Chapter 13: Physiology of respiration

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The rhythmic act of quiet breathing entails an active inspiratory movement in which the diaphragm and the chest wall is pulled outwards by active contraction of the external intercostal muscles. In this way, the volume of the thoracic cage is increased and air is drawn into the airway. The primary function of the lung is to provide a site for gaseous exchange so that oxygen can enter the circulation and carbon dioxide can be eliminated. This gaseous exchange occurs in the terminal branches of the bronchial tree in both the respiratory bronchioles and alveoli, while the remainder of the tracheobronchial tree acts simply as a conduit for air passing to and from these exchange sites.

The system has necessarily evolved sophisticated mechanisms to ensure that air inspired through the nose, mouth and pharynx is adequately filtered, and the added protection of the pharyngeal reflexes and the sphincter action of the larynx ensure that food and other large particles do not enter the airway. In addition, the bronchial tree is continually cleansed by ciliated epithelium with an overlying mucous layer which traps fine particulate matter and clears the airway. Adequate respiratory function also demands complex control mechanisms to ensure that oxygenation of the blood is achieved in a variety of different circumstances while allowing for minor irregularities of flow caused by speed and swallowing.

It is the purpose of this chapter to expand and discuss some of the outlines given of the physiology of respiration together with those respiratory function tests in common clinical usage, and to describe the common abnormalities of respiration seen in upper airway disease and in disorders of the tracheobronchial tree.

Pathophysiology of respiration

Mechanics of ventilation and blood flow

Chest wall and respiratory muscles

Quiet breathing entails an active inspiratory movement in which the diaphragm descends and the chest wall is expanded by active contraction of the external intercostal muscles. This results in the generation of a profound negative intrapleural pressure and causes a rapid expansion of lung volume which draws air into the lungs. In contrast, expiration is largely a passive movement which relies on the elastic recoil of lung substance and chest wall.

Downward displacement of the diaphragm results from contraction of the diaphragmatic crura, and this is supplemented by flattening of the hemidiaphragms caused by the contraction of muscle fibres running from the costal margin to the central fibrous tendon. During quiet breathing there is little movement of the chest wall or activity in the intercostal muscles, and most muscle activity emanates from the diaphragm alone; in these circumstances, any intercostal muscle activity serves to prevent inward collapse of the chest wall during diaphragmatic descent. However, where there is an increased workload and more active respiration is required, the external intercostal muscles are recruited. These muscles
pass downwards and medially from one rib to another causing, by their actions, upward and outward movement of the ribs which, at the same time, become more horizontal. Where there is a requirement for maximum ventilation (such as occurs during extreme exercise), the accessory muscles of respiration are also utilized. These muscles - including the sternomastoid, the trapezius and the scalene group - help to expand the upper ribs and thereby increase further the intrathoracic volume.

In the presence of diseases of the lung parenchyma, the work of breathing is increased by the concomitant loss of lung elasticity and, in some states such as chronic obstructive airway disease, the problem is compounded by air trapping with flattening of the diaphragms. As a result there is loss of diaphragmatic muscle efficiency. Narrowing of the airway increases the airway resistance and this also increases the work of breathing. Where increased work is required, the metabolic load placed on the respiratory muscles is enhanced; in the presence of coexistent hypoxia, hypokalaemia, hypocalcaemia or hypomagnesaemia, muscle fatigue is accelerated and the likelihood of respiratory failure therefore increased.

In disease states with an increased airway resistance, expiratory movements may also become dependent on active muscle contraction. In such circumstances, the internal intercostal and abdominal wall muscles may be required to expel air from the bronchial tree. In other patients, such as those with kyphoscoliosis and ankylosing spondylitis, respiratory embarrassment results from loss of chest wall mobility and expansion of the lungs becomes more dependent on diaphragmatic movement. In contrast, patients with neurological diseases or muscle dystrophias (such as occur in poliomyelitis or the myasthenia of the Guillain-Barré syndrome) have marked diaphragmatic weakness, and in these circumstances those actions of the accessory and intercostal muscles that are preserved assume a great importance.

**Lung volume and dead space**

The major subdivisions of lung volume are shown in the figure. The tidal volume is the volume of air breathed in or out during quiet respiration, and is approximately 500 mL, with a resting respiratory rate of 15-20 breaths per minute. The inspiratory reserve volume represents the maximum volume of air which can be inspired after completing a normal tidal respiration, that is inspired from the end-inspiratory position (2000-3000 mL), and the expiratory reserved volume represents the maximum volume capable of being expired after a normal tidal expiration, that is expired from the end-expiratory position (750-1000 mL). As the lung volume decreases on expiration, there is a progressive narrowing of the small airways; these eventually close, trapping air in the distal airway. Even on forced expiration some air remains, and this is termed the 'residual volume' (1200 mL).

One of the most frequently measured parameters in clinical work is the vital capacity. This is the maximal volume of air which can be expelled from the lungs by a forceful effort following maximal inspiration. The vital capacity averages 4.8 litres in the male and 3.2 litres in the female, but is related to the size and age of the subject. It is reduced in older people and also in diseases of the respiratory tract such as respiratory obstruction, pleural effusion, pneumothorax, pulmonary fibrosis, emphysema and pulmonary oedema. If the vital capacity is measured by means of a spirometer, the volume of air expelled can be timed. Normally, 75% of the vital capacity should be expired in the first second, which is termed the 'forced expiratory volume' (FEV$_1$). Such a measurement provides a much more sensitive index of
obstruction in the airway than does measurement of the vital capacity alone. Studies of vital capacity and its subdivisions are used to assess pulmonary function and are particularly useful prior to surgery in assessing the risks of general anaesthesia.

Also shown in the figure are: the total lung capacity (TLC); the inspiratory capacity, which is the maximal volume of gas which can be inspired from the resting expiratory level; and the functional respiratory capacity (FRC), which is the volume of gas remaining in the lungs at the resting expiratory level. Most of these lung volumes and capacities can be measured by using a simple spirometer, but residual volume, and hence the functional residual capacity and total lung volume, can be assessed only by measurements of nitrogen washout (in a patient breathing pure oxygen), by whole body plethysmography or, most commonly, by helium dilution. Alternatively, radiological techniques may be applied.

As has already been observed, the respiratory tract is divided into conducting passages and gas exchange surfaces. The latter, formed by the respiratory bronchioles and alveoli, comprise a surface area of some 70-80 m² in the adult. Therefore, although much of the surface area of the respiratory system is used for gas exchange, some of the inspired air (about 150 mL) merely fills the conducting air passages between the mouth and nose and respiratory bronchioles; this is called the anatomical dead space. The physiological dead space comprises this volume and also the volume of inspired gas which ventilates alveoli in excess of that which is required to oxygenate blood in the adjacent pulmonary capillaries. In a healthy state, this additional volume is negligible, but in disease states (where there are unequal ventilation/perfusion ratios in parts of the lung) the physiological dead space may greatly exceed that of the anatomical dead space and only a very small volume of the inspired air is then available for gas transfer.

Air flow

In the respiratory tract, air flows through a rapidly branching system which progressively narrows. The resistance to air flow in such a tubular system is inversely proportional to the fourth power of the radius. Therefore, in the normal upper airway and larynx, resistance is low and the flow of air is fast; but if there is narrowing at these sites, turbulence together with a considerable rise in airway resistance will result. As the airway divides, the diameter becomes progressively smaller and hence the resistance to air flow tends to increase. However, this effect is mitigated because the number of airways also rapidly increases and the overall resultant rise in airway resistance is not large. In fact, only 20% of air flow resistance is situated in the small airways and 60% of the overall resistance is found in the medium-sized airways between 2 and 6 mm in diameter.

In the normal subject, minor changes in airway resistance result during different phases of the respiratory cycle. In extrathoracic sites, inspiration tends to collapse the airway, although normal muscle tone and the structure of the airway oppose such forces in order to keep the airway patent. During expiration, the same part of the airway tends to expand as expired air flows from the lungs. In contrast, the major intrathoracic airways expand as the volume of the chest increases during inspiration, and are then compressed by the diminution of lung volume during the expiratory phase. Thus any defect in the extrathoracic airway leads to an increase in the inspiratory resistance, whereas problems in the intrathoracic airways tend to be more acute in expiration. Air passing down the larger airways is therefore subject to
some fluctuation in resistance, but as airway radius decreases, the resistance becomes less phase variable and more dependent on airway diameter alone. Eventually, at about the eleventh generation of bronchi (each generation implying an airway division), bulk flow of air ceases and oxygen and carbon dioxide diffuse to the remainder of the lower part of the pulmonary tree.

**Gas exchange**

Once the inspired air reaches the respiratory bronchioles and alveoli, gas exchange by diffusion across the alveolar membranes and into the pulmonary capillaries occur. It follows that for this exchange to take place, the blood in the capillaries must be in close proximity to ventilated alveoli, and the transport of oxygen and carbon dioxide will be impaired if there is any mismatch between ventilation and perfusion. In a normal person, both the major air flow and perfusion are to the lower lobes since expansion is maximal in the lower part of the chest and pulmonary arteriolar pressure is low at the bases. Many disease processes produce a mismatch: lobar pneumonia (where there is consolidated lung which has a good blood supply but minimal ventilation) and pulmonary embolus (where there is adequate ventilation but poor perfusion) are extreme examples of conditions which produce imbalance, but many lesser degrees of the same phenomenon may occur.

The transport of oxygen across the basement membrane is limited by the poor solubility of this gas, and as its solubility is considerably less than that of carbon dioxide, a ventilation perfusion imbalance tends to lead to hypoxia, without resulting in decreased carbon dioxide transfer and hypercapnia.

**Pulmonary circulation and oxygen transport**

Blood returning from the periphery drains to the vena cavae and hence into the right side of the heart. This is a low pressure circulation with a mean arterial pressure of only 25 mmHg, and a maximum pressure of less than 50 mmHg. This low pulmonary vascular pressure means that when the subject is erect most of the blood flow is diverted to the lower lobes of the lungs and very little reaches the apices where the arterial pressure may be as low as 5-10 mmHg.

The pulmonary circulation may be deranged in a variety of ways. One of the most common is a pulmonary embolus which occurs when detached thrombus passes from a large peripheral vein and traverses the right side of the heart to become lodged in part of the pulmonary arterial tree. This event produces a decrease in local lung perfusion in the presence of normal ventilation, with an increase in pulmonary vascular resistance and increased right ventricular work and strain. The rise in pulmonary artery pressure which accompanies a pulmonary embolus may lead to the opening up of arteriovenous anastomoses, and hence to the shunting of blood to the left atrium, with concomitant bypassing of the lungs; this may produce additional hypoxia.

Occasionally, pulmonary artery pressure rises as the result of a shunt of blood from the left to the right side of the heart: such an event occurs in the presence of an atrial or ventricular septal defect. Such a shunt initially produces dilatation of the pulmonary arteries, but this is followed by pulmonary artery vasoconstriction and a subsequent narrowing of the
pulmonary arterioles with thickening of the vessel walls. As a consequence, there is a diminution of pulmonary perfusion. Conversely, when there is increased back pressure from the heart, as occurs in left ventricular failure, mitral regurgitation or mitral stenosis, the pulmonary veins become overfilled with blood. Initially, there is no accompanying rise in pulmonary venous pressure, but as the system is further filled the pressure rises and, as a result, the postcapillary pressure is elevated. As in the systemic circulation, fluid balance in the pulmonary capillaries obeys Starling's law; thus, fluid normally leaves the capillary circulation at the high pressure arterial end and is reabsorbed at the distal end where the luminal pressure is lower and the oncotic pressure of the blood is sufficient to encourage fluid to return. However, if the pulmonary pressure is raised there is a net movement of fluid into the parenchyma of the lung and pulmonary oedema with decreased lung compliance and hypoxia will result.

Changes in haemoglobin concentration also affect oxygen transport. A reduced concentration of haemoglobin clearly allows less oxygen to be carried in the blood; conversely, an increase in the concentration causes increased blood viscosity with a rise in pulmonary vascular resistance, a reduction in pulmonary capillary perfusion and a diminution in the efficiency of gas transport in the lung. This is particularly likely to occur if the packed cell volume of the peripheral blood exceeds 55% of the total blood volume as this causes a marked rise in viscosity; however, if the packed cell volume remains below 50%, the viscosity of the blood is seldom a limiting factor in gas transport.

The binding of oxygen to, and the dissociation of oxygen from, haemoglobin can be plotted on a dissociation curve. As the partial pressure of oxygen in the tissues falls, oxygen is released from haemoglobin which, as it passes through the alveolar capillaries, is reoxygenated to form oxyhaemoglobin. The oxygen dissociation curve is altered by changes in the acidity of the environment, with a decrease in pH leading to a decreased affinity of haemoglobin for oxygen. The position of the curve is also affected by the concentration of 2,3-diphosphoglycerate in the red cells. This metabolite is produced from cells engaged in active metabolism and is reduced in old cells and particularly in those which have been stored; as a result, transfused blood has a low concentration of diphosphoglycerate which causes a shift in the dissociation curve to the left. A large transfusion, therefore, limits the amount of oxygen which can be delivered to the tissues.

Carbon monoxide also binds to haemoglobin to form carboxyhaemoglobin. This reaction proceeds with an avidity which is more than 250 times the affinity of oxygen. As a result, the binding of this gas is irreversible in practical terms, and any haemoglobin which is linked to carbon monoxide is unavailable for oxygen transport. This becomes clinically relevant in patients who are hypoxic with lung disease and who continue to smoke. Such subjects already have difficulty with ventilation as a consequence of damaged lung tissue, and clearly there will be an added difficulty in providing adequate tissue oxygenation if between 5 and 10% of their circulating haemoglobin is unavailable for oxygen transport on account of its conversion to carboxyhaemoglobin.

**Ventilatory regulation**

Breathing patterns are under both voluntary and automatic control. Automatic control is localized in the 'respiratory centre' which comprises a pool of neurons in the grey matter
of the pons and upper medulla. Evidence from stimulation testing in experimental preparations has made it possible to delineate separate areas within this group which are responsible for inspiration and expiration, but there is close interaction so that inspiration is associated with inhibition of expiratory neurons in the medulla and expiration with reciprocal inhibition of spinal cord neurons. It is also known that feedback from muscle spindles in the intercostal and abdominal muscles, as well as from the accessory muscles of respiration, acts with the input from pulmonary stretch receptors, ‘J’ receptors (junctional receptors in bronchial walls) and irritant receptors by way of the vagus nerves to moderate this activity. Although these centres will develop rhythmic discharge when isolated from the upper brainstem and from afferent input, their activity is usually moderated by both the higher brainstem and by phasic impulse traffic in the vagal nerves.

Experimental evidence has also suggested that activity in these centres is moderated by other parts of the pontine reticular formation. Stimulation of the lateral part of the middle and lower pons induces a sustained inspiratory effort, and this ‘apneustic centre’ is thought to exert a tonic discharge upon the medullary inspiratory centre to promote a more sustained respiratory effort. In turn, this tonic activity is controlled and lessened by vagal efferents, and by an upper pontine centre called the pneumotaxic centre. Even after vagal transection, this latter centre will hold the apneustic centre in check.

It is thought that this somewhat complicated system acts in the following way. The inspiratory centre, under the influence of the stimulus provided by the arterial PCO₂ and the tonic activity of the apneustic centre, discharges through the spinal cord to the anterior horn cells in the cervical and thoracal regions that are responsible for promoting diaphragmatic and chest wall movements; inspiration then occurs. At the same time, the inspiratory centre provokes the pneumotaxic centre and this discharges inhibitory impulses to the apneustic centre. This latter centre is therefore exposed simultaneously to these inhibitory impulses and to inhibition relayed by way of the vagus nerve from the pulmonary stretch receptors. In turn, this inhibition reduces activity in the medullary inspiratory centre. This centre then stops discharging and expiration follows passively. It is assumed that the pneumotaxic centre relays excitatory impulses from higher centres to the expiratory centre when active expiration is required.

Response to changes in oxygen and carbon dioxide tension

A lack of oxygen or an excess of carbon dioxide in the arterial blood affects respiration, with both hypoxia and hypercapnia causing a rise in the respiratory rate. Chemosensitive areas for this reaction are located in the brainstem and in the carotid and aortic bodies. Thus a decrease in the arterial partial pressure of oxygen causes increased discharge in fibres of the glossopharyngeal and vagus nerves serving the peripheral chemoreceptors, while an increase in oxygen tension (above 27 kPa or 200 mmHg) leads to an abolition of activity in the cells in these organs that are sensitive to hypoxia. Similarly, a rising arterial carbon dioxide tension leads to a parallel rise in hydrogen ion concentration in the peripheral chemoreceptors and this, in turn, results in increased activity in this system. Although the response to hypoxia and hyperoxia is mediated solely through peripheral receptors, the greatest response to a rising carbon dioxide level comes from central chemoreceptors located in the base of the fourth ventricle. These cells are responsive to changes in the hydrogen ion concentration in the surrounding cerebrospinal fluid. They
contain a high concentration of the enzyme carbonic anhydrase which catalyses the reaction binding the carbon dioxide and this directly influences the local hydrogen ion concentration by way of the formation of carbonic acid.

Effects of the reticular acting system

The reaction of the respiratory neurons is related to the rest of the brainstem so that a depression of brainstem activity, as is seen in sleep or during anaesthesia, results in a reduction in responsiveness to hypoxia and hypercarbic drives. During sleep, the decrease in these drives is most marked in rapid eye movement (REM) sleep; in this phase, the arterial carbon dioxide in the normal subject may rise by 1 kPa (5-8 mmHg) and the arterial oxygen may fall by 4%. It follows that any patient with a severe respiratory disability, who is only just able to clear carbon dioxide and provide adequate oxygenation when awake, may suffer severe hypoxia and hypercapnia when asleep or anaesthetized.

Higher control of breathing

The respiratory neurons in the brainstem, together with the peripheral receptors and receptors in the fourth ventricle, act in concert to provide a constant arterial oxygen PO$_2$ and PCO$_2$ by adjustment of the respiration rate, respiratory volume and length of the different phases of respiration. If brainstem function is normal, respiration is regular and quiet with a constant pattern of inspiration and expiration. If there is damage to the relevant parts of the brain then this pattern becomes deranged, and either the periodic waxing and waning of Cheyne-Stokes respiration or an irregular gasping pattern of respiration becomes apparent. Superimposed upon the normal patterns of respiration are voluntary and semi-automatic control systems. Therefore, the act of speaking, which requires the coordination of the larynx, pharynx and mouth, and delivery of the correct volume of air to the glottis at an adequate pressure, is not totally involuntary, but necessitates superimposed semi-automatic control which results from coordination learned in childhood. Central organization of this control requires the basal ganglia, cerebellum and cerebrum to act by imposing the desired respiratory pattern upon automatic control while maintaining PO$_2$ and PCO$_2$ levels within normal limits. When this system breaks down, words are produced, but there are difficulties in controlling the volume or tone of the speech; such abnormalities are commonly seen after cerebrovascular accidents. In addition, a few patients have been reported with complete cerebromedullary disconnection. Such subjects also experience an inability to superimpose upon automatic respiration the irregularities of respiration associated with voluntary control. Thus in the normal patient, voluntary, semi-automatic and automatic respiration are superimposed during waking hours, but during sleep semi-automatic and voluntary control is lost and respiration becomes totally automatic. As a result, some patients with deranged brainstem control, but normal semi-automatic and voluntary mechanisms, have normal respiration when awake but show severe respiratory dysrhythmias during sleep. For example, in the Shy-Drager syndrome, abnormalities of central autonomic function cause fluctuations in cardiovascular and respiratory control and irregular and disorganized respiration during sleep, with frequent apnoeic episodes. In some subjects, brainstem control is so severely disrupted that sleep results in total cessation of normal breathing (Ondine's curse).
Respiratory failure

Respiratory failure with its attendant lowering of the arterial PO$_2$ to less than 8 kPa, may occur with damage to the respiratory system at any level. In most cases, there is inadequate gas exchange as a result of lung damage due to either chronic obstructive airway disease or to pulmonary fibrosis. Initially, the resultant high carbon dioxide levels cause an increased respiratory drive, but responsiveness gradually diminishes and tolerance develops. Carbon dioxide drive is usually the major determinant of ventilatory volume and when this fails the PO$_2$ rises. When levels exceed 10 kPa, carbon dioxide acts as a narcotic and the resultant drowsiness and fluctuating consciousness further depress the respiratory drive. A major problem resulting from this decrease in carbon dioxide responsiveness is the increased reliance on hypoxic drives. Such patients are therefore at risk when given high concentrations of inspired oxygen, for a further reduction in ventilatory drive may result in an additional rise in carbon dioxide tension and consequent unconsciousness. It is for this reason that controlled oxygen therapy is used in patients with chronic obstructive airway disease, and blood gases must be checked regularly to ensure that such therapy does not result in carbon dioxide retention. The respiratory depression caused by sedative drugs, narcotics, strong analgesics or anaesthetic agents can exacerbate this situation and lead to high PCO$_2$ levels and severe hypoxia.

Respiratory control of the upper airway

Coordination of muscle activity in the oral cavity, pharynx and larynx depends upon normal central control in the brainstem and intact pharyngeal wall receptors with normal innervation (provided by the glossopharyngeal and vagus nerves). Defects in this system lead to a loss in patency of the upper airway which may be exacerbated by drug ingestion. This problem will be considered in subsequent section of this chapter where upper airway disease is discussed.

Breathlessness

Breathlessness is a subjective sensation which does not always correspond with objective evidence of a compromised respiratory system. To some subjects, breathlessness implies tachypnoea whereas to others it implies the physical difficulty of getting air into or out of the chest, with or without an attendant feeling of distress. These differing views result from the various pathologies which give rise to a perception of breathlessness.

If a subject is asked to hold his breath for as long as possible after maximum inspiration, the resulting sensation of distress will rapidly become severe, which will force the person to exhale and resume a normal breathing pattern; this is called the break point. Such holding of breath after the inspiration of a mixture with a low PO$_2$ or a high PCO$_2$ leads to a shortened breath holding time and an earlier break point. Thus hypoxia and hypercapnia clearly influence breathlessness. However, the duration also depends on lung volume, since the duration of breath hold from total lung capacity is much longer than from functional residual capacity or residual volume. It is known that chest wall muscle receptors (which provide information to the central nervous system about the work of breathing and the volume of the chest) also contribute directly to the sensation of breathlessness, as chest wall paralysis
causes breath holding to lose its element of respiratory distress. All of these factors interact and are in turn overlayed by psychological elements.

Exercise limitation is often the first sign of respiratory insufficiency. The degree of limitation depends on the respiratory reserve, and a subject with only mild pulmonary disease may not notice any abnormality unless he is forced to exert himself maximally; accordingly, there is no complaint of breathlessness. However, when the respiratory reserve has been lost, even mild exertion will cause dyspnoea, and it is usually at this point that there is an objective realization of breathlessness by the patient. Even so, in some cases the patient's awareness of a respiratory problem may be limited in the face of objective evidence of quite severe disease.

Respiratory toilet and defences

The nose

Air passes through the passages of the nose during quiet respiration and is warmed and humidified. Any large particles are trapped on the nasal mucosa and are expelled either by the nasal cilia or by sneezing. Inhaled gases, such as chlorine, cause irritation in the nose, and this produces reflex rhinorrhea and sneezing before affecting the rest of the airway to produce coughing. The cilia of the nose and the mechanisms of their action in the nose and tracheobronchial tree are identical and will be considered later.

The pharynx

There are a large number of irritant receptors in the pharyngeal wall and these can be blocked by topical anaesthesia. These receptors act to protect the airway from noxious fumes or foreign bodies by initiating an expulsive cough when stimulated. Patients with brainstem disease or decreased levels of consciousness may suffer suppression of their pharyngeal cough reflex and this leads to the easier passage of foreign material into the tracheobronchial tree. Functionally, the pharynx, larynx and oesophagus are closely coordinated so that breathing and swallowing can occur without allowing excess aerophagia or aspiration of gastric or oesophageal contents into the bronchial tree. Acid reflux or incoordination in the oesophagus (especially at the level of the cricopharyngeus) is liable to cause aspiration, and this is a particular feature of pseudobulbar and bulbar palsy, and may also be a feature of cerebellar disease. Coordination is also often poor at the extremes of life, and young children and the elderly are therefore prone to choke on food or quietly to aspirate gastric contents while asleep.

The larynx

The laryngeal inlet acts as a sphincter to protect the airway. In addition, the closure of the laryngeal sphincter during expiration allows increased intrathoracic pressure to develop, and this manoeuvre aids the development of a large explosive force of expired air which acts to clear the tracheobronchial tree during coughing. Glottic closure also fixes the chest and diaphragm and allows increased abdominal pressure to be produced when the abdominal muscles contract; this aids defaecation, micturition and parturition.
During swallowing, an elevation of the larynx towards the base of the tongue is effected by contraction of the inferior constrictor and palatopharyngeus and stylopharyngeus muscles; this also brings the pharyngo-oesophageal opening towards the bolus of food. At the same time there is a cessation of air flow as a result of reflex central inhibition, and laryngeal closure occurs at both the glottic and supraglottic levels to prevent food passing into the trachea. As the bolus passes, the epiglottis passively tilts and the shape of its upper surface assists in guiding the swallowed material towards the oesophagus.

The laryngeal sphincters are arranged in three tiers. The first layer is formed by the aryepiglottic folds and epiglottis, the second by the false cords and the third by the true vocal cords. The aryepiglottic sphincter lies almost vertically and consists of a thick band formed by the thyroarytenoid and interarytenoid muscles. This sphincter closes the pharynx above from the laryngeal vestibule, and sphincteric closure is completed anteriorly by the tubercle of the epiglottis and posteriorly by the bodies of the arytenoid cartilages.

The false cords lie above the true cords from which they are separated by the laryngeal ventricle. Each fold has a free medial border, and the folds extend from the thyroid cartilage anteriorly to the anterolateral surface of the arytenoid cartilages posteriorly. The main substance of the folds consists of a mixture of fibrous and elastic tissue which is covered with pseudostratified columnar epithelium containing mucous glands. At rest, these folds do not project as far medially as the true cords, but when the muscle fibres external to these ventricular bands contract, the bodies of the arytenoid cartilages are approximated.

The true cords extend from the angle between the laminæ of the thyroid cartilages to the vocal processes of the arytenoid cartilages. The fibrous element is condensed at the medial border of these folds with the elastic tissue of the upper border of the conus elasticus; the muscle element is provided by fibres of the thyroarytenoid muscle. The upper surface of this cord is flat but the lower surface shows a downward concavity. This shape provides a more efficient valve than a simple sphincter for preventing air entry during inspiration, and the dome-shaped undersurface of the cord concentrates the infraglottic air pressure onto the sloping free margins of the folds, which has the effect of abducting the cords during expiration.

During closure of the laryngeal sphincters, the true vocal cords are the first to approximate and these establish contact progressively from the front backwards. This is followed by a similar adduction and closure of the false cords, with short segments at the posterior commissure being the first to close as the arytenoid cartilages adduct and rotate medially under the influence of the interarytenoid, thyroarytenoid and lateral cricothyroid muscles. The remaining parts of the false cords then close from the front backwards, and closure is finally completed by the forward tilt of the arytenoids.

The trachea and bronchial tree

The trachea and bronchial tree are lined with a ciliated epithelium which contains mucous cells. Between 100 and 200 mL of mucus are produced each day and thus contains small quantities of sialic acid, neutral polysaccharides, albumin, secretory immunoglobulin (IgA) and lysozyme, together with water which forms 95% of the total volume. Air which has passed through the nose is humidified and is 90-95% saturated with water vapour, but the
The presence of mucus in the bronchial tree serves to diminish any water loss in the lower airways as well as providing a surface protection against inhaled chemicals, organisms and other irritants. In chronic bronchitis there is an increase in the number of mucus-producing cells with a resultant increase in bronchial secretions; this mucus may be difficult to cough up as there may also be a simultaneous reduction in ciliary beating.

Normally, the cilia which are present in the trachea, the larynx and the nose move mucus in streams away from the lower airways towards the pharynx where it can be swallowed. Ciliary structure is shown in the figure. Each cilium consists of two central fibres enclosed in a sheath and these are connected to nine pairs of peripheral fibres which are interlinked with dynein arms. Radial secondary fibres connect the central and peripheral fibres and the whole is enclosed in an outer membrane. The cilia move with a beating motion and this provides the mucous escalator which traps particular matter. Inflammation, cigarette smoke and other irritants all reduce ciliary activity, but in a small number of patients the cilia are immobile as a result of structural abnormalities. Whatever the cause, reduced clearance of mucus leads to pooling with secondary infection and bronchial damage which predisposes to bronchiectasis. In the case of the nose, the consequence is chronic inflammatory changes with sinusitis. The clinical picture is seen in patients with Kartagener's syndrome, where immobile cilia are responsible for a clinical picture which includes sinusitis and bronchiectasis, as well as infertility attributable to immobility of the spermatozoa.

Although small particles are cleared by the ciliary escalator, larger debris is cleared by coughing. Stimulation of irritant receptors in the bronchial tree passes by way of the vagus to the brainstem and an inspiratory effort then follows, which is followed by forced expiration initiated with the glottis closed to raise the intrathoracic pressure. With relaxation of the laryngeal sphincters, a rapid flow of air up the trachea results and the irritant is expelled. In the presence of bronchial hyperreactivity there is a decreased threshold for activation of irritant receptors, and spasmodic coughing may therefore occur spontaneously or after minimal stimulation (for example by cold air).

**Measurement of respiratory function**

**Measurement of lung volume**

The early measurements of lung volume were carried out by means of a wet spirometer. The subject was asked to inspire maximally and then to exhale through a tube into a bell that contained air floating in a bath of water; air entry caused the bell to rise and thus allowed measurement of the vital capacity to be made. Today, dry spirometers are employed with a bell which are expanded by the gas blown into it, and of these the most commonly used in the UK is the Vitalograph. The subject breathes in to total lung capacity and then exhales to his residual volume. Most spirometers plot the volume of expired gas against time and this allows the forced expiratory volume in one second (FEV1) to be taken from the trace. In turn, this can be used as a measure of air flow limitation. A severe diminution in vital capacity which is below that predicted for the individual on the basis of his sex, height and age is an indication that blood gases should be checked. As a guideline for surgery, a vital capacity of less than 1200 mL is often associated with an increase in anaesthetic and postoperative complications.
Lung volumes may also be measured by using the dilution of gas mixtures to assess the residual volume. In the single breath transfer test, one measured inhalation of a helium and air mixture is taken, held for 10 seconds, and then exhaled. The helium and air mixture is diluted with air already present in the alveolae, and only a proportion of the helium which is breathed in will be blown out, the remainder being left behind in the residual volume. The difference in concentration between the inspired and expired helium allows calculation of the residual volume of the lung and, as the vital capacity was the volume of the gas inspired, the total lung volume may then be calculated.

This single breath method of measuring lung volume is limited as the subject may not take a breath equal to lung capacity, and there may be unequal mixing of gases in the lung. For this reason, rebreathing of a fixed volume of helium and air mixture with compensation for oxygen consumption and absorption of CO₂ is a more accurate method of assessment, and this test should be available in most respiratory function laboratories. Once adequate mixing has had time to occur and the helium concentration in the system has become constant, this method enables a calculation of helium dilution to be performed. At this point, the subject exhales and this allows the measurement of both the vital capacity and the inspiratory and expiratory reserve volumes. Calculation then allows an assessment of the functional residual capacity and residual volume so that the total lung volume may be computed. Full lung volume measurement with body box plethysmography is also possible, but is available in only a limited number of centres and is rarely required clinically. Vital capacity measured with a Vitalograph is usually all that is needed for routine clinical work and more comprehensive measurements are used only for monitoring the progression of disease or for monitoring the effects of treatment.

**Air flow**

**Peak flow**

Peak flow measurement is the most commonly performed respiratory function test, and cheap reliable peak flowmeters are readily available on most hospital wards. The peak expiratory flow rate measured by these machines is the maximum air flow which is maintained for a period of at least 10 ms. In this test, the subject is requested to breathe in to total lung capacity and then to breathe out as fast as he/she can, but unless there is good effort, and unless the expiration starts at maximum lung volume, the peak flow measured will be reduced and inaccurate. A common error with this method, especially with the mini-Wright peak flowmeter, occurs if the subject places his fingers over the slide indicating the peak flow and prevents or reduces its movement; in spite of these limitations, the peak expiratory flow is readily performed in most subjects and is easily repeatable. Measurements of peak flow allow obstructive airway disease from any case to be easily assessed; for example, peak flow is reduced in asthma but rises after treatment with a bronchodilator. In patients with upper airway narrowing, measurement of peak flow allows the conditions of variable intrathoracic obstruction and fixed upper airway obstruction to be assessed with ease. However, if there is variable extrathoracic airway obstruction, the expiratory flows will be normal, and reliance must then be placed on maximum inspiratory flows to detect the abnormality. These conditions and the change in peak flow associated with them will be considered in the section on abnormalities of upper airway function.
Forced expiratory volume

When a spirometer is used to measure vital capacity, the expiratory spirogram is usually plotted as volume against time. This allows the volume of air exhaled in the first second of forced expiration (FEV₁) to be measured. FEV₁ provides information on air flow in large and medium-sized airways and is reduced in asthma and upper airway disease. With disease of the trachea or larynx, the FEV₁ is reduced less than the peak flow, and this forms the basis of the Empey Index which is the FEV₁ (in mL) divided by the peak flow (in L/min). In the normal subject, this ratio is less than 10. In the presence of upper airway disease, the peak flow is reduced more than the FEV₁, and the Empey Index will rise; if the Empey Index exceeds 10, this would suggest that there is fixed airway or variable intrathoracic airway narrowing. Variable extrathoracic airway narrowing only reduces inspiratory flows and does not affect the Empey Index (see later).

Flow-volume loops

Measurement of the peak flow are limited as they provide recordings of flow obtained at only one lung volume. The flow-volume loop provides information on the maximum flows obtained at all lung volumes, both in inspiration and expiration. In this test, flow is measured with a pneumotachograph or is obtained by differentiation of the volume signal from a dry spirometer. Flow is plotted on the y axis and lung volume on the x axis of a graph, with total lung capacity at the origin and residual volume on the right. By convention, expiratory flows are plotted as positive and inspiratory flows as negative values. This investigation allows a large amount of physiological information to be obtained and is particularly useful in the management and investigation of patients with upper airway or tracheal disease. As in any lung function test, the cooperation of the subject and the production of a maximum effort are necessary for a meaningful result. If there has been a breath of subvital capacity volume or of inadequate effort, this can often be identified from the trace so that unwarranted diagnosis and conclusions are not made. Flow-volume loop measurement is available in most district general hospitals, and the details of the different loops obtained in different airway pathologies are discussed in the final section of this chapter.

Other tests

Body plethysmographic methods are available for the measurement of airway resistance and conductance. Forced oscillation methods allow measurement of the resistance to air flow of both the lungs and chest wall, and measurement of transpleural pressures allows the compliance of the lung to be assessed. A detailed examination of the flow-volume loop obtained with a pneumotachograph can be made by using a computer analysis. All of these methods of assessment are available in only a limited number of centres and are of little value in clinical management. Measurements of peak flow and FEV₁, in combination with recordings of the flow-volume loop, allow sufficient physiological information to be assembled in most instances.

Gas transfer

The simplest method of measuring gas transfer in the lungs is to measure the concentrations of oxygen and carbon dioxide carried in the arterial blood. Hypoxia in a patient
breathing room air implies that the transfer of oxygen across the lungs is reduced. If the patient is already breathing oxygen-enriched air, subtraction of the arterial PO$_2$ from the inspired PO$_2$ (obtained by calculation) allows the alveolar/arterial gradient to be estimated and this reflects the efficiency of the lungs. Similarly, comparison of the arterial PCO$_2$ with that in the environment allows the efficiency of clearance of CO$_2$ to be assessed and an estimate of the efficiency of respiratory drives and control to be made.

The most commonly used method for assessing the transfer of gas across the lung is the single breath carbon monoxide transfer test. A mixture of air, helium and carbon monoxide is inhaled and held in the lungs for 10 seconds before being expired. Helium is not absorbed across the lung basement membrane, but some helium mixes with the residual volume and thus the concentration expired is lower than that which is inspired. Knowledge of the concentration of gas inspired and its volume allows the residual volume of the lung to be calculated and hence the total lung volume (vital capacity plus residual volume) to be derived. The gas mixture contains a small quantity of carbon monoxide and this crosses the basement membrane of the lung and is bound strongly to haemoglobin. If the concentration of carbon monoxide, which is inspired and expired, is measured, the quantity of carbon monoxide absorbed (as mL/min per mmHg) can be calculated; this is the transfer factor and depends on the size of the lung as well as on its efficiency in gas transfer. Correction for the alveolar volume allows the transfer coefficient (K$_{CO}$) to be assessed.

The transfer coefficient is reduced if there is pulmonary oedema, pulmonary fibrosis or ventilation perfusion mismatch, but it can also be increased if there is intrapulmonary haemorrhage as carbon monoxide will be bound to intrapulmonary haemoglobin and will appear to have transferred into the circulation. As only a single breath is used for this test there are many sources of potential error; certainly, if the breath is not held adequately or if inspiration is not to vital capacity the efficiency of the test will be impaired.

Exercise testing

Many patients with altered lung function are limited in their capacity to exercise. However, most lung function tests measure respiration at rest, and these tests correlate only moderately well with exercise tolerance. A major disadvantage of any test of lung function is that it cannot allow for limitations of exercise capacity caused by other factors such as cardiac failure or angina, previous cerebrovascular disease or musculoskeletal disorders. All of these may increase the work for a given amount of exercise.

Exercise testing can vary from the very simple to the extremely complex. This section describes currently available methods of testing in order of increasing complexity.

Clinical assessment

The patient may be able to quantify, in terms of years or of number of stops for a measured distance, how far he/she can walk before stopping. Alternatively, the number of steps or flights of stairs that the patient can climb before he/she needs to stop can be recorded. However, as most subjects have difficulty in quantifying distance, this limits the usefulness of these questions. In towns, the distance between lamp posts is usually 25 metres and this represents a measured distance which may be used in the assessment of exercise.
tolerance. The ability to climb the stairs to an out-patient clinic was for many years used by cardiothoracic surgeons as a measure of respiratory function; if a patient could easily ascend two flights of stairs then he would be able to withstand cardiothoracic surgery.

**Walking**

McGavin and his colleagues in Edinburgh introduced a timed walk as a measure of exercise tolerance. They asked patients to walk as fast as they could for 6 min (resting when necessary) and then measured the distance covered during the time. They found that this test correlated well with lung function and with the patients' symptoms, and that it gave a repeatable measure of exercise limitations. Several forms of these tests have now been tried, using a 12-min walk, a 2-min walk or the time to walk 100 metres.

**Treadmill exercise testing**

The testing of a patient on a treadmill, while walking either at a constant speed or with increasing speed, allows exercise ability to be quantified. If blood gases can be measured before and after the exercise, the degree of hypoxia caused by exercising can be assessed, which will provide an indication of the efficiency of the lungs for a given exercise load.

In the case of patients who have cardiac dysrhythmias or angina, exercise testing by means of the treadmill allows the exercise to be carried out with constant monitoring of the patient. This type of test has the obvious advantage that patients may be observed more closely than when they are undertaking an unsupervised walk up and down a hospital corridor.

**Physiological measurement**

The most complicated of all exercise tests comprises a full physiological assessment of respiration on exercise. In these tests, such factors as ventilation, oxygen consumption, oxygen saturation and carbon dioxide production can be measured to assess the physiological response to exercise. These tests are usually carried out by using an exercise cycle, and they provide a considerable amount of information concerning the exercise capacities of the subject. However, because such tests require a large amount of equipment and are expensive to perform, they are available in only a few centres. Such complex measurements of respiratory function are rarely indicated in the routine assessment of patients, and are much more part of research into respiratory disease and its effects than of an overall assessment which would be of use to the clinician.

The most useful assessment of exercise is that of the history combined with either the 6-min or the 2-min walk. This combination usually gives a good assessment of the patient's functional abilities.
Abnormalities of upper airway function

Introduction

Phase variation in airway resistance has been described in a previous section. During inspiration, the intrathoracic airway is held patent as the chest and lungs expand, but during expiration the lungs are in a state of collapse, resulting in external compression of the trachea. Therefore, in disorders of the trachea or bronchi, obstruction tends to be most marked during expiration, and this produces expiratory wheezing. In contrast, inspiration induces a negative pressure in the pharynx, larynx and extrathoracic trachea which leads to collapse of the airway in the absence of mechanisms to ensure patency. Patency during inspiration is ensured as follows: the pharynx is kept open by protrusion of the tongue resulting from action of the genioglossus, the pharyngeal circumferential muscle contracts similarly to prevent inward flopping of the pharyngeal wall and the vocal cords are abducted. In addition, the tracheal rings keep the trachea patent and prevent collapse. On the other hand, expiration leads to an increase in upper airway air pressure which tends to keep the extrathoracic airway patent.

Snoring and obstructive apnoea

During sleep there is a decrease in the tone of the genioglossus and the circumferential pharyngeal muscles which maintain upper airway patency. This allows the tongue to fall back and the pharynx to collapse inwards during inspiration, with partial air flow obstruction and inspiratory snoring. Such partial pharyngeal obstruction occurs most commonly when the person is supine as gravity itself causes the tongue to fall back. Snoring is therefore most common in the supine position, and can often be prevented by turning the person on their side; waking the person also increases respiratory drives and muscle tone, and hence helps to remove obstruction. Snoring may be aggravated by the use of sedatives and muscle relaxants and, of these agents, alcohol is the most common offender as it leads to sedation, reduction in respiratory drive, and acts as a muscle relaxant. Any lesion causing a partial blockage of the extrathoracic airway will tend to predispose to upper airway collapse and may thus lead to snoring.

A more complete obstruction to air flow occurs in obstructive sleep apnoea, where there are episodes of complete cessation of air flow resulting from collapse of the pharynx during inspiration. Once obstruction to air flow occurs in the awake person there is respiratory distress, and increased muscle tone ensures pharyngeal patency. In light sleep, the respiratory drives are partially reduced and airway obstruction tends to lead to arousal and waking; however, in rapid eye movement sleep, the respiratory drives are all reduced to a considerable extent and there is an additional reduction in muscle tone.

During rapid eye movement sleep, obstruction to the upper airway does not necessarily produce instant arousal and wakening. However, as the duration of air flow obstruction continues, hypoxia and hypercapnia will result, leading to an increase in pulmonary artery pressure and a parallel increase in systemic blood pressure. Inspiration against a closed or obstructed upper airway (the Müller manoeuvre), as occurs in obstructive sleep apnoea, leads to an increase in vagal activity which produces bradycardia. Vagal overactivity in the presence of hypoxia also may be associated with the development of cardiac dysrhythmias, and these may be both atrial and ventricular in origin and lead potentially to asystole and sudden death.
In spite of these effects, obstructive apnoea rarely leads to death. More commonly, after a period of upper airway collapse and apnoea with hypoxia, there is arousal with increased respiratory drives and the relief of obstruction. A patient with obstructive sleep apnoea will thus suffer the problems of both hypoxia and vagal overactivity combined with frequent wakening. Rapid eye movement sleep and even light sleep can become so fragmented that the patient will sleep extremely poorly (possibly less than 60 min per night) and will experience sleep deprivation, which in itself can lead to a reduction in respiratory drives and cause the episodes of obstruction to occur even more frequently. The patient will also suffer from daytime hypersomnolence. In turn, recurrent hypoxia leads to an increase in pulmonary artery pressure and pulmonary vascular resistance, which culminates in fixed pulmonary hypertension with cor pulmonale. If hypoxia is prolonged there will be an increase in erythropoietin production with a concomitant increase in red cell production and thus an increased red cell mass and polycythaemia. This picture of cor pulmonale, polycythaemia and severe hypoxia with cardiac dysrhythmia is seen only in patients with frequent and prolonged obstructive sleep apnoea.

The severity of the sleep apnoea syndrome depends both on the number of apnoeic attacks and on their duration. Obstructive sleep apnoea syndrome is said to be present only if there are more than 30 episodes of obstruction each of which lasts more than 10 seconds during 6 hours of sleep. Even this number of apnoeic attacks is unlikely to produce more than frequent wakening with tiredness and possibly daytime sleepiness. Many patients who demonstrate the more severe sequelae of obstructive apnoea show, by contrast, several hundred apnoeic attacks per night (severe hypoxia with haemoglobin oxygen saturations of less than 50% with each apnoeic attack longer than a minute in duration and terminated by wakening and hyperkinetic activity).

**Causes of upper airway obstruction**

- Deviated nasal septum.
- Postnasal space tumours.
- Abnormal soft palate.
- Tonsils.
- Macroglossia.
- Adenoids.
- Micrognathia.
- Obesity / narrowed pharynx.
- Epiglottis.
- Retropharyngeal mass.
- Short, thick neck.

**Nose**

In obligate nose breathers, such as a feeding baby, nasal obstruction may lead to severe respiratory embarrassment. In most people, nasal obstruction produces only partial upper airway problems as breathing through the mouth alone provides adequate compensation. However, a partial obstruction may lead to snoring and occasionally to sleep apnoea; thus snoring is common with upper respiratory tract infection and rhinitis, and obstructive sleep
Apnoea has been reported in patients with deviation of the nasal septum or polyps and can be produced with nasal packing.

**Mouth and pharynx**

Partial occlusion of the oropharynx during sleep has already been discussed. The enlarged tongue seen in acromegaly, Down’s syndrome, and occasionally in hypothyroidism, may also cause sleep apnoea as may shortening of the anteroposterior diameter of the oropharynx (which occurs with the bird-like face of the Pierre-Robin, Treacher Collins, Prader-Willi and Kearns-Sayre syndromes, and, occasionally, in patients with temporomandibular joint subluxation). This also predisposes to obstructive sleep apnoea. In these cases, lengthening of the lower jaw with bilateral osteotomy reduces or removes the obstruction and prevents obstructive apnoea.

Inflammation of the tonsils, adenoids and epiglottis may also lead to airway narrowing and obstruction, as can simple tonsillar and adenoidal hypertrophy. Patients with myxoedema, acromegaly and the mucopolysaccharidoses deposit myxoid material around the pharynx, and this circumferential narrowing of the airway also causes partial airway obstruction. Similarly, extremely obese patients deposit fat around the pharynx, and the consequent narrowing of the airway can be seen on computerized tomographic (CT) scanning of the neck. Retropharyngeal masses caused by tumour, enlarged lymph nodes or abscesses also reduce the pharyngeal size and may produce airway obstruction. Some patients have a very large uvula and soft palate with large mucosal folds which may close off the entrance to the pharynx and lead to air flow obstruction, snoring and obstructive apnoea. In these cases, removal of the uvula and trimming of the redundant soft palate (uvulopalatopharyngoplasty), will reduce obstruction and may cure sleep apnoea in 60-70% of the patients. The short fat neck may also be associated with upper airway obstruction as there is a reduction in the length of the pharynx from nasopharynx to larynx, and the lateral and posterior walls of the pharynx tend to bulge into the lumen. If obesity also develops and fat is deposited around the pharynx, these subjects are especially at risk of developing severe snoring and obstructive apnoea.

**The larynx**

The larynx is the narrowest point in the upper airway and fixed narrowing of the larynx leads to upper airway obstruction and stridor. Recurrent laryngeal nerve palsy also compromises the larynx, causing loss of laryngeal dilatation in inspiration, and predisposing to stridor and obstructive apnoea. Polychondritis (where the cartilage becomes infiltrated with inflammatory cells and destroyed by anticartilage antibody) destroys cartilage in both the larynx and trachea, and the resulting laryngeal stenosis may produce a floppy trachea which collapses during maximum inspiration.

**Trachea**

As noted in the introduction to this section, extrathoracic airway obstruction becomes worse in inspiration and characteristically causes stridor. In contrast, the intrathoracic airway is smallest during expiration, and narrowing typically produces wheezing. The trachea, passing as it does from the extrathoracic larynx down into the thoracic cavity, may show either or both of these abnormalities. Fixed tracheal stenosis, as occurs with an enlarged thyroid or
mediastinal mass pressing upon the trachea, leads to a reduction in both inspiratory and expiratory flow. Variable tracheal narrowing, which occurs with a floppy trachea following polychondritis or with a pedunculated tumour, will produce differing symptoms, depending on its size. There may be stridor from extrathoracic collapse during inspiration, or wheezing from intrathoracic obstruction; this may be confused with the wheezing of obstructive airway disease. Although post-tracheostomy scarring produces some fixed obstruction, the cartilage destruction associated with such a stoma allows variable tracheal collapse during inspiration and therefore produces signs compatible with both fixed and variable airway narrowing.

**The investigation of upper airway disease**

Plain X-rays of the neck, thorax and thoracic inlet allow the upper airway to be measured and should show the site of fixed airway narrowing. Tomography and CT scanning of the neck allow greater accuracy in identification of mass lesions and will also identify peripharyngeal deposits of fat. None of these techniques will necessarily allow a laryngeal site of obstruction to be identified. Examination of the upper airway by direct vision, by indirect or direct laryngoscopy and by bronchoscopy enable fixed areas of narrowing to be seen and a biopsy to be made, but a floppy trachea or a pharynx which collapses will not necessarily be identified.

Respiratory function tests allow both identification of the physiological nature of an upper airway obstruction and characterization according to whether the latter is fixed or variable, intrathoracic or extrathoracic. However, more precise identification is not possible. Occasionally, muscle weakness of chest wall stiffness may produce a similar flow-volume loop appearance to upper airway obstruction.

Although when taken individually, neither direct vision, radiology nor respiratory function tests will provide all the answers in the examination of a patient with upper airway disease, when taken together, the site, nature and severity of the lesion may usually be reasonably ascertained.

**Spirometry and the Empey Index**

Air flow is fat in the upper airway, and obstruction therefore limits the maximum possible flow. The peak expiratory flow rate (PEFR) may thus be reduced to a greater extent than the forced expiratory volume in one second (FEV₁). A fixed airway narrowing reduces expiratory flows in both the extrathoracic and intrathoracic large airways, whereas a variable airway narrowing reduces expiratory flow only in the intrathoracic airway. Therefore, measurements of peak expiratory flow rate and the FEV₁ are useful in the assessment of intrathoracic variable airway obstruction, and in both intrathoracic and extrathoracic fixed obstruction. The greater reduction in peak expiratory flow rate when compared to the forced expiratory volume in one second is made use of in the Empey Index (FEV₁ in mL; PEFR in L/min). If there is a significant fixed upper airway narrowing or intrathoracic variable airway narrowing there will be a FEV₁/PEFR ratio of greater than 10. However, the test will be useless in identifying extrathoracic variable airway disease, for which examination of the inspiratory flow pattern is necessary. In spite of its limitations, the Empey Index is easy to measure and can be of considerable use in following the progress of a patient with upper airway disease.
Flow-volume loop

It is possible to display flow and volume recorded by a pneumotachograph or obtained by differentiation of the volume recording from a spirometer, in order to produce synchronous flow and volume measurements which can be used to examine the air flow through the upper airway. Flow-volume loops which display only the expiratory portion of a maximum effort are of limited use as they do not provide information on airway collapse during inspiration. Both the shape of the trace and any irregularity of flow are useful. If there is a variable airway narrowing, as occurs with a collapsible pharynx, the oscillation of both inspiratory and expiratory flows gives a sawtooth appearance on the trace. Such a sawtooth pattern is seen in the figure and is from a patient with obstructive sleep apnoea. In this latter condition, the variable collapse of the upper airway results in such a sawtooth pattern in 60% of subjects, and this is superimposed on the flow-volume loop appearance of variable extrathoracic obstruction. The flow-volume loop appearance in fixed intrathoracic and extrathoracic obstruction, and in variable intrathoracic and extrathoracic obstruction, is shown in the figure.

Fixed extrathoracic obstruction

Fixed extrathoracic obstruction is found in laryngeal stenosis or pharyngeal stenosis caused by a mass lesion. There is a fixed obstruction of air flow which occurs in both inspiration and expiration, and curves for maximum inspiration and expiration are therefore reduced. As a result, the flow-volume loop has a flattened appearance and the Empey Index is raised. This appearance is partially duplicated if there is severe muscle weakness, such as occurs in muscular dystrophy, myasthenia and polyneuritis, although in these instances inspiratory flows usually exceed those achieved in expiration and the resultant curves are therefore asymmetrical.

Fixed intrathoracic obstruction

Fixed intrathoracic obstruction may be caused by tracheal stenosis but is more commonly a result of extrinsic compression of the trachea from an intrathoracic mass. In such circumstances, the flow-volume loop shows a pattern which is similar to that which is found in fixed extrathoracic obstruction and the Empey Index is again raised. However, if only one main bronchus is affected the pattern is normal. It therefore follows that, if there is a flattening of the flow-volume loop, the obstruction must be in the upper airway above the carina.

Variable extrathoracic obstruction

The most common cause of variable extrathoracic obstruction is pharyngeal collapse. Variable obstruction also occurs if the trachea collapses as the result of tracheomalacia; this may follow a tracheostomy where the tracheal wall has been permanently scarred, or in polychondritis where the tracheal cartilages are absent or floppy. Occasionally, tracheal or laryngeal obstruction may be the result of a pedunculated tumour, and flow will be reduced over only part of the respiratory cycle. In this group of patients, the Empey Index is normal but the flow-volume loop shows a cut-off of the inspiratory limb with reduced maximum inspiratory flow as the trachea collapses.
This pattern may also be seen in inspiratory muscle weakness and bilateral diaphragmatic paralysis. It is also reproduced in those subjects who have a fixed chest wall with limited inspiratory excursions, but who are able to retain expiratory flows by diaphragmatic movement. Such fixation of the chest wall should be obvious and not difficult to differentiate from extrathoracic variable airway obstruction. However, muscle weakness may be much less apparent unless maximum inspiratory and expiratory pressures are measured.

**Intrathoracic variable obstruction**

Intrathoracic variable obstruction tends to obstruct air flow during expiration, but inspiration is unaffected since the intrathoracic contents, including the major airways, are expanded as the thorax enlarges. A reduction of expiratory flow results with a normal inspiratory pattern. The flow-volume loop is again characteristic and this, in conjunction with the Empey Index (see above), should allow definition of the site of obstruction and its degree of variability.