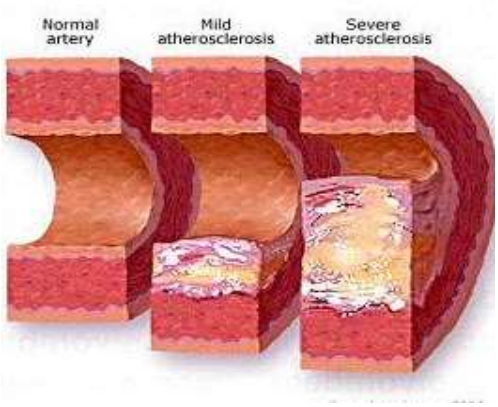
Diseases of Blood vessels

Atherosclerosis (Atheroma)

This is patchy thickening of the intima of arteries by lesions composed of deposited lipids surrounded by proliferating connective tissue. Each of these lesions is called: atheroma



Risk factors:

- Hypertension is a major risk factor
- High levels of plasma lipids (hypercholesterolemia) cause endothelial damage
- Smoking causes endothelial damage
- Diabetes Mellitus
- Life style: Lack of exercise, stress, obesity
- Familial hereditary factors

Pathological features

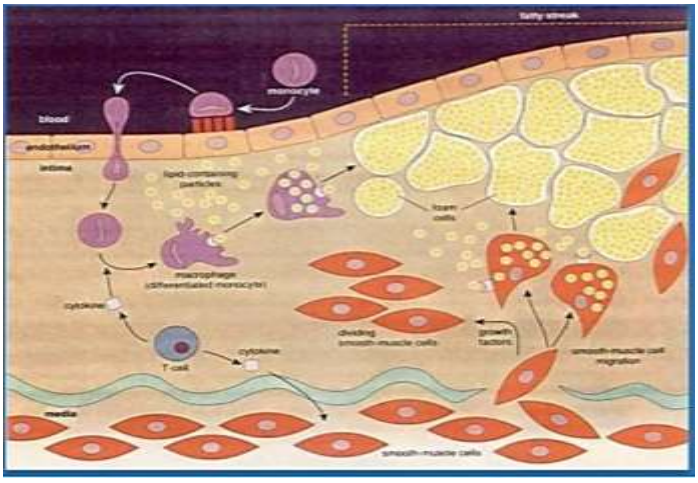
Sites of atherosclerosis:

- Large arteries: aorta and its main branches
- Small arteries: coronaries, cerebral and renal arteries
- Medium sized arteries as Femoral artery

Atherosclerosis is mostly due to Chronic endothelial damage

*Caused by:

- Vascular stress (hypertension)
- Toxic products of cigarettes



*Endothelial injury → allows trapping of lipids (cholesterol) in the sub-endothelial part of the intima

*Also endothelial injury → enhance the adherence of platelets → release of platelet factors → stimulation of proliferation of connective tissue & smooth muscles

Pathology of the Cardiovascular system

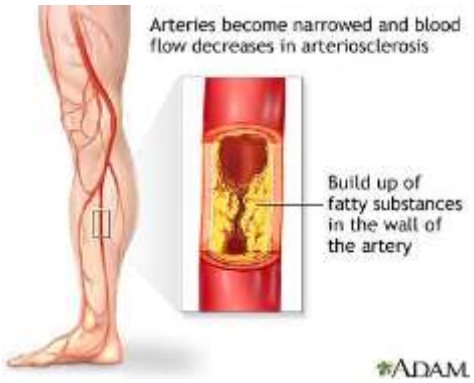
Effects & complications:

A) Ischemic effects:

- Ischemia may be incomplete i.e. narrowing or complete occlusion

➢ **Small arteries: Coronaries:**

- Narrowing → atherosclerosis heart diseases
- Occlusion → myocardial infarction

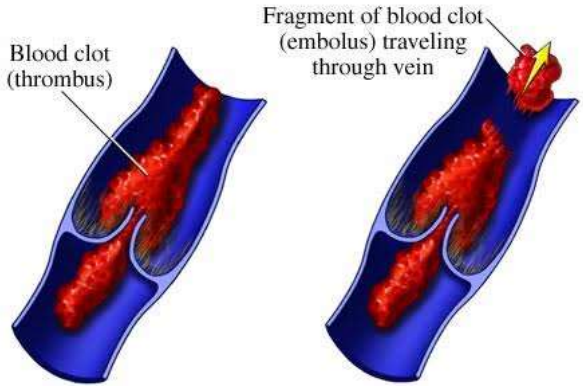


➢ **Femoral artery**

- Narrowing → intermittent claudication (in legs)
- Occlusion → dry gangrene of leg (amputation)

➢ **Large arteries: Aorta:**

- Thrombosis may develop over atheromata and this may be detached to form thrombo-emboli which can cause systemic embolism leading to infarctions in different organs



B) Aneurysm formation:

- A local enlargement of an artery

- They are due to stretch of the atrophic media

- The most common are:

a. The cerebral arteries
b. The aorta → death



Hypertension

Definitions:

Hypertension is persistent elevation of blood pressure above normal. The normal adult pressure not more than 140 / 90 mmHg.

Types:

- **Primary (essential) hypertension: 90% is unknown etiology→ idiopathic**
- **Secondary hypertension: 10%**

Causes of Secondary hypertension

1. **Endocrinal causes:**
   a. **Thyrotoxicosis**
   b. **Pheochromocytoma** are tumors arising from the adrenal gland. They may secrete Catecholamines (adrenaline & nor-adrenaline)
   c. **Cushing's syndrome** is due to prolonged exposure to cortisol
   d. **Hyperaldosteronism:** Medical condition in which too much aldosterone is produced by the cortex adrenal glands
2. **Toxemia of pregnancy**

   (increased hormones → increased blood pressure)
3. **Renal causes:**
   a. **Polycystic kidney** (cysts cause urine collection & obstruction of release)
   b. **Renal stones**
   c. **Inflammation of kidney** (Glumerulonephrotis or Pyelonephritis)
   d. **Amyloidosis** (deposition of extracellular substances)
   e. **Renal artery stenosis**
4. **Vascular diseases:**

   as Coarcation of the aorta

Effects of hypertension (complications)

1. **Eye:** Arterial narrowing and retinal damage
2. **Heart:** Left ventricular hypertrophy & heart failure
3. **Cerebral hemorrhage**
4. **Kidney:** Varying degrees of renal damage which may result in uremia

Thrombosis

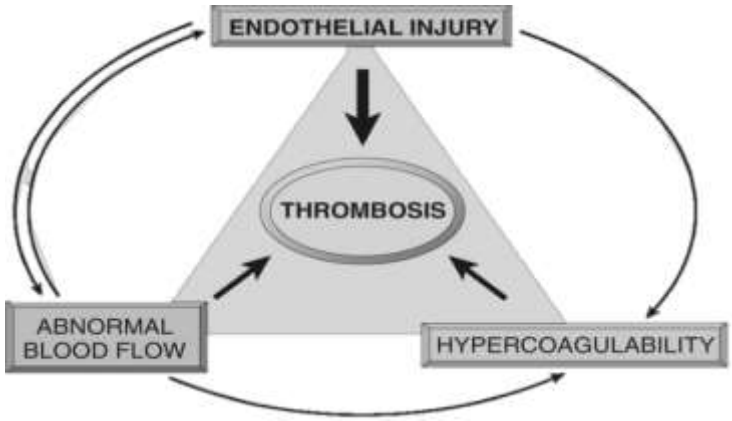
- **Thrombus** is a solid compact mass formed inside the cardiovascular system during life from circulating blood constituents

Main features:

1. **Intravascular**
2. **Mass of coagulated blood composed of platelets, fibrin, cells and plasma proteins. Early the lines of Zahn are present which are alternating layers of platelets and fibrin**
3. **Adherent to the internal surface of the vessel**

Etiology of thrombosis → Virchow's triad (3 factors)

1. **Endothelial Injury**
2. **Abnormal Blood flow**
3. **Hypercoagulability**



Classification of Thrombi

According to occlusion:

1. **Non-occlusive thrombus:** (does not close the vessel) in the heart and aorta (mural thrombi)
2. **Occlusive thrombus:** (close the vessel) in vascular lumen

According to site of thrombi:

1. **Arterial thrombi**
2. **Cardiac (heart) thrombi**
3. **Venous thrombi**
4. **Capillary thrombi**

Fate of Thrombi

1. **Lysis:** The role of **fibrinolytic agents in the blood**
2. **Propagation: Enlargement and extension of the thrombus**
3. **Organization: Fibrosis of the thrombus**
4. **Recanalization:** During organization **new channels may** form within the thrombus; these may **allow renewed blood flow** through the **obstructed vessel.**

Complications of Thrombi

1. **Infarction: Reduced blood flow to a tissue/organ: result in ischemia or infarction**
2. **Thrombo-embolization:** part of the thrombus breaks off → occludes distant blood vessel

Embolism

• **Definition**:
Occlusion of a vessel by a mass of material (i.e. embolus) that is transported in blood stream

• **Embolus**:
It is a **detached intravascular solid, liquid or gaseous mass**, carried by the blood to a site distant from its point of origin.
Most common type is due to fragments of circulating thrombus (**Thromboemboli**)

• **Main types of embolus**:

1- Thromboembolism (99% of all emboli) These emboli may be **septic or aseptic**

Classified according to whether they lodge in the pulmonary or systemic circulation:
- **Pulmonary thromboembolism (originate from venous thrombosis as DVT)**
- **Systemic thromboembolism (originate from arterial thrombosis)**

2- Fat embolism → (broken femoral bone → bone marrow to blood)

3- Gas embolism (Air embolism) → (Decompression sickness of divers)

4- Amniotic fluid embolism (Liquid emboli) → (pregnant during delivery → amniotic fluid to blood)

5- Bacterial Embolism

Disease of blood vessels:

Pathophysiology of B V D;

Endothelial cells of blood vessels contribution of nitric oxide (NO) to endothelial – dependent vasodilation, greater in large conduit arteries compared to small resistance vessels. These regional biochemical and phenotypic differences between endothelial cells extend to their susceptibility to injury in the face of cardiovascular risk factors such as hypercholesterolemia, diabetes and smoking.

Endothelial dysfunction is pivotal in the development of cardiovascular diseases such as atherosclerosis and hypertension.

The are four major pathways underlying endothelium dependent modulation of vascular tone;

NO, arachidonic acid metabolites,

endothelium dependent hyper polarization (EDH)

and endothelin.

1- **Reductions in no bioavailability, is a hallmark of endothelial dysfunction associated with cardiovascular risk factors such as hypercholesterolemia, smoking, diabetes and obesity. loss of NO tip the homeostatic balance in favor of vasoconstriction, proliferation, activation of platelets and blood clot formation, and inflammation. These pathological processes contribute to clinical manifestations such as hypertension, atherosclerosis and arterial thrombosis, which are associated with significant morbidity and mortality.**

2- **Cyclooxygenases:** **COX enzymes metabolize arachidonic acid to endoperoxide, then converted to (prostacyclin; PGI_1 , thromboxane A_2) cyclooxygenase are found in the endothelium, regarded as vascular protective, production PGI_2, which act on postanoid (IP) ,**

receptor to cause vasodilation and inhibition of platelet aggregation via activation of adenylyl cyclase and subsequent elevation of intracellular cyclic-adenosine monophosphate (cAMP). PGI_2 also inhibits platelet and lymphocyte adhesion to endothelium, limits vascular smooth muscle cell proliferation and migration, and counteracts the production of growth factors.

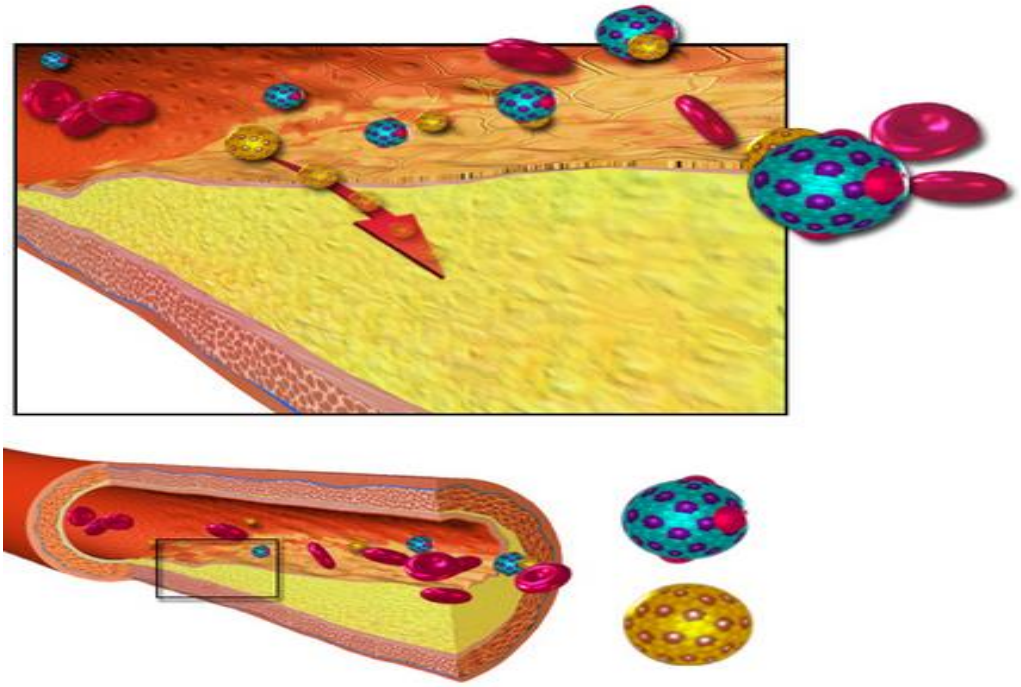
Atherosclerosis,(Atheroma).

is a chronic inflammatory vascular disease.

This is thickening of the intima of arteries by lesions composed by deposited of lipids surrounded by proliferating connective tissue. Each of these lesions is called atheroma.

Atheroma: (consist of a lipid core containing cholesterol crystals, lipids, and cellular debris. Surrounding this core is a fibrous cap composed of smooth muscle cells, collagen and other connective tissue components. Calcification, marked by the deposition of calcium salts within the plaque, can render the plaque rigid and more prone to rupture. The presence of inflammatory cells, particularly macrophages, contributes to plaque instability and progression. The stability and size of the fibrous cap play critical roles in determining the risk associated with atheromatous).

An atheroma, or atheromatous plaque, is an abnormal accumulation of material in the inner layer of an arterial wall, the lumen of the artery, narrowing it and restricting blood flow.



Atheroma and atherosclerosis:

Atheroma: fatty material that clogs arteries. It builds up over time and can lead to complications.

Atherosclerosis: Is atheroma (plaque) defining feature of a disease called atherosclerosis. an atheroma begins to form at the site and it grows over time causing complication " blood circulation disturbances".

risk of atherosclerosis?

atherosclerosis risk factors can trigger the buildup of plaque in arteries.

Diabetes:

High blood sugar can damage the inner layers of the arteries, causing plaque buildup.

Family history:

Genes may raise risk, especially if have a common inherited cholesterol disorder called familial hypercholesterolemia. This condition affects about 1 in 300 people.

Inflammatory diseases:

When have a condition such as rheumatoid arthritis or psoriasis, high levels of inflammation can injure blood vessels, which can lead to plaque buildup.

Lack of physical activity:

Spending little time moving each day while spending a lot of time in(LAZY LIFE)is linked to unhealthy cholesterol levels that lead to atherosclerosis.

High blood pressure:

Over time, high blood pressure can damage artery walls, allowing plaque to build up. In the United States, high blood pressure accounts for more deaths linked to atherosclerosis than any other risk factor .

Older age:

For most people, plaque buildup starts in childhood and gets worse as they get older. In men, the risk increases after age 45. In women, the risk increases after age 55. The risk is even higher for women who have endometriosis or polycystic ovary syndrome, or if they had gestational diabetes or preeclampsia during a pregnancy.

Overweight or obesity:

Overweight and obesity raise the risk for heart disease and are linked to many other health problems, including type 2 diabetes and cancer.

Race:

Black Americans' risk of death from heart disease is 30% higher than White Americans' risk. People of South Asian origin (Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka) also have a higher heart disease risk.

Smoking and secondhand smoke:

Almost one-third of deaths caused by coronary heart disease are linked to smoking or exposure to secondhand smoke. Secondhand smoke can cause atherosclerosis-linked disease and stroke.

Unhealthy diet:

Eating a lot of foods high in fat, can increase cholesterol levels. Saturated fats are found in meat and dairy products (except nonfat dairy). Also, drinking too much alcohol or binge drinking can raise total cholesterol level.

Effect of atherosclerosis disease " blood circulation disturbances" .

When this plaque buildup may lead to:

A- Ischemic effect:-

1. Aortoiliac occlusive disease. (iliac or femoral arteries): Leg pain that starts when active and goes away when rest (claudication).

2. Carotid artery disease. Arteries that supply blood to brain (carotid arteries): (Stroke).

3. Coronary artery disease. (coronary arteries): Chest pain or discomfort that starts when active and goes away when rest (stable angina). May progress with time to myocardial infarction.

4. Mesenteric ischemia. Arteries that supply blood to intestines (mesenteric arteries): Stomach pain after eat.

   (postprandial cramps, also known as “abdominal angina”).

5. Peripheral artery disease. Peripheral artery disease (PAD) may not cause symptoms, or symptoms may be mild.
   PAD symptoms include:

   Leg pain when walking.
   Muscle pain or cramping in the arms or legs, often in the calf.
   Muscle pain begins with exercise and ends with rest.
   Painful cramping in one or both of the hips, thighs or calves after walking or climbing stairs or other activities.
   Pain when using the arms, such as aching and cramping when knitting or writing.
   Coldness in the lower leg or foot, especially when compared with the other side.

6. Renal artery disease. Arteries that supply blood to kidneys (renal arteries): Secondary hypertension and potentially reduced kidney function.

7. Vertebral artery disease. Vertebrobasilar insufficiency (VBI) is when blood flow to the back of brain reduces or stops.

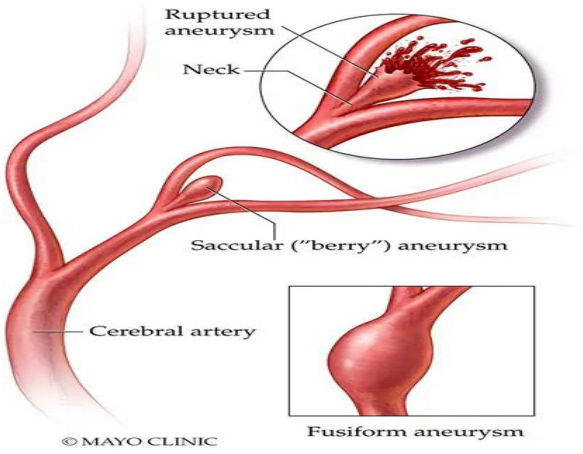
   VBI affects the parts of brain that control balance and movement. Atherosclerosis of vertebrobasilar artery often causes condition disturbances balance and movement, as well as increases risk of stroke.

B- Aneurysmal effect:-

- A local enlargement of an arterial atheroma by compressing and stretching of the atrophic media ……. ↔ create aneurysm.

The most common sites are:-

1- The cerebral arteries; when rupture cause stroke or death.



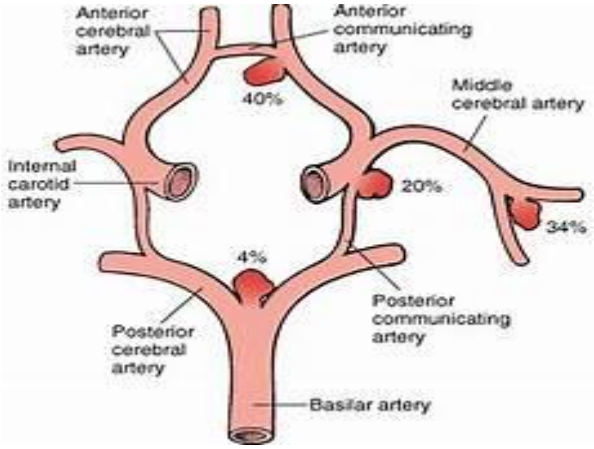
Saccular and fusiform cerebral aneurysms

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- **saccular aneurysm.**

  It's a round, blood-filled sac that protrudes from the main artery or one of its branches. It usually forms on arteries at the base of the brain. A berry aneurysm is the most common type of aneurysm.

- **Fusiform aneurysm.** This type of aneurysm causes bulging on all sides of the artery.
- **Mycotic aneurysm.** This type of aneurysm is caused by an infection. When an infection affects the arteries in the brain, it can weaken the artery wall.



2- The aorta ; when rupture cause rapid mortality (death).

involve the progressive expansion and weakening of the three layers of the aorta: the intima, media, and adventitia.

Multiple pathological processes including :
extracellular matrix (ECM) breakdown,
inflammation,
phenotype switching of vascular smooth muscle cells (SMCs),
medial layer of the arterial wall is composed mainly of vascular smooth muscle cells, under physiological conditions, VSMCS are contractile phenotype and primary function is to regulate

vascular tone. In atherosclerosis switching these cells by matrix protein and proteases cause weakness in wall and dilatation .

oxidative stress, and neovascularization;
also contribute to this process. Furthermore, these biological mechanisms are thought to initiate the degradation of elastic fibers and alterations in collagen composition, ultimately compromising the structural integrity and reducing the flexibility of the aortic wall.

