Measurement of respiratory function: an update on gas exchange

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Abstract

Gas exchange is the main function of the lungs. Oxygen and carbon dioxide diffuse along their partial pressure gradient across the alveolar-capillary membrane. Lungs have a large reserve for gas exchange. Alveolar ventilation and pulmonary circulation are closely matched to provide efficient gas exchange in the lungs. Hypoxaemia often results from mismatch in ventilation–perfusion. Gas exchange can be impaired in various disease states. Measurement of the diffusing capacity for carbon monoxide (DLCO) provides estimation of the gas exchange function. A low DLCO indicates an impairment of oxygen transfer across the alveolar-capillary membrane. Anaesthesia and surgery adversely affect pulmonary function, many of which adverse effects can be prevented.

Keywords Alveolar-capillary membrane; carbon dioxide; carbon monoxide; diffusion; diffusing capacity; gas exchange; general anaesthesia; oxygen; ventilation–perfusion matching

Royal College of Anaesthetists CPD matrix: 1A01

Learning objectives

After reading this article you should understand the:
- physics of pulmonary gas exchange, including the factors affecting the rate of diffusion of gases
- functional histology of respiratory membrane and factors affecting its function
- diffusing capacity, how it is measured, and its clinical implications
- normal and abnormal distribution of ventilation and pulmonary circulation, and the zones of lung
- effects of anaesthesia on the respiratory function

Precise physiological processes help to achieve the efficient gas exchange which is the primary function of the lungs. Gas exchange also occurs in the body tissues at the cellular level where O_2 and CO_2 diffuse into and out of the mitochondria. Our bodies maintain normal levels of O_2 and CO_2 through chemical and neural mechanisms of control of breathing. The level of CO_2 plays an important part in influencing the pH of the blood. Metabolic activity of the body determines the work load imposed upon the lungs. The earliest signs of respiratory impairment are noticed during exercise when respiratory reserves are used. This review article discusses the physiological processes involved in the gas exchange, including the physics of gas exchange, the alveolar-capillary membrane, the diffusing capacity, the pulmonary ventilation, the pulmonary circulation, the ventilation/perfusion and respiratory changes occurring with anaesthesia.

Physics of gas exchange

Pulmonary gas exchange is a two-way *diffusion* process where oxygen (O_2) and carbon dioxide (CO_2) diffuse in opposite directions across the alveolar-capillary membrane driven by the gradients of their partial pressures. Being highly soluble in lipids, the physiologically important gases diffuse easily through the cell membranes. Diffusion of gas through the water in the alveolar lining is a limiting factor for the movement of gases. As such, diffusion of gases through the respiratory membrane and other tissues is almost equal to the diffusion of gases in water.

Factors affecting the rate of diffusion of gases

Some facts about the gas exchange are briefly listed in Box 1. According to Fick's law of diffusion, the rate of diffusion of gases[1] in the fluids depends on various factors (Box 2) which are expressed in the formula:

$$D \propto \frac{P \times A \times S}{d\sqrt{MW}}$$

The **partial pressure difference** (P) between the alveoli and the pulmonary capillary blood is a measure of the net tendency for

Some gas facts for the gas exchange

Dalton's law states that the partial pressure of a gas in a gas mixture is the pressure that this gas would exert if it alone occupied the total volume of the mixture. In the alveoli:

$$PT = PN_2 + PO_2 + PCO_2 + PH_2O$$

Gases flow from high pressure to low pressure areas and also along their molar concentration

Graham's law states that the rate of diffusion of a gas is inversely proportional to the square root of its molecular weight

Henry's law of solubility states that the amount of gas (O_2) physically dissolved in the water is proportional to its partial pressure in the gas phase

Solubility and dissolved volumes of O_2 and CO_2 in alveoli

$$O_2\text{—}0.225\ \text{ml/litre/kPaO}_2\text{—}0.225 \times 13.33 = 3\ \text{ml}$$

$$CO_2\text{—}5.1\ \text{ml/litre/kPaCO}_2\text{—}5.1 \times 5.33 = 27.2\ \text{ml}$$

Fick's law describes the rate of diffusion of O_2 and CO_2 from lungs to the pulmonary blood

Box 1

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Factors affecting the rate of diffusion of gas in a fluid

- Partial pressure gradient of the gas
- Surface area available
- Distance through which the gas must diffuse (thickness of alveolar-capillary membrane)
- Solubility of the gas in the fluid
- Molecular weight of the gas
- Temperature of the fluid — normally constant in the body

Box 2

the gas molecules to move across the membrane. For a given pressure difference, carbon dioxide diffuses about 20 times as rapidly as oxygen.

The **surface area of the respiratory membrane** (A) available for gas exchange may be reduced in certain conditions e.g. pneumonectomy and emphysema. When the total surface area is decreased to about one-third to one-quarter of normal, gas exchange is significantly reduced even under resting conditions. While during sports and strenuous exercise, even the slightest decrease in surface area of the lungs can seriously decrease the gas exchange.

The rate of diffusion through the membrane is inversely proportional to the **thickness of the membrane** (d). When thickness of the respiratory membrane increases to more than two to three times the normal (e.g. in pulmonary oedema and fibrosis), it can significantly interfere with the normal exchange of gases.

The **solubility** (S) and **molecular weight** (MW), two characteristics of a gas itself, determine the **diffusion coefficient of the gas**. The rate of diffusion of a gas at a given partial pressure is proportional to its diffusion coefficient ($S/\sqrt{MW}$).[1] It would be difficult for the larger molecules to pass easily through the cell membranes. Depending upon the molecular weights (O_2 is 32 and CO_2 is 44) one expects the diffusion of CO_2 to be slower than that of O_2. Actually CO_2 diffuses 20 times faster than O_2 and O_2 twice as rapidly as nitrogen. This is because CO_2 is 30 times more soluble in water than O_2 and taking the square root of these molecular weights reduces the difference between the gases. Taking the diffusion coefficient of oxygen as 1, the relative diffusion coefficients of other gases are: carbon dioxide 20.3; carbon monoxide 0.81; nitrogen 0.53 and helium 0.95.[1]

Alveolar-capillary membrane

The gas exchange area is about the size of a tennis court packed into the two lungs. It is estimated that there are about 300×10^6 alveoli. The unit of gas exchange in the lungs is called the *acinus*. It consists of a group of alveoli with its respiratory bronchiole surrounded by pulmonary capillaries (Figure 1).[2] The average diameter of an alveolus is 0.1–0.2 mm^3.

The alveoli are lined with two types of epithelial cells: type I and type II pneumocytes. The flat alveolar epithelial cells (type I pneumocytes) are the site of gas exchange, whereas type II pneumocytes are linked with surfactant production. The distance between the alveolar epithelium and the capillary basement membrane is 0.4 μm only.[3] The mean diameter of the pulmonary capillaries is about 7 μm. This means that the red cells travel in very close contact with the alveolar-capillary membrane (Figure 2),[2] thus facilitating the diffusion of O_2 and CO_2.

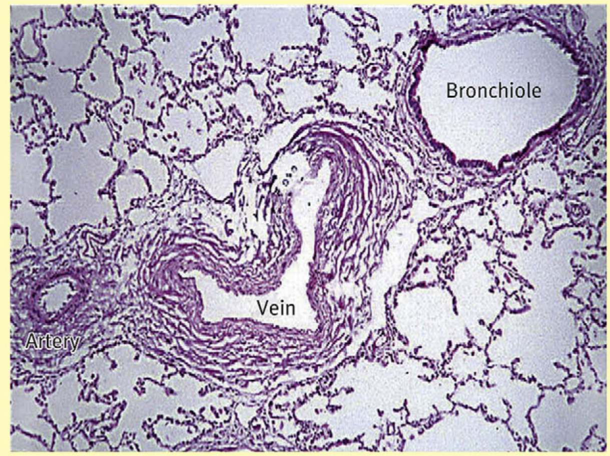

Figure 1 Microscopic view of normal lung tissue. Courtesy Dr A Hussain, Royal Victoria Hospital, Newcastle upon Tyne (UK).

Gas exchange equilibrium (i.e. full saturation) is reached normally in 25–30% of the capillary distance (~one-third of the transit time) in the pulmonary capillary bed.[4,5] Little or no further gas transfer occurs in the remaining pulmonary capillary transit. During exercise, a longer capillary distance is required before equilibrium is reached but the transit time remains much the same as blood passes faster through the capillary and the lower mixed venous PO_2 speeds up the diffusion.[6]

Several factors may affect the respiratory membrane (Box 3).[2] The rate of diffusion of gases is reduced when the respiratory membrane is thickened. A thickened alveolar-capillary membrane (e.g. in pulmonary fibrosis and vascular diseases) will prolong the equilibration process and may cause hypoxaemia. Patients suffering from these diseases require the whole capillary distance (and whole pulmonary capillary circulation time) to oxygenate the blood.

Schematic representation of alveolar capillary membrane

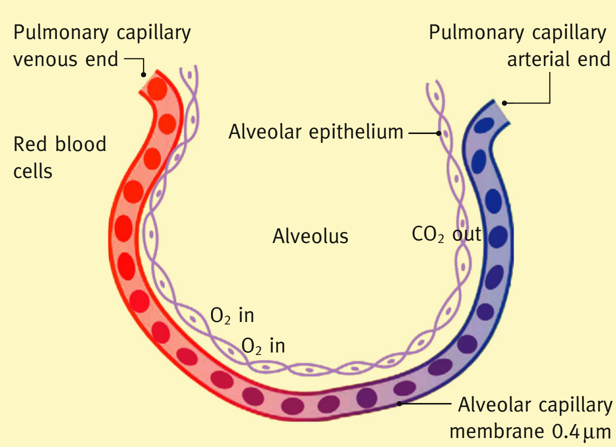

Figure 2

