



Advanced Physiology

Lec.5 Respiratory system

By: Pro D
muneef Saab Ahmed

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Introduction

The respiratory system allows oxygen delivery to, and carbon dioxide removal from, the bloodstream, which are mediated via the conducting airways and a gas-exchange region. The exchange of gases is termed respiration.

Functional components of the respiratory system

1-The pump that drives ventilation: chest wall and pleura; respiratory muscles (intercostals and diaphragm). These can be supplemented by the accessory muscles of respiration (sternomastoids, scaleni, pectorals, latissimus dorsi) in situations where the work of breathing is increased. Inspiration is an active process, being brought about by negative intra-pleural pressure generated by contraction and descent of the diaphragm and rib cage elevation by the intercostal muscles. The contraction of the diaphragm expands the chest wall laterally (bucket handle effect) and antero-posteriorly (pump handle effect). The phasic action of the intercostal muscles helps in stabilisation of the chest wall. Expiration is mainly passive and dependent on the elastic recoil of the lungs and chest wall. Active expiration occurs during exercise and in hyperventilation states and primarily involves the anterior abdominal wall musculature, assisted by the internal intercostal muscles.

2- The distribution of ventilation: upper respiratory tract, conducting airways, respiratory bronchioles. Apart from air conduction, these air passages are involved in the humidification and warming of inspired air.

3- Perfusion: pulmonary arteries and veins, capillaries.

4- Bronchial clearance: muco-ciliary escalator; macrophages.

5- Alveolar clearance and defence: alveolar macrophages; pulmonary lymphatics; humoral mediators. The process of gas exchange itself involves:

Ventilation of the lungs;

Capillary perfusion of ventilated alveoli;

Diffusion across the alveolar-capillary membrane

The upper respiratory tract

This comprises:

1- The nose, which serves the following functions:

Air conduction.

Particle and micro-organism clearance by the muco-ciliary mechanism, which comprises the pseudostratified ciliated epithelium, mucous blanket and the mucus-producing glands. The inspired air is thereby cleaned and filtered. In general, particle diameter requires to be greater than 10 μ m to allow nasal filtration.

Humidification and warming of inspired air by a counter-current heat and fluid exchange mechanism.

Perception of smell, via the olfactory neuroepithelial receptors.

Contributes to more than 50% of total airway resistance normally.

2- The pharynx, which is involved in swallowing, while simultaneously preventing aspiration of food into the lungs.

3- The larynx, which is involved with:

The production of speech, which comprises the three components of phonation, resonance and articulation.

Providing a sphincter for protection of the lower airway from soiling, especially during swallowing and vomiting.

Acting as a sphincter in cough and expiration.

Regulating airflow in and out of the lungs. When open, ventilation of the lungs is allowed.

The **Valsalva manoeuvre**, of forced expiration against a closed glottis, which is involved in the control of venous return and also facilitates defaecation.

Providing sensory input for respiratory control.

The paranasal sinuses are lined by ciliated stratified or pseudostratified columnar epithelium. They may subserve the following functions:

Humidification and warming of inspired air;

Regulation of intra-nasal pressure;

Provision of resonance to the voice;

Increase in the surface area of the olfactory mechanism;

Lessening the density and weight of the skull;

Nasal function testing

This can be carried out by:

1- Airflow measurements

Rhinomanometry: simultaneous trans-nasal pressure and airflow recording; which can be anterior, posterior or post-nasal; Peak nasal airflow; Acoustic rhinometry; Radiological imaging to assess the cross-sectional area of the nasal passages (computed tomography or magnetic resonance imaging).

2- Ciliary function testing: saccharin taste test, which measures the time taken to taste saccharin in the back of the throat after application to the anterior tip of the inferior nasal turbinate. A time greater than 30 minutes is abnormal. Ciliated epithelium can be obtained by nasal brush biopsy of the inferior nasal turbinate and the sample is processed at 37 °C to determine ciliary beat frequency, and to assess the ciliary beat pattern by slow motion analysis. Ciliary ultrastructure can be assessed by transmission electron microscopy.

3- Tests of olfaction using smell bottles.

Functional anatomy of the lower respiratory tract (Weibel)

The tracheo-bronchial tree can be described as a symmetrical dichotomous branching system of airways, comprising around 23 generations of airway from the trachea to the alveolar sacs. It comprises:

1- Trachea: generation 0. This is 25 cm long in the adult and supported by 15–20 horseshoe-shaped cartilaginous rings that are joined posteriorly by smooth muscle.

2- Main, lobar and segmental bronchi: generations 1–4. The major site of airways resistance to gas flow is at the level of the 3rd and 4th generation airways, contributing 60%–70% of total airways resistance.

3- Small bronchi: generations 5–11. Bronchioles: generations 12–14. There is no cartilage in the wall at this level, and the air passages are held open not by structural rigidity but by elastic recoil.

4- Respiratory bronchioles: generations 15–18.

5- Alveolar ducts: generations 19–22.

6- Alveolar sacs: generation 23. The 23rd generation airways possess a total

cross-sectional airway diameter much greater than that of the trachea. Airway calibre is determined by the coupling of airway wall elasticity and airway transmural pressure. The topological unit of the lung is the bronchopulmonary segment, which is supplied by a principal branch of a lobar bronchus and its accompanying pulmonary artery.

Features of the pulmonary acinus (or terminal respiratory unit)

- 1- The functional gas exchanging unit of the lung.
- 2- The zone supplied by a first order respiratory bronchiole.
- 3- Includes the respiratory bronchioles, alveolar ducts and alveolar sacs distal to a single terminal bronchiole, typically representing generations 15–23.
- 4- A human lung contains between 30 000 and 50 000 acini, each with a diameter of about 3.5 mm and containing about 10 000 alveoli.
- 5- This provides a total gas volume of 2500 ml and a surface area of between 50–80 square metres, through which gas exchange by diffusion can occur.
- 6- The acini are connected by channels in the alveolar walls known as pores of Kohn, which act as portals for collateral ventilation and the transit of macrophages.

Respiratory epithelium

The **functions of respiratory epithelium** include:

Humidification of inspired air;
Chemical barrier and particle clearance;
Defence against infection.

Respiratory (bronchial) epithelium consists of the following cell types:

- 1- Pseudostratified columnar ciliated epithelial cells, with 200–300 cilia per cell.
- 2- Mucus-secreting (goblet) cells.
- 3- Basal cells, which anchor the goblet and ciliated cells to the extracellular matrix.
- 4- Mast cells, which secrete histamine, lysosomal enzymes, leukotrienes, plateletactivating factor, neutrophil and eosinophil chemotactic factors and serotonin.
- 5- Non-ciliated bronchiolar epithelial (Clara) cells, which are specialised secretory cells in the terminal bronchioles. These cells synthesise, store, and secrete specialised lipids, proteins and glycoproteins.
- 6- APUD (amine precursor uptake, decarboxylase) cells, which have a high content of amine and peptide hormones including serotonin, dopamine, noradrenaline and vasoactive intestinal peptide.
- 7- Dense-core granulated cells (Kulschitzky cells)

Classification of alveolar cell types

Capillary endothelial cells with loose junctions.

Alveolar epithelial cells:

Type I: squamous lining cells, which comprise 90%–95% of the alveolar surface.

Type II: secretory cells: synthesise, secrete and store surfactant; cuboidal; microvilli; osmophilic inclusion bodies.

Alveolar macrophages, which are responsible for the phagocytosis of particles, viruses and bacteria.

Neutrophils.

Pulmonary defence mechanisms

These can be categorised as:

Mechanical

Filtration in the upper airways, especially the nose.

Humidification of the inspired air.

Epiglottic function.

A competent larynx allowing an effective cough reflex.

Ciliary action of respiratory epithelial cells, which allows upward clearance of mucus from the tracheo-bronchial tree – the muco-ciliary escalator. This characterises epithelial cells to the 17th generation of airways. There are over 200 cilia per cell.

Mucus blanket. Mucus is a mixture of water, electrolytes and macromolecules (lipids, mucins and enzymes) secreted by the goblet cells and mucosal glands.

Surfactant preventing alveolar atelectasis.

Glycoproteins (Fibronectin).

Immune defences

Immunoglobulins, especially IgA and IgG;

Complement factors, classical and alternative;

Cellular defence mechanisms (alveolar level): alveolar macrophages and T-lymphocytes; polymorphonuclear cells.

Diffusion

The air–blood barrier is about 2 mm thick and comprises:

The capillary endothelium; The fused basement membranes of the endothelial and epithelial layers;

The epithelial type I and II pneumocytes.

The pulmonary interstitium separates the linings of the alveoli and of the capillaries. It comprises:

A fibrous scaffold of collagens and elastic fibres;

Extracellular matrix of vessel wall;

Fibroblasts, smooth muscle cells and macrophages;

Lymphatic vessels.

The rate-limiting steps for oxygen diffusion

These are:

The rate of passage of oxygen across the alveolo-capillary membrane;

The rate of combination of oxygen with haemoglobin in the red blood cells;

The driving pressure for diffusion, i.e. the differences in pressures between pO_2 in the alveolus and pO_2 in the red blood cell.

Diffusing capacity

This is measured using carbon monoxide as a tracer gas. The single breath-hold method involves the following steps:

* A single breath-hold for 10 seconds is followed by rapid inspiration from the residual volume to the total lung capacity of a gas mixture of 0.3%–0.4% carbon monoxide, helium, oxygen and nitrogen. This represents a vital capacity breath of gas from a reservoir bag.

- * Slow even exhalation back to the residual volume follows. The first portion of the expired gas (750 ml) represents the anatomical and system dead space. The second portion (the last 75–100 ml) of the expired gas (the end-tidal gas) is collected and taken as representing alveolar gas.
- * Carbon monoxide and helium concentrations are measured in alveolar gas.
- * The carbon monoxide tension in pulmonary capillary blood is close to zero, owing to the long time required for the plasma to equilibrate with alveolar gas.
- * The rate at which carbon monoxide leaves the alveoli depends on the rate of diffusion through the alveolar-capillary membrane.
- * The diffusing capacity for carbon monoxide is equal to the volume of carbon monoxide transferred into the blood per minute per mm Hg of carbon monoxide partial pressure, i.e. the rate of uptake of carbon monoxide.

In the steady state method, the patient rebreathes the gas until equilibrium is reached.

Transport mechanisms for solute and water across the capillary endothelial cell

These include:

Passive diffusion: transcellular or paracellular

Pinocytosis

Via endothelial channels

Via inter-endothelial junctions

Dead space

Anatomical dead space

This refers to the volume of the conducting airways, and is around 130–180 ml (2 ml/kg throughout life) in the adult, i.e. about 1/3rd of the tidal volume (dead space ventilation (VD)/tidal volume (VT) ratio = 0.3). It can be measured by

Fowler's method:

- 1- A single breath of 100% oxygen is inhaled and followed by a single expiration.
- 2- On expiration, nitrogen concentration is continuously measured at the mouth. Nitrogen is measured as it does not participate in gas exchange. A simultaneous measurement of expired gas volume is carried out.
- 3- The nitrogen concentration in the expired gas gradually rises as 100% oxygen is washed out of the conducting airways by alveolar gas. It plateaus when only alveolar gas is being exhaled.
- 4- The volume of the anatomical dead space is equal to the volume that occurs half-way to the plateau point.

Physiological dead space

This refers to the proportion of the tidal volume that does not participate directly in gas exchange. It consists of the anatomical dead space and the alveolar dead space (the volume of gas in alveoli that are ventilated but not perfused, and thereby not participating in gas exchange, i.e. wasted ventilation). It comprises

25%–35% of the normal tidal volume (the VD/VT ratio). It can be measured by

Bohr's method, which is based on the following principles:

- * Air ventilating perfused lungs will equilibrate with carbon dioxide in the blood. Alveolar pCO₂ is thus similar to arterial pCO₂.
- * Inspired air contains virtually no carbon dioxide.

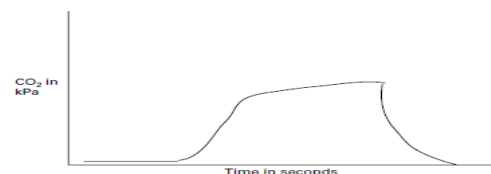


Figure 7.1 Expired CO₂ concentration during a normal breath.

- The product of the alveolar carbon dioxide concentration and the amount of inspired air reaching the alveoli equals the expired carbon dioxide concentration (multiplied by the tidal volume).

$$VD = \frac{(PaCO_2 - PECO_2)}{PaCO_2} \times VT$$

where

PaCO₂ = arterial PCO₂

PECO₂ = expired gas PCO₂

In general, alveolar dead space increases in disease and anatomical dead space increases with increasing age. Anaesthetic circuits and equipment will increase