Lung disease

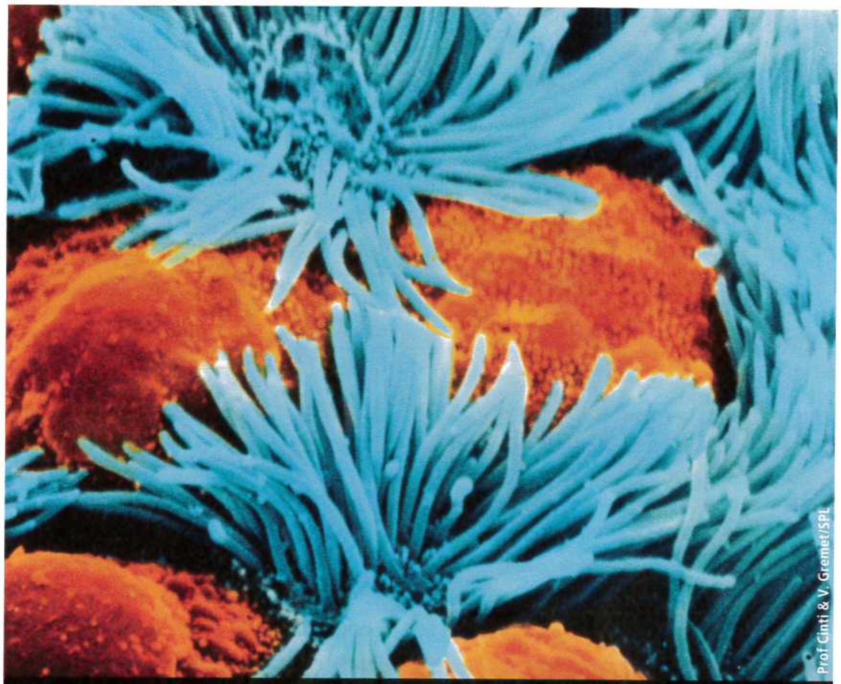
Sarah Herrick

Breathing is essential to keep us alive, but problems can occur when diseases such as asthma and emphysema damage our lungs

Lung disease can lead to impaired lung function. It is important for us to understand lung disease so that we can improve treatments for debilitating conditions such as asthma and emphysema.

The lungs are responsible for gas exchange. They are where oxygen enters the body and carbon dioxide is removed. When we breathe in, air enters our airways through our mouth and nose. These passageways warm, filter and humidify the air, which passes into the lower airway consisting of the trachea, bronchi, bronchioles and alveoli.

The trachea is a tube supported by cartilage that spans the length of the throat and branches into right and left bronchi. Each bronchus branches into smaller tubes known as bronchioles. Each bronchiole ends in a cluster of air-filled sacs called the alveoli (see Figure 1). As the airways get narrower, the amount of cartilage around each tube decreases and is replaced by smooth muscle. Tension in the smooth muscle can alter the diameter of the bronchioles and therefore alter the resistance to airflow. Relaxation of the muscle results in an increase in airway diameter (bronchodilation), whereas contraction causes airway narrowing (bronchoconstriction).



Coloured scanning electron micrograph of the bronchial epithelial lining of the lung. The cilia (blue) and goblet cells (orange) help to keep the lungs free from disease (×7000)

The alveoli are the sites of gas exchange. Each adult human lung contains around 150 million alveoli — equivalent to the surface area of a tennis court. Gas exchange occurs by diffusion of gases between air in the alveolar sac and blood in capillaries surrounding the alveoli. It is an extremely efficient system, as the distance between the blood in the capillaries and air

Key words

Lung
Gas exchange
Asthma
Emphysema
Disease

Figure 1 Simplified airway branching pattern of the left lung

in the alveolus is very small (see Figure 2). Gases that are dissolved in the blood are pumped around the body through the circulatory system.

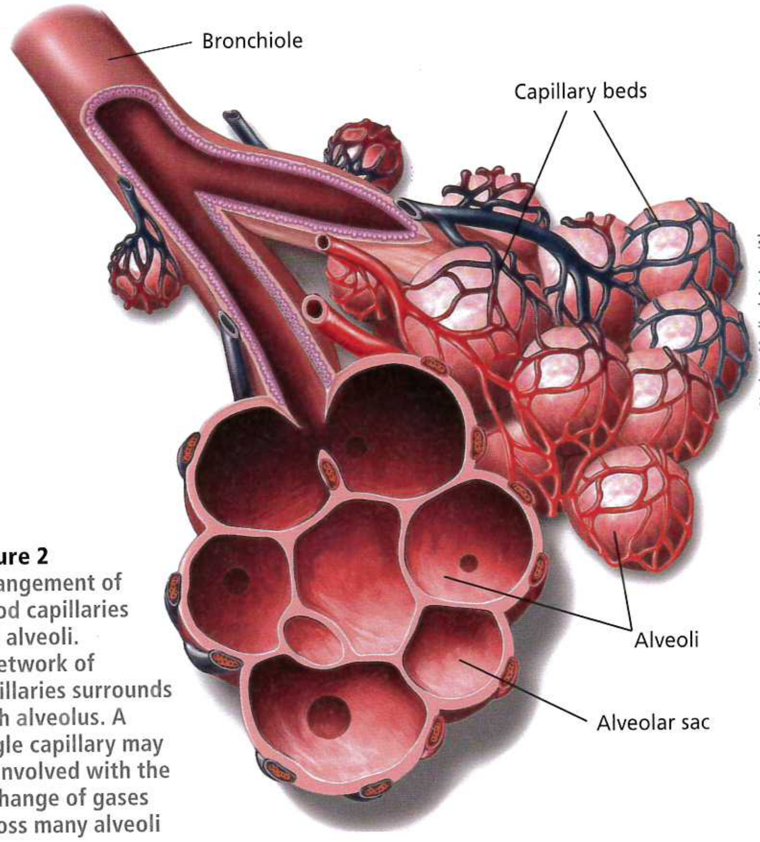


Figure 2 Arrangement of blood capillaries and alveoli. A network of capillaries surrounds each alveolus. A single capillary may be involved with the exchange of gases across many alveoli

Mechanics of breathing

When we inhale, the **intercostal muscles** contract to pull the rib cage up and out, and the **diaphragm** contracts and flattens. This increases the volume of the chest cavity and causes the lungs to expand. The pressure in the lungs is reduced and so air is drawn in. When we exhale, our intercostal muscles relax, causing our rib cage to drop and our diaphragm returns to its usual dome-like shape. This squeezes air out. Even in this relaxed state, less than one-tenth of the air in the lungs leaves the body to be replaced by the same amount of fresh air breathed in. This is known as the resting tidal volume and may be measured using a spirometer (see Box 1).

Our demand for oxygen changes — for example, when we exercise. One way we cope with this is through changes in breathing volume and rate. The normal breathing rate for an adult at rest is 13–17 breaths per minute, with each inhalation containing about 500 cm^3 of air. During vigorous exercise, up to 80 breaths per minute may be taken, with each inhalation

Box 1 Spirometry

Spirometry is the most common way of measuring how we breathe. It measures lung function and monitors the volume and flow of air that can be breathed in and breathed out.

Spirometry is an important tool for helping to diagnose lung conditions such as asthma, pulmonary fibrosis, cystic fibrosis, and emphysema. The test is performed with a spirometer. Measurements of lung function are displayed on graphs called spirograms. A number of measurements can be recorded (see Figure A):

- Tidal volume (TV) is the amount of air that you inhale and exhale at each breath in a resting relaxed state (a normal healthy reading is around 0.5 dm^3).
- Expiratory reserve volume (ERV) is the amount of air that you can voluntarily exhale after you have completed a normal relaxed phase of breathing (a normal healthy reading is around 1 dm^3).
- Inspiratory reserve volume (IRV) is the amount of air that you can inhale over and above the tidal volume (a normal healthy reading is around 3 dm^3).
- Vital capacity (VC) is the maximum amount of air you can forcibly expel from your lungs after a maximum inhalation. It is equal to IRV + TV + ERV. A normal adult has a VC between 3 and 5 dm^3. A human's VC varies with age, sex, height, body mass and ethnicity.

For diagnosis, patients are asked to breathe normally in a relaxed state. They are then asked to take the deepest inhalation they can, then exhale into the sensor as hard as possible and for as long as possible (see Figure B). Measurements of the volumes of air expelled by the patient are compared with average values from healthy individuals.

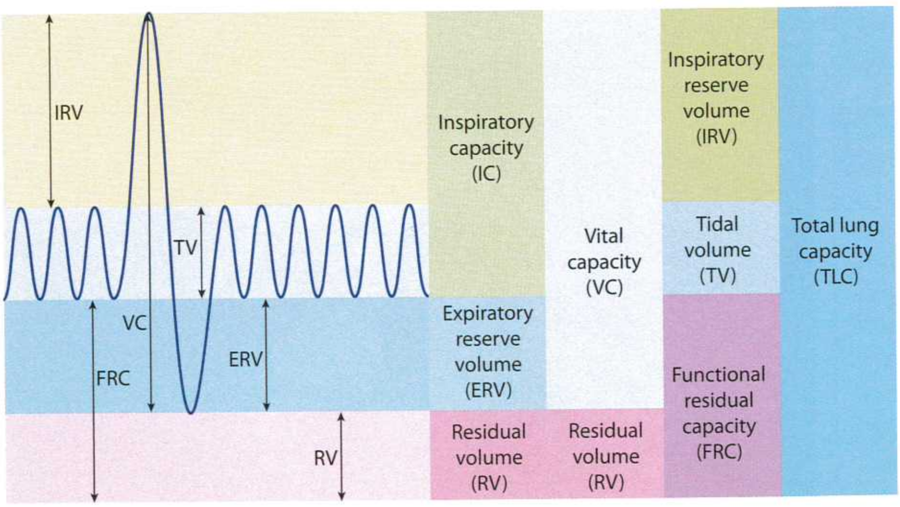


Figure A Spirometry graph

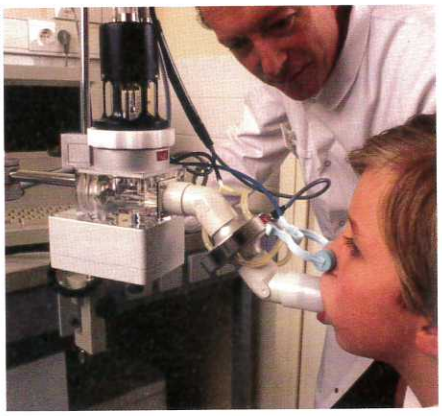


Figure B Using a spirometer

containing up to 4 dm^3 of air (an increase of almost ten times).

Diseases of the airway

Our airway is lined with a variety of specialised cells with different functions. The lining of the trachea and bronchi consists of a surface layer of **epithelial cells** covered in cilia, on top of a connective tissue layer containing mucus glands. **Goblet cells** in the epithelial lining discharge mucus, which traps debris and microorganisms. The cilia on the surface of the epithelial cells sweep the mucus towards the throat, where it is swallowed. Most particles are removed by this system, called the mucus escalator. However, they can also be engulfed and cleared by inflammatory cells such as **macrophages** (see BIOLOGICAL SCIENCES REVIEW Vol. 25, No. 4, pp. 2–6).

Some lung diseases are caused by external factors that are inhaled, such as allergens (asthma), bacteria (pneumonia) and asbestos (mesothelioma) (see Table 1). Such diseases may develop in different parts of the respiratory system. For example, hay fever affects the upper nasal airway and is caused by breathing in pollen, whereas pleurisy is inflamation of the outer lining of the lungs and is usually caused by a virus.

Diseases often cause damage that changes the structure of the airway and affects lung function. It is important to understand how external factors disrupt lung structure. A better understanding of these processes may lead to new ways of treating diseases and preventing them from becoming life threatening.

Asthma and emphysema are two common, **chronic** airway disorders where affected people show a reduction in lung function and often have difficulty breathing. However, there are distinct differences between the two conditions in terms of what causes them, how each develops, and which part of the lung is affected.

Asthma

Asthma affects over 300 million people worldwide. Most cases involve an allergic response in which the bronchi become narrowed, causing shortness of breath, wheezing, coughing and tightness across the chest. Asthma usually begins in childhood but can develop at any age.

Triggers

Airborne substances that can trigger an asthma attack include house dust mites, mould, pollen and cat and dog fur. These substances are harmless to most people but in others they irritate the delicate epithelial lining of the airway and stimulate an immune response and inflammation. This is followed by tissue repair. The repeated cycle of damage and repair leads to changes in the structure of the bronchiole wall and is known as airway remodelling. This includes damage to the surface of epithelial cells, a build-up of scar tissue, increased mucus production and smooth muscle expansion (see Figure 3).

During an asthma attack inflammatory substances such as histamine and prostaglandins are released. These stimulate the muscles lining the bronchi to contract uncontrollably. This leads to difficulty in breathing and hence low concentrations of oxygen in the blood. Over time, the narrowing of the airway may become irreversible as scar tissue builds up and excess mucus accumulates. Asthma attacks vary in severity from mild breathlessness to respiratory failure and death.

Diagnosis and treatment

A peak flow meter can be used to measure the airflow through the bronchi and thus the degree of obstruction in the airways. People may also have skin-prick tests to determine whether they have any allergies. There is no cure for asthma, but it can usually be managed with drugs that either relax the muscles around the airway (bronchodilators) or reduce the inflammation (anti-inflammatories) or both.

Table 1 Lung diseases and their causes

Lung condition	Possible cause	Typical location	General features
Mesothelioma	Asbestos	Lining of the lung	Malignant tumour
Asthma	Allergens	Bronchi/bronchioles	Narrowing of airway/ inflammation/excess mucus
Emphysema	Cigarette smoke	Alveolar walls	Fewer, larger air spaces
Pneumonia	Bacteria and viruses	Small bronchioles and alveoli	Fluid-filled air spaces
Cystic fibrosis	Genetic inheritance	Bronchi	Overproduction of mucus
Hay fever	Grass pollen	Nasal passages	Allergic response with nasal irritation/ excess secretion
Pleurisy	Viruses	Lining of the lung	Inflammatioin of the pleural layers

Terms explained

Chronic Long term and persistent.

Diaphragm The muscle that separates the thoracic and abdominal cavities.

Epithelial cells Cells lining the lumen of the airways.

Goblet cells Mucus-producing cells found in the epithelial layer.

Intercostal muscles Muscles between the ribs that help move the rib cage up and down during breathing.

Macrophage A type of white blood cell that can engulf foreign particles and produce a multitude of growth factors.

Neutrophil A type of white blood cell that clears cell debris and is one of the first cells to arrive at a site of damage.

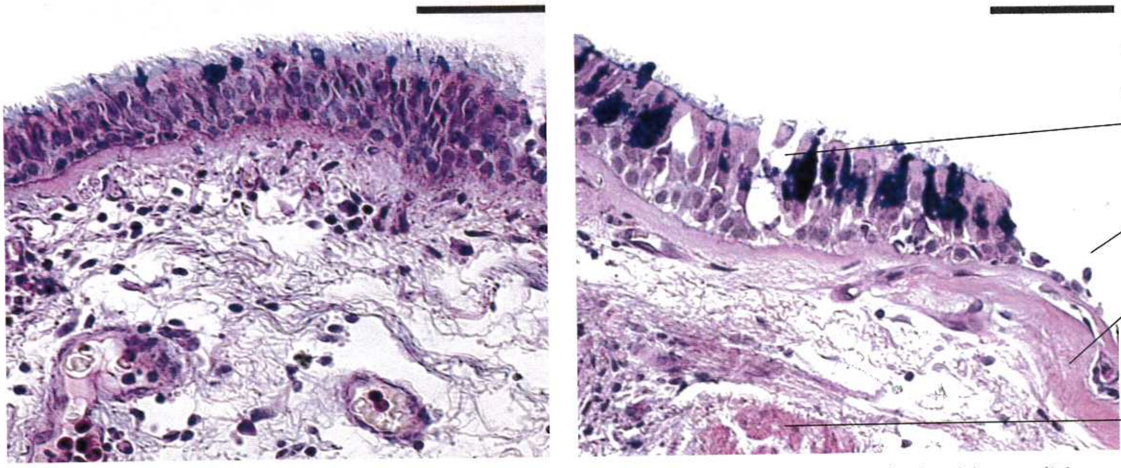


Figure 3 Light microscope images of a histological section of an airway wall showing the healthy condition on the left and the asthmatic condition on the right. In asthma, surface epithelial cells are damaged and there is an increase in the number of goblet cells (dark purple) releasing mucus. Scale bar = 100 micrometres

Emphysema

Emphysema is another chronic inflammatory disease in which the lungs become increasingly damaged over time. People with emphysema experience shortness of breath and find it hard to exercise.

Causes

Emphysema is usually a direct result of cigarette smoking (see Figure 4), although pollution and infections may make it worse. Tobacco smoke and other pollutants cause damage and inflammation in the bronchioles, leading to constriction of the smooth muscle. Nicotine in tobacco smoke reduces the efficiency of the mucus escalator, so mucus is not easily cleared. Mucus production is also increased and this can itself lead to chronic bronchitis (inflammation of the epithelium). Emphysema and bronchitis together form part of a condition known as chronic obstructive pulmonary disease.

Inflammation associated with emphysema causes damage to the alveolar surface. Inflammatory cells such as **neutrophils** move into the lung tissue and produce damaging enzymes and harmful by-products. The delicate alveolar walls are disrupted and their air sacs merge to form fewer, larger spaces and hence less surface area for gas exchange. As the lung tries to repair itself, scar tissue forms in the alveolar wall, increasing the distance gases must diffuse to reach the blood in the surrounding capillaries. Over time, the lungs become less elastic and so are less efficient at gas exchange.

In the early stages of emphysema there are no obvious symptoms, but as the disease progresses and the lungs acquire more damage, sufferers experience increasing shortness of breath, wheezing and a chronic cough. Eventually, the concentration of oxygen in the blood starts to fall and, in some cases, patients start to turn blue owing to a lack of oxygen in their blood.

Figure 4 Section through a lung from a patient with emphysema. Note the black deposits in the air spaces from the tar in the cigarette smoke that has been inhaled

Diagnosis and treatment

Doctors can make a diagnosis based on these obvious symptoms, together with a variety of tests. Analysis of a blood sample from an artery informs the doctor of the concentrations of oxygen and carbon dioxide in the blood. Chest X-rays are taken to exclude the possibility of other diseases and to determine how large an area of lung is affected. Spirometry tests reveal the extent of reduced lung function (see Box 1).

Once damage to the lungs has occurred, there is no treatment that can reverse it. However, if patients

Further reading

Charities with information on lung disease:

British Lung Foundation: **www.blf.org.uk**

Asthma UK: **www.asthma.org.uk**

give up smoking they can greatly reduce the rate at which the lungs deteriorate further. Badly affected patients may need a continuous supply of oxygen for breathing.

Personalised treatment

Both asthma and emphysema are complex diseases involving multiple factors and different pathways of progression and rates of deterioration of lung function. It is now thought that each of these conditions may actually be a combination of a number of diseases, with differing causes and mechanisms.

Current research is trying to tease apart all these multiple diseases. Large groups of patients, each with well-known histories of their diseases and symptoms, are being studied using advanced technologies. The aim is to measure individual differences in the genetic make-up, gene expression and cell biochemistry of these patients. Drug treatment can then be tailored for particular individuals or groups of patients depending on the particular characteristics of their diseases.

Things to do

- Blow up a round balloon and give yourself a score of 1–5 according to how much effort it took (1 = easy, 5 = hard).
- Now blow up a long thin balloon and again give an effort score of 1–5. This represents the airway narrowing with asthma.
- Now surround the deflated round balloon with sellotape (representing scar tissue and airway wall remodelling) and try blowing it up again, giving a new effort score.

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Key points

- The respiratory system begins with the trachea, which divides into two bronchi. These continue to form a series of branches that become narrower and finally terminate in clusters of alveoli.
- Alveoli in the lower airway have thin walls that allow the exchange of gases between the respiratory system and the circulatory system.
- Inhalation of air involves contraction of the diaphragm and a rise of the rib cage; exhalation depends on the relaxation of the diaphragm and the fall of the rib cage.
- Different lung diseases may affect different parts of the airway system.
- Lung diseases may be caused by inhalation of foreign particles, pathogens or allergens.
- Most lung diseases affect the structure of the airways and hence the ability to breathe.