Vessels types of vessels

- Arteries
- Veins
- Capillaries

Composition of the wall of an artery:

- Layer of connective tissue (intima)
- Smooth muscle layer (media)
- Tunica adventitia (externa)

Arteriosclerosis — condition in which the arterial walls become thickened and lose elasticity
caused by migration of the smooth muscle cells + fibroblasts into the tunica intima resulting in thickening of the tunica intima + loss of elasticity.

As tunica intima thickens + elasticity is lost, the lumen of the artery becomes narrowed → decreasing blood flow through the artery.

Atherosclerosis is the leading cause of atherosclerosis.
It is the leading cause of coronary artery disease + stroke.

In atherosclerosis there is a localized buildup of fat (lipids) in the arterial wall that hardens to form an atherosclerotic plaque.
Plaque formation is initiated by damage to the endothelium of the artery.

- Hypertension
- Smoking
- AGEs
- Immune Rxns

↓

injury to endothelium

↓

endothelial cells that are damaged stop secreting cytokines that normally prevent platelets and monocytes from sticking

↓

monocytes and platelets stick at site of damage

↓

monocytes convert into macrophages that start secreting enzymes and free radicals

↓

Free radicals oxidize low-density lipoproteins (LDLs)
Oxidized free radicals penetrate into the connective tissue layer of the tunica intima and cause inflammation.

The inflammation attracts the macrophages stuck to the endothelium into the tunica intima.

Macrophages phagocytose the LDLs in the tunica intima but can't digest them.

Macrophages become filled with LDLs and convert into “Foam cells”.

Accumulation of foam cells in the tunica intima forms a lesion called a “Fatty Streak”.
The foam cells of the fatty streak secrete chemotactic factors that attract smooth muscle cells and fibroblasts into the fatty streak where these cells proliferate.

The accumulation of cells in the fatty streak causes it to thicken and start to occlude the lumen of the artery.

The fibroblasts secrete collagen into the fatty streak.

As the collagen walls off the fatty streak from the surrounding tissues of the arterial, the fatty streak becomes a "fibrous plaque."
As the process continues the fibrous plaque becomes progressively larger, progressively occluding the arterial lumen.

A plaque that gets large enough can rupture through the endothelium of the artery.

When collagen of the plaque is exposed to the blood it triggers the coagulation cascade → formation of a blood clot that is stuck to the ruptured plaque → further occluding the lumen of the artery. The ruptured plaque with a thrombus stuck to it is called a "Complicated lesion"
The thrombus can break loose from the plague forming an embolus in the blood.
The embolus will circulate in the blood until it becomes lodged in a blood vessel, causing ischemia in the tissues supplied by the vessel, and tissue death if blood flow is completely blocked.

Treatments:
Directed at minimizing or eliminating risk factors:
- Cessation of smoking
- Control of blood pressure
- Reduction of dietary fat intake
- Increase in dietary intake of
Omega 3 fatty acids
- anti-inflammatory properties
- decrease platelet adhesion
- have blood thinning properties

- Drug therapy to reduce blood levels of LDLs.
  (ex. Lipitor)

- If ischemia or occlusions have occurred these may need to be addressed.

Excess homocysteine in the blood is also believed to contribute to plaque formation.

Homocysteine is a by-product of the metabolism of methionine. Methionine is abundant in red meat and dairy products.
Diets high in red meat and dairy products result in high methionine intake that is converted in the body into homocysteine.

Homocysteine promotes plaque development by:

— Reacts with the LDLs in the blood causing them to aggregate making them easier to phagocyte

— Promotes formation of free radicals in the blood — contribute to endothelial damage.
Hypertension

"High Blood Pressure"

- Clinical definition -
  Consistent elevation of BP
  > 140/90 mmHg
  measured on 3 separate occasions

  caused by a combination of:
  - increased cardiac output (CO)
  - increase in total peripheral vascular resistance (TPR)

  CO

  The volume of blood pumped by the left ventricle per minute

  Depends on:
  - Stroke volume of the LV
  - Heart rate
CO is expressed by formula:

\[ CO = SV \times HR \]

\[ \frac{4900}{min} = 70ml \times 70 \text{beats/min} \]

Any factor that causes increased SV and/or HR will \( \rightarrow \) increased CO \( \rightarrow \) TPR

**TPR**

Depends on diameter of the arteries and viscosity of the blood

Conditions that cause an increase in blood viscosity (e.g., Polycythemia vera) and/or chronic decrease in arterial diameter \( \rightarrow \) TPR \( \downarrow \) BP
Two categories of hypertension

Primary Hypertension
a.k.a. - essential hypertension
or
idiopathic hypertension

A chronic elevation in BP that has no single identifiable cause

Secondary Hypertension

A chronic elevation in BP caused by a disease or condition
ex. hypertension due to Grave's Disease
Chronically elevated BP results in injury to the arterial vessel walls:

- Increases inflammation in arterial wall
- Causes edema
- Causes increase in permeability of arterial wall
- Causes constriction of smooth muscle in arterial wall

Causes hypertrophy and hyperplasia of arterial wall smooth muscle:

Decreases diameter of lumen of the artery
Systemically this process results in increased resistance to blood flow through the arteries (i.e. HTPR).

This will cause further hypertension.

So, chronic hypertension causes a positive feedback loop that further increases the hypertension.

"Hypertension begets Hypertension!"

Treatments are directed at maintaining BP below 140/90 mmHg.

If it is secondary hypertension then condition causing the hypertension must be addressed.
For primary hypertension, initial treatment involves lifestyle modifications:
- cessation of smoking
- losing weight
- regular exercise
- decrease dietary salt intake
- Restricting alcohol intake

If these fail to resolve the hypertension, then drug therapy is initiated.

Diuretics — promotes water excretion → ↓ Blood volume → ↓ BP

β-blockers — block sympathetic β receptors on the pacemaker cells & heart muscle cells
"ACE Inhibitors"

Angiotensin converting enzyme inhibitors

Angiotensin is part of the RAAS in this system.

\[ AG \rightarrow AGII \rightarrow \text{stimulates synthesis and secretion of aldosterone} \]

\( \downarrow \) potent vasoconstrictor

ACE inhibitors inhibit the enzyme that converts AG into AGII.

Reduces levels of AGII in blood \( \rightarrow \text{vaso dilation of arteries} \)

Also reduces aldosterone levels \( \rightarrow \text{Na}^+ \) reabsorption from kidney filtrate
Angiotensin II receptor blocking agents

block ATII receptor on smooth muscle of arteries preventing vasoconstrictive effects of ATII

- Calcium channel blockers
decrease SV by blocking Ca**+** channels on heart muscle cells, reducing force of contraction.
Also reduce Ca**+** entering the smooth muscle cells of arteries reducing vasoconstriction

- Centrally acting adrenergic inhibitors
act by decreasing sympathetic output from CNS → vHR, BSV, and v vasoconstriction of arteries
Orthostatic Hypotension

A fall in blood pressure upon standing

Normally, BP drops 10-20 mmHg when you are laying down or sitting. When you stand up quickly, your CV system adjusts to prevent the blood in your head from being pulled down into your body by gravity.

This is prevented by the baroreceptor reflex that increases sympathetic output from the CNS upon standing.

The sympathetic output acts to NH, TSV and VS to constrict the arteries to SBP and keep blood from draining out of your head.
In orthostatic hypotension this reflex mechanism fails resulting in a drop in blood pressure in the head causing:

- dizziness
- blurred vision
- fainting

Orthostatic hypotension is caused by:

- Lesion in the CNS due multiple sclerosis, diabetes mellitus, etc., that cause lesions in autonomic centers in the brain
- Drugs that decrease sympathetic output
- Prolonged immobility
- Low blood volume
- Idiopathic (cause can't be identified)

Treatment
Primarily directed at addressing underlying cause.

No treatment for idiopathic hypotension other than administration of drugs to raise BP to help reduce it.

Aneurysm

Localized dilation or outpouching of a blood vessel or heart chamber.

Result from weakening in the wall of the blood vessel or heart chamber.

Most common cause is an atherosclerotic plaque that damages the wall of the vessel, or disrupts blood flow.
to a part of the heart chamber wall causing death of cells in the heart chamber wall and weakening of the wall.

Heart muscle cells are always active and rely on aerobic metabolism to generate the ATP they need.

So, they need a steady supply of O2 and nutrients, and to have their wastes carried away.

If an occlusion of a coronary artery occurs, ischemia and hypoxia will occur in the part of the heart normally supplied by that artery.
when this happens the heart muscle cells in that part of the heart shift to anaerobic metabolism. Heart muscle cells can be sustained for up to 20 min by anaerobic metabolism, but if full blood is not restored, then the cells start to die resulting in myocardial infarction (cardiac muscle cell death).

Ischemia of the heart muscle is usually accompanied by chest pain (angina pectoris).

In early stages of coronary artery disease, ischemia and angina may occur only upon exertion.
"Silent ischemia" can occur, where there is no angina associated with the ischemia.
Normal ECG deflections

Atrial depolarization

Ventricular depolarization

Ventricular repolarization

ST segment depression

T wave inversion

ST segment elevation

Depolarization of walls of the ventricles

Repolarization of walls of the ventricles

Ischemia causes changes in the ST segment of the ECG.