RSC301 – Asthma Management

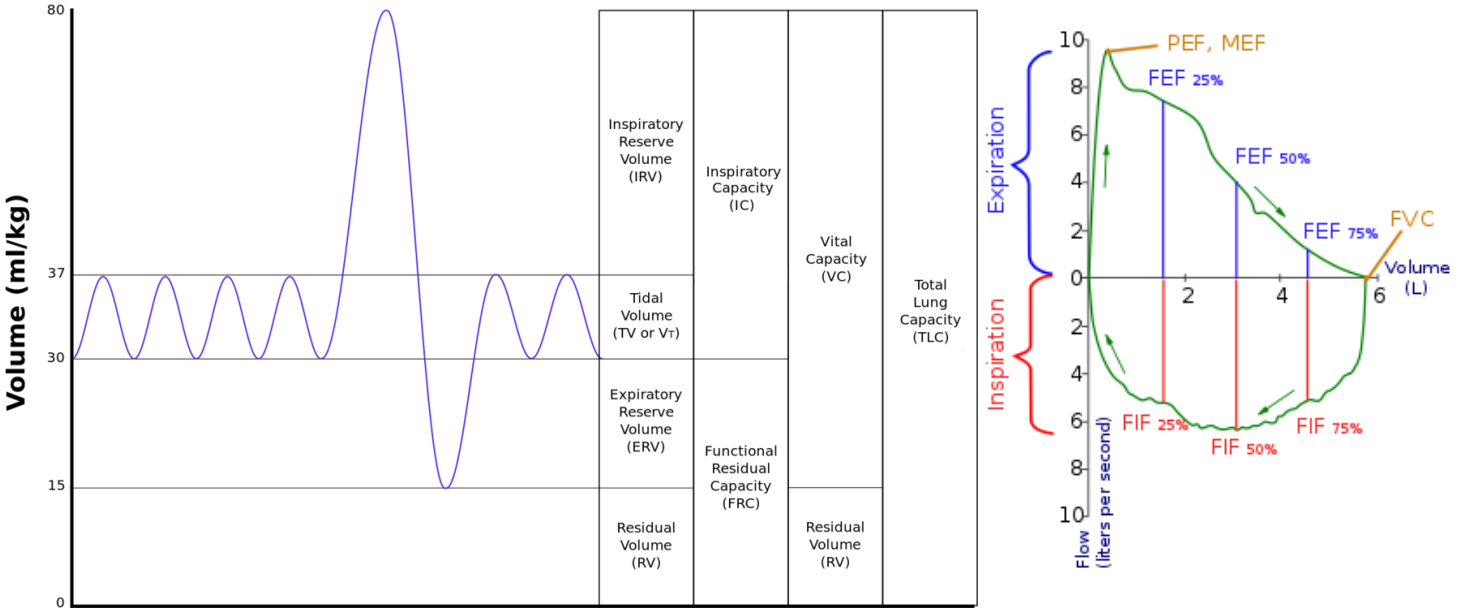
Contents

Previous expected knowledge:

Respiratory anatomy and physiology:

- The lungs sit within a pleural cavity
- Chest expands, pressure within the pleural cavity is lowered, and air moves in via the trachea and bronchi
- Breathing is controlled by the respiratory centre in the medulla, and muscles innervated include:
    - Diaphragm
    - Intercostal muscles
- During heavy breathing, the pectorals muscles, sternocleidomastoid muscles and scalenes may be used to provide further expansion of the thoracic cavity
- Normal lung function varies between people
    - dependent on age, sex, height, weight, race
    - plateau in lung function 20-30 years of age, then steady decline
    - FEV1 (volume of air forcefully breathed out in one second from inhaling to maximal capacity) declines about 30-35mL per year.
    - Smokers decline 100mL per year

- Lung volumes
    - Forced vital capacity (FVC) – total amount of air that can be forcefully inhaled and exhales
    - FEV1 – forced expiratory ratio of air in one second from FVC
    - FEV1:FVC ratio – normally more that 0.8 (i.e. 80% breathed out in the first second of forced exhalation)
    - Respiratory rate – breaths per minute
    - Tidal volume – volume of air in a normal breath (normally about 500mL)



- Spirometry involves a patient breathing in as much air as they can (to forced vital capacity), then forcefully exhaling and breathing out all the air they can as fast as possible.
- Asthma is a chronic inflammatory response in the airways
    - wheezing, cough, dyspnoea, tight chest, tachycardia, fatigue, anxiety, difficulty speaking
    - often reversible
    - short-term changes:
        - bronchoconstriction due to histamine, IL-4, IL-5, IL-13 and other inflammatory mediators – increase airway resistance, harder to get air in
        - excessive mucus production leads to mucus plugs
        - airway inflammation and oedema
    - long-term changes:
        - remodelling of lung tissue
        - thickening and fibrosing of basement membrane
        - hyperplasia of mucus glands
- COPD
    - emphysema → enlargement of airspaces and destruction of lung tissue
    - chronic obstructive bronchitis → obstruction of the small airways
    - bronchiectasis → permanent dilation of the airways resulting from destruction of smooth muscle following prolonged infection and inflammation (more dead space, less air for gas exchange)

Module 1

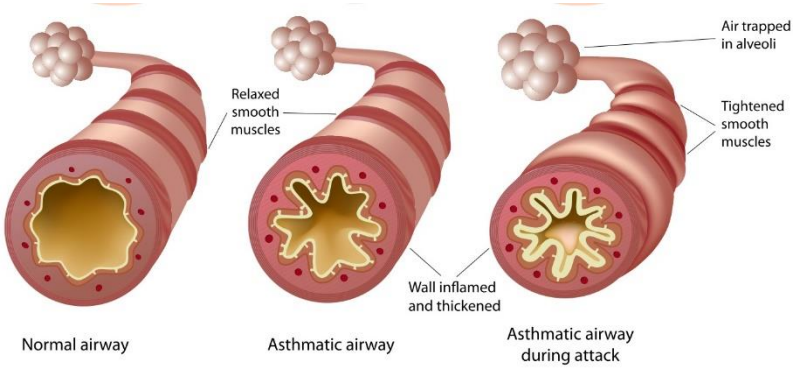
Topic 1: Pathogenesis

Airway inflammation and hyperactive airway musculature narrowing bronchioles to result in a flow obstruction

- Not in all grades of asthma
- Airway inflammation leads to muscular hyperactivity
    - Muscle contracts, constricting airways, bronchoconstriction
- Mediators involved include histamine, thromboxane and leukotrienes
- Chronic inflammation of airways results in permanent changes

Allergic response

- Due to inhaled allergenic particles in the nose, bronchi or bronchioles
- Immune system cells (mast cells, eosinophils, basophils, and neutrophils) release cellular mediators (histamine, leukotrienes, other mediators)
- Response is beneficial in the short term



- In asthmatic individuals, inflammatory response is via the Th2 pathway (T-helper cell 2)
- Inflammation leads to redness and oedema, and desquamation of airway epithelium
    - Airway lining sheds off

Asthma response pathway

Allergen lands on airway mucosa
↓
Digested by allergen-presenting cell (APC) or dendrite (immune cell, not the part of the neuron)
↓
Cells migrate to the lymph nodes and present the degraded allergen to T-cells
↓
T-cells prime B-cells to produce allergen-specific antibodies which bind to mast cells
↓
Mast cell releases histamine, attracting eosinophils to the site
↓
T-cells proliferate and release cytokines (IL-4 and IL-5)

Allergic and non-allergic responses:

- Allergic individuals produce more IgE (the allergy immunoglobulin)
- Non-allergic individuals produce more IgG (the standard immunoglobulin)
- Allergic individuals produce more IL-4 and IL-5 (Th2 pathway)
- Non-allergic individuals produce more INF-γ
    - INF-γ inhibits IL-4 and IL-5

IL-4 and IL-5

- Interleukin-4 and interleukin-5
- IL-4 is involved in stimulating production of Th2 cells from precursor Th0 cells
- IL-4 also promotes inflammation of tissues by activating macrophages
- IL-4 also promotes switching of immunoglobulin class to IgE (allergic response)