Arterial Vascular Disorders

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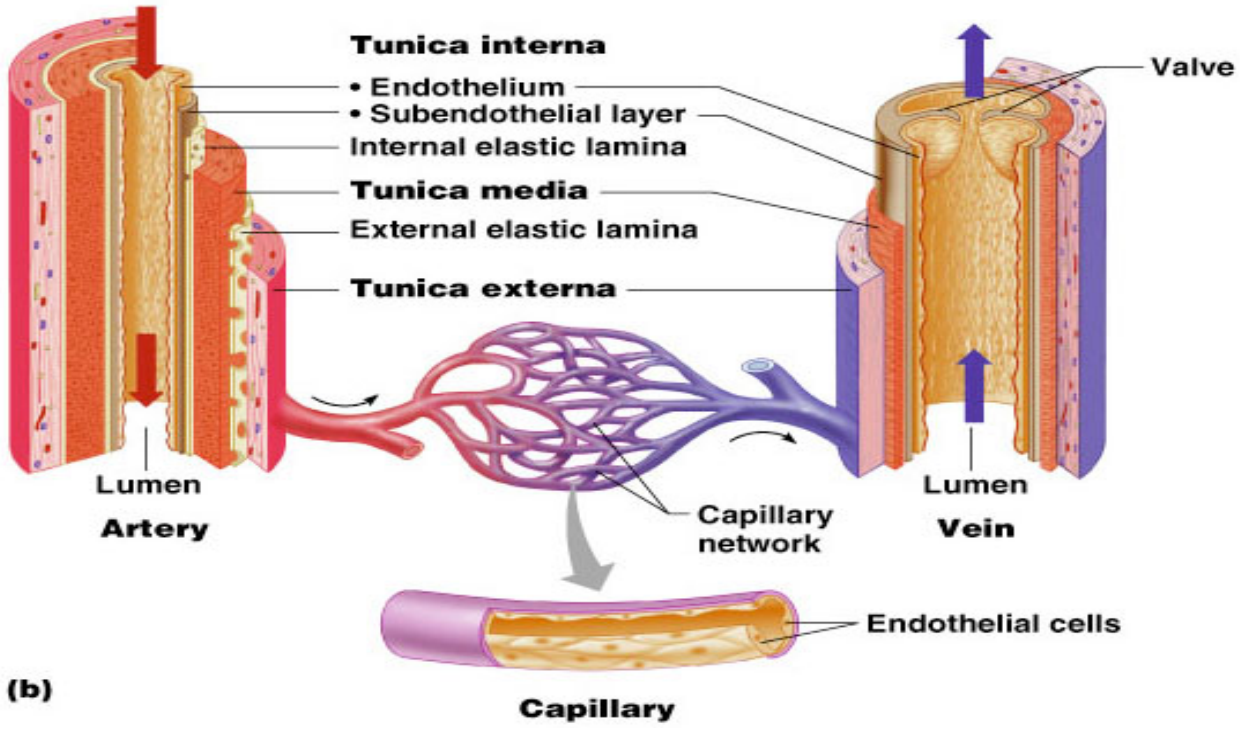
Basic Vascular Structure: Arteries

- **Tunica Intima**
  - Innermost layer of flattened endothelial cells
  - Basement Membrane- Layer of glycoproteins that keeps the endothelial cells in place
  - Layer of fibrous connective tissue below BM
- **Tunica Media**
  - Thickest part of arterial wall
  - Elastic connective tissue
  - Internal elastic lamina- thin, strong elastic tissue separating tunica interna from media
  - Surrounded by the external elastic lamina- another layer of elastic connective tissue
- **Tunica Adventitia**
  - Outermost of three layers
  - Protective layer of loosely organized fibrous connective tissue
- **Vasa Vasorum**
  - Network of small vessels outside tunica adventitia
  - Supply blood to cells that make up outer layers of large arteries
- All layers can become more rigid (i.e. higher collagen content) with age

Basic Vascular Structure: Veins

- Have thinner walls and larger <u>luminal spaces</u>
  - No internal or external elastic lamina
    - Tunica intima has thinner connective tissue layer outside of it
    - Tunica media is thinner
  - More “anastomosed” throughout the body
  - Many have valves to prevent backflow
    - Especially veins in extremities
    - Projections from the Tunica intima wall



Two main pathologies occurring with arteries

Arteriosclerosis is the stiffening or hardening of the artery walls.

Atherosclerosis is the narrowing of the artery because of plaque build-up. **Atherosclerosis** is a specific type of **arteriosclerosis**.

Arteriosclerosis

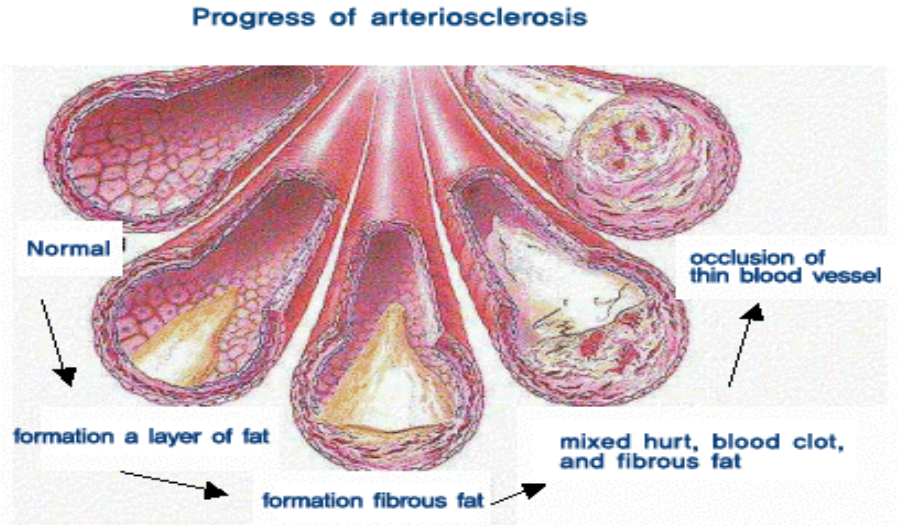
- Chronic disease of the arterial system
  - Abnormal thickening and hardening of the vessel walls
  - Smooth muscle cells and collagen fibers migrate to the tunica intima
- Often referred to as Hypertensive Vascular Disease
  - Very common
  - Usually found in smaller arteries/arterioles
  - Arterial walls get thicker- looks much like hyalinization
  - Caused by deposition of proteins, lipids, and basement membrane components in the Tunica intima and media

Atherosclerosis

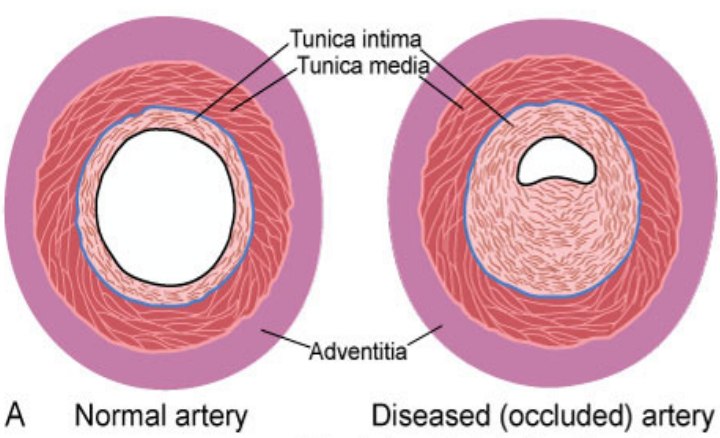
- Form of arteriosclerosis
  - Thickening and hardening caused by accumulation of lipid-laden macrophages in the arterial wall
  - Plaque development

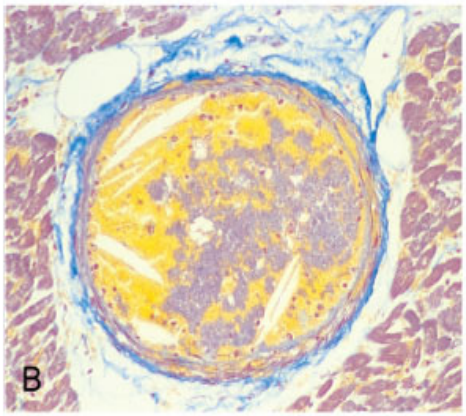
Diseases of the Arteries and Veins

- **Atherosclerosis Progression**
  - Inflammation of endothelium
  - Cellular proliferation
  - Macrophage migration and adherence
  - LDL oxidation (foam cell formation)
  - Fatty streak
  - Fibrous plaque
  - Complicated plaque
  - Result in—inadequate perfusion, ischemia, necrosis



- **Atherosclerosis Risk Factors**
  - **Hyperlipidemia- elevated levels of fat in the blood**
    - High Blood LDL (**Low Density Lipoproteins**) - cholesterol carrying particles between liver and other tissues that metabolize cholesterol
    - **HDL –** transports fat from the blood into the liver. Once in the liver, it is converted to become less atherogenic. “Good Cholesterol”
    - **LDL –** transports fat from liver to blood, where it becomes atherogenic to the arterial walls. “Bad Cholesterol”
  - Familial Hypercholesterolemia - elevated plasma cholesterol due to defective LDL receptors
  - Hypertension
  - Smoking
  - Diabetes Mellitus
  - Gender (males more predisposed)
  - Genetic Predisposition
  - Secondary factors- obesity, stress, inadequate exercise, excessive (or no) alcohol use


Tunica intima
Tunica media
Adventitia
A
Normal artery
Diseased (occluded) artery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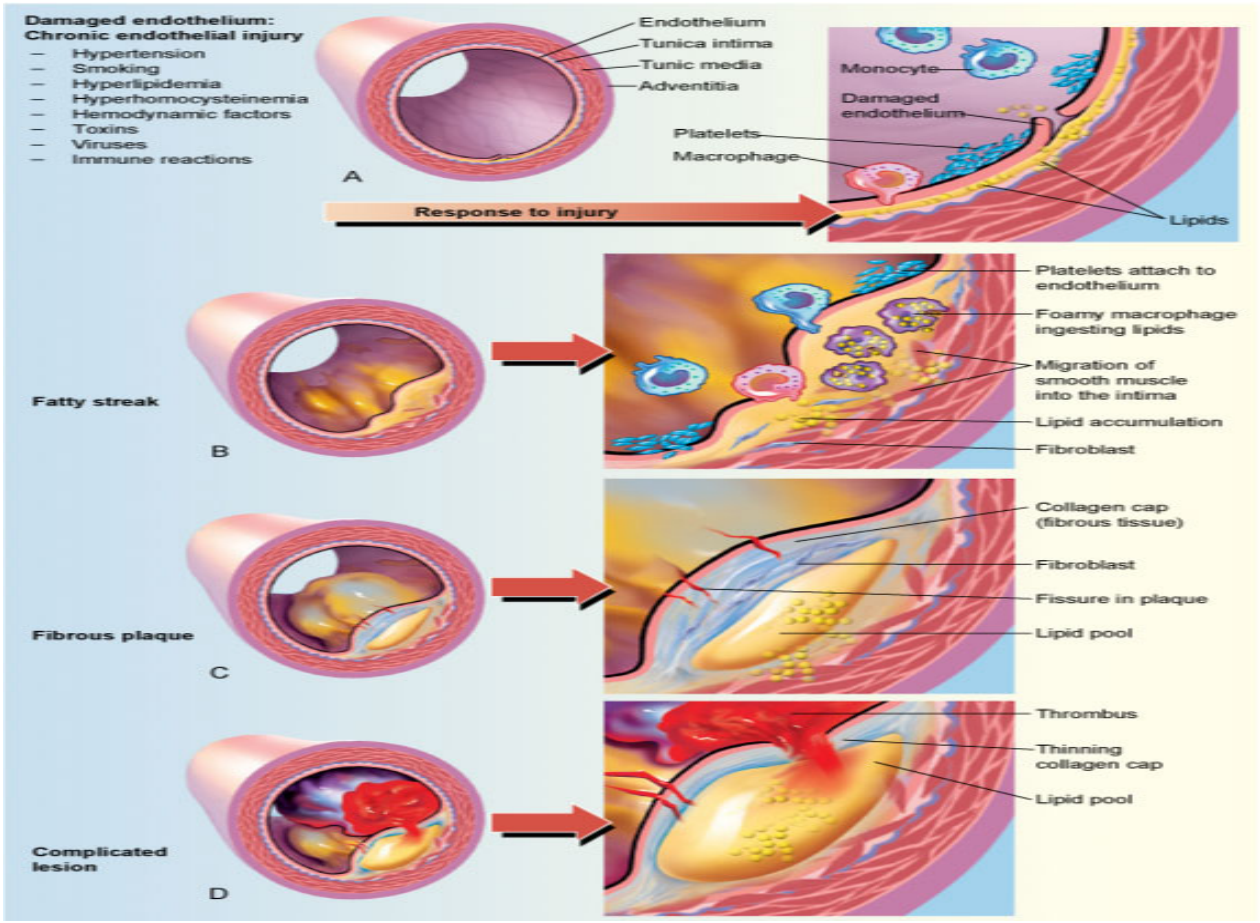
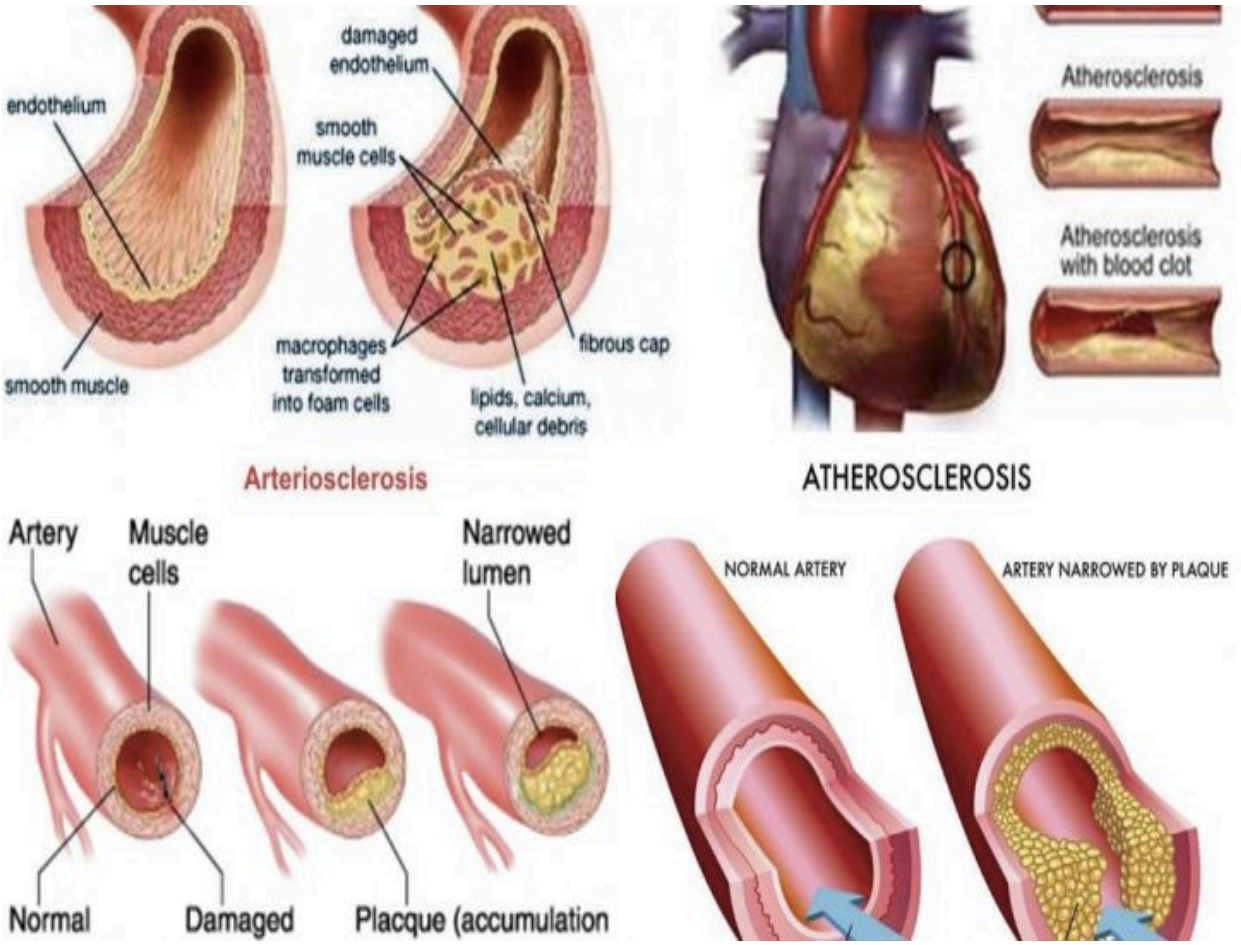

Damaged endothelium:
Chronic endothelial injury
– Hypertension
– Smoking
– Hyperlipidemia
– Hyperhomocysteinemia
– Hemodynamic factors
– Toxins
– Viruses
– Immune reactions
Endothelium
Tunica intima
Tunic media
Adventitia
A
Monocyte
Damaged endothelium
Platelets
Macrophage
Response to injury
Lipids
Fatty streak
B
Platelets attach to endothelium
Foamy macrophage ingesting lipids
Migration of smooth muscle into the intima
Lipid accumulation
Fibroblast
Fibrous plaque
C
Collagen cap (fibrous tissue)
Fibroblast
Fissure in plaque
Lipid pool
Complicated lesion
D
Thrombus
Thinning collagen cap
Lipid pool



There are three complications of atheroma

- **Ischemia**
  - The lumen of the artery narrows and distal vascular flow is lowered
- **Thrombus**
  - The presence of the atheroma increases the clot risk, which forms a thrombus
  - This can close off the lumen causing an infarct – tissue death
- **Aneurysm**
  - The atheroma can weaken the arterial wall causing a ballooning of the wall which can burst

Hemodynamic Disorders

- Any disorder that arises from an interruption in blood flow in the body

Thrombus - Mass of platelets, RBCs, WBCs, and fibrin
Thrombosis - Thrombus forming in an inappropriate place (i.e. vessel)

Ischemia

- Reduced blood supply results in decreased perfusion of cells, tissues and organs distal to the narrowed lumen
- The ischemia causes the tissues to become hypoxic, which makes it hard for the cells and tissues to carry on normal cell metabolism.
- This causes aerobic (In the presence of oxygen) metabolism to be converted into anaerobic (without oxygen) metabolism.
- The anaerobic metabolism causes and accumulation of waste products to accumulate in the tissues.

Effects of lactic acid on arterial walls

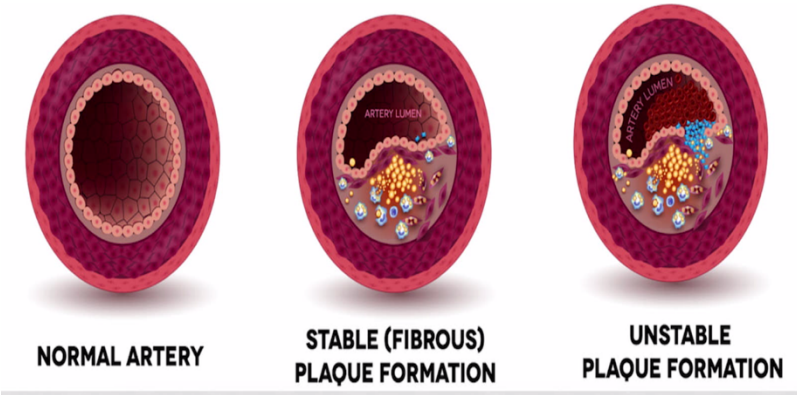
- The anaerobic metabolism is only intended to be a short term emergency measure in the body and was not meant to be a long term fix.
- If it is not washed away by sufficient blood flow, it tends to stick to the walls which causes more hypoxia.
- When this occurs in muscles it causes cramping and pain.
- Smooth muscles around organs can cramp and close off.
- When a smooth muscle cramps around a hollow organ it is referred to as colic.
- Lactic acid accumulation in the heart is called angina.

Thrombus

- Because of the platelets, blood is meant to clot to protect us from hemorrhaging
- Blood inside the lumen is liquid and when it clots it is a thrombus, which is stationary
- There are three main causes of thrombus formation in the arterial walls:
    - Disorders of the endothelial lining
    - Decreased rates of blood flow
    - Increased coagulability of blood

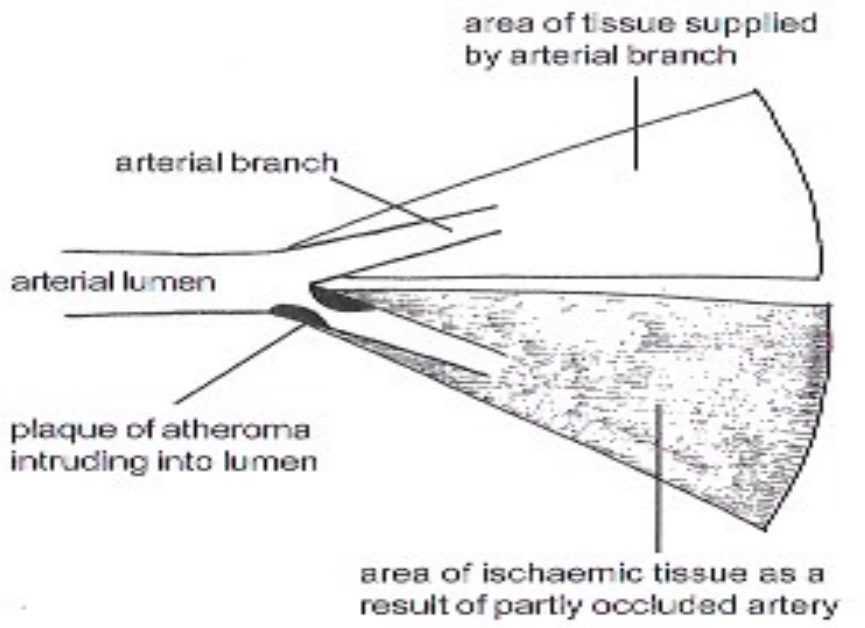
Virchow's Triad

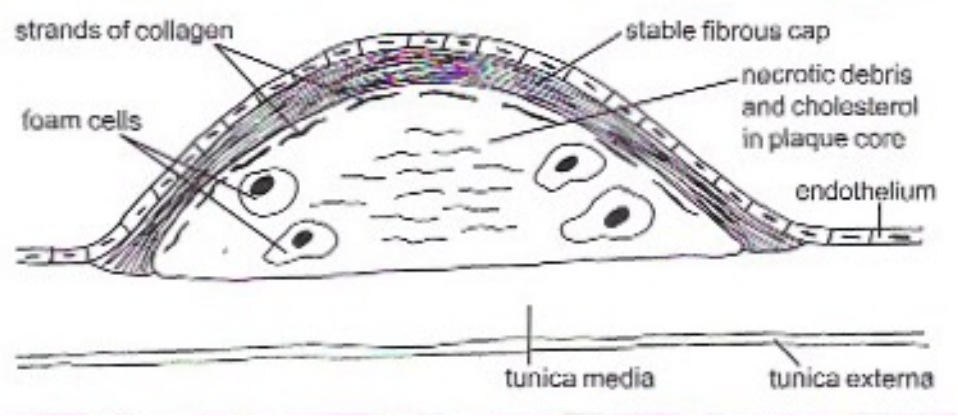
- Disorders of the endothelial layer
    - The atheroma under the endothelial lining greatly increases the risk of a thrombus development or plaque formation
        - A stable or simple plaque has an intact fibrous cap and a layer of vascular endothelium separating the plaque from coming in contact with the blood. This makes a thrombus formation unlikely because platelets and other clotting factors do not get to the core
        - An unstable plaque occurs when there is a crack or fissure or ulcer of the endothelial lining and clotting factors can get to the core. Inflammatory chemicals can also cause this.



Thrombus - continued

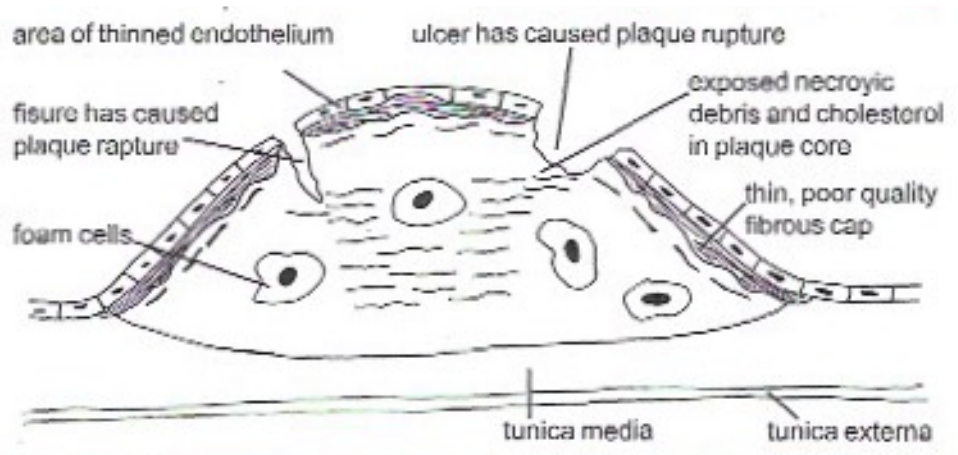
- Sluggish or abnormal blood flow
    - This is a risk because when the blood moves slower, it allows platelets and other clotting factors more time to stick to the arterial walls.
    - In the legs, this can cause DVT – deep vein thrombosis
    - In AF, atrial fibrillation, the atria do not fully contract and some blood stays behind and can form clots
- Increased blood coagulability
    - Anything that changes the viscosity of blood to being thicker increases the risk of thrombus formation.
    - Can be caused by dehydration or at high altitudes, where more RBC are needed to survive.
    - Smokers produce more RBCs because the hemoglobin in inactivated in the presence of carbon monoxide.
    - Thrombocytosis – increased platelet count
    - Whenever there is a hemorrhage (surgery, trauma, childbirth), more young platelets are released from the spleen. Young platelets are more likely to stick to arterial walls.





Stable Thrombus Plaque

The thrombogenic core and the blood are kept apart by the presence of a stable fibrous cap and an intact layer of vascular endothelial cells. The central core contains foam cells, which are macrophages full of LDL, cholesterol, and necrotic cell debris.



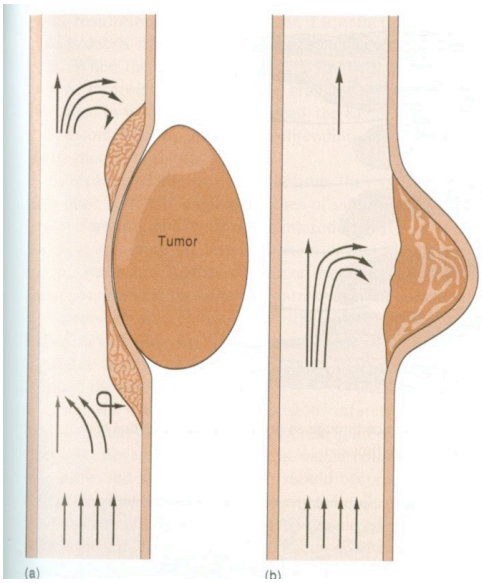
Unstable Thrombus Plaque

In the unstable (complicated) thrombus plaque, inflammatory chemicals have thinned the fibrous cap and caused it to become unstable. This can result in the plaque rupturing. As a result, the blood comes into contact with thrombogenic collagen and a clotting factor produced from the foam cells.

Statin drugs have anti-inflammatory properties as well as lowering LDL cholesterol. As a result, statins prevent anti-inflammatory processes thereby preventing inflammatory thinning of the fibrous cap.

Vessel Distortions

Pressure on vessel wall by a tumor →



Aneurysm bulging of wall

Thrombosis Sequela

- **Resolution**
  - Thrombus doesn't continue to develop (stable)
- **Organization**
  - *Phagocytes* digest thrombus 2-3 days after it forms
  - *Platelets* and *fibrin* are replaced by fibrous connective tissue
  - Endothelium forms over the tissue
  - Recanalization - Small channels form in a thrombus to allow blood flow, reducing ischemia
- **Recanalization of a thrombus.**
  - Newly formed thrombus partially restores flow.
- **Propagation**
  - Thrombus extends along the vessel and may obstruct other vessels
- **Infarction**
  - *Infarct* - A region of necrosis near a thrombus caused by ischemia
  - Necrotic tissue broken down and replaced by scar tissue
  - More serious in arteries because veins are branched
- **Embolism**
  - Cause: Blood flow is suddenly stopped by an embolus, an abnormal mass in the bloodstream
  - Embolism is a common cause of infarction

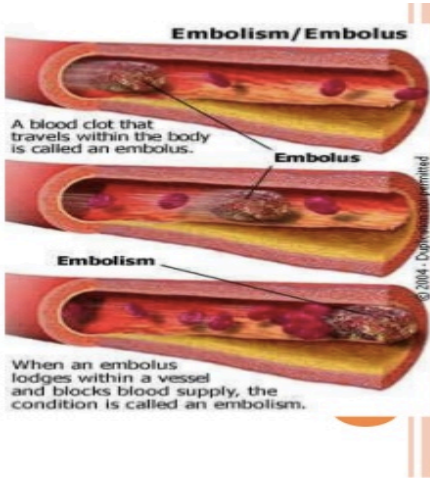
Types of Embolism

- **Thromboembolism**
  - Embolus is a *thrombus* or *fragmented thrombus* that breaks away from its source
  - Cause of fragmentation: Temporary pressure change from resuming activity after a period of inactivity
  - Two types of thromboemboli:
    - Arterial Thromboemboli - Thromboembolus in arteries is carried to smaller vessels until it becomes lodged
    - Venous Thromboemboli - Thromboembolus in veins is carried to larger vessels until it becomes lodged in the heart or lungs
- **Fat Embolism**
  - Forms when fat-rich marrow gains access to blood
  - Causes: Long bone fractures and liver damage
- **Air Embolism**
  - *Air* or *gases* form bubbles in the blood
    - Volume over 100 mL is dangerous
    - Heart is damaged by volume of 300 mL
    - Type of air embolism: The Bends
    - *Nitrogen gas* leaves blood and forms emboli, resulting in quick reduction in pressure
- **Foreign Body Embolism**
  - Foreign material impedes blood flow
- **Amniotic Fluid Embolism (rare)**
  - Infant's cells are shed into amniotic fluid and enter circulation via cuts in the placental membrane

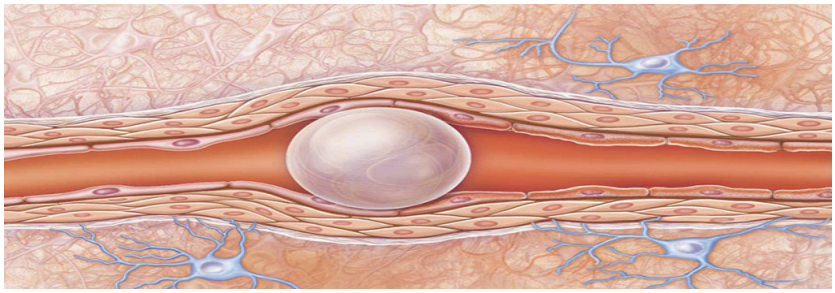
Fat Emboli: Fat particles or droplets that travel through the circulation

Fat Embolism: A process by which fat emboli passes into the bloodstream and lodges within a blood vessel.

Fat Embolism Syndrome (FES): serious manifestation of fat embolism occasionally causes multi system dysfunction, the lungs are always involved and next is brain



Air Embolism →

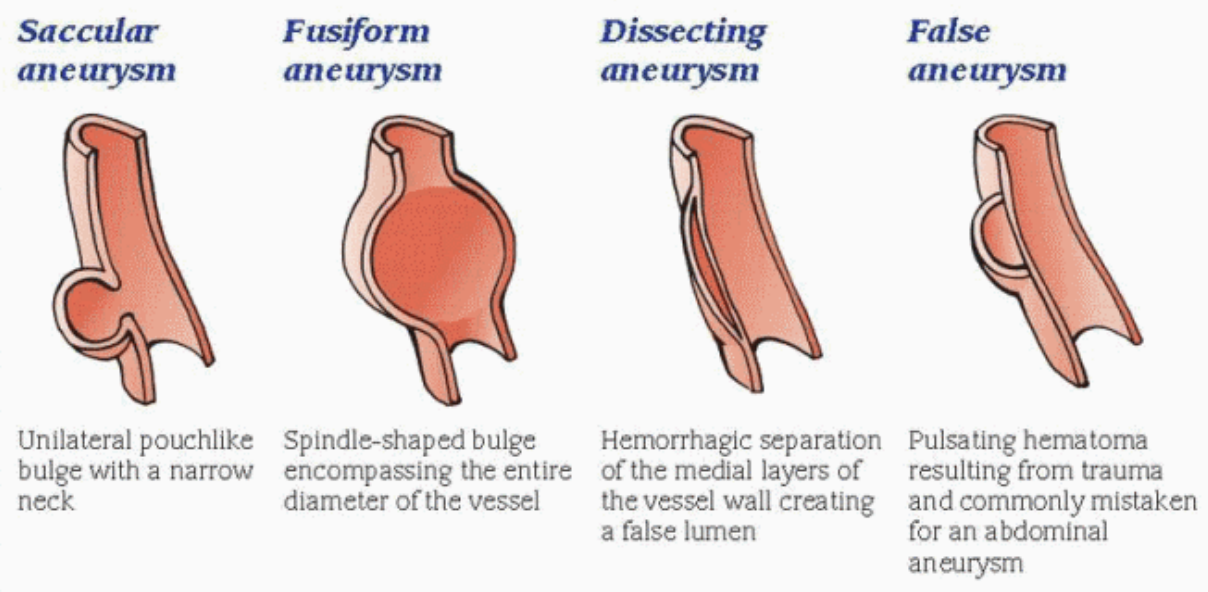


Thromboembolism Therapy

- **Anticoagulant Therapy**
  - Interferes with blood coagulation
  - Example: *Heparin* blocks thrombin and fibrin formation
- **Activation of the Fibrinolytic System**
  - Promotes breakdown of clotting factors
  - Example: *t-PA (tissue plasminogen activator)*
- **Antiplatelet Therapy**
  - Decreases platelet aggregation and activation
  - Example: *Aspirin*

Aneurysm

- Enlargement of the artery or ballooning of the wall
- The growing atheroma and thinning of the wall causes the arterial pressure to increase, which only further weakens the wall
- Two causes of aneurysm are increased blood pressure and weakened arterial walls.



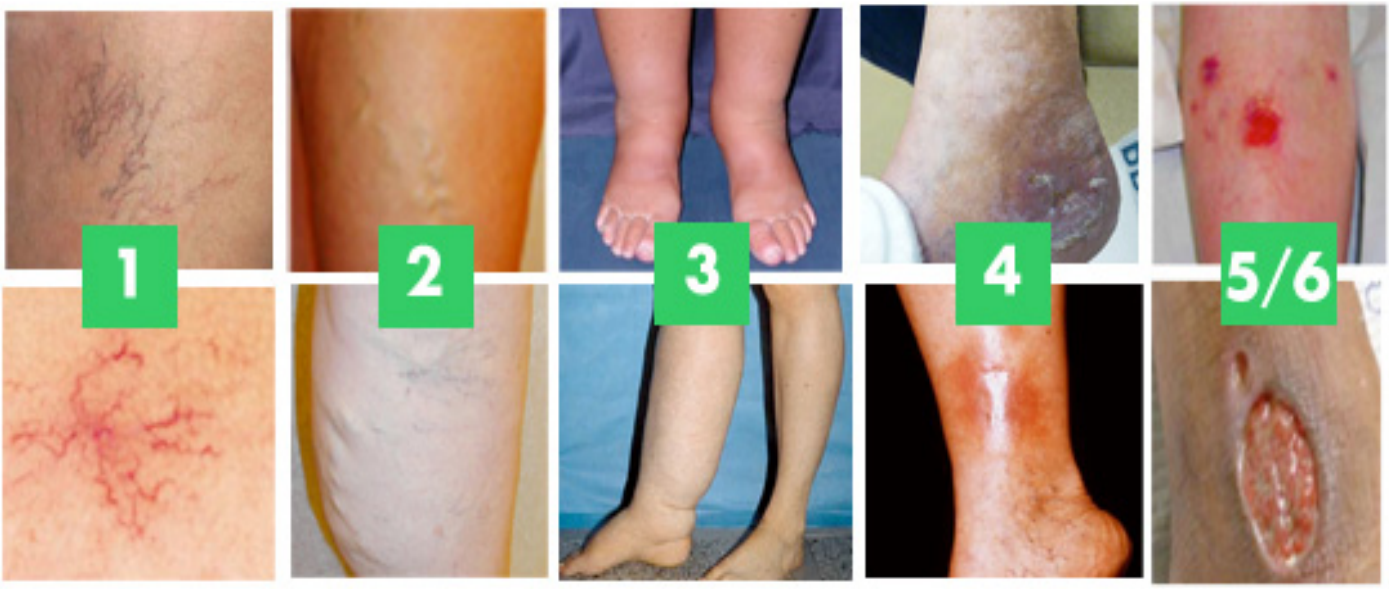
Other vascular disorders caused by disrupted arterial circulation

- **Gangrene –** necrotic dead tissue
- **Pressure sores**
- **Coronary arterial disease**
- **Strokes – cerebral vascular accidents**
- **Raynaud's disease**
    - Excessive constriction of small arteries and arterioles
    - Usually seen in fingers and toes
    - Affects about 5% of population
- **PVD – Peripheral Vascular Disease**
    - Intermittent claudication of extremities
    - More common over 50-years-old and in smokers

Vein Disorders

- Common, but usually not life-threatening
- **Thrombophlebitis**
    - Inflammation of a vein as a result of thrombosis (usually in deep leg veins)
    - Risk of thromboembolism

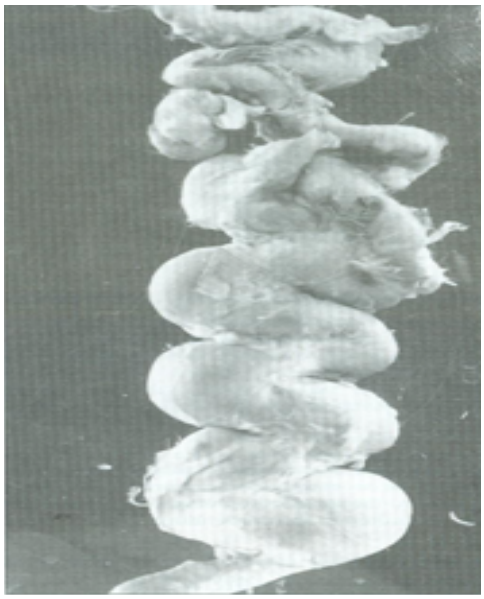
Vein Disease Stages from Spider Veins to Ulcers

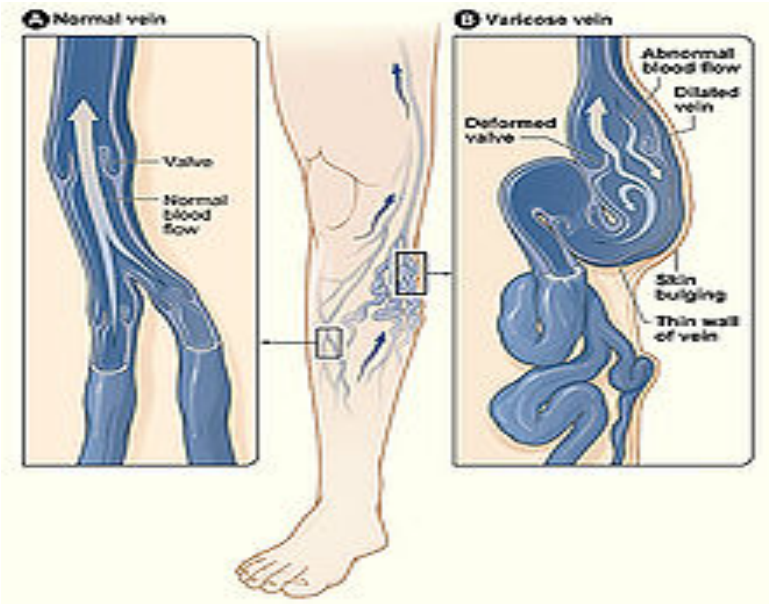


Vein Disease Stages from Spider Veins to Ulcers

- Class 1 - Vein Disease: **Spider Veins** (**Telangectasias**)
    - This describes diseases that occur in tiny veins in the skin
    - The dilated veins and capillary vessels are called telangectasis or spider veins.
    - Occurs in 40% of woman and 18% of men. Over half of the population has this form of vein disease

- Class 2 – Vein Disease: **Varicose Veins**
  - Often referred to as dilated superficial veins
  - Affects 15% of the population
  - Varicose veins are veins that are tortuous and dilated because of leaky valves
  - This is the stage in which people often become aware of vein disease.
  - 75% of patients at this stage states that it interferes with daily activity.
  - Heredity, prolonged standing, obesity, pregnancy





- Class 3 – Vein Disease: **Leg Edema**
  - Slightly more advanced vein disease causes swelling of the legs.
  - The backflow in the venous system interferes with the body's ability to reabsorb fluid leading to swelling of the leg.
  - This swelling resolves at the end of the day when legs are elevated.
  - Vein disease is the most common cause of leg swelling.
- Class 4 - Vein Disease: **Skin Changes**
  - Over time the venous congestion leads to changes in the skin.
  - The skin becomes thinner and **discolored to reddish brown or whitish** in color.
  - At this vein disease stage the skin is easily injured and heals slowly.
- Class 5 & 6 – Vein Disease: **Leg Ulcers**
  - These are the most advanced forms of superficial vein disease.
  - Venous ulcers are caused by venous congestion that has progressed to point that it interferes with ability for blood flow to provide nutrition to skin. This makes any skin injury heal very slowly, if at all.
  - Without treatment of the underlying vein disease, 20% of these ulcers remain unhealed at 2 years.
  - Class 5 Vein is used to describe legs with healed venous ulcers.
  - Class 6 Vein Disease is used to describe legs with active ulcers.
  - Venous disease is the most common cause of ulcers on the leg.

Deep Vein Thrombosis

- The formation of a blood clot in a deep vein
- Symptoms may include pain, swelling, redness or warmth of the area
- Half of the cases have no symptoms.
- Complications may include pulmonary embolism, as a result of detachment of a clot which travels to the lungs, and post-thrombotic syndrome.
- Risk factors include recent surgery, cancer, trauma, lack of movement, obesity, smoking, hormonal birth control, pregnancy, and the period following birth.
- The underlying mechanism typically involves some combination of decreased blood flow rate, increased tendency to clot, and injury to the blood vessel wall.
    - The three factors of Virchow's triad — Venous stasis, hypercoagulability, and changes in the endothelial blood vessel lining (such as physical damage or endothelial activation)—contribute to DVT and are used to explain its formation