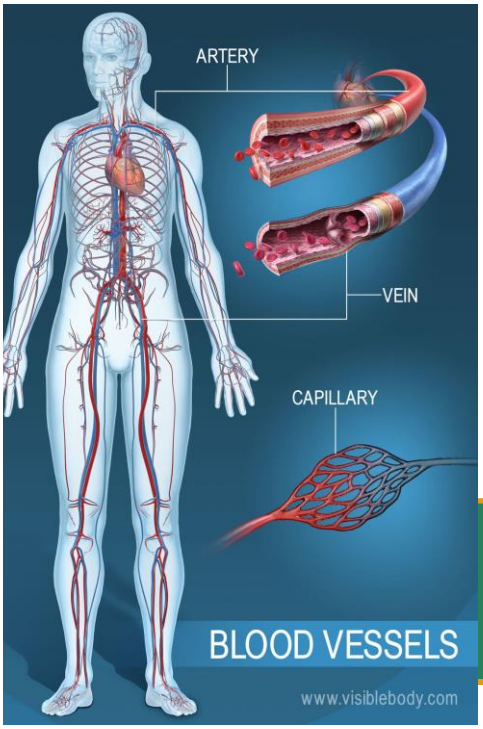
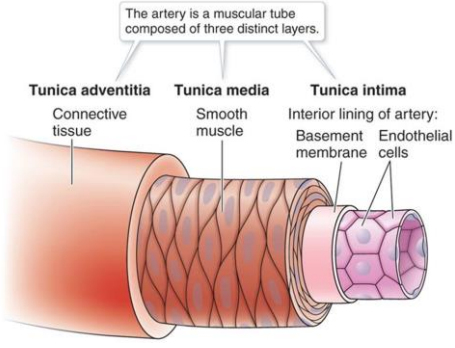


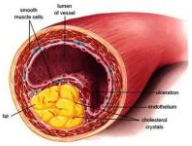
Chapter 15

Arterial Disorders

1

Basic Concepts





Arteries

- Muscular-walled blood vessels
- Move blood away from heart
- The high the pressure, in the vessels → the greater the resistance the heart must work against

Arteriosclerosis

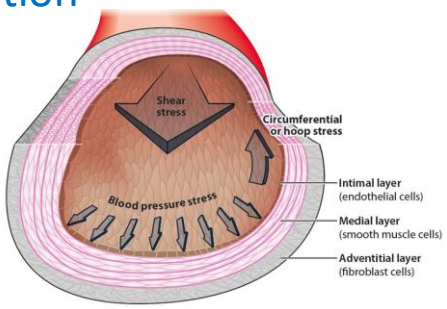
- Hardening and narrowing of arteries

Atherosclerosis

- Plaque build up on arterial wall

2

Arterial Wall Composition

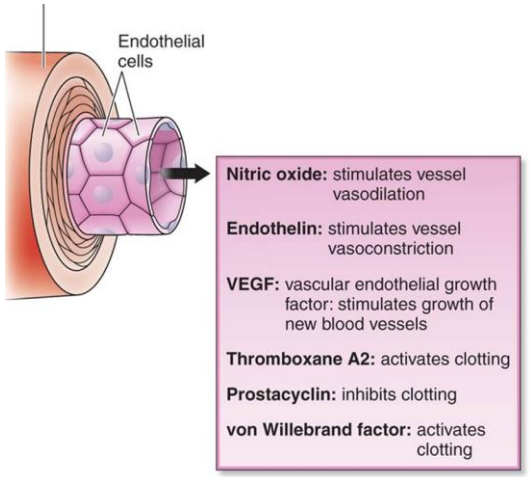


- Tunica intima
  - Inner lining of endothelial cells
  - Damage may lead to arteriosclerosis and atherosclerosis
- Tunica media
  - Smooth muscle
  - Regulate blood flow
    - Alpha-adrenergic nerve fibers: vasoconstriction
    - Beta-adrenergic nerve fibers: vasodilation
  - Calcium: vasoconstriction
    - Calcium channel blockers (CCB): vessel relaxation
- Tunica externa (adventitia)
  - Outer covering

3

Endothelium Function

- Fluid filtration, maintain blood vessel tone, semipermeable barrier, neutrophil chemotaxis
- Vessel dilation
  - Nitric oxide (NO)
- Vessel constriction
  - Endothelin
- Angiogenesis
  - VEGF
- Diuresis
  - C-type natriuretic peptide
- Clot prevention
  - Prostacyclin
- Clot formation
  - Thromboxane A2



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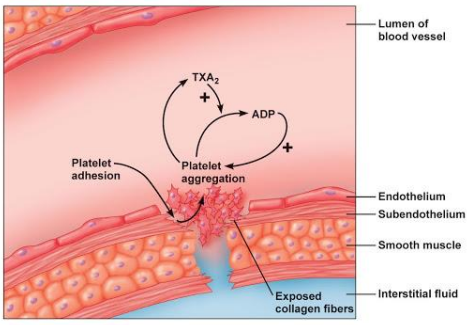
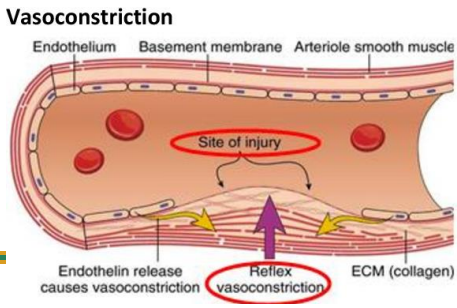
Endothelial Injury

- Leads to arteriosclerosis and atherosclerosis
- Endothelial injury attracts WBCs
  - Initiates inflammation
  - vWF released increasing platelet aggregation
  - Foam cells (lipid-rich macrophages) form
  - NO release inhibited causing vasoconstriction
  - Plaque formation



(a) Damaged blood vessel endothelium



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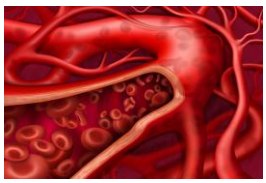
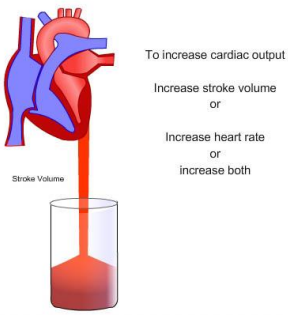
Blood Flow Regulation

- **Blood flow inversely related to diameter of vessel**
  - Flow from large diameter to small diameter reduces flow and increases pressure
  - Resistance is affected by → vessel diameter, vessel length, and blood viscosity
- **Blood flow = blood pressure/resistance**
  - Blood flow = CO (cardiac output)
  - Blood pressure = BP
  - Resistance = PVR (peripheral vascular resistance)



- **Cardiac output (CO)**
  - Amount of blood from LV per minute
  - CO = BP/PVR
  - BP = CO × PVR
  - Factors can be adjusted independently
    - To raise BP:
      - Increase CO
      - Increase peripheral vascular resistance (PVR)



To increase cardiac output

Increase stroke volume
or

Increase heart rate
or
increase both

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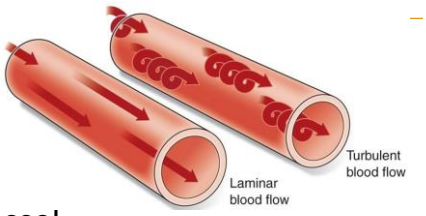
Turbulent vs Laminar Flow

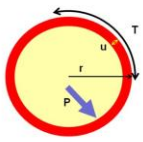


- Laminar
  - Smooth flow parallel to vessel
- Turbulent
  - Rough flow perpendicular to vessel
  - Endothelial injury can lead to turbulent flow
  - "Whooshing" sound known as *bruit*
- Sluggish, stagnant, or turbulent blood flow increases risk of thrombus formation

Arterial Wall Tension and Distension

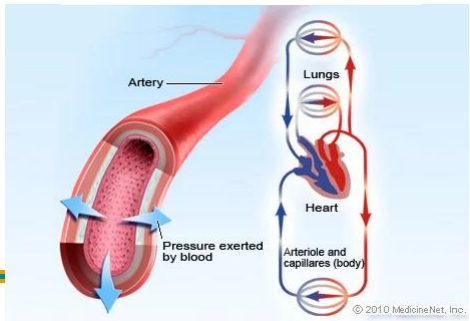
- Arterial wall tension
  - Force opposing the distending pressure inside the vessel
  - Laplace's Law
    - Intraluminal pressure = tension/radius

LaPlace's Law



$$\text{Wall Tension (T)} = \frac{\text{Transmural Pressure (P)} \times \text{Radius (r)}}{2 \times \text{Wall Thickness (u)}}$$

- Hypertension (HTN)
  - Vessel walls hypertrophy (enlargement of an organ or tissue from the increase in size of its cells.), reducing tension and wall stress
- Compliance
  - Distending capacity of a blood vessel



Blood Pressure Regulation

- Systole
  - Cardiac contraction
- Diastole
  - Cardiac relaxation
- SBP/DBP: 120/80 mm Hg
- Pulse pressure
  - Difference between SBP and DBP
  - Ideal: approximately 40 mm Hg

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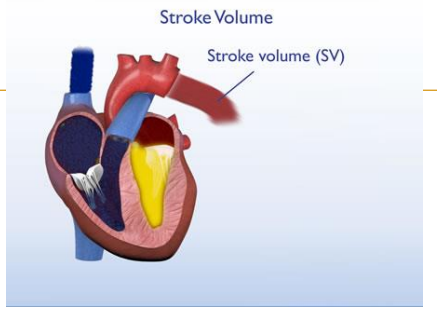
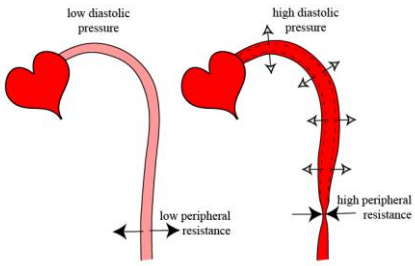
Cardiac Factors



- Stroke volume (SV) = Amount of blood ejected per beat
- CO = HR × SV (per minute)
  - Approximately 5 L/min at rest
  - 70 bpm × 70 ml/beat = 4.9 L/min
- The body has to adjust PVR and BP inversely to maintain CO.
  - For example, to maintain CO when BP decreases → the body has to raise peripheral vascular resistance by arterial vasoconstriction
    - CO = BP/PVR or BP = CO × PVR



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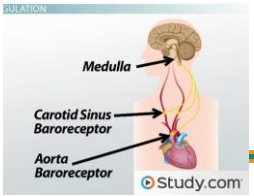
Pressure Relationships

- CO = BP/PVR or BP = CO × PVR
- ➔ *Flow, resistance, and pressure are all related*
- Factors can be changed
  - ANS innervation affects PVR by changing vessel diameter
  - Changes in PVR affect BP
  - Changes in BP affect CO
  - Changes in HR and SV can affect CO and BP

Baroreceptors: Neural Regulation of BP

- Short-term regulation of BP changes
  - *Example:* lying down to standing
- Located in walls of aorta and carotid arteries
- Sense stretch of vessel wall
- Send signal to cardioregulatory center
  - Medulla oblongata and pons
  - *BP too high:*
    - Activate PNS
    - Decrease HR, contractility, vasoconstriction
  - *BP too low:*
    - Activate SNS
    - Increase HR, contractility, vasoconstriction



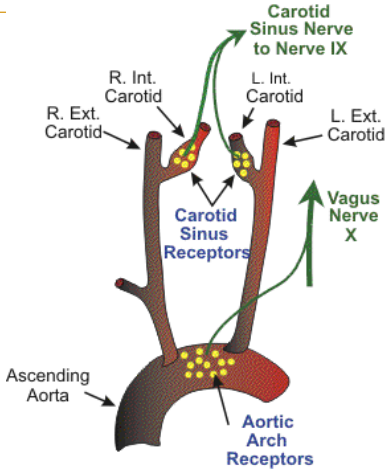


Figure 1. Location and innervation of arterial baroreceptors.

Orthostatic Hypotension

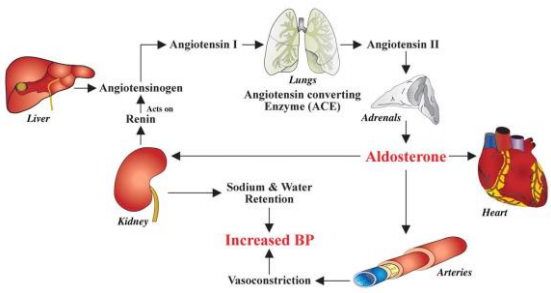
- Drop in BP when changing position from lying down to standing
- Decreased cerebral perfusion
  - Dizziness
- Decreased BP sensed by baroreceptors
- Activation of SNS increases HR to compensate
- Very common in the elderly

Renin-Angiotensin-Aldosterone System (RAAS)

Key role in BP regulation

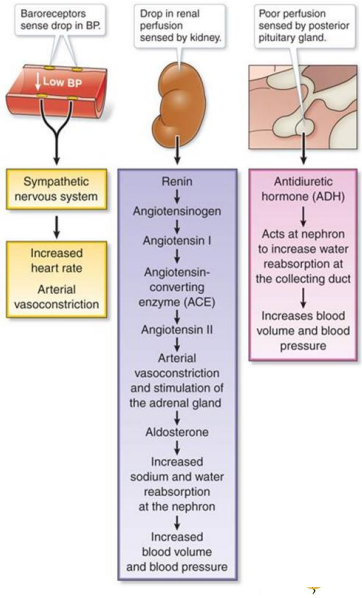
- **Renin**
  - From JG (juxtaglomerular) cells of kidneys in response to low pressure or perfusion
  - Converts angiotensinogen (from liver) to angiotensin I
- **Angiotensin I converted to angiotensin II**
  - ACE (angiotensin-converting enzyme) **in the lungs**
- **Angiotensin II**

  a) Potent vasoconstrictor -- b) Activates aldosterone for adrenal cortex
- Aldosterone stimulates sodium and water retention by kidneys to increase blood volume and pressure
- Combination of vasoconstriction (angiotensin II) and fluid retention (aldosterone) serve to elevate BP



Antidiuretic Hormone (ADH)

- From posterior pituitary
  - ADH = vasopressin
  - Released in response to drop in BP and/or blood volume or increased blood osmolarity
- Increases water reabsorption by kidneys
- Raises blood volume and blood pressure



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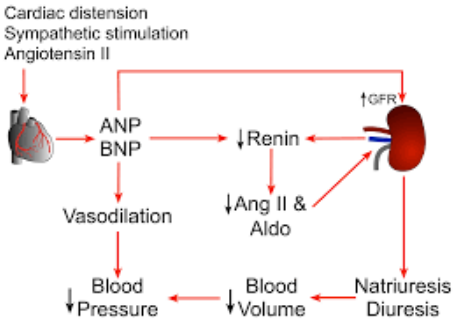
Natriuresis (natural diuresis promoted by the heart and brain)

- in response to excess water in the bloodstream→ the heart releases atrial natriuretic peptide (ANP) and the brain releases brain natriuretic peptide (BNP)
  - These act at the nephrons to release excess water into the urine.
  - The reduction of blood volume can contribute to a lowering of BP.
  - When BP and blood volume return to normal, water and sodium excretion cease.



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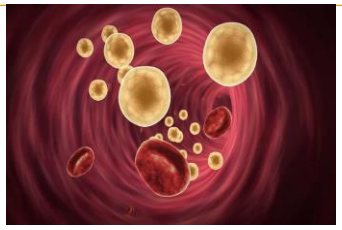
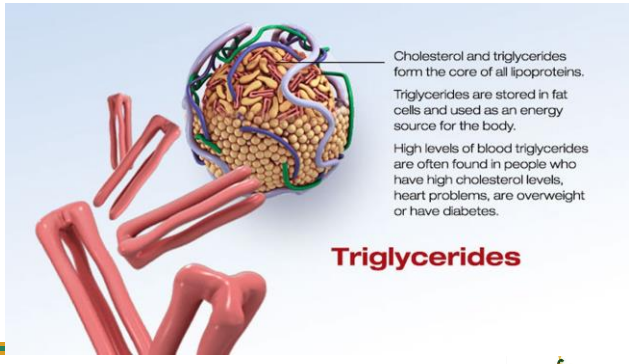
Lipids

- Cholesterol
  - Ingested from diet, but mainly made by liver
  - Used in cell membrane and hormone synthesis
- Triglycerides
  - Ingested in diet
  - Stored in adipose tissue





Lipoproteins

- Transport lipids in blood
  - LDL: low-density lipoprotein
    - "Bad" cholesterol as involved in plaque formation in arteries
  - HDL: high-density lipoprotein
    - "Good" cholesterol as it helps excrete cholesterol from body ("reverse cholesterol transport")

Effect of Glucose on Arteries

- Glucose injures endothelial cells
  - Glycoslation (glycation)
  - Forms AGEs (advanced glycosylation end products)
- Inflammation and plaque formation may result
- AGEs increase endothelin release leading to **vasoconstriction**
- Reason for diabetes mellitus being a risk factor for CAD

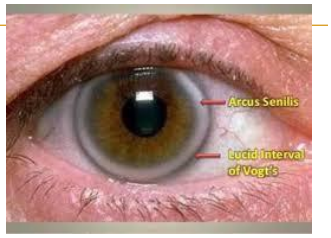
Other Factors Affecting the Arteries

- Free radicals
  - Damage cell membrane of endothelial cells, causing inflammation
- Nicotine
  - Potent vasoconstrictor, especially coronary arteries; increase BP, SNS activation
- Homocysteine
  - Damages endothelial linings (deficiencies in vitamin B_{12} or folic acid decrease homocysteine breakdown)

Hypelipidemia

- CVD
  - Associated with elevated LDL and low levels HDL
- Elevated lipid risk factors
  - Familial hypercholesterolemia (FH)
  - Diabetes mellitus
  - Obesity
  - Hypothyroidism
  - Sedentary lifestyle
  - Diet high in saturated fats
  - Medications: progestins, corticosteroids

Hyperlipidemia (continued_1)



- Plaque formation along vessel walls
- Lipid-filled WBCs (foam cells)
- Overt signs and symptoms may be lacking
- Review family history and look for risk factors for cardiovascular disease
- **S/S**
  - Xanthoma: cholesterol deposits under skin
  - Xanthelasma: cholesterol deposits around eyes
  - Arcus senilis: yellow-white ring around cornea
- **Diagnosis**
  - Blood sample to evaluate lipids
  - Rule out causes that may elevate lipids
    - *Example:* hypothyroidism
  - Also: hs-CRP; homocysteine levels
- ASCVD: Atherosclerotic Cardiovascular Disease Risk

Hyperlipidemia—Treatment

- Lifestyle modifications
  - Dietary cholesterol less than 300 mg/day
  - Limit saturated fats
  - Regular physical activity
- Medications
  - **Statins**
    - HMG-CoA reductase inhibitors
    - Decrease liver cholesterol synthesis and may also reduce plaque
- **Bile acid sequestrants**
  - Block bile acid absorption
  - Cholesterol is key component of bile
- **Fibrates**
  - Decrease triglyceride secretion by liver
- **Monoclonal antibody medications**
  - Block enzyme, which degrades LDL receptors
  - LDL levels in blood are reduced

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Hypertension = Elevated BP

- "Silent killer"
- General criteria:
  - 2 or more BP readings of DBP greater than 80 or SBP greater than 130 mm Hg
- 5 Categories
  - Normal
  - Elevated BP
  - Stage 1 HTN
  - Stage 2 HTN
  - Hypertensive crisis
- Controversy about recommended BP goals for different populations
- Primary HTN: 95%
  - Etiology unknown
- Secondary HTN
  - Due to underlying disease
    - *Example:* Cushing's disease

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Hypertension (continued_1)

- ~1 in 3 adults in U.S.
- Risk factors
  - Age
  - African American ethnicity
  - Obesity
  - Family history
  - Diabetes mellitus
  - Tobacco use
  - Stress
  - Excessive alcohol intake
  - Hypersensitivity to angiotensin II
  - High renin secretor

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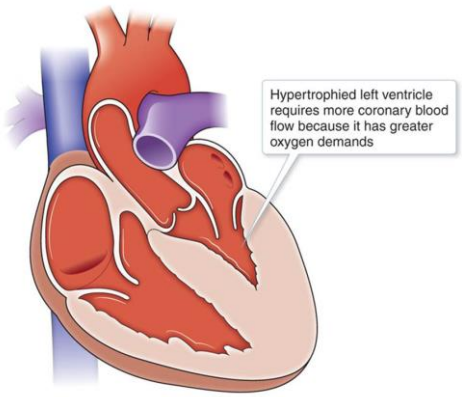
Hypertension (continued_2)

- Two major pathological effects (complications)
  - High shearing stress on arterial walls
    - Damage to organs:
      - Injury to retina, kidneys, brain, lower extremities
  - LV hypertrophy (LVH)
    - Coronary blood supply unable to support additional ventricular tissue



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Complications of Hypertension

- Left Ventricle Hypertrophy
  - May lead to MI or heart failure
- Aneurysms
  - Bulge in weakened area of arterial wall
- Cerebral hemorrhage
- Hypertensive encephalopathy
- Hypertensive retinopathy
  - Arteriovenous nicking
- Renal disease
  - Glomerular injury

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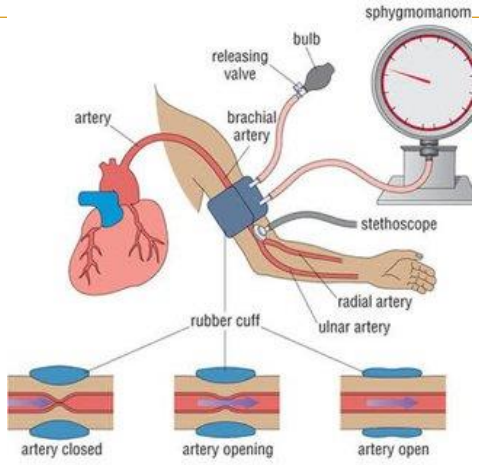
Hypertension (continued_3)

- Often no symptoms
  - Target organ damage may present with headaches, chest pain, vision disturbances, dizziness
  - Check for disorders and medications known to elevate BP
- BP measurement
  - Seated for 5 minutes
  - No caffeine, exercise, smoking within prior 30 minutes
  - 2 measurements: use average
  - HTN: 2 separate measurements of elevated BP on separate days
  - Ambulatory BP monitoring may be used



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Hypertension Assessment

- Fundoscopic exam to examine retinas (HPT places excess pressure on arteries and arterioles)
- Chest → Alteration in PMI (point of maximal impact); When listening to the heart, the clinician may hear an S4 sound, which occurs before S1 because of a less compliant left ventricle in LVH.
- Bruits → Artery walls can become weakened and form aneurysms. Turbulent blood flow within an aneurysm can be heard as a bruit through the stethoscope.
- Peripheral arteries of lower extremities → check perfusion: Temperature, sensation, pulses
- **Diagnosis:** Rule out underlying diseases that may elevate BP; 12-lead ECG; urinalysis (checking for protein in urine which may occur with HTN damage of kidneys); CBC

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Hypertension—**Treatment**

- **Diet:** DASH (Dietary Approaches to Stop Hypertension)
- **Stress** reduction and physical **activity**
- **Smoking** cessation
- **Medications**
  - Diuretics
  - ACE inhibitors (The angiotensin converting enzyme (**ACE**) is an enzyme that converts angiotensin I to angiotensin II. Angiotensin II helps increase blood pressure by causing small blood vessels constriction.)
  - ARBs (angiotensin II receptor blockers)
  - Calcium channel blockers (block vasoconstriction of arteries)
  - Beta-adrenergic blockers (Beta blockers diminish the effects of the SNS on the heart and arteries, thereby decreasing HR and blocking vasoconstriction)

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Atherosclerosis

- Gradual process by which atherosclerotic plaques build up on arterial wall
- Contributes to CAD, cerebrovascular disease, peripheral arterial disease
- Result of endothelial injury and inflammation
  - Lipids, elevated glucose levels, free radicals, shearing force of BP

Atherosclerosis Risk Factors

- Gender
- Age
- Diabetes mellitus
- Family history
- Tobacco use
- Hypertension
- Obesity
- Lifestyle factors
  - Sedentary lifestyle
  - Diet high in saturated fats

Atherosclerosis Pathophysiology

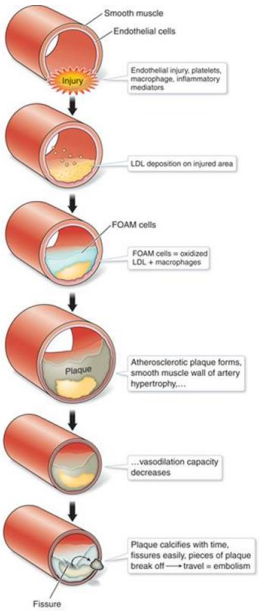
- Injury to endothelium
- Produce adhesion molecules that attract WBCs
  - Vascular cell adhesion molecule 1 and chemoattractant protein-1
- WBCs differentiate into macrophages and fill with LDLs
  - Become foam cells

Atherosclerosis Pathophysiology (continued_1)

- Foam cells store cholesterol until they undergo apoptosis and release lipids into tunica media layer
- Inflammatory cytokines attract fibroblasts
- Fatty streaks form leading to plaques
- Arterial wall becomes less elastic
- Plaques calcify and are covered with fibrous platelet cap

Atherosclerosis Pathophysiology (continued_2)

- Plaque rupture causes bleeding
- Plaque can break loose and travel to area and obstruct blood flow
- hs-CRP: high sensitivity CRP
  - Measures CRP levels
  - CRP associated with inflammation and increased plaque formation



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Clinical Manifestations of Atherosclerosis

- Gradual, so may have no symptoms until end organ dysfunction
- Examine for CVD
  - Obesity, shortness of breath, cyanosis, rapid pulse, elevated BP, weak pulses in extremities, etc.
- Bruits
- Arteriosclerotic changes to retina

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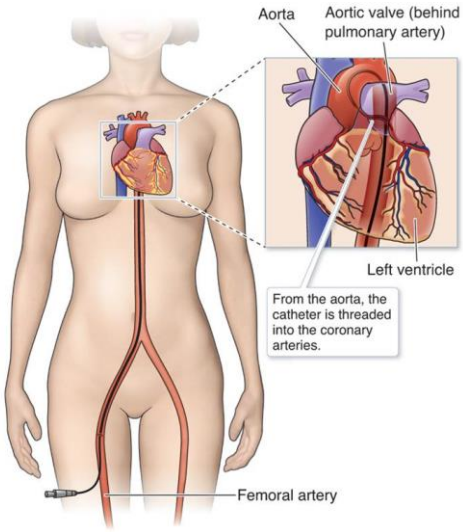
Diagnosis of Atherosclerosis

- Lipid profile
  - Cholesterol, TG's, LDL, HDL
- Endothelial function assessment
  - Intracoronary Doppler technique
  - Ultrasound of brachial artery
- C-reactive protein
  - CRP acute phase protein from liver: inflammation
  - hs-CRP (high sensitivity CRP): increased levels associated with elevated CVD risk
- Homocysteine levels
  - High levels associated with endothelial injury
- Calcium computerized tomography scan
  - CT scan detects calcified plaques
- Cardiac angiography
  - Radiopaque dye study using cardiac catheterization to examine blocked vessel
- Intravascular ultrasonography
  - Via catheterization provides cross-sectional image of coronary arteries

Atherosclerosis Treatment

- Same as for hyperlipidemia
- Use coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI), such as angioplasty with stent placement, to reperfuse ischemic areas of heart

Cardiac Catheterization and Coronary Angiography



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Peripheral Arterial Disease—PAD

- Arteriosclerosis and atherosclerosis outside coronary arteries
  - Most common site: femoral artery above knee
- Same risk factors as atherosclerosis
  - Diabetes mellitus accelerates process
    - Peripheral neuropathy may be present
- Gradual onset
  - Usually symptoms don't present until 70% occlusion

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Peripheral Arterial Disease—PAD (continued_1)

- Intermittent claudication: primary sign
  - Pain with exertion, relieved by rest
  - Occlusion decreases oxygenation of tissue, leading to ADP and lactic acid formation
  - Reducing activity enables oxygen levels to meet metabolic demand, eliminating pain
- Metabolic changes in muscle occur with ischemia and reperfusion cycles

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Peripheral Arterial Disease—PAD (continued_2)

- Examine for signs of arteriosclerosis and atherosclerosis
  - HTN, hyperlipidemia, diabetes, CAD, MI
- Assessment of patient symptoms:
  - pain and numbness with exertion alleviated by rest, etc.
  - Examine for diminished or absent pulses (bilateral comparison), palpable coolness, paresthesia, pallor, sensation distal to proximal

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Peripheral Arterial Disease—PAD (continued_3)

- Diagnosis
  - Ankle-brachial index (ABI): compare upper and lower extremity BP
    - Normal: 1 or slightly greater
    - Less than 1 indicates PAD
  - Serum labs: CBC, ESR, CRP
  - Arterial plethysmography, conventional angiography, arteriogram, CT scan, MRI, capillary refill time (normal refill less than 2 seconds)

Peripheral Arterial Disease—PAD (continued_4)

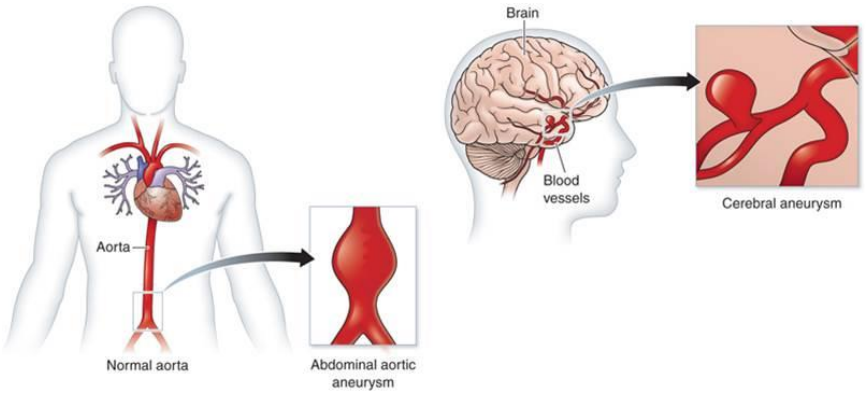
- Treatment
  - Lifestyle modification
    - Exercise stimulates collateral circulation
  - Medications
    - Cholesterol lowering, anti-hypertensive, platelet inhibitors, vasodilators
    - Thrombolytic agents may be used
  - Peripheral arterial revascularization procedures help restore circulation
  - Open surgical vascular bypass grafting

Aneurysm

Weakening of arterial wall causing bulging or dilation

- Locations
  - Cerebral arteries
    - Sometimes called “berry aneurysms”
  - Aorta
    - Most common: abdominal aortic aneurysm (AAA)
- Normally caused by arteriosclerotic damage
  - Also genetic predisposition, infection, vascular disease
- Risk factors for rupture
  - Atherosclerosis, smoking, HTN

Aneurysm (continued_2)



Aneurysm (continued_2)

- Classified by size, shape, location
  - True aneurysm
    - Involves all 3 layers of vessel wall
  - False aneurysm
    - Hematoma where the clot is outside arterial wall
  - Fusiform shape
    - All layers of vessel wall dilate equally
  - Saccular shape
    - Weakness on one side of vessel

Aneurysm (continued_3)

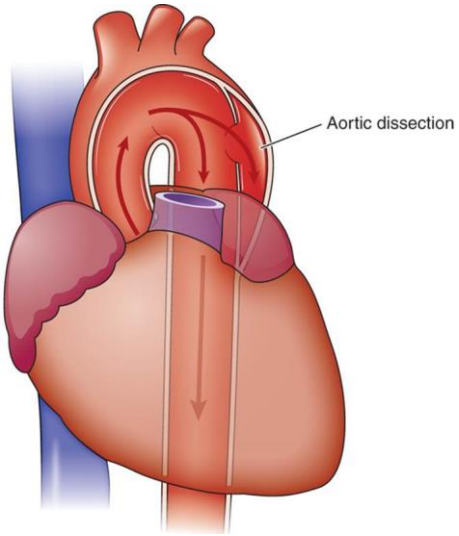
- Presentation depends on size, location, and integrity
  - May be missed until rupture occurs
- AAA: may present with abdominal or back pain
  - May compress organs causing nausea and vomiting
  - In thin patient, may see pulsatile mass
  - Deep palpation should not be performed
  - Bruit may be present
- Cerebral aneurysms are normally silent
  - If rupture: subarachnoid hemorrhage

Aneurysm (continued_4)

- Diagnosis
  - Found incidentally
  - Ultrasonography
- Treatment
  - Smoking cessation, BP regulation
  - AAA: periodic follow up
  - Surgical treatment may be necessary

Aortic Dissection

- Tear in lining between tunica intima and media of aorta leading to a splitting of layers
  - Blood flows between layers
- Potentially lethal
- Symptom onset is sudden
  - Patient hears “ripping” or “tearing” sound
  - Pallor, tachycardia, BP presentation may be variable depending on dissection location



Aortic Dissection (continued_2)

- Signs may include bounding pulse, wide pulse pressure, diastolic murmur, and signs of heart failure
- Cardiac tamponade may occur
- 20% of cases present with neurological deficit, such as syncope
- Diagnosis
  - ECG, chest CT scan or MRI, transesophageal echocardiogram
- Treatment
  - Surgery

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Vasculitis

Inflammation of arterial walls, autoimmune

- Classified based on vessel size
  - Large-sized
    - Temporal arteritis (TA) and Takayasu arteritis
  - Medium-sized
    - Polyarteritis nodosa (PAN) and Kawasaki disease
  - Small-sized
    - Raynaud's disease and thromboangitis obliterans (TAO)

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Temporal Arteritis

Inflammation of superficial temporal arteries, although may affect other arteries

- Exact etiology is unknown; infectious pathogens may be trigger
- Headache is most common symptom, changes in vision may also occur, scalp ischemia and necrosis
- ESR and CRP may be elevated (in 20% of patients, no such elevation)
- Temporal artery biopsy for definitive diagnosis
- Steroid treatment

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Takayasu Arteritis

Inflammation of aorta and its major branches

- Unclear etiology, autoimmune component
- Microorganisms may serve as etiologic agents
- 3 stages
  - 1st is flulike symptoms
  - 2nd involves inflammatory changes in arteries
  - 3rd involves fibrotic changes
- Diagnosis
  - ESR, CRP, antiendothelial antibodies, angiography
- Treatment
  - Corticosteroids

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Polyarteritis Nodosa

Necrotizing inflammation in small- and medium-sized arteries anywhere in body

- Occurs mainly at bifurcation points
- Entire arterial wall affected

- Leads to aneurysms, thrombosis, ischemia
- Viral infections associated
- Can have single-organ involvement or multiorgan failure, peripheral neuropathy often present
- Corticosteroids are standard treatment

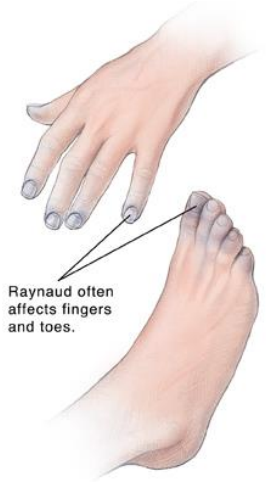
Kawasaki's Disease

- Affects children and is associated with infections
- Predominantly affects coronary arteries
  - Death may occur from MI
- Initial presentation is often with fever that persists
  - Four stages: acute, subacute, convalescent, and recovering

Raynaud's Disease

Vasospasm in arterioles of hands and sometimes feet

- Usually no serious complications
- Thought to be exaggerated SNS response leading to vasoconstriction
- Low levels of NO and high levels endothelin
- Signs
  - Bilateral pain, blanching, and numbness of digits
  - Classic triad: pallor, cyanosis, and rubor in fingers
- No specific lab tests
  - May see elevated CRP, ESR, alpha 1-trypsin
- Diagnosis
  - Echocardiogram
- Treatment
  - IV immunoglobulin and aspirin



Thromboangiitis Obliterans (TA)

- Small- and medium-sized arteries and veins of hands and feet
- Usually young, adult males
- Cigarette smoking associated with the disease
- Symptoms
  - Deep red skin color; coolness of extremities; claudication of hands and feet
- No specific laboratory tests
  - Angiogram may be used
- Treatment
  - Smoking cessation, vasodilators and exercise

Arterial Ulcers

- Ischemic skin wounds due to lack of blood flow
  - Pale, diminished pulses in extremities with delayed capillary refill
  - Ulcers usually located distally at tips of toes, heel, lateral malleolus
- Antibiotics may be needed to prevent infection
- Preventive measures to lessen further injury to skin