preserve intact brain function until further measures are taken to restore spontaneous blood circulation and breathing in a person who is in cardiac arrest. It is recommended in those who are unresponsive with no breathing or abnormal breathing, for example, agonal respirations.
CPR involves chest compressions for adults between 5 cm (2.0 in) and 6 cm (2.4 in) deep and at a rate of at least 100 to 120 per minute. The rescuer may also provide artificial ventilation by either exhaling air into the subject's mouth or nose (mouth-to-mouth resuscitation) or using a device that pushes air into the subject's lungs (mechanical ventilation). Current recommendations place emphasis on early and high-quality chest compressions over artificial ventilation; a simplified CPR method involving chest compressions, is only recommended for untrained rescuers. In children, however, only doing compressions may result in worse outcomes, because in children the problem normally arises from a respiratory, rather than cardiac problem. Chest compression to breathing ratios is set at 30 to 2 in adults.

CPR alone is unlikely to restart the heart. Its main purpose is to restore partial flow of oxygenated blood to the brain and heart. The objective is to delay tissue death and to extend the brief window of opportunity for a successful resuscitation without permanent brain damage. Administration of an electric shock to the subject's heart, termed defibrillation, is usually needed in order to restore a viable or "perfusing" heart rhythm. Defibrillation is effective only for certain heart rhythms, namely ventricular fibrillation or pulseless ventricular tachycardia, rather than asystole or pulseless electrical activity. Early shock when appropriate is recommended. CPR may succeed in inducing a heart rhythm that may be shockable. In general, CPR is continued until the person has a return of spontaneous circulation (ROSC) or is declared dead.

Methods:
Compressions with rescue breaths
A universal compression to ventilation ratio of 30:2 is recommended for adults. With children, if at least 2 trained rescuers are present a ratio of 15:2 is preferred. According to AHA 2015 Guidelines In newborns a ratio is 30:2 if One rescuer and 15:2 if 2 rescuers.
If an advanced airway such as an endotracheal tube or laryngeal mask airway is in place, artificial ventilation should occur without pauses in compressions at a rate of 8–10 per minute. The recommended order of interventions is chest compressions, airway, breathing or CAB in most situations, with a compression rate of at least 100 per minute in all groups. Recommended compression depth in adults and children is at least 5 cm (2 inches) and in infants it is 4 centimetres (1.6 in). As it can be difficult to determine the presence or absence of a pulse, the pulse check has been removed for lay providers and should not be performed for more than 10 seconds by healthcare providers. In adults, rescuers should use
two hands for the chest compressions, while in children they should use one, and with infants two fingers (index and middle fingers).

**Compression only**

For adults with cardiac arrest, compression-only (hands-only or cardiocerebral resuscitation) CPR which involves chest compressions without artificial ventilation is recommended as the method of choice for the untrained rescuer. In adults with out-of-hospital cardiac arrest, compression-only CPR by the lay public has an equal or higher success rate than standard CPR. It is hoped that the use of compression-only delivery will increase the chances of the lay public delivering CPR.

Compression-only CPR is not as good for children who are more likely to have cardiac arrest from respiratory causes. Two reviews have found that compression-only CPR had no more success than any CPR whatsoever. Rescue breaths for children and especially for babies should be relatively gentle. Either a ratio of compressions to breaths of 30:2 or 15:2 was found to have better results for children. Both children and adults should receive a hundred chest compressions per minute. Other exceptions besides children include cases of drownings and drug overdose. In both these cases, compressions and rescue breaths are recommended if the bystander is trained and is willing to do so.

**Prone CPR**

Standard CPR is performed with the person in supine position. Prone CPR, or reverse CPR, is performed on a person lying on their chest, by turning the head to the side and compressing the back. Due to the head being turned, the risk of vomiting and complications caused by aspiration pneumonia may be reduced.
Urinary System

The urinary system is the main excretory system and consists of the following structures:

- 2 kidneys, which secrete urine
- 2 ureters that convey the urine from the kidneys to the urinary bladder
- the urinary bladder, which collects and stores urine
- the urethra through which urine leaves the body.

The urinary system plays a vital part in maintaining homeostasis of water and electrolytes within the body. The kidneys produce urine that contains metabolic waste products, including the nitrogenous compounds urea and uric acid, excess ions and some drugs. The main functions of the kidneys are:

- formation of urine, maintaining water, electrolyte and acid–base balance
- excretion of waste products
- production and secretion of erythropoietin, the hormone that stimulates formation of red blood cells
- production and secretion of renin, an important enzyme in the control of blood pressure. Urine is stored in the bladder and excreted by the process of micturition.
Kidneys

The kidneys lie on the posterior abdominal wall, one on each side of the vertebral column, behind the peritoneum and below the diaphragm. They extend from the level of the 12th thoracic vertebra to the 3rd lumbar vertebra, receiving some protection from the lower rib cage. The right kidney is usually slightly lower than the left, probably because of the considerable space occupied by the liver.

Kidneys are bean-shaped organs, about 11 cm long, 6 cm wide, 3 cm thick and weigh 150 g. They are embedded in, and held in position by, a mass of fat. A sheath of fibrous connective tissue, the renal fascia, encloses the kidney and the renal fat.

As the kidneys lie on either side of the vertebral column, each is associated with different structures.

Right kidney
Superiorly the right adrenal gland
Anteriorly the right lobe of the liver, the duodenum and the hepatic flexure of the colon
Posteriorly the diaphragm, and muscles of the posterior abdominal wall.

Left kidney
Superiorly the left adrenal gland
Anteriorly the spleen, stomach, pancreas, jejunum and splenic flexure of the colon
Posteriorly the diaphragm and muscles of the posterior abdominal wall.
**Gross structure of the kidney**

There are three areas of tissue that can be distinguished when a longitudinal section of the kidney is viewed with the naked eye:

- an outer fibrous capsule, surrounding the kidney
- the cortex, a reddish-brown layer of tissue immediately below the capsule and outside the renal pyramids
- the medulla, the innermost layer, consisting of pale conical-shaped striations, the renal pyramids.

The hilum is the concave medial border of the kidney where the renal blood and lymph vessels, the ureter and nerves enter.

Urine formed within the kidney passes through a renal papilla at the apex of a pyramid into a minor calyx. Several minor calyces merge into a major calyx and two or three major calyces combine forming the renal pelvis, a funnel shaped structure that narrows when it leaves the kidney as the ureter. The walls of the calyces and renal pelvis are lined with transitional epithelium and contain smooth muscle. Peristalsis, intrinsic contraction of smooth muscle, propels urine through the calyces, renal pelvis and ureters to the bladder.

![Structure of the kidney](image)

**Microscopic structure of the kidney**

The kidney contains about 1–2 million functional units, the nephrons, and a much smaller number of collecting ducts. The collecting ducts transport urine through the pyramids to the calyces, giving the pyramids their striped appearance. The collecting ducts are supported by connective tissue, containing blood vessels, nerves and lymph vessels.
**The Nephron**

The nephron is essentially a tubule closed at one end that joins a collecting duct at the other end. The closed or blind end is indented to form the cup-shaped glomerular capsule (Bowman’s capsule), which almost completely encloses a network of tiny arterial capillaries, the glomerulus. These resemble a coiled tuft. Continuing from the glomerular capsule, the remainder of the nephron is about 3 cm long and described in three parts:

- the proximal convoluted tubule
- the medullary loop (loop of Henle)
- the distal convoluted tubule, leading into a collecting duct.
- The collecting ducts unite, forming larger ducts that empty into the minor calyces.

The kidneys receive about 20% of the cardiac output. After entering the kidney at the hilum, the renal artery divides into smaller arteries and arterioles. In the cortex an arteriole, the afferent arteriole, enters each glomerular capsule and then subdivides into a cluster of tiny arterial capillaries, forming the glomerulus. Between these capillary loops are connective tissue phagocytic mesangial cells, which are part of the monocyte–macrophage defence system. The blood vessel leading away from the glomerulus is the efferent arteriole. The afferent arteriole has a larger diameter than the efferent arteriole, which increases pressure inside the glomerulus and drives filtration across the glomerular capillary walls. The efferent arteriole divides into a second peritubular (meaning ‘around tubules’) capillary network, which wraps around the remainder of the tubule, allowing exchange between the fluid in the tubule and the bloodstream. This maintains the local supply of oxygen and nutrients and removes waste products. Venous blood drained from this capillary bed eventually leaves the kidney in the renal vein, which empties into the inferior vena cava.

The walls of the glomerulus and the glomerular capsule consist of a single layer of flattened epithelial cells. The glomerular walls are more permeable than those of other capillaries. The remainder of the nephron and the collecting duct are formed by a single layer of simple squamous epithelium.

Renal blood vessels are supplied by both sympathetic and parasympathetic nerves. The presence of both divisions of the autonomic nervous system controls renal blood vessel diameter and renal blood flow independently of autoregulation.
The kidneys form urine, which passes to the bladder for storage prior to excretion. The composition of urine reflects exchange of substances between the nephron and the blood in
the renal capillaries. Waste products of protein metabolism are excreted, water and electrolyte levels are controlled and pH (acid–base balance) is maintained by excretion of hydrogen ions.

**Water balance and urine output**

The source of most body water is dietary food and fluid although a small amount (called ‘metabolic water’) is formed by cellular metabolism. Water is excreted as the main constituent of urine, in expired air, faeces and through the skin as sweat. The amount lost in expired air and faeces is fairly constant; the amount of sweat produced is associated with environmental and body temperatures. The balance between fluid intake and output is controlled by the kidneys. The minimum urinary output, i.e. the smallest volume required to excrete body waste products, is about 500 mL per day.

**Electrolyte balance**

The kidneys play an important role in electrolyte and water balance. Changes in the concentration of electrolytes in the body fluids may be due to changes in:

- the body water content, or
- electrolyte levels.

Several mechanisms maintain the balance between water and electrolyte concentration.

**Ureters**

The ureters carry urine from the kidneys to the urinary bladder. They are about 25–30 cm long with a diameter of approximately 3 mm. The ureter is continuous with the funnel-shaped renal pelvis. It passes downwards through the abdominal cavity, behind the peritoneum in front of the psoas muscle into the pelvic cavity, and passes obliquely through the posterior wall of the bladder. Because of this arrangement, as urine accumulates and the pressure in the bladder rises, the ureters are compressed and the openings into the bladder are occluded. This prevents backflow (reflux) of urine into the ureters (towards the kidneys) as the bladder fills and also during micturition, when pressure increases as the muscular bladder wall contracts.

**Structure**

The walls of the ureters consist of three layers of tissue

- an outer covering of fibrous tissue, continuous with the fibrous capsule of the kidney
- a middle muscular layer consisting of interlacing smooth muscle fibres that form a functional unit round the ureter and an additional outer longitudinal layer in the lower third
an inner layer, the mucosa, composed of transitional epithelium.

**Function**

Peristalsis is an intrinsic property of the smooth muscle layer that propels urine along the ureter. Peristaltic waves occur several times per minute, increasing in frequency with the volume of urine produced, sending little spurts of urine along the ureter towards the bladder.

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**Urinary bladder**

The urinary bladder is a reservoir for urine. It lies in the pelvic cavity and its size and position vary, depending on the volume of urine it contains. When distended, the bladder rises into the abdominal cavity.

**Structure**

The bladder is roughly pear shaped, but becomes more balloon shaped as it fills with urine. The posterior surface is the base. The bladder opens into the urethra at its lowest point, the neck.

The peritoneum covers only the superior surface before it turns upwards as the parietal peritoneum, lining the anterior abdominal wall. Posteriorly it surrounds the uterus in the female and the rectum in the male. The bladder wall is composed of three layers:

- the outer layer of loose connective tissue, containing blood and lymphatic vessels and nerves, covered on the upper surface by the peritoneum
the middle layer, consisting of interlacing smooth muscle fibres and elastic tissue loosely arranged in three layers. This is called the detrusor muscle and when it contracts, it empties the bladder

the inner mucosa, composed of transitional epithelium that readily permits distension of the bladder as it fills.

When the bladder is empty the inner lining is arranged in folds, or rugae, which gradually disappear as it fills. The bladder is distensible but as it fills, awareness of the need to pass urine is felt. The total capacity is rarely more than about 600 mL.

The three orifices in the bladder wall form a triangle or trigone. The upper two orifices on the posterior wall are the openings of the ureters; the lower orifice is the opening into the urethra. The internal urethral sphincter, a thickening of the urethral smooth muscle layer in the upper part of the urethra, controls outflow of urine from the bladder. This sphincter is not under voluntary control.

**Urethra**

The urethra is a canal extending from the neck of the bladder to the exterior, at the external urethral orifice. It is longer in the male than in the female. The male urethra is associated with both the urinary and reproductive systems.

The female urethra is approximately 4 cm long and 6 mm in diameter. It runs downwards and forwards behind the symphysis pubis and opens at the external urethral orifice just in front of the vagina. The external urethral orifice is guarded by the external urethral sphincter, which is under voluntary control.

The wall of the female urethra has two main layers: an outer muscle layer and an inner lining of mucosa, which is continuous with that of the bladder. The muscle layer has two parts, an inner layer of smooth muscle that is under autonomic nerve control, and an outer layer of striated (voluntary) muscle surrounding it. The striated muscle forms the external urethral sphincter and is under voluntary control. The mucosa is supported by loose fibroelastic connective tissue containing blood vessels and nerves. Proximally it consists of transitional epithelium while distally it is composed of stratified epithelium.
Urine Formation

There are three processes involved in the formation of urine:

- Filtration
- Selective reabsorption
- Secretion.

Filtration

This takes place through the semipermeable walls of the glomerulus and glomerular capsule. Water and other small molecules readily pass through, although some are reabsorbed later. Blood cells, plasma proteins and other large molecules are too large to filter through and therefore remain in the capillaries. The filtrate in the glomerulus is very similar in composition to plasma with the important exceptions of plasma proteins and blood cells.

Filtration takes place because there is a difference between the blood pressure in the glomerulus and the pressure of the filtrate in the glomerular capsule. Because the efferent arteriole is narrower than the afferent arteriole, a capillary hydrostatic pressure of about 7.3 kPa (55 mmHg) builds up in the glomerulus. This pressure is opposed by the osmotic pressure of the blood, provided mainly by plasma proteins, about 4 kPa (30 mmHg), and by filtrate hydrostatic pressure of about 2 kPa (15 mmHg) in the glomerular capsule. The net filtration pressure is, therefore:

$$7.3 - (4 + 2) = 1.3 \text{kPa} \text{ or }$$
$$55 - (30 + 15) = 10$$

The volume of filtrate formed by both kidneys each minute is called the glomerular filtration rate (GFR). In a healthy adult the GFR is about 125 mL/min, i.e. 180 litres of filtrate are formed each day by the two kidneys. Nearly all of the filtrate is later reabsorbed from the kidney tubules with less than 1%, i.e. 1–1.5 litres, excreted as urine. The differences in volume and concentration are due to selective reabsorption of some filtrate constituents and tubular secretion of others.

Autoregulation: Renal blood flow, and therefore glomerular filtration, is protected by a mechanism called autoregulation, whereby renal blood flow is maintained at a constant pressure across a wide range of systolic blood pressures (from around 80–200 mmHg). Autoregulation operates independently of nervous control, i.e. if the nerve supply to the renal blood vessels is interrupted, autoregulation continues to operate. It is therefore a property inherent in renal blood vessels; it may be stimulated by changes in blood pressure in the renal arteries or by fluctuating levels of certain metabolites, e.g. prostaglandins.
In severe shock, when the systolic blood pressure falls below 80 mmHg, autoregulation fails and renal blood flow and the hydrostatic pressure decrease, impairing filtration within the glomeruli.

**Selective reabsorption**

Most reabsorption from the filtrate back into the blood takes place in the proximal convoluted tubule, whose walls are lined with microvilli to increase surface area for absorption. Many substances are reabsorbed here, including some water, electrolytes and organic nutrients such as glucose. Some reabsorption is passive, but some substances, e.g. glucose, are actively transported. Only 60–70% of filtrate reaches the medullary loop. Much of this, especially water, sodium and chloride, is reabsorbed in the loop, so that only 15–20% of the original filtrate reaches the distal convoluted tubule, and the composition of the filtrate is now very different. More electrolytes are reabsorbed here, especially sodium, so the filtrate entering the collecting ducts is actually quite dilute. The main function of the collecting ducts is to reabsorb as much water as the body needs.

Active transport takes place at carrier sites in the epithelial membrane, using chemical energy to transport substances against their concentration gradients. Some ions, e.g. sodium and chloride, can be absorbed by both active and passive mechanisms depending on the site in the nephron.

Some constituents of glomerular filtrate (e.g. glucose, amino acids) do not normally appear in urine because they are completely reabsorbed unless blood levels are excessive. Reabsorption of nitrogenous waste products, such as urea, uric acid and creatinine is very limited. The kidneys’ maximum capacity for reabsorption of a substance is the transport maximum, or renal threshold.

For example, the normal blood glucose level is 3.5–8 mmol/L (63 to 144 mg/100 mL) and if this rises above the transport maximum of about 9 mmol/L (160 mg/100 mL), glucose appears in the urine. This occurs because all the carrier sites are occupied and the mechanism for active transport out of the tubules is overloaded. Other substances reabsorbed by active transport include sodium, calcium, potassium, phosphate and chloride.

The transport maximum, or renal threshold, of some substances varies according to body need at a particular time, and in some cases reabsorption is regulated by hormones.

**Hormones that influence selective reabsorption**

**Parathyroid hormone:** This is secreted by the parathyroid glands and together with calcitonin from the thyroid gland regulates the reabsorption of calcium and phosphate from
the distal collecting tubules, so that normal blood levels are maintained. Parathyroid hormone increases the blood calcium level and calcitonin lowers it.

**Antidiuretic hormone:** ADH. This is secreted by the posterior pituitary. It increases the permeability of the distal convoluted tubules and collecting tubules, increasing water reabsorption. Secretion of ADH is controlled by a negative feedback system.

**Aldosterone:** Secreted by the adrenal cortex, this hormone increases the reabsorption of sodium and water, and the excretion of potassium. Secretion is regulated through a negative feedback system.

**Atrial natriuretic peptide, ANP:** This hormone is secreted by the atria of the heart in response to stretching of the atrial wall when blood volume is increased. It decreases reabsorption of sodium and water from the proximal convoluted tubules and collecting ducts. Secretion of ANP is also regulated by a negative feedback system.

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**Tubular secretion**

Filtration occurs as blood flows through the glomerulus. Substances not required and foreign materials, e.g. drugs including penicillin and aspirin, may not be entirely filtered out of the blood because of the short time it remains in the glomerulus. Such substances are cleared by secretion from the peritubular capillaries into the filtrate within the convoluted tubules. Tubular secretion of hydrogen ions (H+) is important in maintaining normal blood pH.
Composition of urine

Urine is clear and amber in colour due to the presence of urobilin, a bile pigment altered in the intestine, reabsorbed then excreted by the kidneys. The specific gravity is between 1020 and 1030, and the pH is around 6 (normal range 4.5–8). A healthy adult passes from 1000 to 1500 mL per day. The volume of urine produced and the specific gravity vary according to fluid intake and the amount of solute excreted. The constituents of urine are:

- Water 96%
- Urea
- Uric acid
- Creatinine
- Ammonia
- Sodium
- Potassium
- Chlorides
- Phosphates
- Sulphates
- Oxalates

Water balance and urine output

The source of most body water is dietary food and fluid although a small amount (called ‘metabolic water’) is formed by cellular metabolism. Water is excreted as the main constituent of urine, in expired air, faeces and through the skin as sweat. The amount lost in expired air and faeces is fairly constant; the amount of sweat produced is associated with environmental and body temperatures.

The balance between fluid intake and output is controlled by the kidneys. The minimum urinary output, i.e. the smallest volume required to excrete body waste products, is about 500 mL per day. Urinary volume in excess of this is controlled mainly by antidiuretic hormone (ADH) released into the blood by the posterior pituitary gland.

Sensory nerve cells in the hypothalamus (osmoreceptors) detect changes in the osmotic pressure of the blood. Nerve impulses from the osmoreceptors stimulate the posterior pituitary to release ADH. When the osmotic pressure is raised, i.e. the blood is becoming more concentrated, ADH output is increased and as a result, water reabsorption by the distal convoluted tubules and collecting ducts is increased, reducing the blood osmotic pressure and
ADH output. This negative feedback mechanism maintains the blood osmotic pressure (and therefore sodium and water concentrations) within normal limits. This negative feedback mechanism may be over-ridden even though there may be an excessive amount of a dissolved substance in the blood. For example, in diabetes mellitus when blood glucose levels exceed the transport capacity of the renal tubules the excess glucose remains in the filtrate, drawing water with it. Large volumes of urine are passed (polyuria), which may lead to dehydration despite increased ADH secretion. However acute thirst and increased water intake usually compensate for the polyuria, at least to some extent.

When blood volume is increased, stretch receptors in the atria of the heart are stimulated and cardiac muscle cells release atrial natriuretic hormone (ANP). This reduces reabsorption of sodium and water by the proximal convoluted tubules and collecting ducts, meaning that more sodium and water are excreted. In turn, this lowers blood volume and reduces atrial stretching, and through the negative feedback mechanism ANP secretion is switched off. Raised ANP levels also inhibit secretion of ADH and aldosterone, further promoting loss of sodium and water.

**Electrolyte balance**

Changes in the concentration of electrolytes in the body fluids may be due to changes in:

- The body water content, or
- Electrolyte levels.

Several mechanisms maintain the balance between water and electrolyte concentration.

**Sodium and potassium balance**

Sodium is the most common cation (positively charged ion) in extracellular fluid and potassium is the most common intracellular cation. Sodium is a constituent of almost all foods and, furthermore, salt is often added to food during cooking. This means that intake is usually in excess of the body’s needs. It is excreted mainly in urine and sweat. The amount of sodium excreted in sweat is usually insignificant unless sweating is excessive. This may occur when there is pyrexia (fever), a high environmental temperature or during sustained physical exercise. Normally the renin–angiotensin–aldosterone mechanism maintains the concentration of sodium and potassium within physiological limits. When excessive sweating is sustained, e.g. living in a hot climate or working in a hot environment, acclimatisation occurs in approximately 7 to 10 days and electrolyte secretion lost in sweat is reduced.

Sodium and potassium occur in high concentrations in digestive juices – sodium in gastric juice and potassium in pancreatic and intestinal juice. Normally these ions are reabsorbed by
the colon, but following acute and prolonged diarrhoea they may be excreted in large quantities causing electrolyte imbalance.

**Renin angiotensin system (RAS)**

Renin angiotensin system ACE = angiotensin converting enzyme.

Sodium is a normal constituent of urine and its excretion is regulated by the hormone aldosterone, secreted by the adrenal cortex. Cells in the afferent arteriole of the nephron release the enzyme renin in response to sympathetic stimulation, low blood volume or by low arterial blood pressure. Renin converts the plasma protein angiotensinogen, produced by the liver, to angiotensin 1. Angiotensin converting enzyme (ACE), formed in small quantities in the lungs, proximal convoluted tubules and other tissues, converts angiotensin 1 into angiotensin 2, which is a very potent vasoconstrictor and increases blood pressure. Renin and raised blood potassium levels also stimulate the adrenal gland to secrete aldosterone. Water is reabsorbed with sodium and together they increase the blood volume, which reduces renin secretion through the negative feedback mechanism. When sodium reabsorption is increased potassium excretion is increased, indirectly reducing intracellular potassium. Profound diuresis may lead to hypokalaemia (low blood potassium levels).
Calcium balance
Regulation of calcium levels is maintained by secretion of parathyroid hormone and calcitonin.

pH balance
In order to maintain normal blood pH (acid–base balance), the proximal convoluted tubules secrete hydrogen ions into the filtrate where they combine with buffers:
- Bicarbonate, forming carbonic acid
  \[ H^+ + HCO_3^- \rightarrow H_2CO_3 \]
- Ammonia, forming ammonium ions
  \[ H^+ + NH_3 \rightarrow NH_4^+ \]
- Hydrogen phosphate, forming dihydrogen phosphate
  \[ H^+ + HPO_4^{2-} \rightarrow HPO_4^{3-} \]
Carbonic acid is converted to carbon dioxide (CO2) and water (H2O), and the CO2 is reabsorbed, maintaining the buffering capacity of the blood. Hydrogen ions are excreted in the urine as ammonium salts and hydrogen phosphate. The normal pH of urine varies from 4.5 to 8 depending on diet, time of day and other factors. Individuals whose diet contains a large amount of animal proteins tend to produce more acidic urine (lower pH) than vegetarians.

Micturition
In infants, accumulation of urine in the bladder activates stretch receptors in the bladder wall generating sensory (afferent) impulses that are transmitted to the spinal cord, where a spinal reflex is initiated. This stimulates involuntary contraction of the detrusor muscle and relaxation of the internal urethral sphincter, and expels urine from the bladder – this is micturition or voiding of urine.
When bladder control is established, the micturition reflex is still stimulated but sensory impulses also pass upwards to the brain and there is awareness of the need to pass urine as the bladder fills (around 300–400 mL in adults). By learned and conscious effort, contraction of the external urethral sphincter and muscles of the pelvic floor can inhibit micturition until it is convenient to pass urine.
Urination can be assisted by increasing the pressure within the pelvic cavity, achieved by lowering the diaphragm and contracting the abdominal muscles. Over distension of the bladder is extremely painful, and when this occurs there is a tendency for involuntary relaxation of the external sphincter to occur allowing a small amount of urine to escape, provided there is no mechanical obstruction. Incontinence is the involuntary loss of urine after bladder control has been established.

Disorders of Urinary System

Glomerulonephritis (GN)
This term suggests inflammatory conditions of the glomerulus, but there are several types of GN and inflammatory changes are not always present. In many cases GN has an autoimmune component which leads to production of immune complexes that may lodge in the glomerular capillaries causing inflammation and impairment of glomerular filtration. Other immune mechanisms are also implicated in GN.

Classification of GN is based on a number of features: the cause, immunological characteristics and findings on microscopy. Microscopic distinction is based on:

- The extent of damage:
  - Diffuse: affecting all glomeruli
  - Focal: affecting some glomeruli

- Appearance:
  - Proliferative: increased number of cells in the glomeruli
  - Membranous: thickening of the glomerular basement membrane.

Diabetic nephropathy
Renal failure is the commonest cause of death in young people with diabetes mellitus (p. 236), especially if hypertension and severe, long-standing hyperglycaemia are also present. Diabetes causes damage to large and small blood vessels throughout the body, although the effects vary considerably between individuals. In the kidney, these are known collectively as diabetic nephropathy or diabetic kidney and include:

- Progressive damage of glomeruli, proteinuria and nephrotic syndrome
- Ascending infection leading to acute pyelonephritis
- Atheroma of the renal arteries and their branches leading to renal ischaemia and hypertension
- Chronic renal failure
Acute pyelonephritis

This is acute bacterial infection of the renal pelvis and calyces, which spreads to the kidney substance causing small abscesses. Bacteria usually reach the kidney by travelling up the urinary tract from the perineum but are sometimes blood-borne. This condition is accompanied by fever, malaise and loin pain.

Ascending infection: Upward spread of bacteria from the bladder is the most common cause of this condition. Reflux of infected urine into the ureters when the bladder contracts during micturition predisposes to upward spread of infection to the renal pelves and kidney substance. Normally the relative positions of the ureters and bladder prevents reflux that permits ascending access of bacteria to the kidneys.

Blood-borne infection: The kidneys are susceptible to blood-borne infection due to their large blood supply (20% of cardiac output). Bacteria may reach the kidney directly in sepsicaemia or travel there from distant sites e.g. a respiratory tract infection, infected wound or abscess.

Reflux nephropathy

Previously known as chronic pyelonephritis, this is almost always associated with reflux of urine from the bladder to the ureter allowing spread of infection upwards towards the kidneys. A congenital abnormality of the angle of insertion of the ureter into the bladder predisposes to this, but it is sometimes caused by an obstruction that develops later in life. Progressive damage to the renal papillae and collecting ducts may lead to chronic renal failure and concurrent hypertension is common.

Renal failure

Acute renal failure

The causes of acute renal failure are classified as:

- Prerenal: the result of reduced renal blood flow, especially as a consequence of, e.g., severe and prolonged shock
- Renal: due to damage to the kidney itself, e.g. Acute tubular necrosis, glomerulonephritis
- Postrenal: arises from obstruction to the outflow of urine, e.g. Disease of the prostate gland, tumour of the bladder, uterus or cervix, large calculus (stone) in the renal pelvis.

There is a sudden and severe reduction in the glomerular filtration rate and kidney function that is often reversible over days or weeks if treated. Oliguria or anuria is accompanied by
metabolic acidosis due to retention of H+, electrolyte imbalance and accumulation of mainly nitrogenous waste products. This occurs as a complication of conditions not necessarily associated with the kidneys.

**Acute tubular necrosis (ATN)**

This is the most common cause of acute renal failure. There is severe damage to the tubular epithelial cells caused by ischaemia or, less often, by nephrotoxic substances. Oliguria, severe oliguria (less than 100 mL of urine per day in adults) or anuria may last for a few weeks, followed by profound diuresis. There is a reduction in glomerular filtration, selective reabsorption and secretion by the tubules, leading to:

- Heart failure due to fluid overload
- Generalised and pulmonary oedema
- Accumulation of urea and other metabolic wastes
- Electrolyte imbalance which may be exacerbated by the retention of potassium (hyperkalaemia) released from damaged cells anywhere in the body.
- Acidosis due to retention of hydrogen ions.

Profound diuresis (the diuretic phase) occurs during the healing process when the epithelial cells of the tubules have regenerated but are still incapable of selective reabsorption and secretion. Diuresis may lead to acute dehydration, complicating the existing high plasma urea, acidosis and electrolyte imbalance. If the patient survives the initial acute phase, a considerable degree of renal function is usually restored over several weeks (the recovery phase).

**Renal calculi**

Calculi (stones) form in the kidneys and bladder when urinary constituents normally in solution usually oxalate and phosphate salts, are precipitated. They are more common in males and after 30 years of age and often recur. Most originate in the collecting tubules or renal papillae. They then pass into the renal pelvis where they may increase in size. Some become too large to pass through the ureter and may obstruct the outflow of urine, causing kidney damage. Others pass to the bladder and are either excreted or increase in size and obstruct the urethra. In developing countries and often in children, stones sometimes originate in the bladder. Predisposing factors include:

- **Dehydration**: this leads to increased reabsorption of water from the tubules but does not change solute reabsorption, resulting in a low volume of highly concentrated filtrate in the collecting tubules
- **pH of urine**: when the normally acid filtrate becomes alkaline, some substances may be precipitated, e.g. phosphates. This occurs when the kidney buffering system is impaired and in some infections

- **Infection**: necrotic material and pus provide foci upon which solutes in the filtrate may be deposited and the products of infection may alter the pH of the urine. Infection sometimes leads to alkaline urine

- **Metabolic conditions**: these include hyperparathyroidism and gout.

**Urinary tract infections (UTIs)**

Infection of any part of the urinary tract may spread upwards causing acute pyelonephritis and kidney damage.

**Ureteritis**

Inflammation of a ureter is usually due to the upward spread of infection in cystitis.

**Cystitis**

This is inflammation of the bladder and may be due to:

- Upward spread of commensal bacteria of the bowel (Escherichia coli and Streptococcus faecalis) from the perineum via the urethra, especially in women

- Trauma, with or without infection, following health-care interventions, e.g. Radiotherapy, insertion of a urinary catheter or instrument into the bladder.

**Urinary incontinence**

In this condition normal micturition is affected and there is involuntary loss of urine. Several types are recognised and described below. In addition to the mechanisms below, neurological abnormalities can also impair voluntary control of micturition, e.g. spinal cord injury, multiple sclerosis.

**Stress incontinence**

This is leakage of urine when intra-abdominal pressure is raised, e.g. on coughing, laughing, sneezing or lifting. It usually affects women when there is weakness of the pelvic floor muscles or pelvic ligaments, e.g. after childbirth or as part of the ageing process. It occurs physiologically in young children before bladder control is achieved.

**Urge incontinence**

Leakage of urine follows a sudden and intense urge to void and there is inability to delay passing urine. This may be due to a urinary tract infection, calculus, tumour or hypersensitivity of the detrusor muscle.
Overflow incontinence
This occurs when there is chronic overfilling of the bladder and may be due to retention of urine due to incomplete voiding when there is obstruction of urinary outflow, e.g. enlarged prostate gland or urethral stricture and/or impaired contraction of the detrusor muscle during micturition. It may also arise as a complication of pelvic nerve damage caused by e.g. surgery, trauma, or when the cauda equina is compressed by a tumor or prolapsed intervertebral disc.