Cardiovascular and Respiratory Disease

1. Cardiovascular disease
2. Respiratory disease
1. Cardiovascular disease

- **Atheroma** is a disease of *unknown aetiology* in which **fatty plaques** form on arterial walls
  - **Atherosclerosis** is the complicated process by which **atheromatous plaques** are formed
    - Highest incidence in men under 50 with high **LDL cholesterol** intakes
    - Affects all vessels above 1mm diameter – particularly at sites of haemodynamic stress
    - Foamy **histiocytes** (long-lived macrophages) accumulate under the intima forming **fatty streaks**
    - **Myocytes** migrate from the media to form a fibrotic cap over a lipid and cholesterol core
  - Once formed these plaques can then become **complicated** by various destabilising factors
    - **Calcification** of the fatty core reduces the **contractility** of the vessel promoting **hypertension**
    - **Ulceration** of the fibrous cap exposes the core which attracts coagulants causing **thrombosis**
    - **Fissures** penetrating under the plaque **destabilise** the entire structure resulting in **embolism**
  - Partial luminal **narrowing** restricts **blood flow** causing local **ischaemia** in structures the vessel supplies
    - Symptoms generally only arise in cases of severe narrowing
    - Resulting clinical conditions include **angina**, **intermittent claudication** and ischaemic colitis
  - Total luminal **occlusion** abruptly stops **blood flow** causing local **infarction** in related structures
    - Infarction of central sites such as the **heart** and **brain** are potentially fatal and always serious
    - Peripheral infarction e.g. of the leg results in **gangrene**
  - Ruptured thrombotic plaques releasing **emboli** can cause **ischaemia** or **infarction** in distant vessels
    - **Transient ischaemic attacks** (TIAs) can result from emboli lodging in small cerebral vessels
    - **Ischaemic strokes** can result from larger emboli occluding cerebral vessels causing **infarction**
  - **Atherosclerotic aneurysms** most common in the **abdominal aorta** may cause a fatal **haemorrhage**

- **Thrombosis** is the formation of a **solid mass** of **blood constituents** within vasculature in life
  - **Thrombi** comprise fibrin, platelets and various blood cells (erythrocytes and leucocytes) in serum
  - Changes in the vessel wall, blood flow or blood **constituents** promote **thrombosis** (Virchow’s Triad)
    - The **intrinsic clotting cascade** is activated when blood contacts a negatively charged surface
    - The **extrinsic clotting cascade** is activated in response to tissue damage
  - Clots are normally degraded through **fibrinolysis** via tPA catalysing plasmin formation from plasminogen
    - **Oclusive** clots may be partially lysed in **recanalisation** – formation of small canals
    - **Mural** clots may rupture and release emboli
  - **Cardiac thrombosis** of the heart walls or valves may give rise to systemic or pulmonary emboli
    - **Atrial** thrombosis may occur as a result of atrial fibrillation
    - **Myocardial** thrombosis may occur following **infarction** (MI)
    - **Valvular** thrombosis (forming vegetations) may occur following endocarditis or rheumatic fever
  - **Prolonged immobility** and the **oral contraceptive pill** may increase the risk of **venous thrombosis**
    - **Deep vein thrombosis** (DVT) may initially be *asymptomatic* but lead to **pulmonary embolism**
    - **Lines of Zahn** (pale platelet-rich stripes) may be seen post-mortem on thrombotic veins
  - **Embolism** is defined as the **sudden total occlusion** of an artery by an obstructive body of remote origin
    - **Pulmonary embolism** can cause severe respiratory **dysfunction** and may be fatal
    - **Systemic embolism** can affect any part of the body causing remote infarct and may be fatal
    - Microscopic **fat-based emboli** may arise in severe trauma but are generally self-resolving
    - **Infective endocarditis** affects the heart valves and may produce infective emboli

- **Ischaemia** is the *inadequate perfusion* of a tissue that may result in **necrosis** and **infarction**
  - **Cerebral** and **cardiac** tissue are the most susceptible to **ischaemic damage** and **infarction**
    - Common causes include **atheroma**, **thrombosis**, **embolism**, vasculitis and hypertension
    - In **shock** the reduced flow can damage vulnerable areas such as the cerebral **watershed zones**
Infarction triggers polymorphic nucleocytes to phagocytose necrotic tissue, angiogenesis and fibrosis
  - First signs of infarction visible morphologically 24 hours after the insult
  - After 3 days the tissue may appear pale or yellow with a hyperaemic border
  - After several weeks a firm fibrous scar will appear pale or red with multiple blood supplies

- Occlusion of the coronary arteries or their subsidiary vessels can result in myocardial infarction (MI)
  - Occlusion of the left coronary artery (LCA) precipitates an anterolateral MI
  - Occlusion of the right coronary artery (RCA) precipitates a posteroinferior MI
  - Occlusion of the left anterior descending artery (LAD) precipitates an anteroseptal MI
  - Occlusion of the left circumflex artery (LCX) precipitates a lateral MI

- **Hypertension** is sustained abnormally elevated pressure in a vascular compartment
  - Systemic hypertension is most commonly essential but may be secondary to numerous other conditions
    - Potentially causative renal pathologies include glomerulonephritis and renal artery stenosis
    - May be caused by hormonal imbalance such as excess adrenaline from a phaeochromocytoma
    - Other causes include aortic coarctation and prolonged corticosteroid or NSAID use
  - Essential hypertension may be linked to RAS dysfunction, sodium retention or excess catecholemines
    - Increases risk of atherosclerosis and causes fibrosis and smooth muscle degradation in vessels
    - Increased cardiac workload may lead to ventricular hypertrophy and eventually to heart failure
  - Malignant hypertension is usually secondary to renal dysfunction and can be life-threatening
    - Diastolic blood pressure may rise abruptly to over 130mmHg
    - Arterioles undergo fibrinoid necrosis promoting thrombosis and local haemorrhage
    - Widespread microvascular damage may precede blindness, stroke and cardiac or renal failure

- **Aneurysms** are abnormal permanent vascular dilatations forming sacs prone to haemorrhage
  - Aneurysms can occur anywhere but are most common in the abdominal aorta and cerebral vessels
    - Atherosclerotic aneurysms (abdominal aorta) may haemorrhage into the retroperitoneal space
    - Dissecting aneurysms result from a tear in the intima causing blood accumulation in the media
    - Berry aneurysms occur on the Circle of Willis and may cause subarachnoid haemorrhage
    - Microvascular aneurysms may occur in hypertension (diabetes) causing retinopathy or stroke
    - False aneurysms can arise in trauma as extravascular masses forming against a normal lumen
  - When aneurysms haemorrhage (usually retroperitoneal or cerebral) they are often fatal

- **Valvular disease** may cause abnormal narrowing (stenosis) or regurgitation (incompetence)
  - Mitral valve disease is invariably caused by rheumatic heart disease leading to left atrial hypertrophy
    - Initially asymptomatic followed by progressively worsening dyspnoea and haemoptysis
    - May result in atrial fibrillation, systemic emboli (particularly cerebral) and heart failure
  - Aortic valve stenosis is most commonly caused by calcific valvular disease affecting the elderly
    - Initially asymptomatic followed by exertive syncope, angina and eventually heart failure
    - Atherosclerosis may give rise to calcified fibrous nodules on the valvular cusps
    - Increased cardiac workload induces left ventricular hypertrophy and myocardial ischaemia

- **Cardiac failure** involves inadequate functioning of the heart leading to pulmonary effusion
  - Causes include cardiac ischaemia, hypertension, valvular disease and respiratory disease (e.g. COPD)
    - Relatively common, typically involving both sides of the heart with a poor prognosis
    - B-type natriuretic peptide (BNP) is released in myocardial stress and indicates cardiac failure
    - Left heart failure results in poor renal perfusion, RAS activation and excessive fluid retention
2. Respiratory disease

- **Pneumonia** is classically defined as **bacterial pulmonary inflammation** with consolidation
  - Alveoli fill with **inflammatory exudate** causing **induration** (hardening) of the lung tissue
    - May involve **hepatisation** from a blood-stained exudate that subsequently degrades
    - Symptoms include those typical of infection as well as **coughing** and **chest pain**
    - Type of pneumonia is generally classified by **X-ray appearance**
  - **Lobular pneumonia** is seen as **multiple patchy shadows** within a localised region
  - **Lobar pneumonia** affects an entire lobe but is restricted to that lobe
    - Majority caused by **pneumococcus** — some by Legionella
    - Normally **resolved** as opposed to repaired but may lead to abscess, empyema, fibrosis etc.
  - **Bronchopneumonia** is **widespread** infection causing acute inflammation in bronchi and bronchioles
    - Majority caused by **Streptococcus pneumoniae** — some by H. influenzae and Pseudomonas
    - Normally **resolved**
  - **Atypical pneumonias** may have **viral inclusions** or involve **penicillin-resistant bacteria**
    - Generally not suppurative — no consolidation
    - Causes include mycoplasma, Chlamydia, Pneumocystis carinii and fungi
  - **Lung abscess** involves a localised **suppurative necrosis** that more commonly affects the **right lung**
    - Majority caused by **gram-negative** organisms or Staphs and Streps
    - Those under coma or **anaesthesia** particularly at risk

- **Tuberculosis** is caused by **Mycobacterium tuberculosis** and characterised by **nodular lesions**
  - Typically transmitted by **inhalation** particularly affecting the **immunosuppressed**
  - The **first time** an individual is infected the resulting disease pattern is called **primary tuberculosis**
    - Organism forms a single **primary tubercle** (Ghon focus) and migrates to local **lymph nodes**
    - Often **asymptomatic** but may spread through infectious **coughing** and **sneezing**
    - Often **repairs** spontaneously with scarring but may persist chronically as **latent tuberculosis**
  - Subsequent **re-infection** of a sensitised individual results in **secondary tuberculosis** (active disease)
    - Multiple lesions form — immune response is **granulomatous** and leads to **necrosis**
    - Symptoms include **pyrexia**, productive cough, night sweats, weight loss and **haemoptysis**
  - In some cases the organism enters the **bloodstream** causing **disseminated tuberculosis**
    - May affect a single organ/system (e.g. **tuberculous meningitis**) or multiple (**miliary tuberculosis**)
    - With correct treatment even widespread disseminated tuberculosis has a **good prognosis**
  - Tuberculosis is treated with **multiple antibiotic therapy** over 6 months (12 months if disseminated)
    - Isoniazid — inhibits production of a crucial **cell wall** component unique to mycobacterium
    - Rifampicin — potent **bactericide** with infrequent but serious side-effects e.g. hepatotoxicity
    - **Bacteriostatic** agents **ethambutol** and **pyrazinamide** used as adjuncts for first 2 months

- **Obstructive airways disease** causes **resistance to flow** — **reduced FEV1** with a **normal TLC**
  - Emphysema is defined as the **abnormal permanent dilatation** of distal airspaces with wall destruction
    - Mostly **asymptomatic** until destruction becomes relatively **widespread** (33% of tissue)
    - Smoking tends to lead to **centriacinar emphysema** of the **upper lobes** sparing distal alveoli
    - **Oxygenation of blood** is limited resulting in tissue hypoxia, **weight loss** and **muscle wasting**
  - Chronic bronchitis results in a **persistent cough** with **sputum** for at least 3 months over 2 years
    - Repeated inhalation of irritants and chronic infections cause **hypertrophy** of **mucous glands**
    - Results in mild **dyspnoea** and **sleep apnoea**, oedema possibly leading to **cor pulmonale**
  - Asthma is a **chronic relapsing disorder** resulting from abnormal **reversible** narrowing of the bronchi
    - Usually **early onset** with symptoms of coughing, wheezing and generalised breathing difficulties
• Usually triggered as part of a type I hypersensitivity reaction, infections, over-exertion etc.
• Treated with bronchodilators (β₂ agonists e.g. salbutamol) through aerosols or nebulisers

• **Tumours of the lung** are almost exclusively **malignant** and strongly associated with **smoking**
  o Malignant neoplasms present non-specifically with coughing, weight loss, dyspnoea and chest pain
    ▪ Many associated with paraneoplastic syndromes e.g. SIADH
    ▪ Most managed with surgery with or without radiotherapy
    ▪ Overall 5-year survival rate is 10%
  o Peripheral adenocarcinomas are common with glandular differentiation and often mucous production
  o Peripheral bronchoalveolar carcinomas are the least common but tend to have the best prognosis
  o Central squamous cell carcinomas have the strongest association with smoking and may be keratinised
  o Central small cell carcinomas are the most aggressive although appear primitive histologically
    ▪ Generally inoperable – treated with chemotherapy

• **Pneumoconiosis** is a non-neoplastic fibrotic reaction to chronic inhalation of mineral dusts
  o Can be caused by a range of substances including asbestos, coal and silica – usually occupational
    ▪ Resident macrophages phagocytose inhaled dust particles triggering toxin and cytokine release
    ▪ May lead to restrictive interstitial lung disease – chronic inflammation, alveolar fibrosis
  o Asbestosis is a diffuse interstitial fibrosis and pneumoconiosis associated with asbestos exposure
    ▪ Fibres may be serpentine (silicate compound) or amphibole (needle-like – more pathogenic)
    ▪ Symptoms arise up to 20 years post-exposure – may result in malignant mesothelioma
  o Malignant mesothelioma usually affects the pleura and is almost exclusively associated with asbestos
    ▪ May be epithelioid (more common) or sarcomatoid (more aggressive) – all have poor prognosis
    ▪ Symptoms may arise up to 40 years post-exposure
  o Silicosis is a nodular dense pulmonary fibrosis resulting from prolonged exposure to silica particles
    ▪ Activated macrophages trigger fibroblasts to deposit collagen forming nodules
    ▪ Not considered to be a predisposing factor for neoplasia