Lecture 1 – Ischaemic Heart Disease

Objectives:

- Understand the epidemiology of ischaemic heart diseases (IHD)
- Understand the risk factors and causes of IHD
- Understand the pathophysiology of IHD
- Understand the common presentations of IHD
- Understand the basic investigations modality/treatment outline

Summary:

Normal Anatomy

- 3 layers of tissue
  - Pericardium – the "bag", membranous coat that the heart sites in
    - Serous pericardium (Parietal + Visceral) + Fibrous pericardium
  - Myocardium – cardiac muscle, consisting of cardiomyocytes
  - Endocardium – lining of endothelium within the heart
- Haematoxylin and Eosin staining
  - Cardiac muscle – ordered muscle fibres, one centrally located nuclei, intercalated disks + branched
  - Skeletal muscle – ordered muscle fibres (can see the dark and light striations) + nuclei seen

Heart Disease

- Congenital = fault during development usually pertaining to a physical deformity (cells haven't divided properly)
  - < 20% of heart disease
- Acquired heart disease = >80% (multifactorial disease, usually due to atherosclerosis)
- Myocardium receives insufficient blood (ischamaeic) due to coronary artery atherosclerosis (>75% of the normal luminal cross-section)
  - Epidemiology: IHD accounts for ~30% of deaths in women aged +6- and ~33% in men
- Two manifestations or levels
  - Gradual occlusion of the coronary artery → angina pectoris (chest pain)
  - Sudden occlusion of the coronary artery → myocardial infarction (heart attack)

Atherosclerosis

- Hard risk factors
  - *Hyper-cholesterolaemia* – deposition of fats in the blood vessel walls i.e. ↑ LDL-C
  - *HTN* – >140/95; Increases risk by 5-fold; damages the endothelium and vessel from excessive pressure
  - *Smoking* – increases risk by 70 – 200%
  - *Diabetes mellitus* – increased risk by 2%
  - *Genetics* – influences the HDL-C:LDL-C levels + the risk of HTN/DM
  - These are **multiplicative** (not additive); tend not to be altered easily and closely related to the disease
- Soft risk factors
  - Hormonal factors – protection of estrogen before menopause + some influence of HDL:LDL by estrogen
  - Diet – influences the blood lipid levels (Risk = high fat/cholesterol, low fibre, low fruit/vegetables)
  - Obesity/lack of exercise, stress, lifestyle factors (stereotypical/classic multi-factorial disease)
- **Non-modifiable risk factors** = age, gender, family history, stress, personality, increased triglycerides + *HTN*
- **Modifiable risk factors** = smoking, obesity, sedentary lifestyle, diabetes, alcohol, increased cholesterol + *HTN*
- Clinical manifestations
  - Intermittent ischaemic effects due to narrowing of the arterial lumen reducing tissue blood flow
    - Typical atheromatous plaque
  - Manifests as **angina pectoris** (chest pain), **intermittent claudication** (reduced blood flow to the legs causes cramping during exercise), **neurological impairment** and secondary **hypertension** (known cause)
- 3 layers of a blood vessel
  - *Inside:* **tunica intima** = most hypertrophied; some channels can be made through the blockage (dissection-like) + tunica media + adventitia: *Outside*
- Lipids accumulate in the intima
  - Lipid core is between the tunica intima and the media as foams cells (macrophages with lipids within)
  - Fibrous caps of intima forms from collagen by smooth muscle cells that have migrated from the tunica intima
    - The thickening of this cap increases the size of the atheroma/ decreased luminal size
    - If the fibrotic cap is weak → burst → lipids escapes (can also be achieved with anti-fibrotics)

- **Factors increasing lipid core stress** = thin fibrous cap, large lipid pool, less stenotic lesions + more cholesterol
- **Factors weakening the cap** = decreased collagen synthesis, increased collagen degradation, increased macrophages and T cells to the area + decreased smooth muscle cells (make collagen)
- Chronology of atherosclerosis (develop over years)
    - Ongoing exposure to risk factors promotes growth of atheroma
    - For majority of time the natural history is subclinical; when it is clinical it is too late → occlusion/rupture
- Partial occlusion
    - Effector of luminal size reduction by atheroma; low grade ischaemia of the heart = pain felt
    - During periods of increased exertion → increased tissue demand BUT not met due to restriction
    - Clinical effects of atherosclerosis = angina pectoris, left-sided sharp chest pain on exertion (lasting ~10 – 15mins) and anaerobic metabolites building up in the heart muscle
- Complete occlusion
    - Effect of a super-posed thrombosis (usually formed elsewhere) plugging the lumen of existing atherogenic artery (decreased lumen) → complete occlusion
    - Characterised by persistent chest pain, unrelated to cardiac workload, given ischaemic at rest

<u>Myocardial Infarction</u>

- MI sequelae/consequences
    - Sudden death – associated with extensive necrosis of the heart muscle due to hypoxia
    - Death within 2 days – due to shock and subsequent heart failure
    - Congestive HF with pulmonary oedema – heart doesn't have the capacity (enough tissue left) to eject blood → mismatch of outputs → oedema + HF
    - Fibrosis + healing – occurs in 6+ weeks, with damaged tissue being replaced with collagen
    - Pericarditis – acute inflammation within the pericardium (friction rub with AI)
- Localisation of myocardial infarction
    - Given the infarct region is discrete is can be localised in histology sectioning post mortem
        - In vivo can be identified on ECG as changes, due to no electrolyte movement and the radionuclide trace will show the extent
            - Sub-endocardial infarct = T-wave inversion; transmural = ST segment elevation
        - Gross pathology later in natural history when fibrosis has occurred appears pale against normal
    - Sub-endocardial (inside, not full thickness of ventral LV) and transmural infarctions are important because necrotic muscle in the endocardium can stimulate thrombosis in the LV → thromboembolism → brain or lung → stroke or PE
- Types of arterial occlusions
    - Left anterior descending coronary artery occlusion
        - Supplies blood to the apex, anterior LV and some of the septum (interventricular = IV)
        - Anterior, apical infarction = ~50% of cases
    - Right coronary artery occlusion
        - Posterior infarction = ~30% of cases with infarct of the posterior LV and posterior septum
        - This artery supplies the LV (site of most severe infarcts given level of vascularisation)
    - Left circumflex coronary artery occlusion
        - Causes lateral infarction of the LV = ~20% of cases
        - Extent and size of infarct is highlighted on ECG trace and radionuclide perfusion imaging
- Laboratory investigations
    - **High blood lipids** – especially total cholesterol, LDL and HDL
    - **Troponins** – proteins associated with the tropomyosin on actin; Immediately after infarction, able to detect cTnT (up to 7 – 10 post MI) and cTnI (up to 5 days post MI)
    - **Cardiac enzymes** – creatine phosphokinase (CPK), lactic dehydrogenase (LDH), Serum glutamic-oxaloacetic transaminase (SGOT), Hydroxybutyric dehydrogenase (HDH; up to 12d post MI)
        - BUT skeletal muscle damage also raises these
    - **Other** – FBE (increased neutrophils + RBCs); CXR (for cardiomegaly), technetium pyrophosphate scan; radionuclide ventriculogram
- Management
    - Defibrillation – cardioversion to cease fibrillation/arrhythmias
    - Fluid replacement via IV saline
    - Pulmonary oedema – give morphine to ease breathing and vasoconstrict
    - Frusemide; O2 therapy
    - Ionotopic agents – increased ventricular output, e.g digoxin or dobutamine
    - Acute coronary thrombolysis – streptokinase to lyse the thrombus (within 3 hours of symptoms)

- Analgesia – morphine or diamorphine acutely
- Anti-arrhythmic – IV beta-blockers, e.g. lignocaine
- Long term – anti-thrombotic medication (aspirin or warfarin), lifestyle changes + rehabilitation
- Coronary artery stents – can be made from metal or polymers (elastic and springy) to hold vessels open
  - E.g. bare-metal, heparin-coated, cypher (sirolimus), taxus (paclitaxel) or EPC binding stents

- MI complications
  - **Rupture of the heart** – fatal haemopericardium or cardiac tamponade (fluid build-up between the myocardium and the pericardium)
  - **Thickening of the LV** (can be twice the normal thickness) – hypertrophy associated with HTN
    - Infarct area has ballooned (aneurysm) and a thrombus has formed
  - **Extension of MI** (propagating thrombus) – the area may build and extend as more coronary artery branches become involved and more area becomes necrotic
    - Warfarin can be given to prevent the extension
    - But only thrombolysis will remove the thrombus
  - Thromboembolism – thrombus breaks off and travels to the brain → forms an ischaemic/necrotic area
    - **Stroke secondary to MI**
  - **Arrhythmias** (4 types) – infarct region is not contracting normally
    - Premature ventricular complexes
      - Occur irregularly from impulses that originate in the ventricles; develop because of necrotic tissue which cannot pass on electrical impulses
      - The heart doesn't beat in synchrony due to inaccurate signalling
      - Defibrillation is needed
    - Ventricular tachycardia
      - Extremely rapid contraction rate, originating from the ventricles, with insufficient time for ventricular filling
    - Ventricular fibrillation
      - Irregular, uncoordinated, ineffective contractions of individual muscle bundles
    - Asystole
      - Complete absence of contraction

- Healing MI on H&E
  - Adjacent to the pericardium, myocardium is normal, with areas of collagen deposition
  - A region of myocardium has undergone **coagulative necrosis** and replaced with scare tissue at the edge
  - Young collagen fibres (not yet dense and compact), new vascular spouts and macrophages
    - Evidence of degranulation which follows AI
  - Hemosiderin is present in the region of scarring (= granulation tissue) + congested vessels
  - Haemorrhage is evident due to destruction of blood vessels
- Gross MI from early infarction
  - Lots of congestion and haemorrhage → death
  - Infarct regions are localised and effect a small percentage of the tissue + surrounded by normal tissue