ATHEROSCLEROSIS

Atherosclerosis

Atherosclerosis is a disease process affecting the intima of the aorta and large and medium arteries, taking the form of focal thickening or plaques of fibrous tissue and fatty material.

Secondary changes are found in other coats of the vessel wall.

Arterial changes occurring with age

1. Intimal thickening
2. Reduction of elasticity of elastic fibres
3. Changes in lipoprotein composition

Intimal thickening commences in childhood and occurs as follows:

a) Proliferation of intimal collagen and elastic tissue.
   b) Infiltration by smooth muscle cells.
   c) Circular elastic fibres develop immediately beneath the endothelium.
   d) Development of subendothelial connective tissue internal to the circular elastic fibres.

Lesions of atherosclerosis

1. Lipid streaks
   These appear as flat or slightly elevated white or yellow areas of variable size and shape which may be found throughout the arterial system of patients of all ages. They have a high lipid content.

2. Fibrous plaques
   Fibrous plaques appear as raised firm greyish areas which on cross section reveal central yellowish lipid rich debris with surrounding fibrous tissue. The distribution of fibrous plaques is slightly different from that of lipid streaks and although they may be formed in response to irritation by the lipid deposits, there is no clear evidence that the plaques develop from lipid streaks. Possibly several types of lipid streak exist and only the young adult type is a precursor of the fibro-lipid plaque.

Effects of fibrous plaques on vessels

1. Encroach on lumen
2. Media underlying the plaque is thinned.
3. Elastic lamina underlying the plaque is thinned.
**Complicated plaques** are raised fibrous plaques which have increased in size and show one or more of the following features:

1. Calcification.
2. Haemorrhage - may cause sudden enlargement of the plaque and occlusion of the vessel.
3. Ulceration - discharge of the contents may cause distal occlusion.
4. Thrombosis - superimposed thrombus developed due to stasis or release of thromboplastin from damaged intima.

**Aneurysm** formation can occur due to dilatation of the arterial wall where the media is weakened secondarily to atherosclerosis.

**The Theories of Pathogenesis**

There are two main theories of pathogenesis.

1. **Infiltration theory**
   
The infiltration theory postulates that the constituents of the atherosclerotic lesion are derived from the blood in the arterial lumen. These are lipoproteins which pass through the endothelium and are deposited in the intima.

2. **Encrustation theory**
   
The encrustation theory postulates the deposition of fibrin, platelets and other plasma constituents in the form of mural thrombi and incorporation into the intima by endothelialisation.

**Effects of atherosclerosis on vessel walls and blood flow**

1. **Narrowing** - causes distal ischaemia
   - predisposes to thrombosis
2. **Tortuosity** - causes turbulence in blood flow predisposing to thrombosis
3. **Dilatation** - aneurysm formation may result.

**Diseases known to increase severity of atherosclerosis**

1. Hypertension
2. Diabetes Mellitus
3. Familial Hyperlipidaemia

**Factors thought to influence severity of atherosclerosis**

1. Smoking
2. Exercise
3. Intake of cholesterol
4. Unsaturated/saturated fatty acid ratio intake
5. Other factors such as Bran, Vitamin E, etc.
THROMBOSIS

Definition: The formation of a solid mass in the circulation from the constituents of the flowing blood. The mass itself is called a thrombus.

a) occluding thrombus occupies the whole vessel lumen
b) mural or parietal thrombus is attached only at one side.

GROSS APPEARANCE OF THROMBI

Veins: polypoid mural or long cylindrical masses, dark red colour, with pale head, neck and long red tail.

Arteries: compact, pale, alternating laminae of pale and dark red material - head and tail cannot be distinguished.

Heart: mural thrombi on surface of inflamed heart valves, ventricular wall and auricular appendages.

MICROSCOPIC STRUCTURE AND FORMATION OF THROMBI

Thrombosis involves two distinct processes

1. The deposition of platelets on a vascular surface.

2. The formation of a fibrin mass.
   Platelet thrombus = Pale or conglutination thrombus
   Fibrin mass = Red or coagulation thrombus
   Thrombi are usually mixed

In veins thrombi form coral-like system with framework of platelets, fibrin and trapped white blood cells this is a coralline thrombus

Propagation is the extension of thrombus from smaller to larger vessels.

It can occur by 2 methods:

1. Development of thrombus proximal to each next venous tributary.

2. Extension of consecutive thrombus past several tributaries - thrombosis “en masse”.

PREDISPOSING FACTORS IN THROMBOSIS

There are 3 factors and constitute Virchow’s Triad

1. Changes in the vessel wall.
2. Changes in blood flow.
3. Changes in constituents of the blood.

1. Changes in vessel wall involve 2 factors:
   (a) The role of abnormal surfaces
   (b) Other changes in the wall

2. Changes in blood flow involve:
   (a) Stasis and dispersion effect with loss of axial flow
   (b) Eddies

3. Changes in constituents of blood involve:
   (a) Increased platelet number
   (b) Increased platelet adhesiveness
   (c) Increased prothrombin time

SUBSEQUENT CHANGES IN THROMBI

Resolution

Definition: Is the series of changes which reduce the bulk of thrombi persisting beyond the initial stages.

Organisation

Definition: Are the reactive changes which occur in the vessel wall and gradually transform the mass into vascular connective tissue.

Re-canalisation

Definition: Is the differentiation of the newly formed endothelialised channels with reconstitution of the original vessel lumen.

EXAMPLES OF THROMBOSIS IN VARYING SITUATIONS

Venous thrombosis - 2 types:

1. Phlebothrombosis
2. Thrombophlebitis
**Phlebothrombosis** - 5 stages in pathogenesis

1. Primary platelet thrombus
2. Coralline thrombus
3. Occluding thrombus
4. Consecutive thrombus
5. Propagation

**Arterial thrombosis** may occur in:

1. Atherosclerosis
2. Aneurysms

**Thrombosis in the heart** occurs in the following pathological conditions:

1. Mitral stenosis
2. Myocardial infarction and cardiac aneurysms
3. Rheumatic fever
4. Bacterial endocarditis
EMBOLISM AND INFARCTION

EMBOLISM
Definition: The impaction in some part of the vascular system of any undissolved material brought there by the blood stream. The transported material is known as an embolus. The commonest cause of emboli is dislodgement of the whole or part of a thrombus, and unless otherwise specified, the term embolism refers to this process.

FORMATION OF EMBOLI

Occluding and mural thrombi give rise to emboli.

Veins: emboli from occluding thrombi move downstream through the widening veins to the right heart and impact in the narrowing pulmonary arteries.

Arteries: emboli from mural thrombi from the heart or large arteries pass downstream and impact in the narrowing arterial tree to the systemic organs.

THE EFFECT OF EMBOLISM

The primary effect of an embolus is the partial or complete occlusion of a vessel followed by a reduction in blood flow. This leads to ischaemia.

ISCHAEMIA
Definition: Is a condition of inadequate blood supply to an area of tissue. The harmful effects produced are due to anoxia.

FACTORS DETERMINING EXTENT OF ISCHAEMIA IN ARTERIAL OBSTRUCTION

1. Speed of onset.
2. Extent of obstruction.
3. Anatomy of local arterial supply, number and size of collateral vessels.
4. Pathology of the collateral circulation.
5. State of oxygenation of blood.
6. Cardiac state.
7. Vulnerability of tissues to anoxia.

INFARCTION
Definition: The production of a circumscribed area of tissue necrosis as a result of ischaemia. The necrotic focus is termed an infarct.

STAGES IN FORMATION OF AN INFARCT

1. Death of cells (necrosis)
2. Acute inflammation in surrounding tissues
3. Phagocytosis
4. Shrinkage and organisation into fibrous scar

SPECIFIC EXAMPLES OF INFARCTS IN IMPORTANT ORGANS

1. **Cardiac infarction**

2. **Pulmonary infarction** - red infarct; dual blood supply; raised venous pressure.

3. **Renal infarction** - pale infarct. The kidney is susceptible to infarction for 3 reasons:

   a) lack of connexions between terminal arteries
   b) high regional blood flow
   c) tissue rapidly undergoes necrosis from anoxia.

Infarcts usually occur as a result of emboli from the left heart.

4. **Splenic infarction** - pale wedge shaped, usually post-embolic.

5. **Distal limb ischaemia** caused by:

   a) thrombosis of diseased arteries - eg secondary to atherosclerosis.
   b) emboli from mural thrombi on the left heart or main arteries

Serious distal limb ischaemia produces necrosis of the skin and underlying tissues. When this becomes infected by bacteria and putrefaction (rotting) occurs it is called **gangrene**.

**GANGRENE**

*Definition:* Is necrosis of tissue with super-added putrefaction.

6. **Cerebral infarction**

The brain is particularly liable to infarction for 2 reasons.

   a) end arteries
   b) cortical neurons are very sensitive to anoxia.

Cerebral infarcts result from:

   a) emboli from the heart, aorta or carotid arteries
   b) primary thrombosis of cerebral vessels

Cerebral infarcts are pale, ill-defined and are known as **cerebral softenings**.