Pathophysiology I

Unit 2

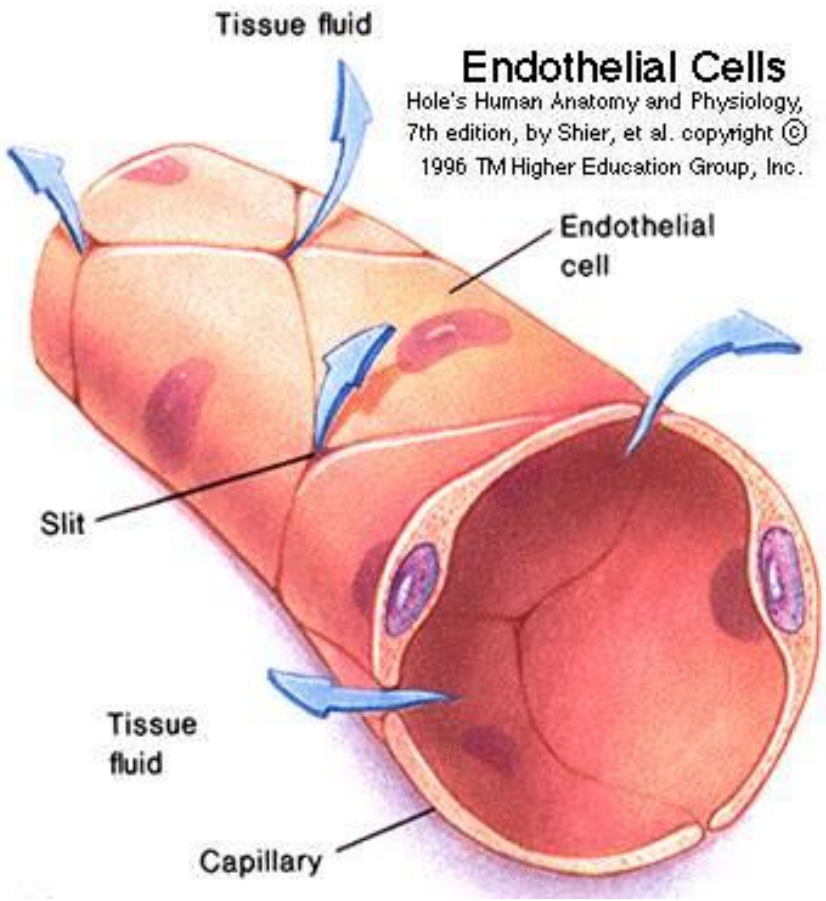
Hematology and Fluid Balance, Cardiovascular Diseases

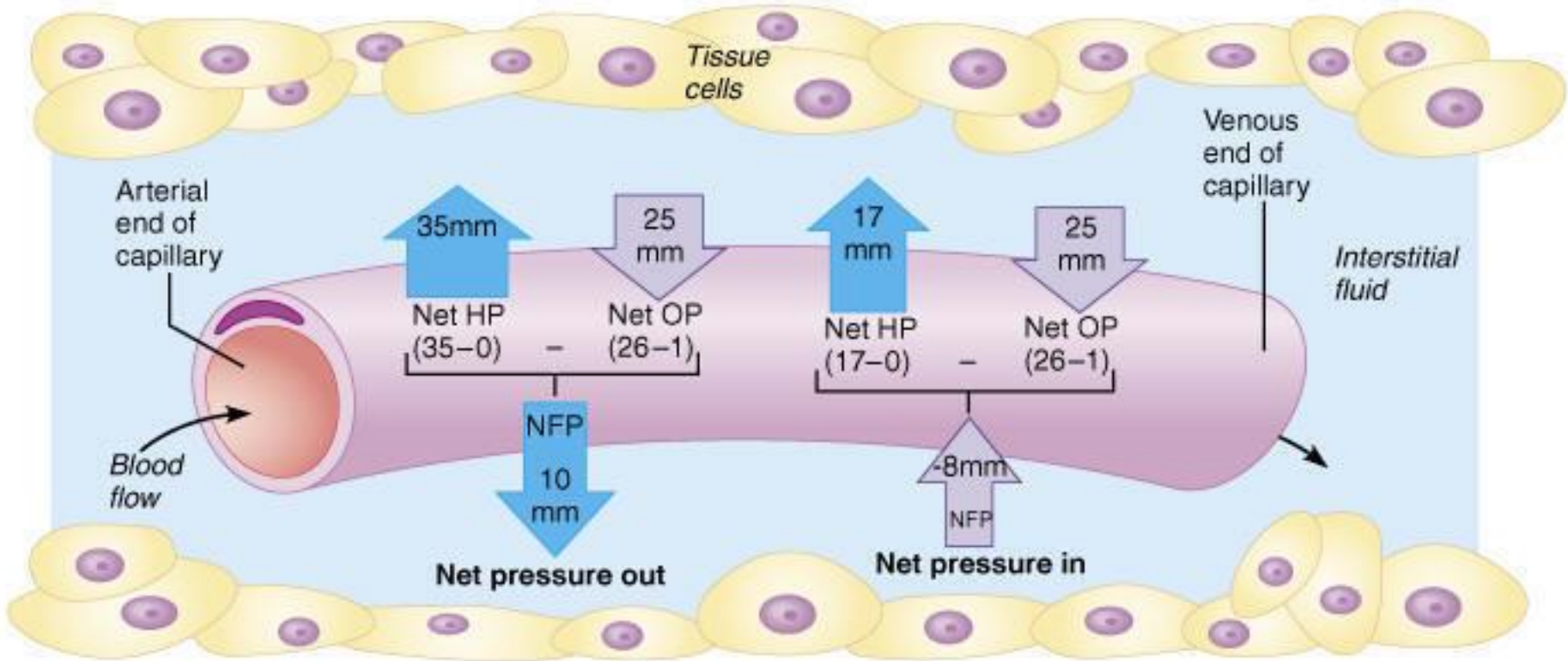
Pathophysiology I

Fluid and Hemodynamic Disorders

Fluids Dynamic in the Body

- Water accounts for approximately 60% of body weight
- Intracellular constitutes 40% of weight
- Extracellular fluid
  - Interstitial fluid (ISF) constitutes 15% body weight
  - Plasma constitutes 5% body weight
- Fluid leaves capillaries to get to cells





Key to pressure values:

HP_c at arterial end = 35 mm Hg HP_{if} = 0 mm Hg OP_{if} = 1 mm Hg

HP_c at venous end = 17 mm Hg OP_c = 26 mm Hg

Fluid and Hemodynamic Disorders

Edema

Edema

- Indicates excessive fluids in the interstitial space and/or body cavities
- It can be localized or generalized
  - Localized
    - May involve any tissue or organ and is deginated descriptively
    - Examples include cerebral edema, pulmonary edema, periorbital edema, etc.
    - Ascites indicates accumulation of fluids in the abdominal cavity
  - Generalized

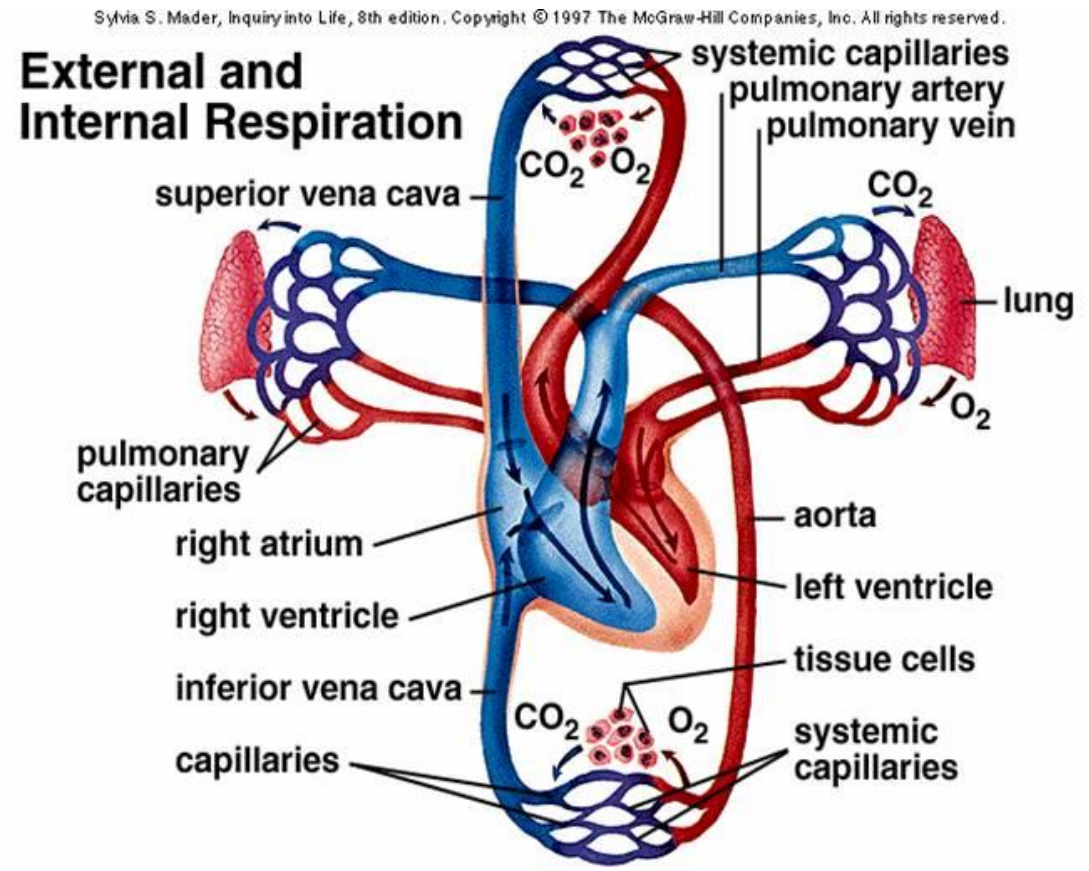
Edema

- Edematous fluid can be classified as an exudate or transudate
- Exudates are rich in protein and blood cells, typical of inflammation
- Transudates contain less protein and fewer cells. Factors causing include:
  - Increased hydrostatic pressure inside blood vessels
  - Decreased oncotic pressure
  - Obstruction of interstitial fluid drainage (obstruction of lymphatics)
  - Increased tissue hydration because of Na retention (Hypervolemic edema)

Edema

- Increased hydrostatic pressure inside blood vessels
  - Most commonly seen with congestive heart failure
  - Most often seen in lower extremities (gravity dependent), and is a pitting edema
- Decreased oncotic pressure
  - Caused by reduction in colloid osmotic pressure (oncotic pressure)
  - Caused by hypoalbuminemia, which in turn is caused by:
    - Protein loss in the kidneys (proteinuria), as seen in nephrotic syndrome
    - Decreased protein synthesis, as seen in chronic liver diseases such as cirrhosis
    - Malnutrition

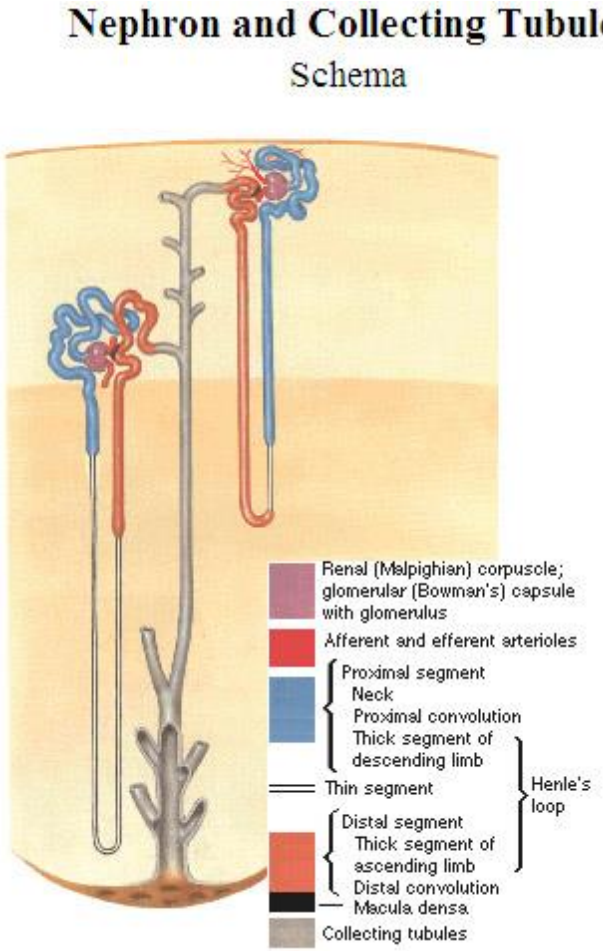
Pitting Edema and CHF



Edema

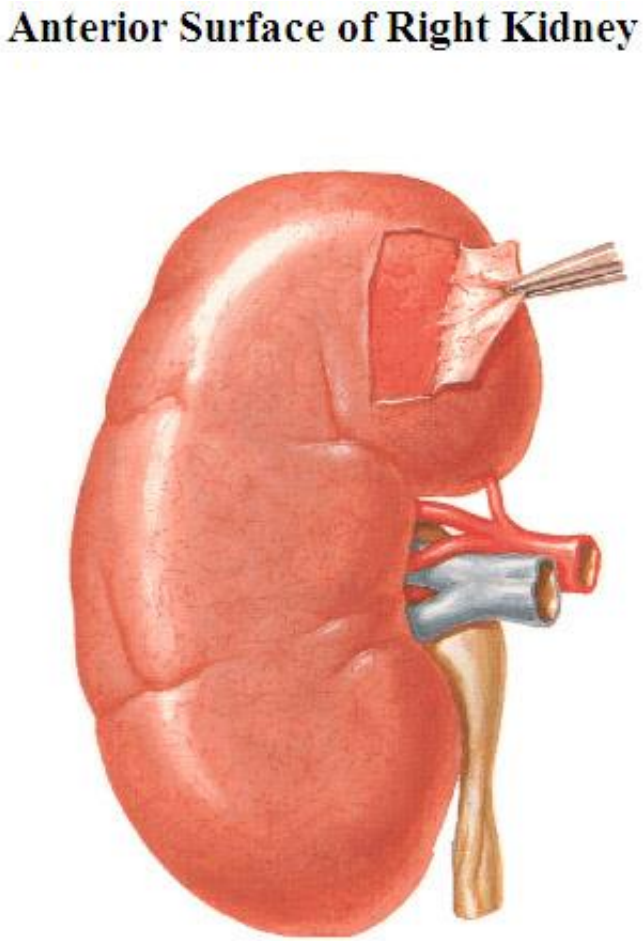
- Obstruction of interstitial fluid drainage (obstruction of lymphatics)
  - Most often occluded by tumor cells or chronic inflammation
- Increased tissue hydration because of Na retention (Hypervolemic edema)
  - Caused by retention of sodium and water
  - Regulation of sodium depends on normal structure and function of kidneys (renin, angiotensinogen, aldosterone)
  - Kidney disease promotes release of renin

Review - Histology of the Kidneys



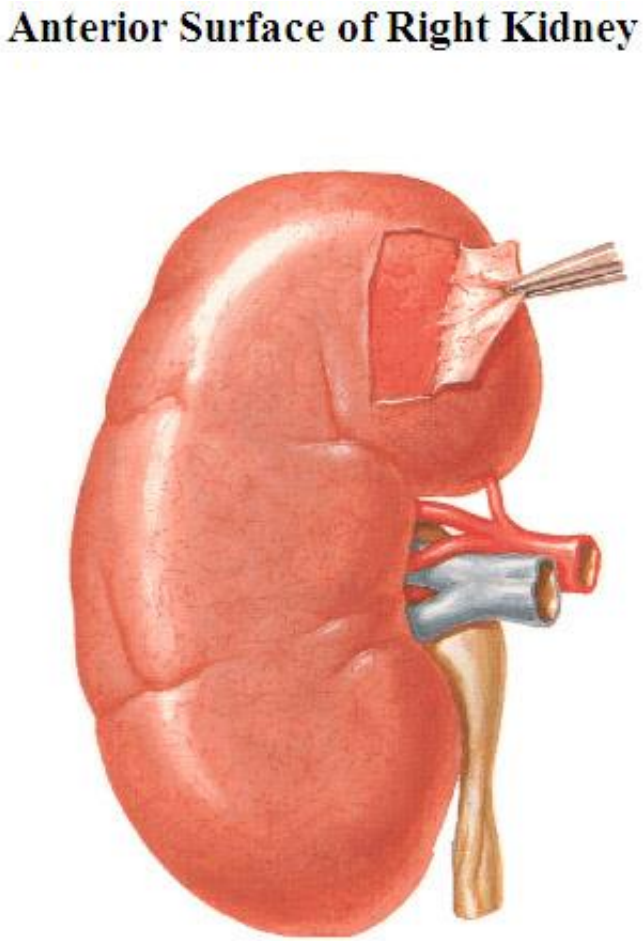
- Nephron
  - The microscopic functional unit of the kidneys which filter wastes and produce urine
- Glomerulus
  - Cluster of arterioles at the entrance of the nephron
  - Contains afferent blood arterioles and efferent arterioles

Review - Fluid Balance



- Vascular supply
  - The kidney is supplied with blood by the renal artery
  - This is a direct branch from the abdominal aorta
  - If someone is volume depleted, the kidneys can initiate the renin-angiotensin mechanism

Review - Fluid Balance



- The renin-angiotensin mechanism regulates blood volume and blood pressure
  - It causes
    - Thirst,
    - Vasoconstriction,
    - Causes adrenal glands to release aldosterone
      - Aldosterone causes more Na (and Water) to be absorbed from the kidneys

Edema

- In clinical practice, edema is often multifactorial
- Edema indicates dysfunction, distribution depends on cause:
  - (Right) Heart failure - edema is in lower extremities (or back if patient is confined to bed)
  - Left ventricular heart failure - results in pulmonary edema and pulmonary hypertension
    - Decreases efficiency of gas exchange
    - Causes dyspnea
  - Renal failure or nephrotic syndrome - edema is typically diffuse
  - Liver failure (such as cirrhosis) - accumulation of fluids is in abdominal cavity (ascites). Attributed to hypoalbuminemia and also due to increased portal venous pressure caused by scarred liver.

Fluid and Hemodynamic Disorders

Hemorrhage

Hemorrhage

- Extravasation of blood, refers to passage of blood outside of the cardiovascular system
- May be sudden onset or chronic, or recurrent
- May be classified as cardiac, aortic, arterial, capillary, venous
  - Hemorrhage could be traumatic or could be secondary to cardiovascular disease
  - Cardiac hemorrhage – trauma or caused by softening of heart wall after myocardial infarction. Often fatal.
  - Aortic hemorrhage – trauma or aortic aneurysm. Often fatal.
  - Arterial hemorrhage - often caused by trauma. Pressure is high and blood loss can be high, leading to death.
  - Capillary hemorrhage - marked by pinpoint droplets of blood appearing on the surface of the skin or mucosa - may be related to trauma, increased venous pressure, weakening of capillary walls, as occurs in vitamin C deficiency (scurvy)
  - Venous hemorrhage - usually traumatic

Hemorrhage
Classification and Terminology

- Hemorrhage is classified as external or internal
  - Internal hemorrhage may fill body cavities
    - Hemothorax
    - Hemoperitoneum
    - Hemopericardium
  - Internal hemorrhage may form a blood filled swelling
    - Hemotoma
  - Hemorrhage can be in the skin
    - Purpura - Between 1 mm ot 1 cm
    - Ecchymosis – larger, blotchy bruise

Hemorrhage
Classification and Terminology

- Clinical terms denoting various forms of hemorrage
  - Hemoptysis
  - Hematemesis
  - Melena
  - Hematuria
  - Metorrhagia

Hemorrhage
Clinical Consequences

- Depends on amount of blood loss, duration, general health of individual
- Massive acute hemorrhage
- Chronic hemorrhage

Fluid and Hemodynamic Disorders

Shock

Shock

- Shock is a life-threatening condition that occurs when the body is not getting enough blood flow. Lack of blood flow means that the cells and organs do not get enough oxygen and nutrients to function properly. Multiple organs can suffer damage as a result. Shock requires immediate medical treatment and can get worse very rapidly. As many 1 in 5 people who suffer shock will die from it.3 types of shock
  - Cardiogenic (due to heart problems)
  - Hypovolemic (caused by too little blood volume)
  - Vasodilation or Anaphylactic (caused by an immune response)
  - Septic shock (due to infections)
  - Neurogenic shock (caused by damage to the nervous system)

Fluid and Hemodynamic Disorders

Thrombosis and Embolism

Thrombosis and Embolism

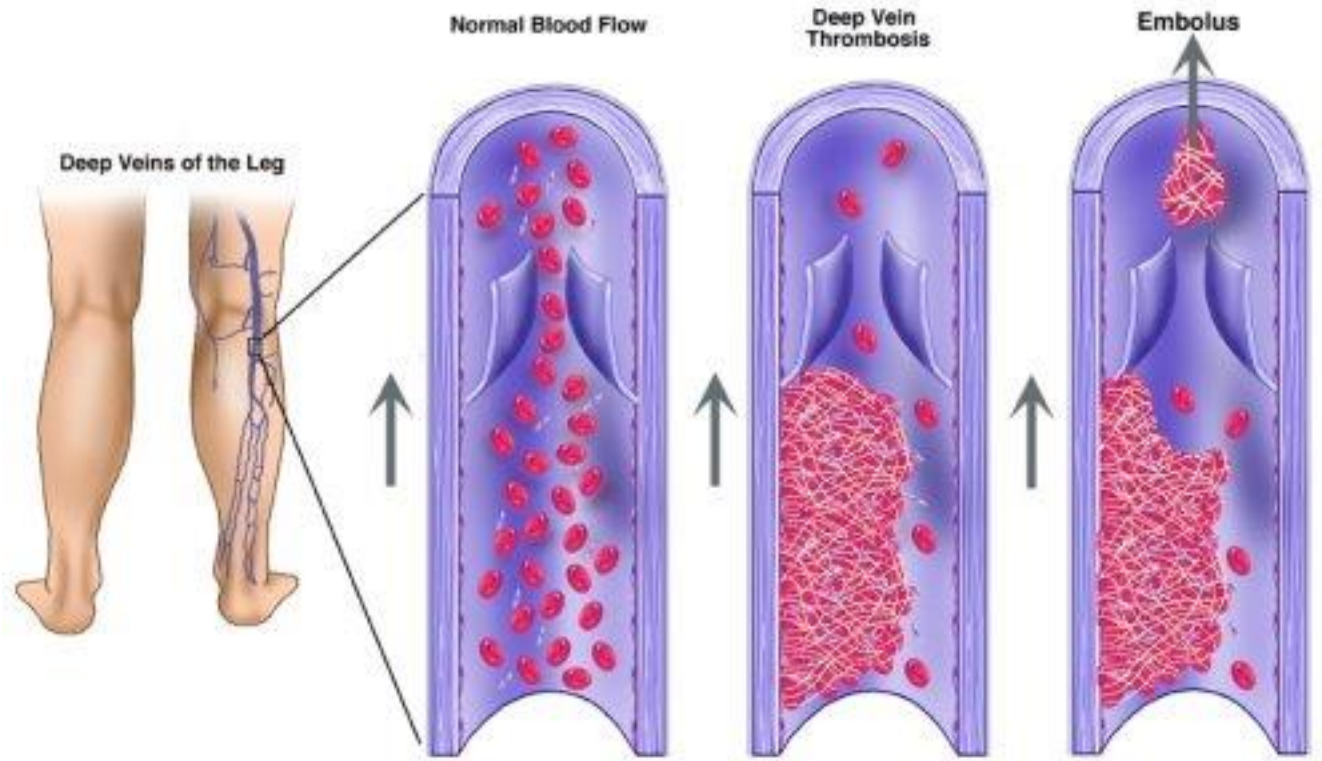
Thrombosis

- Thrombosis - The formation or presence of a blood clot in a blood vessel (thrombus). The vessel may be any vein or artery as, for example, in a deep vein thrombosis or a coronary (artery) thrombosis. The clot itself is termed a thrombus. If the clot breaks loose and travels through the bloodstream, it is a thromboembolism

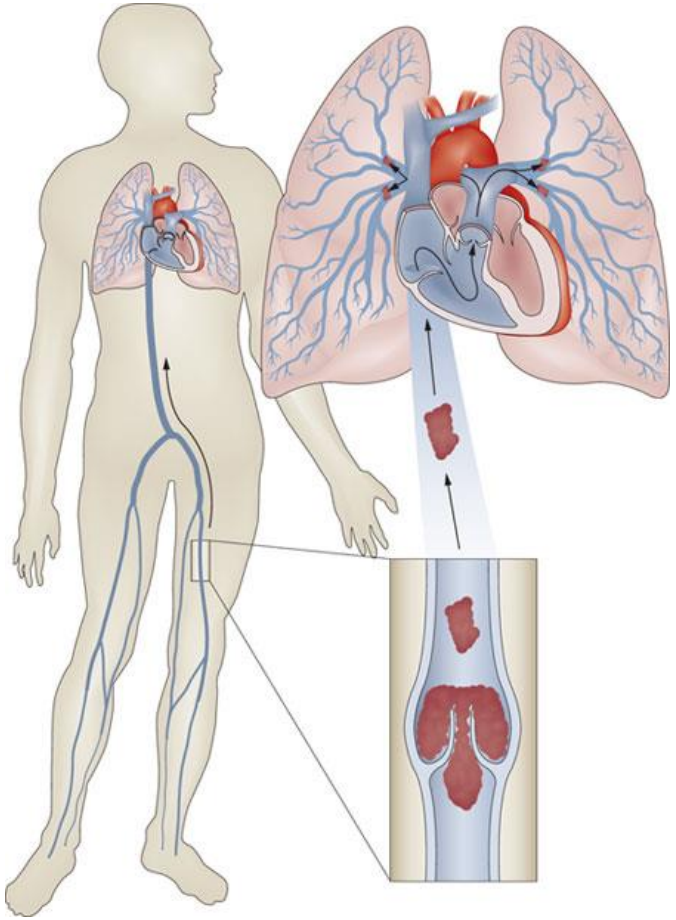
Embolism

- Embolism - the obstruction of a blood vessel by a foreign substance or a blood clot that travels through the bloodstream, lodging in a blood vessel, plugging the vessel. Foreign substances that can cause embolisms include air bubbles, amniotic fluid, globules of fat, clumps of bacteria, chemicals (such as talc), and drugs (mainly illegal ones). Blood clots are the most common causes of embolisms. A pulmonary embolus is a blood clot that has been carried through the blood into the pulmonary artery (the main blood vessel from the heart to the lung) or one of its branches, plugging that vessel within the lung.

Thrombosis and Embolism

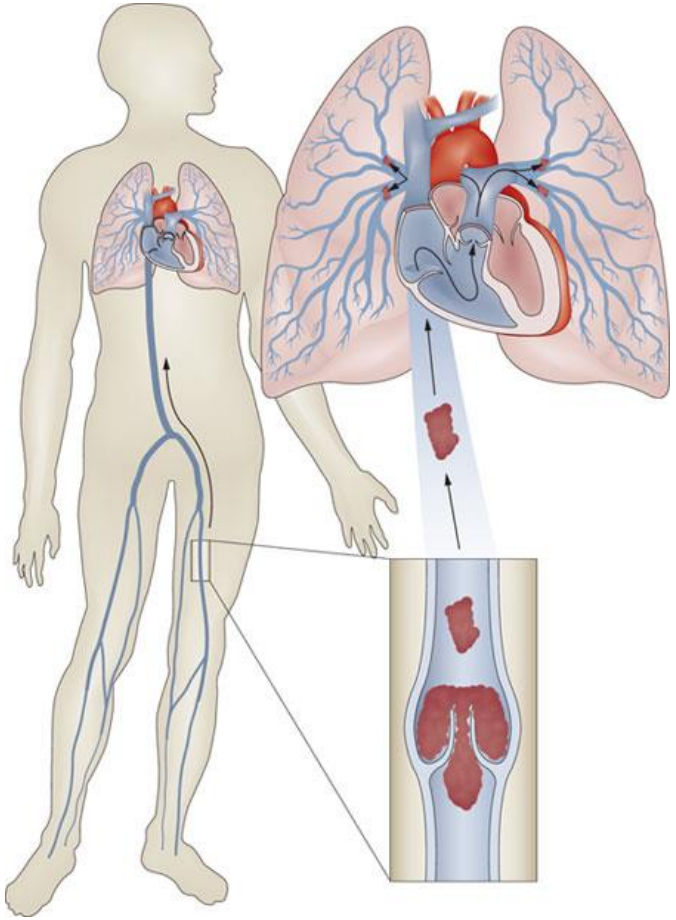


Pulmonary Embolism



- Pulmonary embolism is when one or more pulmonary arteries in your lungs become blocked. In most cases, pulmonary embolism is caused by blood clots that travel to the lungs from the legs or rarely other parts of the body (deep vein thrombosis, or DVT)
- Factors such as immobility, cancer and surgery increase risk.
- Pulmonary embolism can be life-threatening, but prompt treatment can greatly reduce the risk of death.

Pulmonary Embolism



- Common signs and symptoms include:
  - Dyspnea. This symptom typically appears suddenly and always gets worse with exertion.
  - Chest pain, which may be worse with a deep breathe. The pain will get worse with exertion but won't go away when you rest.
  - Cough. The cough may produce bloody or blood-streaked sputum.
- Other signs and symptoms that can occur with pulmonary embolism include:
  - Leg pain or swelling, or both, usually in the calf
  - Clammy or discolored skin (cyanosis)
  - Excessive sweating
  - Rapid or irregular heartbeat
  - Lightheadedness or dizziness

Pathophysiology I

Cardiovascular Diseases

Cardiovascular Disease Introduction

- Cardiovascular disease accounts for more than one half of all mortality in industrialized countries
- The most prevalent causes are atherosclerosis and hypertension
- Atherosclerosis manifestations account for 50% of deaths in adults in the US
- Hypertension is an important complication of athersclerosis, however it can occur independent. It accounts for about 10% of all heart disease

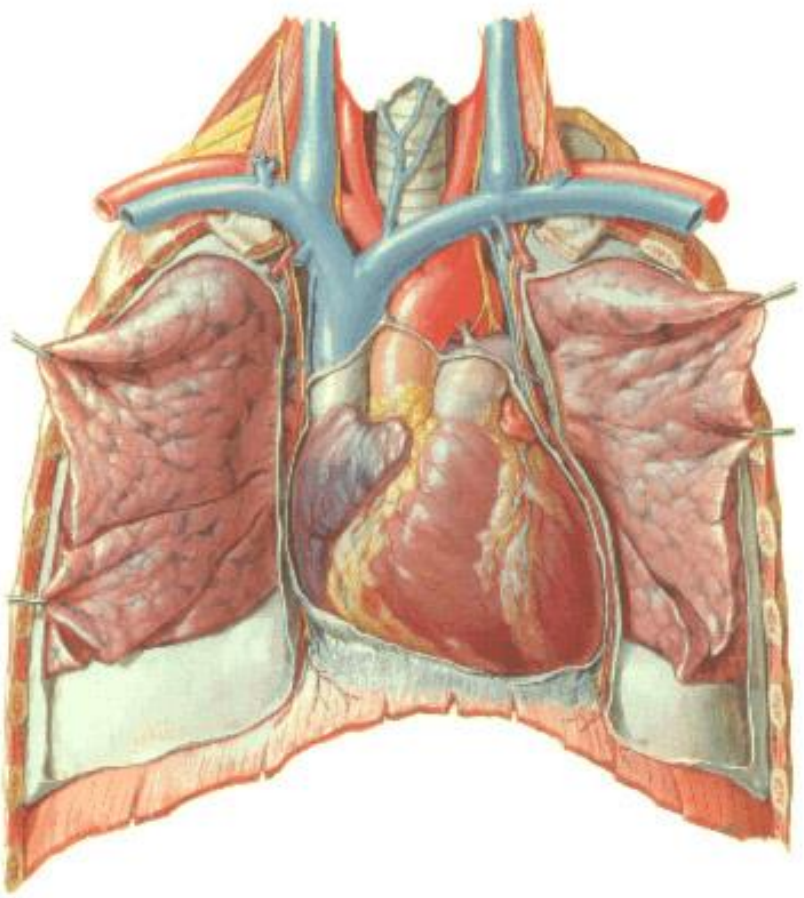
Cardiovascular System

Review of Anatomy

Cardiovascular System Anatomy Review

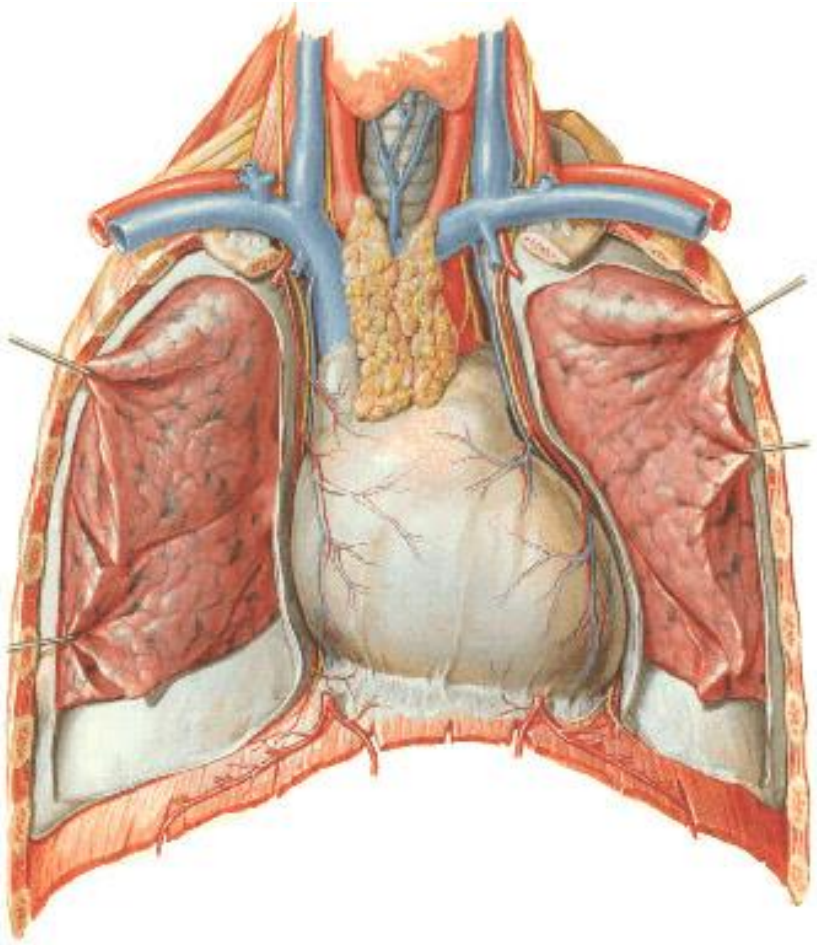
Heart Structure and Circulation

Cardiovascular System



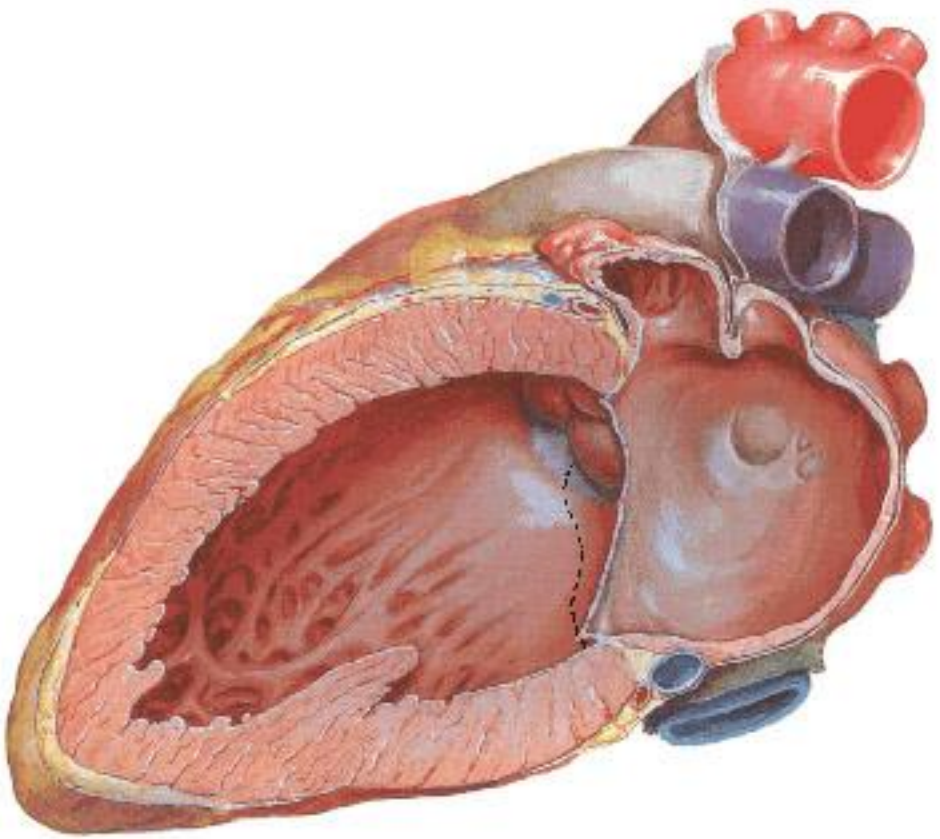
- Cardiovascular system is composed of the
  - Heart
  - Blood vessels
    - Arteries – blood vessels which carry blood away from the heart
    - Veins – blood vessels which carry blood towards the heart
    - Capillaries – exchange vessels
  - Blood
- Its function is to transport nutrients, gases, hormones and other products throughout the body

Pericardium



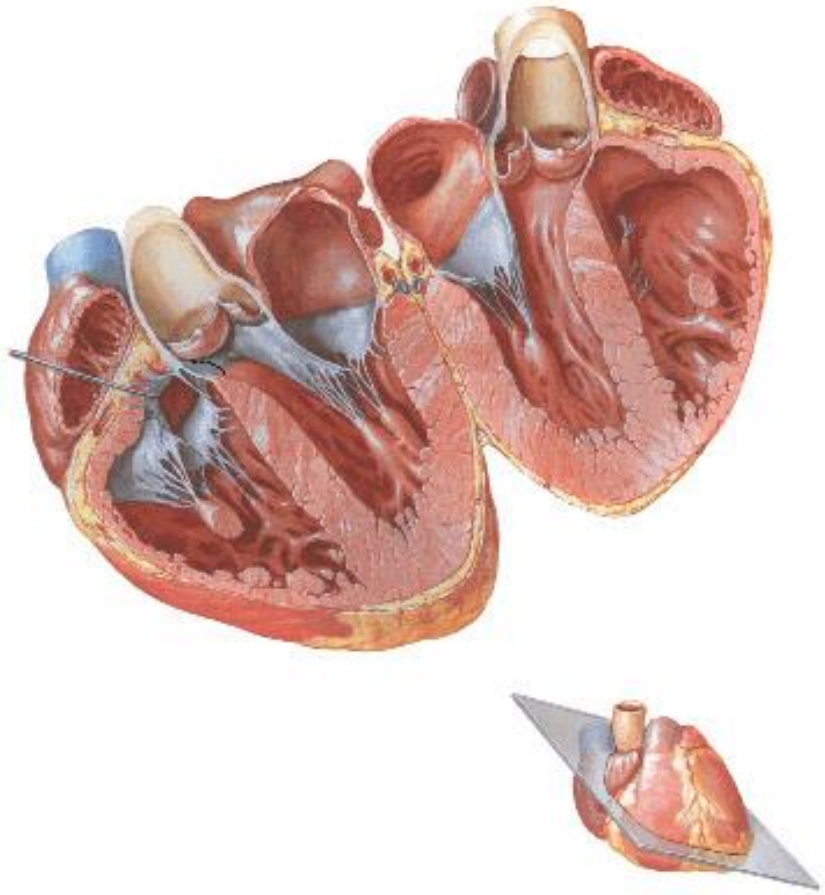
- The heart is surrounded by the pericardium
  - Parietal pericardium is the outer layer. It is a serous membrane
  - The visceral pericardium is the deepest layer and is in contact with the myocardium. It is also a serous membrane

Layers of the Heart



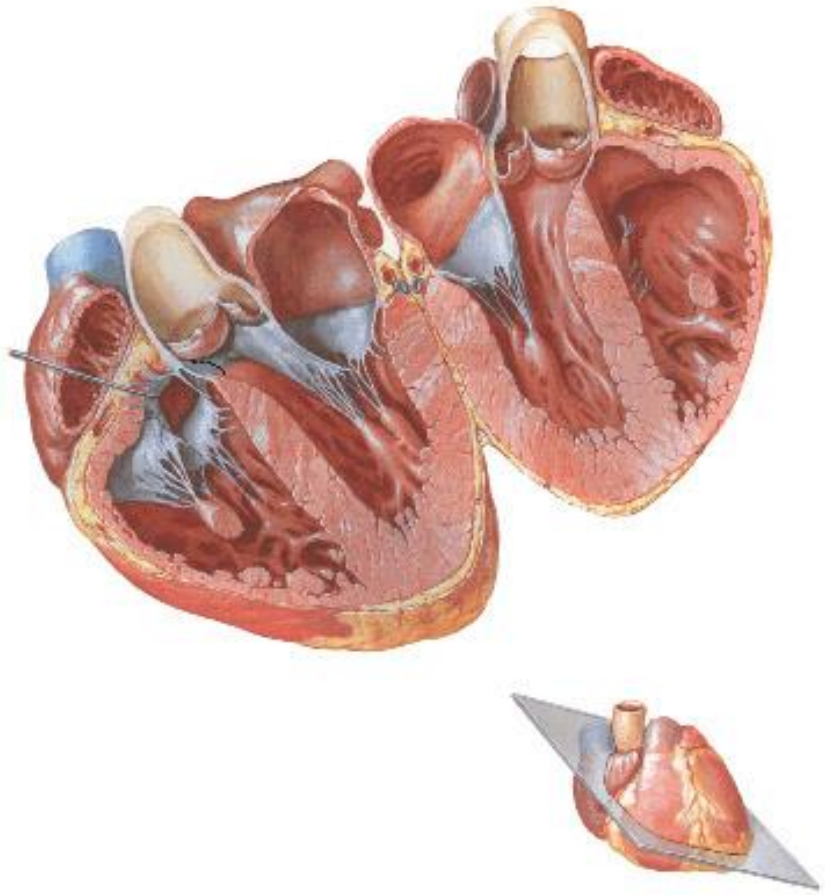
- The heart wall has three layers
  - The epicardium is the outer layer of the heart (it is the same layer as the visceral pericardium)
  - The myocardium is the next muscular layer
  - The endocardium is the inner lining of the heart

Chambers and Valves of the Heart



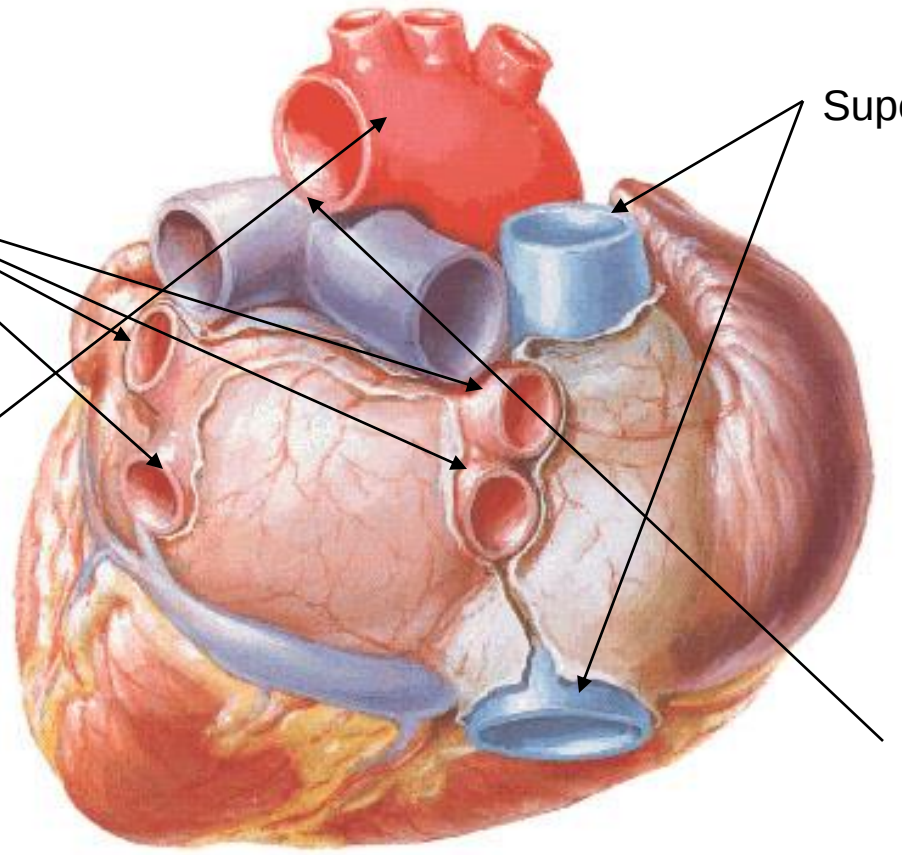
- The heart has 4 chambers and 4 valves
  - Two chambers are receiving chambers which receive blood
    - Right atrium receives blood from the periphery of the body
    - Left atrium receives blood from the lungs
  - Two chamber are discharging chambers
    - Right ventricle discharges blood to the lungs
    - Left ventricle discharges blood to the periphery of the body

Chambers and Valves of the Heart



- Two valves are atrioventricular valves
  - The tricuspid valve allows blood to pass from the right atrium to the right ventricle and prevents backflow
  - The bicuspid valve allows blood to pass from the left atrium to the left ventricle and prevents backflow
- Two valves are semilunar valves
  - The pulmonary semilunar valve allows blood to pass from the right ventricle to the pulmonary artery (and to the lungs)
  - The aortic semilunar valve allows blood to pass from the left ventricle to the aorta (and to the periphery of the body)

Vessels Related to the Heart



Oxygenated blood from the lungs returns to the heart through….

Pulmonary Veins

Blood enters the left artium, travels through the bicuspid (mitral) valve to the left ventricle

Blood travels through the aortic semilunar valve to the aorta to be sent to the body's tissues

Aorta

Superior and Inferior Vena Cava

Deoxygenated blood from the body enters through these vessels into the right atrium

Blood travels through the tricuspid valve to the right ventricle

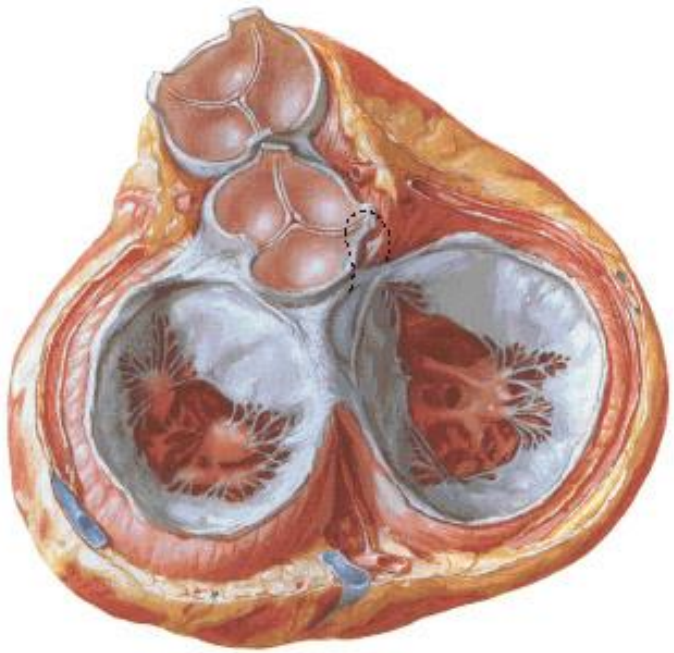
Blood travels through the pulmonary semilunar valve to the pulmonary artery

Pulmonary Artery

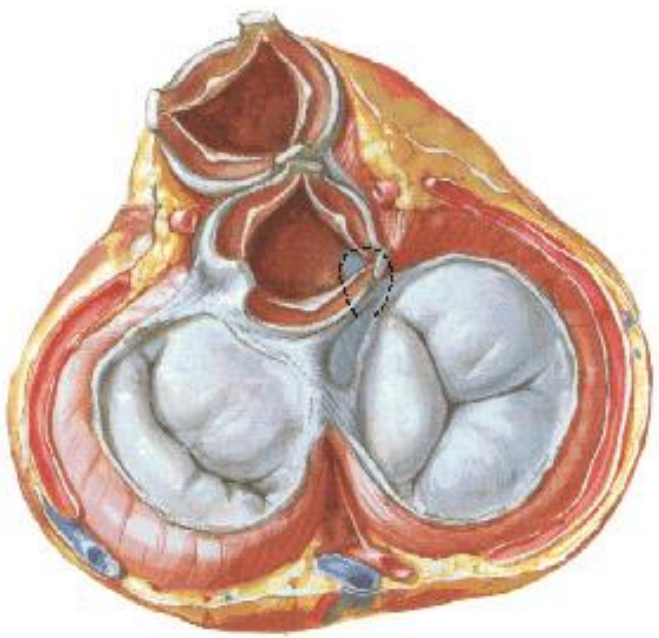
Deoxygenated blood travels to the lungs for gas exchange

Systole and Diastole

Valves of Heart in Diastole



Valves of Heart in Systole



Cardiovascular System Anatomy Review

Heart Conducting System

Heart Conducting System

- Heart cells have an inherent rhythmicity, meaning they beat on their own without nervous system or endocrine control. However they are influenced by the nervous system and endocrine system.
- Cardiac muscle cells are bound to each other via proteins and synapse are electrical. If one cell depolarizes, the cells it is in contact with also depolarizes.
- Cardiac muscle cells beat the fastest at the sinoatrial (SA) node. These cells, therefore set the pace.

Heart Conducting System

- From the SA node, the stimulus spreads across the atrial wall and reaches the atrioventricular (AV) node.
- The AV node delays the stimulus. This allows the atria to contract fully and push blood into the ventricles.
- From the AV node, the signal travels along the interventricular septum within the AV bundle (bundle of HIS) and then branches into Purkinje fibers where it spreads to the muscular wall of the ventricles. This causes the ventricles to contract from the inferior end to pump blood out of the ventricles and through the semilunar valves into the aorta and pulmonary artery.

Animations

- http://www.nhlbi.nih.gov/health/health-topics/topics/hhw/electrical.html
- http://highered.mheducation.com/sites/0072495855/student_view0/chapter22/animation__conducting_system_of_the_heart.html

Cardiovascular System

Pathophysiology

Cardiovascular Disease Classifications

- Congenital Heart Disease
- Ischemic vascular disease
- Hypertension-related disease
- Inflammatory disease (infectious and autoimmune)

General Appearance and Demeanor

- Biomedicine, pg 581

Cardiovascular Diseases

Congenital Heart Diseases

Cardiovascular Disease
Congenital

- Congenital - Abnormal development of the heart during embryological development and present at birth
- Includes:
  - Septal defects
  - Tetralogy of Fallot

Cardiovascular Disease
Factors Contributing to Disease

Septal defects represent the most common form of congenital heart disease
May involve a hole in the atrial or the ventricular septum

Atrial Defects

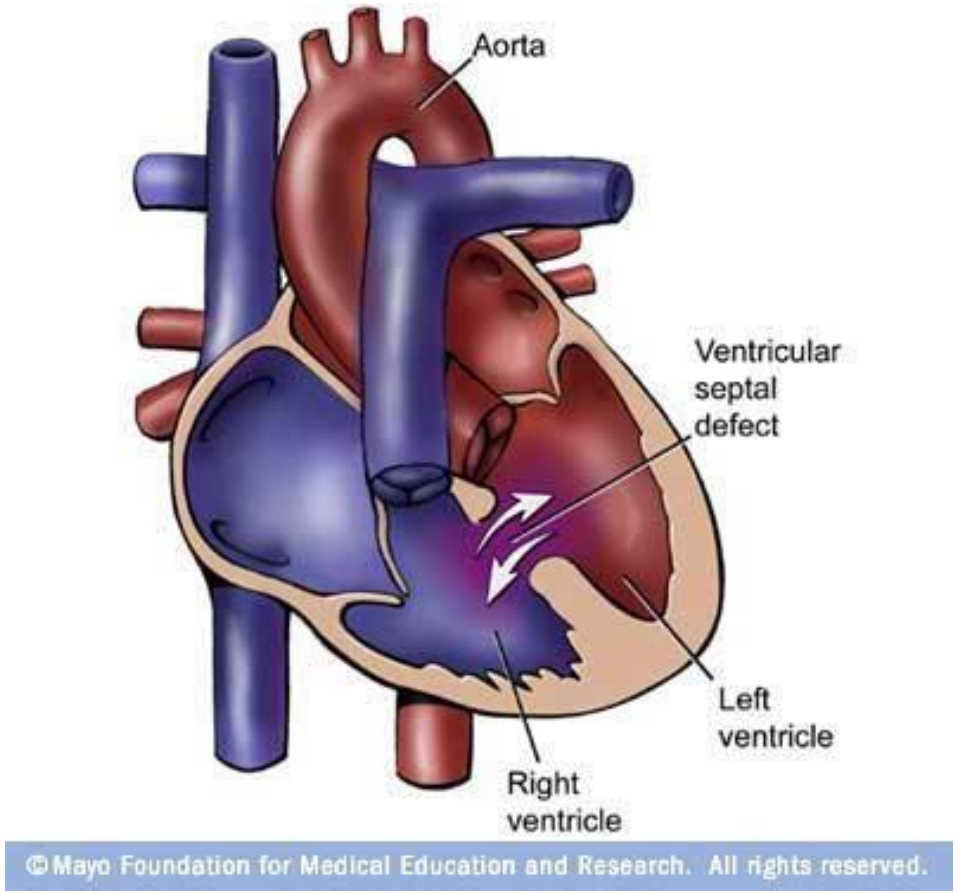
- Atrial defects result from a failure of closure or an incomplete formation of the septum between right and left atrium at birth

Ventricular Defects

- Most common and most serious
- Results in mixing of blood in the left and right chambers
- As it advances, results in cyanosis

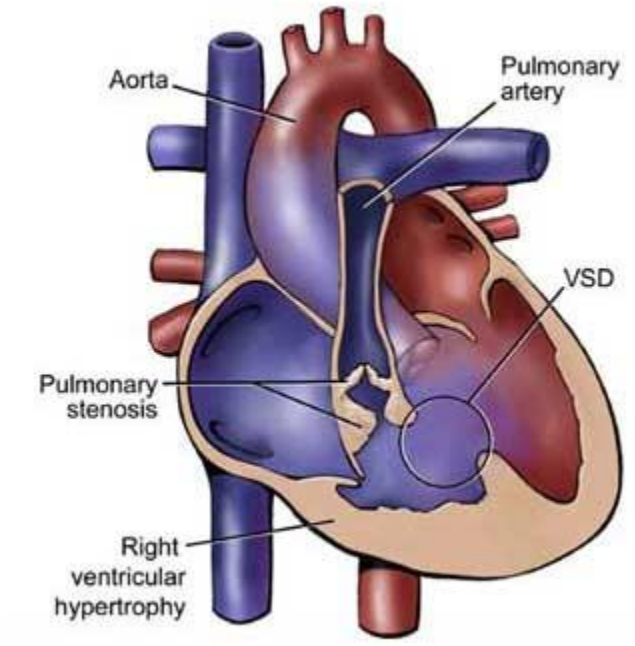
Septal defects produce heart murmurs which can be detected by cardiologists
Some small defects close spontaneously, larger defects require surgery and results are good

Septal Defects



Cardiovascular Disease
Factors Contributing to Disease

- Tetralogy of Fallot
  - Most common cause of cardiac cyanosis in newborn children. Symptoms develop early and children present as "blue babies"
  - Consists of four lesions
    - Valvular stenosis of the pulmonary artery
    - Ventricular septal defect
    - Malposition of the aorta where it receives blood from both the left and the right ventricles
    - Hypertrophy of the right ventricle due to increased workload of the myocardium
  - Often requires surgery and results depend on severity of the deformation



Cardiovascular Diseases

Atherosclerosis

Cardiovascular Disease Atherosclerosis

- Heart action depends on a constant supply of nutrients and oxygen
- Occlusion of the arteries or narrowing of the lumen impedes blood supply and causes ischemia
  - Chronic ischemia leads to pump failure typical of chronic coronary heart disease. This may be associated with bouts of chest pain known as angina pectoris
- Sudden occlusion of arterial blood causes an infarct
- Atherosclerosis is a major contributor to circulation problems
- Animation - http://watchlearnlive.heart.org/CVML_Player.php?moduleSelect=athero

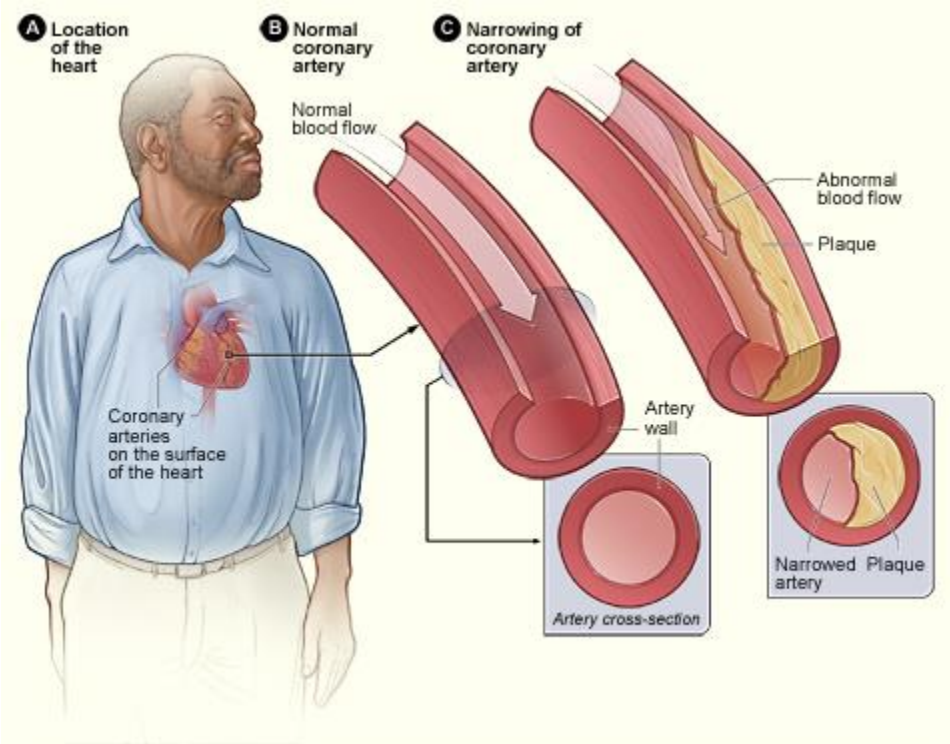
Atherosclerosis Risk Factors

- Risk factors
- Considered a multi-factorial disease with many risk factors. Some are hereditary, but many can be diminished by changing lifestyle

- Risk factors listed in table 7.1
- Main risk factors include:
  - Age and sex
  - Heredity
  - Physical inactivity, Obesity
  - Hyperlipidemia
  - Diabetes mellitus
  - Hypertension
  - Cigarette smoking
  - Stress

Atherosclerosis in the coronary artery (coronary heart disease)

- May have varied presentation depending on amount of occlusion, speed at which it develops and extent of atherosclerosis present in branches, and other factors (Fig 7-13)
- May slowly progress or a sudden occlusion may occur
  - With chronic progressive ischemia angina pectoris might be present. Leads to congestive heart failure
  - Sudden occlusion leads to infarct
- Clinical features include:
  - Congestive Heart Failure
  - Angina Pectoris
  - Myocardial Infarction

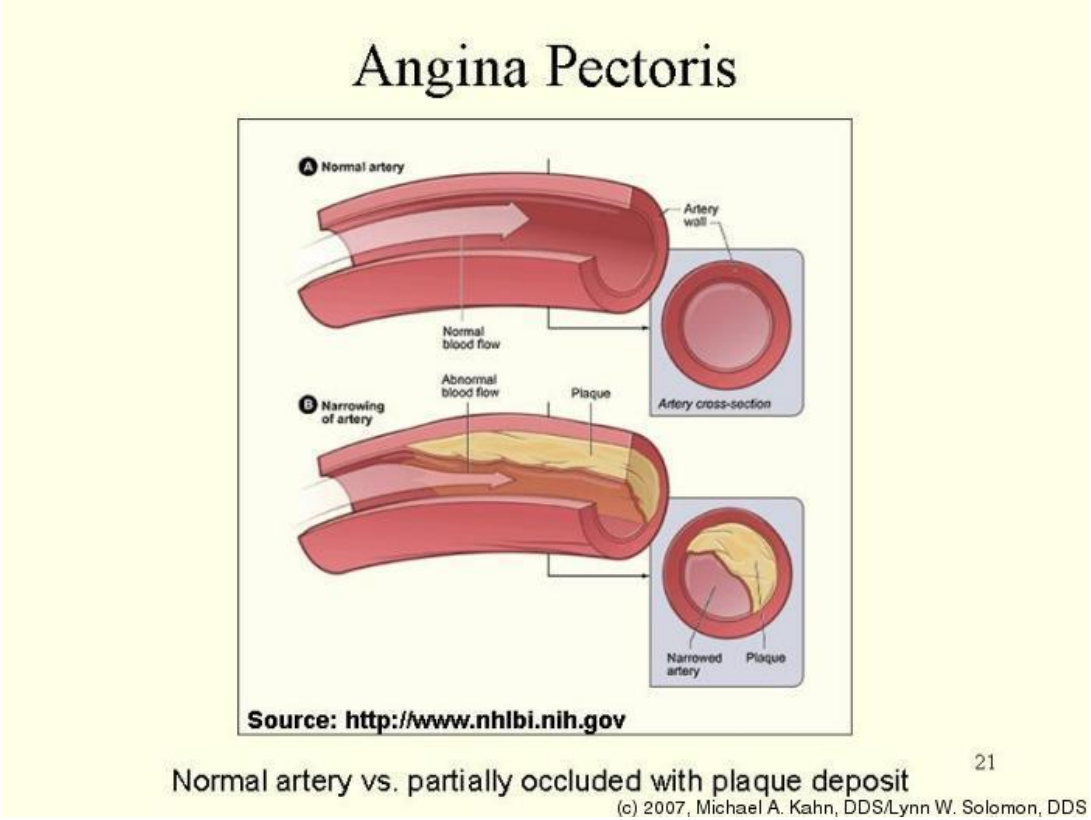


Atherosclerosis in the coronary artery (coronary heart disease)

- Congestive heart failure
  - Hypoxia of the myocardium results in pump failure
  - Blood back flows impedes venous return to heart
  - Right ventricular failure causes congestion of the peripheral organs and extremities, often seen with swelling of the legs (especially towards the end of the day). Can also cause enlargement of the liver and pain below the right costal margin, pressure on the abdominal veins can lead to ascites. (figure 7-19)
  - Left ventricular failure leads to pulmonary congestion and pulmonary edema. Pleural effusion can also develop. Patients develop dyspnea. In severe cases dyspnea is present continuously, in mild cases, only during strenuous activity.

Atherosclerosis in the coronary artery (coronary heart disease)

- Angina pectoris
  - Myocardium may function normally unless more demands are made, in which case there is chest pain
  - Classic signs include:
    - Chest discomfort last 2-5 min., max 10-15 min
    - Patient is motionless, hunched over with closed fist over chest. They have anxiety, sweating, chest tightness
    - Pulse is rapid and bounding, BP is elevated, may be dyspnea



Atherosclerosis in the coronary artery (coronary heart disease)

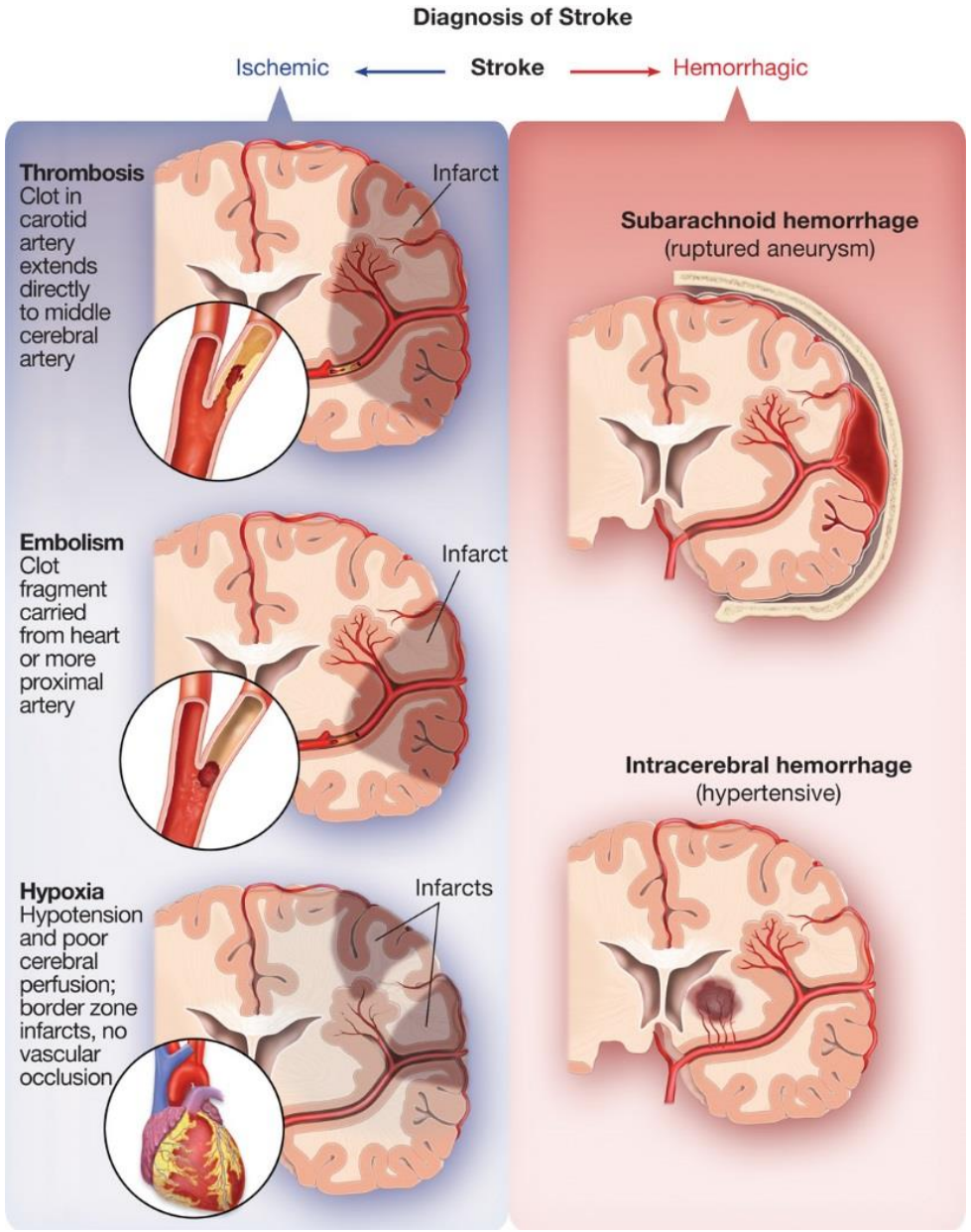
- Myocardial infarction
  - Rapid, sudden occlusion causes an infarct and can cause death
  - Sudden death usually caused by ventricular fibrillation and cardiac arrest (substantial pump failure) (25% of patients)
    - Patients typically experience a crushing chest pain, followed by loss of consciousness
    - Requires immediate attention and still often leads to death
  - Among 75% that survive the acute phase, most develop heart failure and cardiogenic shock
    - Multi-organ failure (especially kidneys) and brain damage can occur
  - Diagnosis made by symptoms (chest pain, SOB, fainting) and labratory findings
    - EKG (electrocardiogram), Troponin, Creatine Phosphokinase (CPK)
  - Treatment
    - 30-40% die within the first year (includes acute mortality)

Atherosclerosis in the coronary artery (coronary heart disease)

- Outcome of myocardial infarction include: fig 7-20
  - Sudden death
  - Early complications
    - Arrhythmia (90%)
    - CHF (60%)
    - Shock (12%)
    - Heart rupture (1%)
  - Late complications
    - CHF (70%)
    - Arrhythmia (20%)
    - Aneurysm (10%)
    - Thromboemboli (10%)
  - Chronic left heart weakness
    - CHF (70%)
    - Recurrent infarcts
    - Arryhthmia

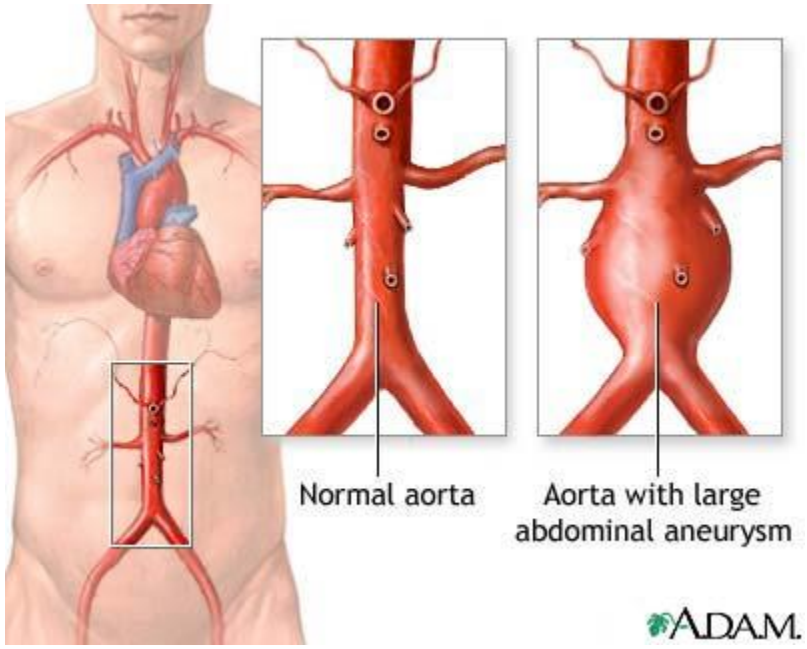
Atherosclerosis of the brain arteries (cerebrovascular disease)

- Atherosclerosis is a common cause of cerebrovascular accident (stroke)
- A CVA has the following etiology:
  - Thrombosis
  - Embolism
  - Hypoxia
  - Hemorrhage



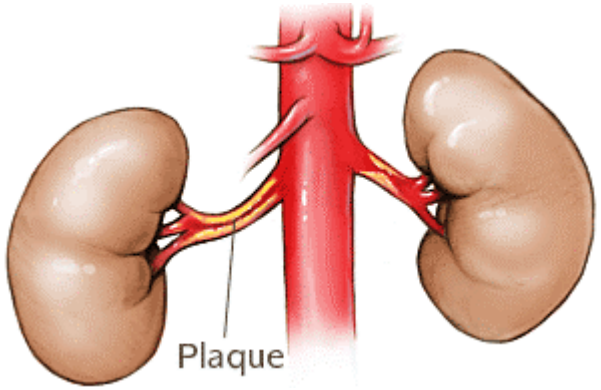
Atherosclerosis of the aorta (presents with aortic calcifications and aortic aneurysms

- Very common in older men
- Lesions can be mild to severe, focal to diffuse
- Most often asymptomatic
- Lesions develop in aorta, become calcified, may be covered with thombi and can narrow the lumen. The aorta becomes rigid and can not expand during cardiac output and leads to an aneurysm (most common in abdominal aorta)
- Major danger is a rupture (associated with high mortality). Aneurysms can be surgically repaired.



Atherosclerosis of the arteries of the extremities (peripheral artery disease)

- Refers to atherosclerosis involving blood vessels to extremities, major abdominal organs
- Common in elderly, diabetics, those with hypertension and hyperlipidemia
- Often affects:
  - Atherosclerosis of the renal artery
  - Atherosclerosis of the intestinal arteries
  - Atherosclerosis of the intestines



Renal Artery Pre- and Post-Treatment

Other Diseases Affecting the Blood Vessels

Arteries

- Polyarteritis nodosa is an autoimmune disease affecting small and medium-size arteries. Involves immune complexes causing damage and fibrinoid necrosis.
- Raynaud's disease is functional disturbance affecting muscular arteries and arterioles causing contraction, especially in cold weather. Causes ischemia in distal parts of body (tips of fingers and toes). Better with warmth.

Veins

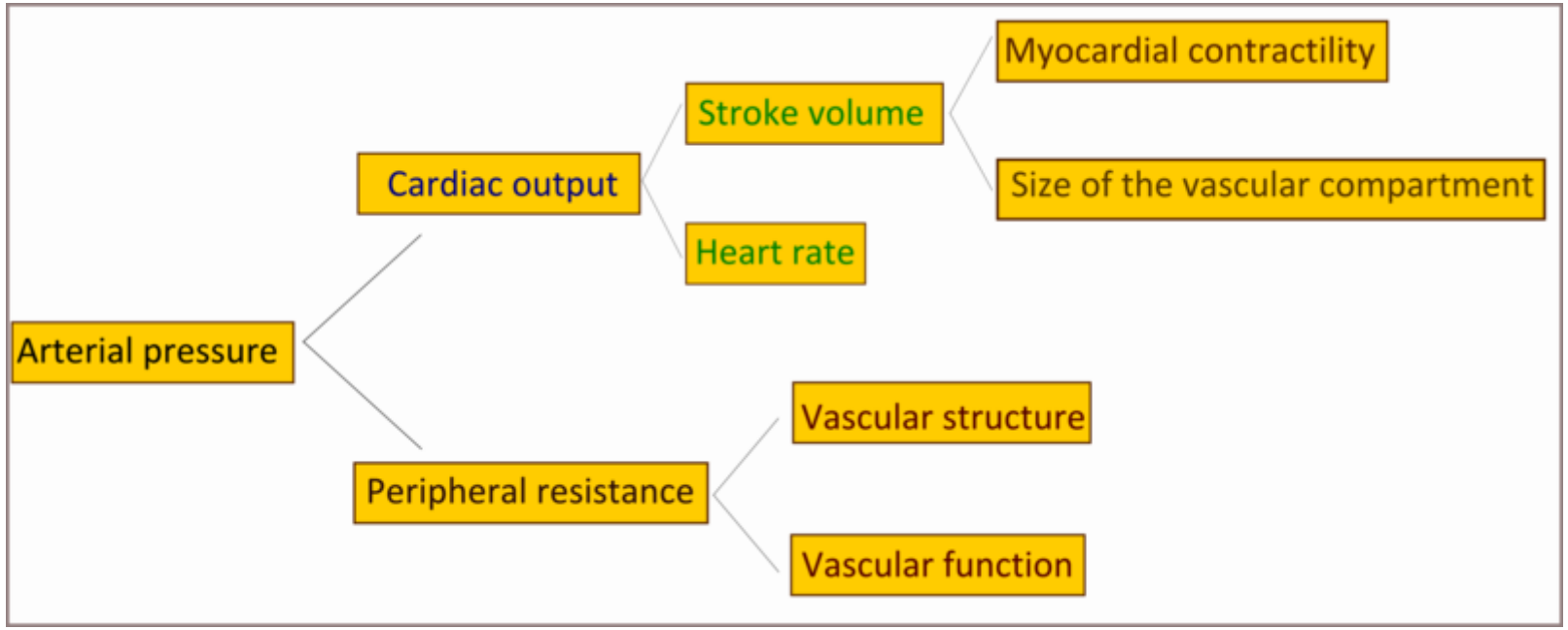
- Varicose veins involves backpressure which cause veins to dilate and distend, negatively affecting the valves.
- Slow flow in veins can more readily lead to clotting. Thrombi can form. This most often occurs in legs. Thrombotic occlusion can lead to inflammation of the vessel wall or thrombophlebitis

Cardiovascular Diseases

Hypertension

Cardiovascular Disease
High Blood Pressure (Hypertension)

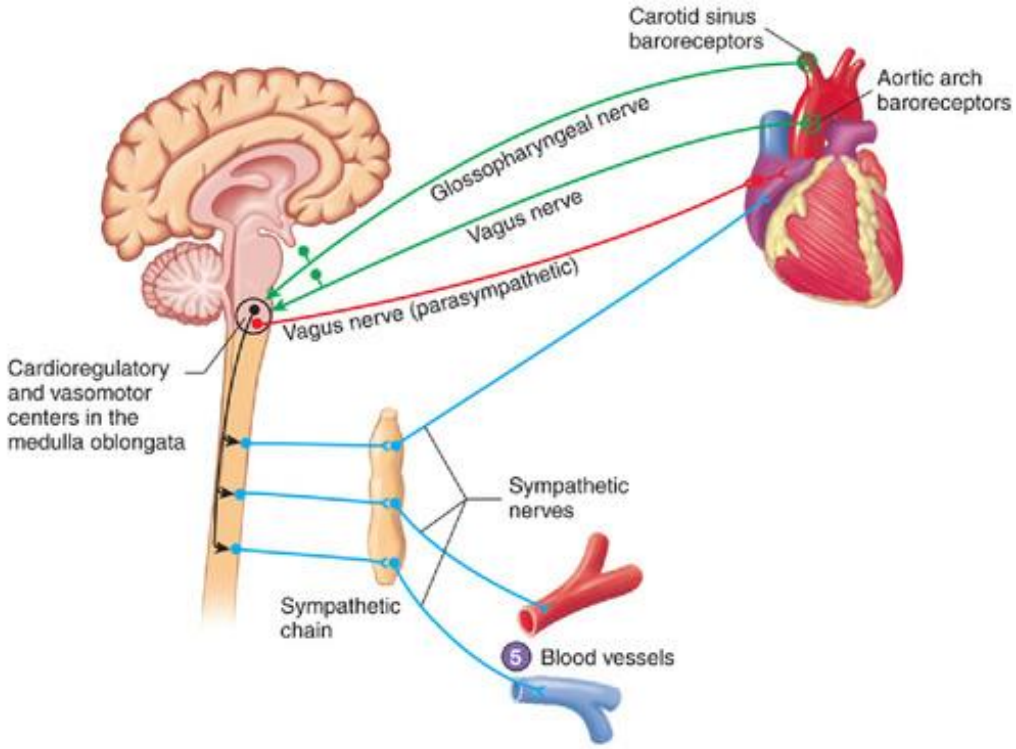
- Arterial blood pressure, which primarily depends on heart action and elastic and contractile properties or arteries and arterioles, is regulated by hormones and biogenic amines.
- Blood pressure measurement includes systolic/diastolic. Blood pressure is influenced by cardiac output (CO) and total peripheral resistance (TPR). BP = CO x TPR
- Hypertension
  - Normal BP is 120 mm Hg / 80 mm Hg
  - Systolic BP over 160 or diastolic BP over 90 is considered hypertensive
  - Clinical hypertension is classified as mild, moderate or severe



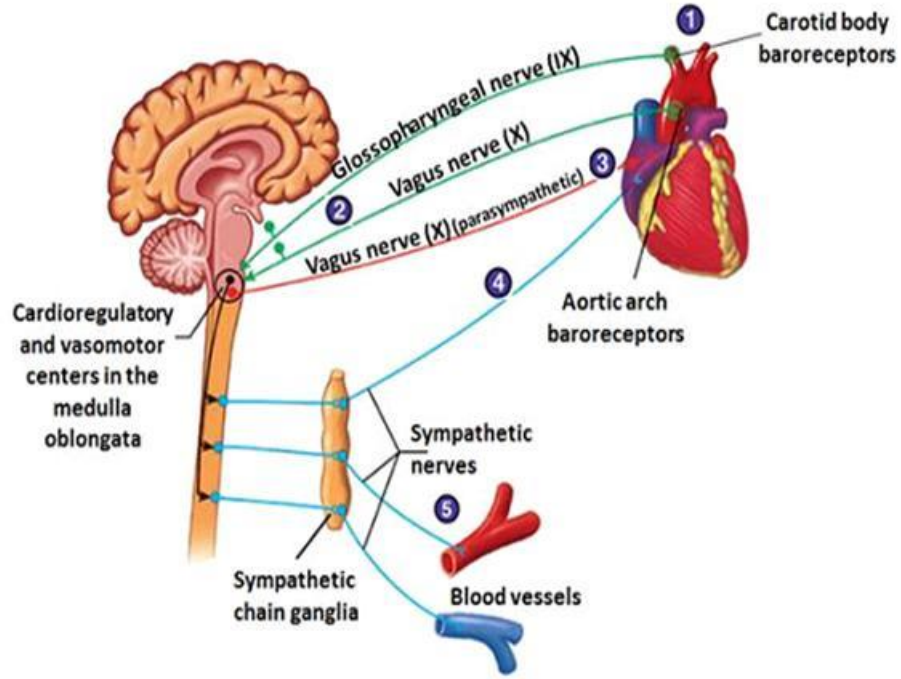
- Systolic is mostly determined by cardiac output (CO)
  - This is influenced by stroke volume and heart rate
- Diastolic is mostly determined by total peripheral resistance (TPR)
  - If arteriole constriction increases, less blood can leave the arteries to capillaries/venous flow and diastolic BP will increase (maybe 90 mm Hg)
  - If arterioles dilate, more blood leaves to capillaries and venous compartment and diastolic pressure will decrease (maybe 60 mm Hg)

Blood Pressure Regulation Nervous System

- Blood pressure is primarily regulated by the nervous system via autonomic nervous system regulation and through the endocrine system via the renin-angiotensin-aldosterone axis
  - Short term – neurological is more important
  - Long term – endocrine control is more important



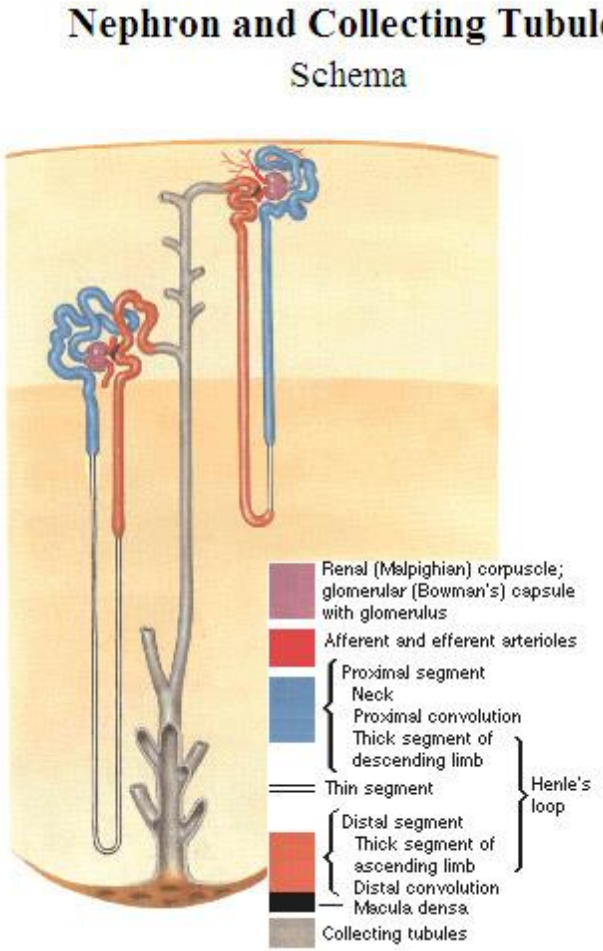
Baroreceptor Reflex Control



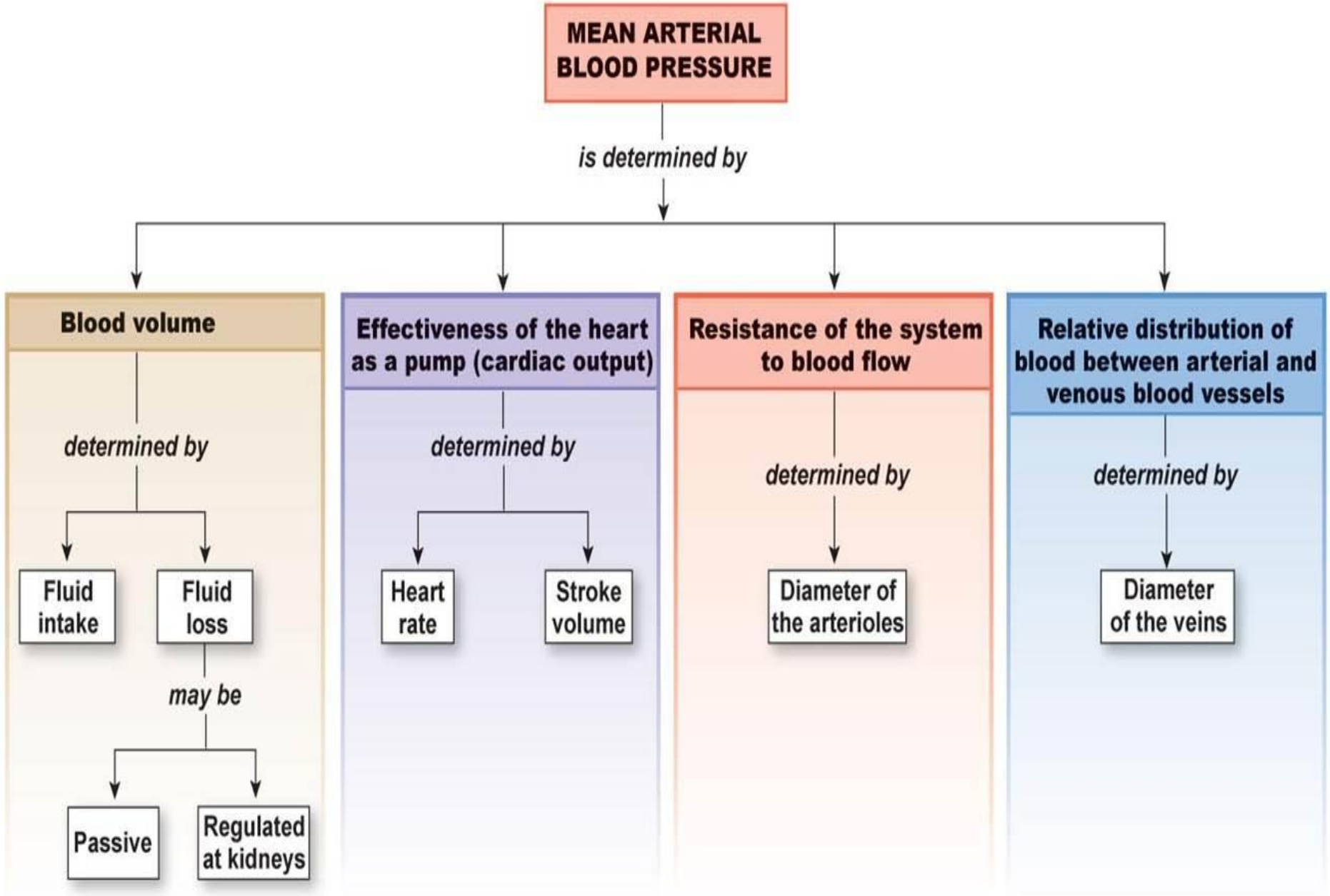
1. **Baroreceptors** in carotid and aortic bodies detect changes in **BP**
2. Impulses are conducted to **cardioregulatory** and **vasomotor** control centers in **medulla oblongata** via the **glossopharyngeal** (IX) and **vagus** (X) nerves
3. ↑BP will cause ↑ parasympathetic stimulation of the heart, which decreases **HR**
4. ↑BP will cause ↓ sympathetic stimulation of the heart, which decreases **HR** and stroke volume
5. ↑BP will causes vasomotor center to ↓ sympathetic stimulation to **BV**, causing vasodilation

Result: **Negative Feedback**
Adjusting HR, SV, and Vasoconstriction allows rapid correction of hyper- or hypotension

Blood Pressure Regulation
Endocrine System



- The renin-angiotensin-aldosterone axis regulates blood volume and blood pressure.
  - Renin is released by the kidneys when there is low blood pressure (volume depletion).
  - Renin causes the liver to release angiotensin I.
  - Angiotensin converting enzymes (ACE) in the lungs converts this to angiotensin II.
  - Angiotensin II causes:
    - Thirst,
    - Vasoconstriction,
    - Causes adrenal glands to release aldosterone
      - Aldosterone causes more Na (and Water) to be absorbed from the kidneys



Cardiovascular Disease
High Blood Pressure (Hypertension)

- Hypertension is classified as primary (essential) or secondary
  - Primary (essential)
    - HBP is not due to anything else going on in the body that would elevate it.
    - Causes sometimes unknown, but contributing factors include genetics, occupation, lifestyle (stress, obesity), and diet (salt intake)
    - Western treatment is drugs and lifestyle change (need for treatment, Biomedicine pg. 612)
  - Secondary
    - Causes include underlying disease, medication, events such as pregnancy
    - Table 7-2

Cardiovascular Disease
High Blood Pressure (Hypertension)

- Morphological changes seen in the heart, peripheral vessels, kidneys, and eyes
  - Cardiomegaly
    - Usually affecting left ventricle, some cells die due to increase in demands. Heart failure occurs leading to increase pulmonary artery pressure
    - This increases the workload in the right ventricle and hypertrophy occurs, leading to failure - cor pulmonale
  - Vasculature
    - Hypertension damages the aorta, major and monir arteries and arterioles, and accelerates atherosclerosis
  - Hypertensive encephalopathy
    - Refers to vascular changes in the brain that cause cerebral ischemia
    - Can lead to stroke cause by sudden rupture or damage of brain arteries
  - Hypertensive retinopathy
    - One of the first changes seen

Cardiovascular Diseases

Blood Born Infections

Cardiovascular Disease
Blood Born Infections

- The large volume of blood passing through the heart makes it susceptible to blood-borne infections (can be caused by bacteria and viruses primarily)
- Bacteria found in infected blood can invade the endothelium of blood vessels and the endocardium of the heart
  - Bacterial endocarditis is the most common infectious heart disease
    - Predisposing lesions from congenital heart defects, deformed valves, mural thormbi can predispose individuals to cardiac infections (clotted blood seems to be the most suitable growth medium)
    - Infected thrombi may give rise to emboli (septic emboli) and bacterial aneurysms in small arteries (mycotic aneurysms)
    - Infected venous thrombi may lead to inflammation of the vessel wall (thrombophlebitis)
  - Viruses can infect and typically cause myocarditis and pericarditis

Cardiovascular Diseases

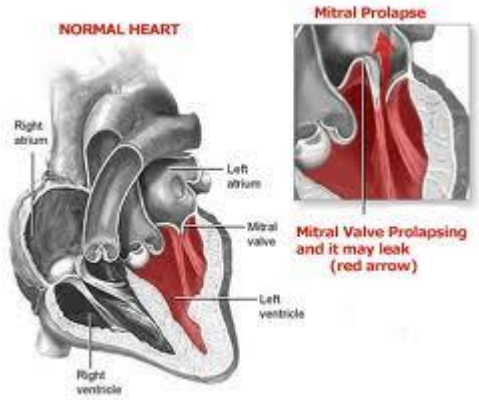
Immune Complexes

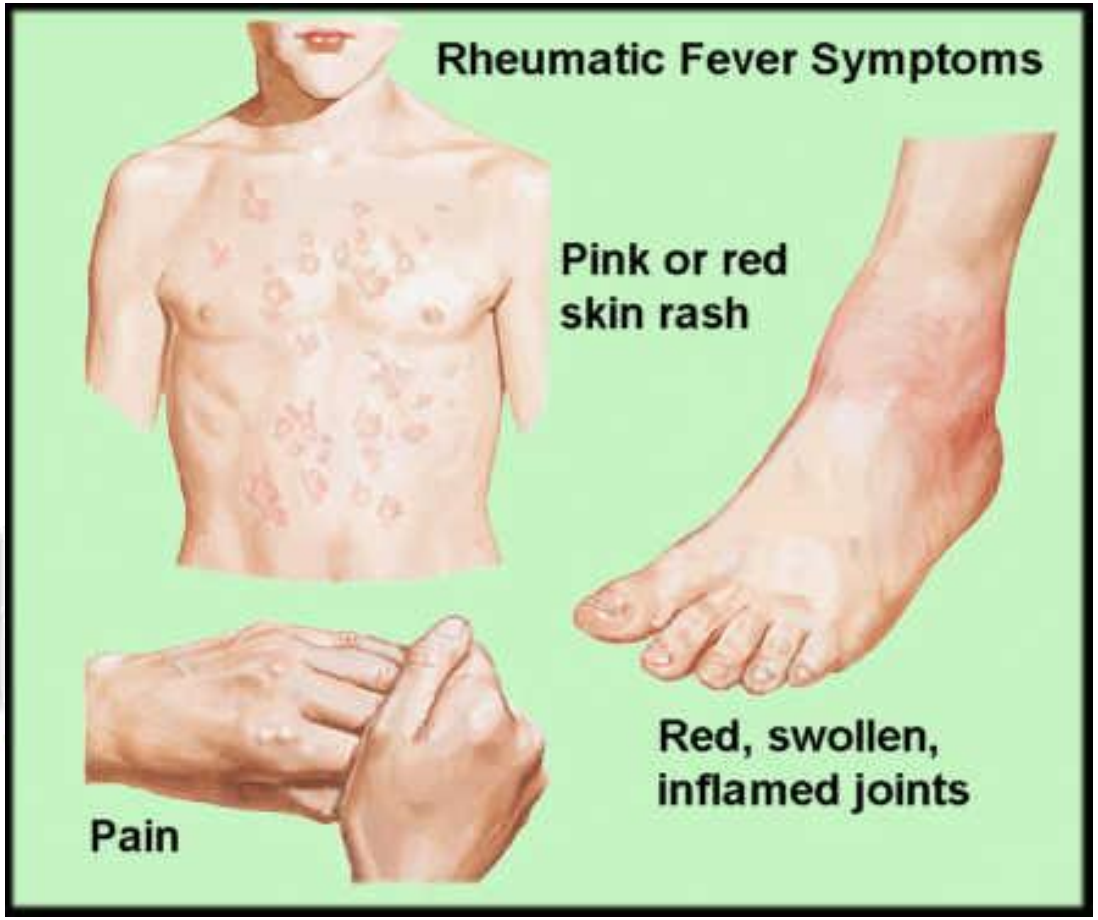
Cardiovascular Disease
Immune Complexes

- Immune complexes in the blood and circulating immune complexes may be deposited in the heart and blood vessels and may cause inflammation and destructive lesions
- Cause vasculitis or endocarditis
- Immune complexes can also form in vessel wall as in polyarteritis nodosa
- Hypersensitivity reactions that causes the body to produce autoantibodies which damage the body's tissue can damage the heart and blood vessels, as in rheumatic fever
  - This is a systemic, immunologically mediated disease related to streptococcal infections
  - Autoantibodies attack the strep, but also attack connective tissue
  - Affects the heart, joints, skin, occasionally the brain

Cardiovascular Disease Immune Complexes

- Rheumatic fever can halve the following symptoms.
- In some cases, autoantibodies attack the heart valves and can damage these, especially the mitral valve. This can cause prolapse (insufficiency) or stenosis of the valve.
- The aortic valve can less frequently be affected.

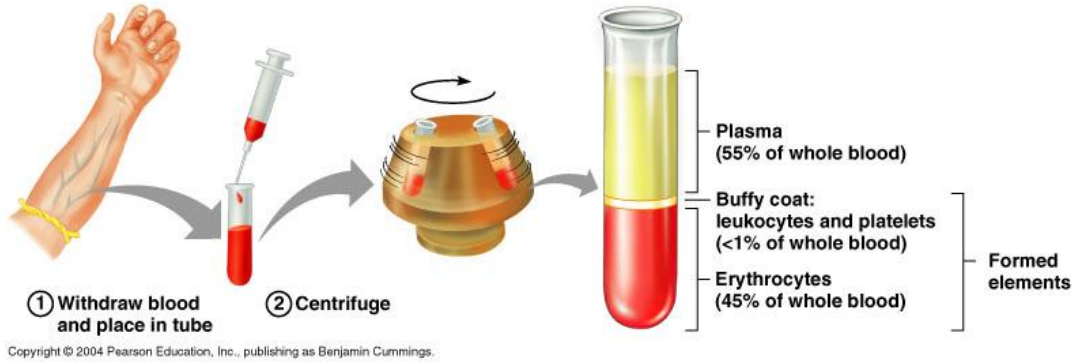




Pathophysiology I

Hematopoietic and Lymphoid System

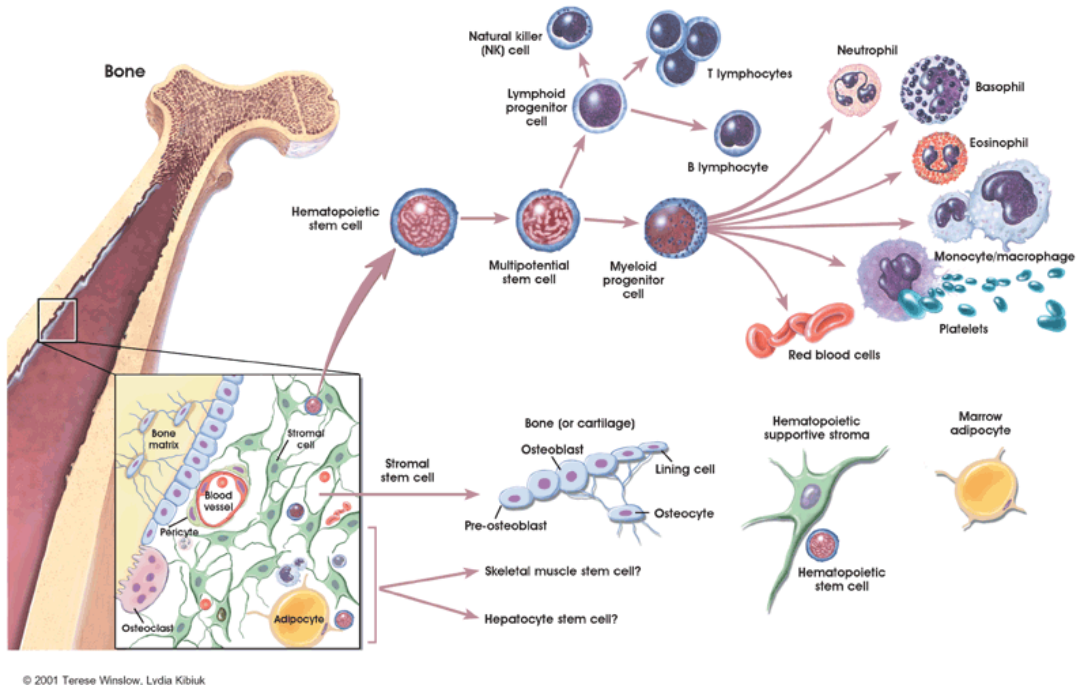
Hematopoietic and Lymphoid System

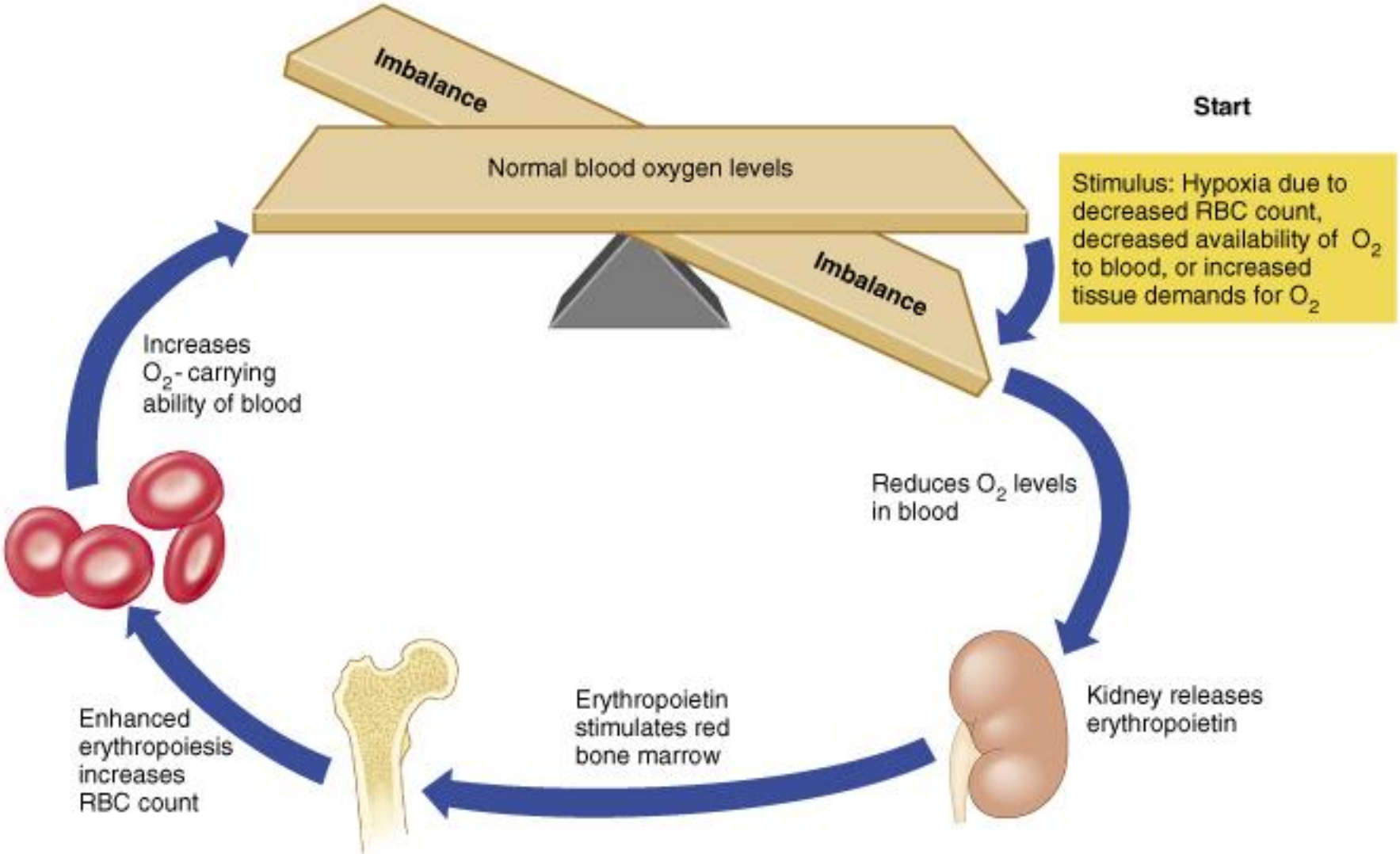


- Analysis of blood provides one of the most important laboratory tests
- Blood consists of plasma and formed elements
- Formed elements consists of the cells (erythrocytes, leukocytes, thrombocytes)
  - In healthy adults, formed elements consist of 40-45% and plasma consists of 55-60%
  - Most consists of RBCs, buffy coat on top contains WBCs and platelets
  - Fig 9.3
- Hematocrit is volume of packed RBCs expressed as a percentage

Hematopoietic and Lymphoid System

- Hematopoiesis occurs in the bone marrow
- The bone marrow is the primary source of hematopoiesis for all blood cells in adults
- Erythrocytes
  - Erythropoietin secreted from the kidneys cause red blood cell formation



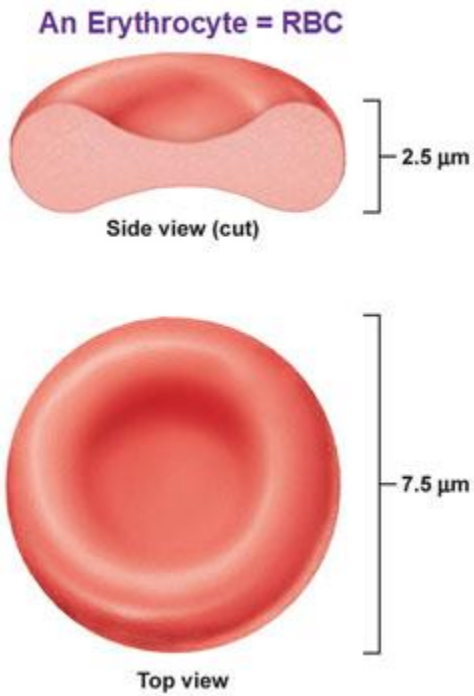


Hematopoietic and Lymphoid System

- Overview of Major Disease
- Hematological disease occurs as a result of abnormal formation, increased destruction, or abnormal structure and function of blood cells
- Includes:
  - Anemia
  - Leukemia
  - Lymphoma
  - Bleeding disorders

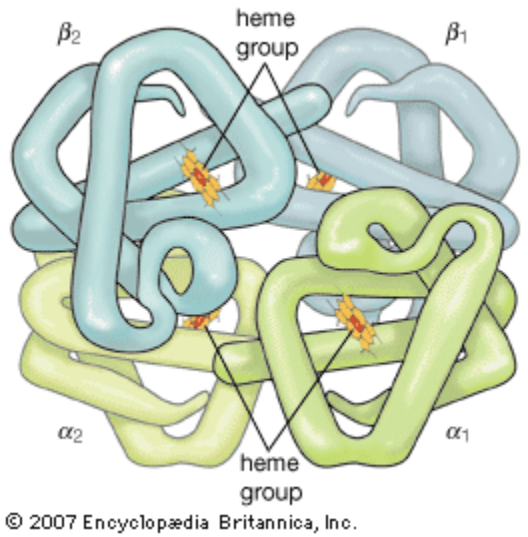
Hematopoietic and Lymphoid System Contributing Factors – Erythrocyte Function

- Erythrocytes are ideally suited for their primary function: transport of oxygen from the lungs into peripheral tissues
  - Shape and make-up of cells allow for ideal transport
  - Shape and lack of nucleus allows for increased surface area, round shape allows them to bend



Hematopoietic and Lymphoid System Contributing Factors – Hemoglobulin Molecules

- Hemoglobin is a complex molecule that consists of four heme groups and four globulin groups
  - RBCs primarily composed of hemoglobin, an iron-containing pigment.
  - Heme portion which involves four rings held together by iron. These molecular structures require iron. Iron deficiency anemia is marked by low Hb levels
  - Globulin portion consists of 4 polypeptide chains which give it a distinctive shape. Abnormal formation of these molecules due to genetic mutations cause abnormal proteins, and abnormal cell shape as seen in sickle cell anemia



Hematopoietic and Lymphoid System Contributing Factors – Hemoglobin Synthesis

- Hemoglobin synthesis requires iron, vitamin B_{12}, vitamin B_6, and folic acid
  - Deficiency of these nutrients cause anemia
  - Anemia may develop because these nutrients are not available, because they are not absorbed, or loss exceeds intake.
  - Iron deficiency can cause anemia and will correspond to particular data seen on a CBC. Loss of blood from things such as a GI bleed need to be considered, especially for men.
  - B_{12} is bound to intrinsic factor in the Stomach. This is necessary for the absorption of B_{12} which takes place in the ileum. Lack of binding of IF in the Stomach and/or lack of absorption in the ileum will cause pernicious anemia. It will result in particular data seen on a CBC

Hematopoietic and Lymphoid System Contributing Factors – RBCs Lifespan

- RBCs live in circulation for 120 days, after which they are removed by the spleen and their components are recycled.
  - Heme is converted to bilirubin which is used to form bile
    - Bilirubin can be checked clinically
    - Clinically, it is referred to as conjugated and unconjugated
    - Unconjugated = indirect
      - Hemolytic anemia results in high indirect bilirubin
        - Reticulocyte count will be high
      - Hepatocellular problems results in high mixed bilirubin
    - Conjugated = direct
      - (Post hepatic) Obstructive liver problems results in high direct bilirubin
        - White stool will be present

Hematopoietic and Lymphoid System Contributing Factors – CBC

- Objective measurements of RBC parameters are done with instruments that estimate the mean size of RBCs and their hemoglobin content
- Complete Blood Count (CBC), measures the following:
  - The number of red blood cells (RBC count)
  - The number of white blood cells (WBC count)
  - The total amount of hemoglobin (Hg) in the blood
  - The fraction of the blood composed of red blood cells (hematocrit)
  - The CBC test also provides information about the following measurements:
    - Average red blood cell size (MCV)
    - Hemoglobin amount per red blood cell (MCH)
    - The amount of hemoglobin relative to the size of the cell (hemoglobin concentration) per red blood cell (MCHC)
    - The platelet count is also usually included in the CBC

Hematopoietic and Lymphoid System Contributing Factors – CBC

- RBC count:
  - Male: 4.7 to 6.1 million cells/mcL
  - Female: 4.2 to 5.4 million cells/mcL
- WBC count:
  - 4,500 to 10,000 cells/mcL
- Hematocrit:
  - Male: 40.7 to 50.3%
  - Female: 36.1 to 44.3%
- Hemoglobin:
  - Male: 13.8 to 17.2 gm/dL
  - Female: 12.1 to 15.1 gm/dL
- Red blood cell indices:
  - MCV: 80 to 95 femtoliter
  - MCH: 27 to 31 pg/cell
  - MCHC: 32 to 36 gm/dL

Hematopoietic and Lymphoid System Contributing Factors – CBC

- CBC and Anemia
- Complete Blood Count (CBC)
  - Low Hb will indicated anemia
  - Normal: Men 14 and women 11.5
- Mean Corpuscular Volume is second line test
  - < 65 microcytic
  - 70-100 normocytic
  - > 100 macrocytic

Hematopoietic and Lymphoid System Contributing Factors – CBC

- Microcytic
  - Iron deficiency
    - TIBC high, Iron low
      - In men, think GI bleed. Hemacult
  - Chronic illness
    - Both low
- Normocytic
  - Bone marrow disease
  - Hemolysis
    - Sickle cell, Thalasiemia, Sperocytosis, Bad heart valve, Antibiotics (Allergy)
  - 2nd line test - reticulocyte count
    - Normal 1-2%
    - Hemolysis will have high reticulocyte count (usually > 4%)
    - Bone marrow disease will have low reticulocyte count (< 1%)
- Macrocytic
  - B12 deficiency
  - Folic acid deficiency
  - 2nd line test - B12, Folic acid

Hematopoietic and Lymphoid System Contributing Factors – CBC

- WBCs participate in the body's defense against infections
- WBC count
  - Normal count 7,000 - 10,000
  - > 10,000 - infection
  - < 7,000 - leukemia
    - Note: some viral infections cause leukopenia (WBC low)

Hematopoietic and Lymphoid System Contributing Factors – WBCs

- Leukemia is cancer of the blood cells. It starts in the bone marrow, the soft tissue inside most bones. Bone marrow is where blood cells are made.
- With leukemia, abnormal white blood cells proliferate.
- Over time, leukemia cells can crowd out the normal blood cells. This leads to serious problems such as anemia, bleeding, and infections. Leukemia cells can also spread to the lymph nodes or other organs and cause swelling or pain.

Hematopoietic and Lymphoid System Contributing Factors – WBCs

- Classifications of Leukemia
  - Acute Lymphoblastic Leukemia
    - Most common form in children
    - Characterized by a massive infiltration of bone marrow with immature lymphoid cells which spill over into blood
  - Acute Myelocytic Leukemia
    - Too many WBCs produced and not enough room for RBCs (normocytic anemia)
    - Not enough room for platelets - bleeding
    - White bllod cells not functioning well - infections
  - Chronic Lymphocytic Leukemia
  - Chronic Myelocytic Leukemia
  - Both chronic are mostly diseases of adulthood

Hematopoietic and Lymphoid System Contributing Factors – WBCs

- Lymphoma is a cancer of the lymphoid system.
- There are many types of lymphoma. One type is Hodgkin disease. The rest are called non-Hodgkin lymphomas.
- Non-Hodgkin lymphomas begin when T cell or B cell, becomes abnormal and proliferate. These abnormal cells can spread to almost any other part of the body.

Hematopoietic and Lymphoid System Contributing Factors – WBCs

- Hodgkin’s and Non-Hodgkin lymphoma can cause many symptoms, such as:
  - Swollen, painless lymph nodes in the neck, armpits or groin
  - Unexplained weight loss
  - Fever
  - Soaking night sweats
  - Coughing, trouble breathing or chest pain
  - Weakness and tiredness that don't go away
  - Pain, swelling or a feeling of fullness in the abdomen
- Tests
  - Physical examination
    - Lymph nodes swollen, painful - infection
    - Lymph nodes swollen, not painful - indicates cancer (especially if does not move)
  - Biopsy
    - Presence of Reed Sternberg cell - indicates Hodgkin's Lymphoma
    - No Reed Sternberg cell - indicates NonHodgkin's Lymphoma

Hematopoietic and Lymphoid System Contributing Factors – WBCs

- Multiple Myeloma
  - Disease of plasma cells
  - B cells transform into plasma cells with antigenic stimulation. Plasma cells proliferate and produce antibodies.
  - Diseased plasma cells multiply in the bone marrow and destroys surrounding bone
  - Tests
    - X-ray - detects punched out holes in bones
    - Blood (CBC) - Ca is high (Ca is released from bone)
    - Proteinuria - immune complexes excreted at and damage kidneys
    - Specific test - serum protein electrophroesis

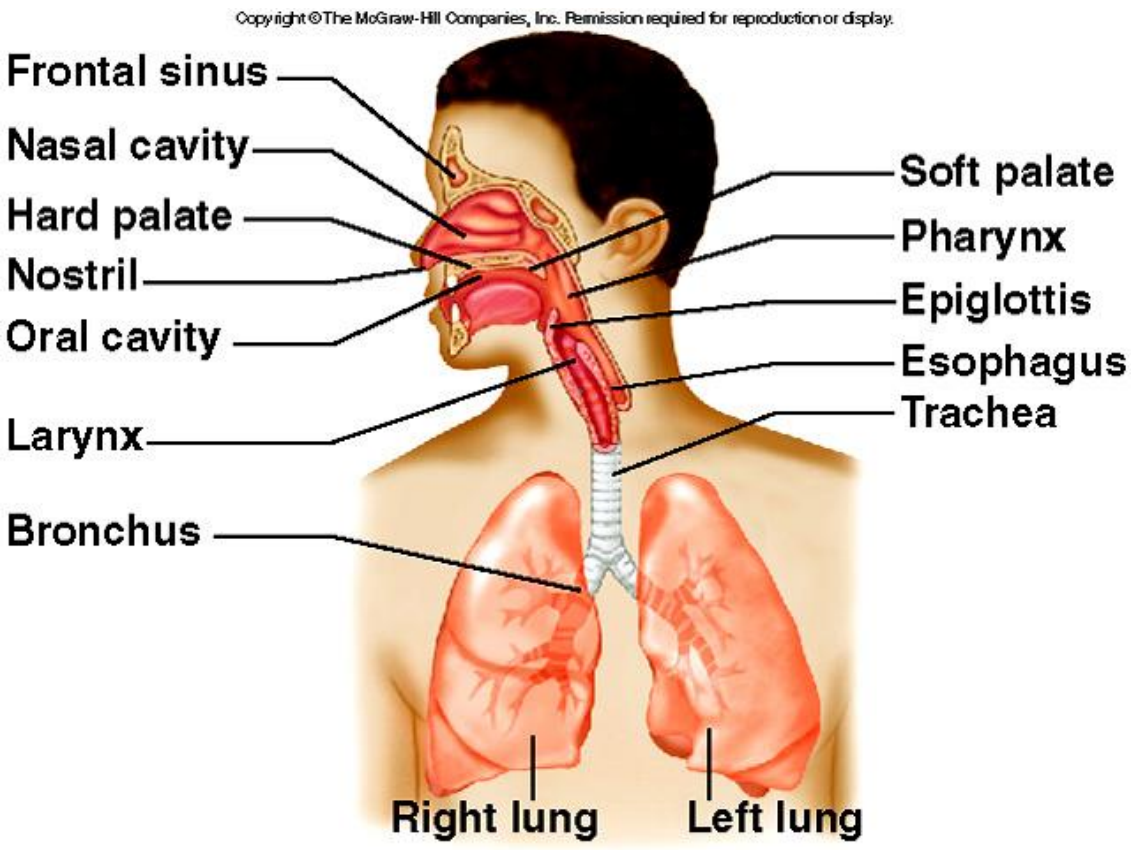
Pathophysiology I

Respiratory System Diseases

Respiratory System

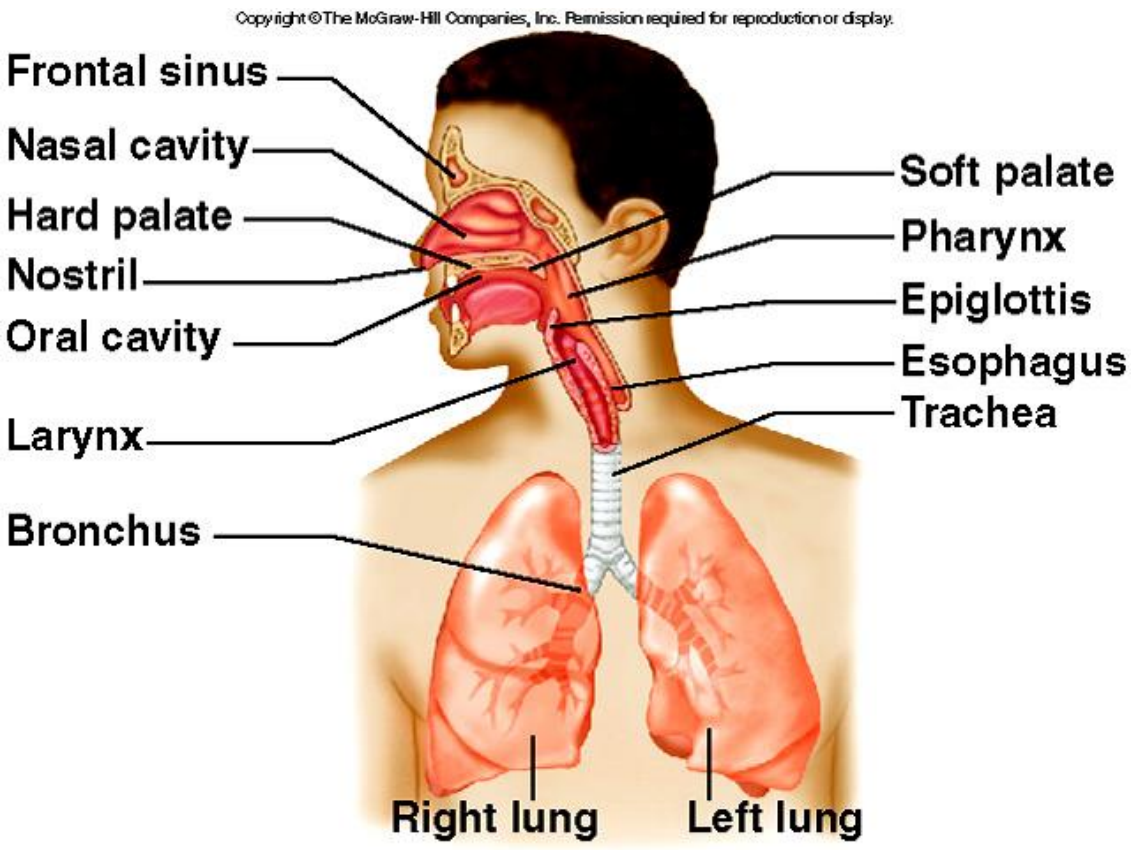
Anatomy Review

Respiratory System Structures



- Organs include lungs and the respiratory tract which is divided into upper and lower respiratory tract
  - Upper consists of
    - Nose
    - Naval cavity
    - Sinuses
    - Pharynx
  - Lower consists of
    - Larynx
    - Trachea
    - Bronchial tree (bronchi and bronchioles, alveoli)
    - Lungs

Respiratory Tract Functions

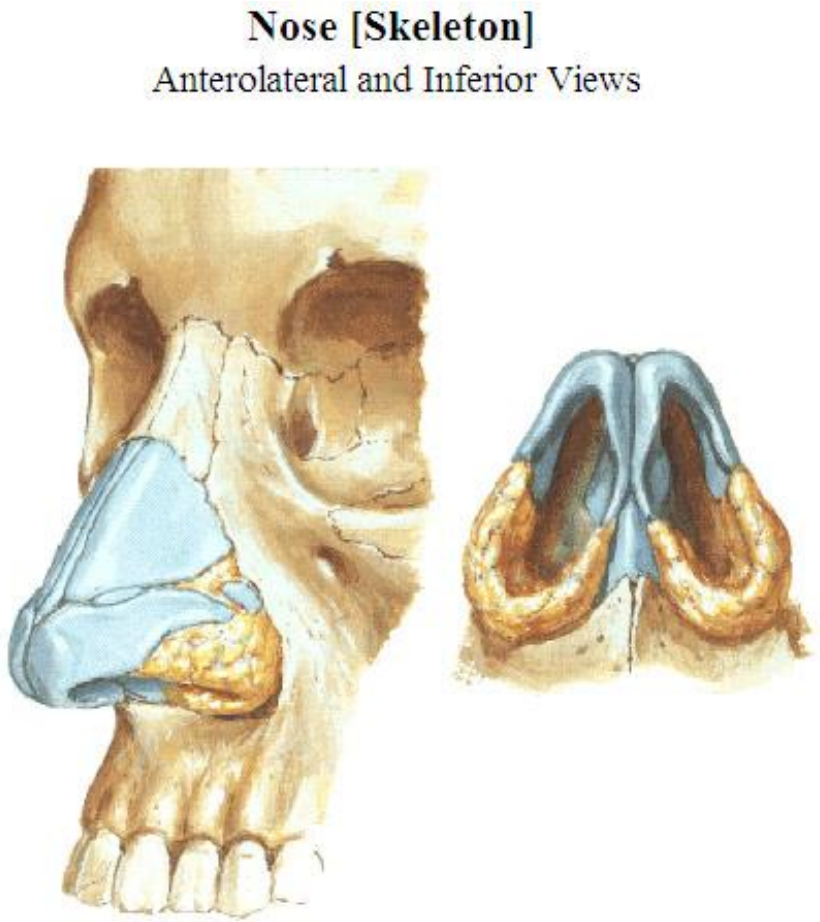


- Pulmonary ventilation – the exchange of gases between external environment to alveoli
- External respiration – the exchange of gases between alveoli and blood stream
- *Note: Internal respiration involves gas exchange between the blood and the interstitial space and cellular respiration between the interstitial space and the cell.*
- Produces sound for communication

Respiratory System Anatomy Review

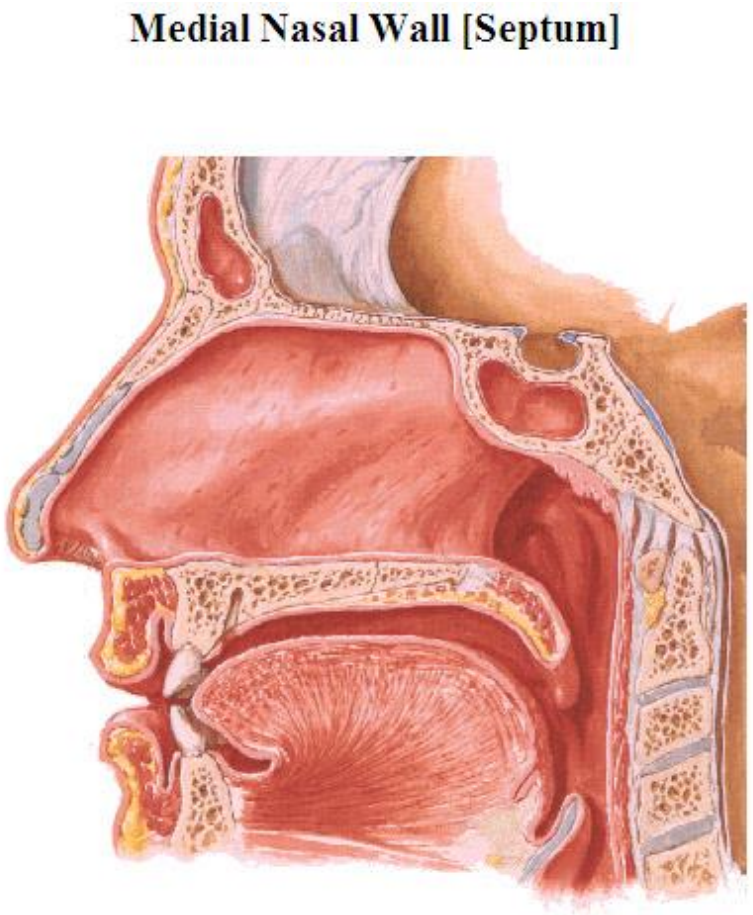
Nose and Paranasal Sinuses

Nose



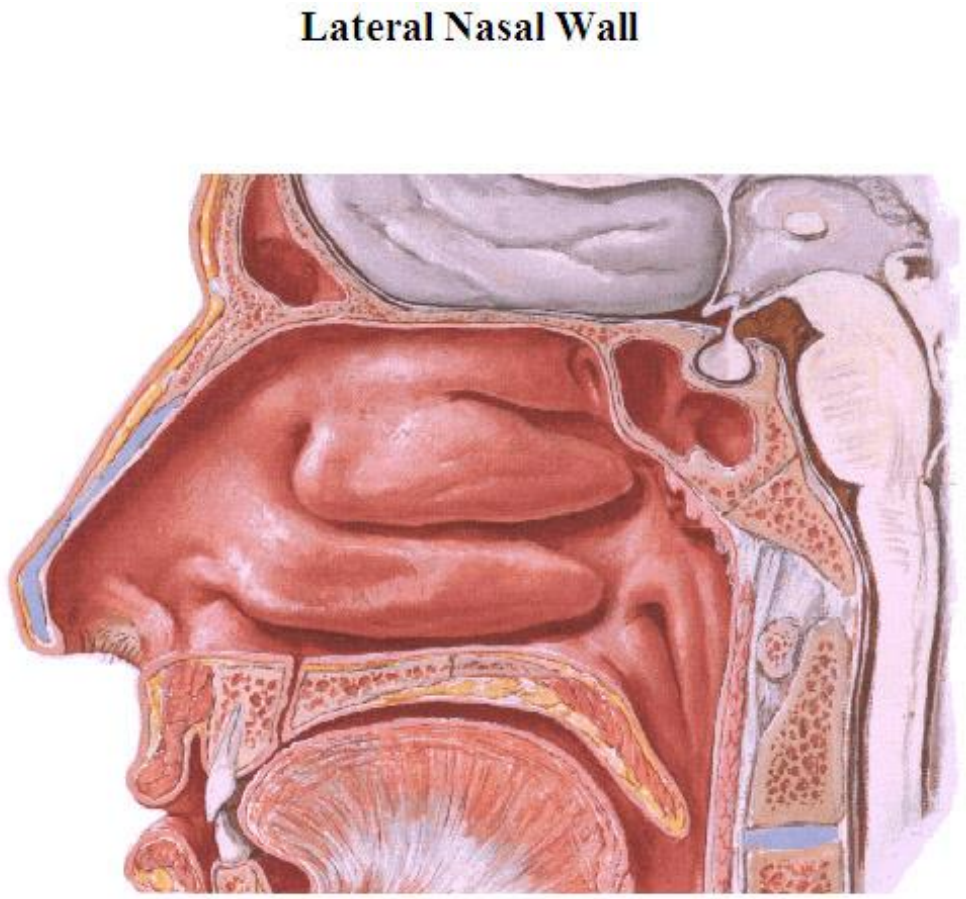
- Lined with mucous membrane, Epithelium is ciliated cuboidal epithelium
- Supported by bone and cartilage
- Provides an entrance for air in which air is filtered by coarse hairs inside the nostrils

Nasal Cavity

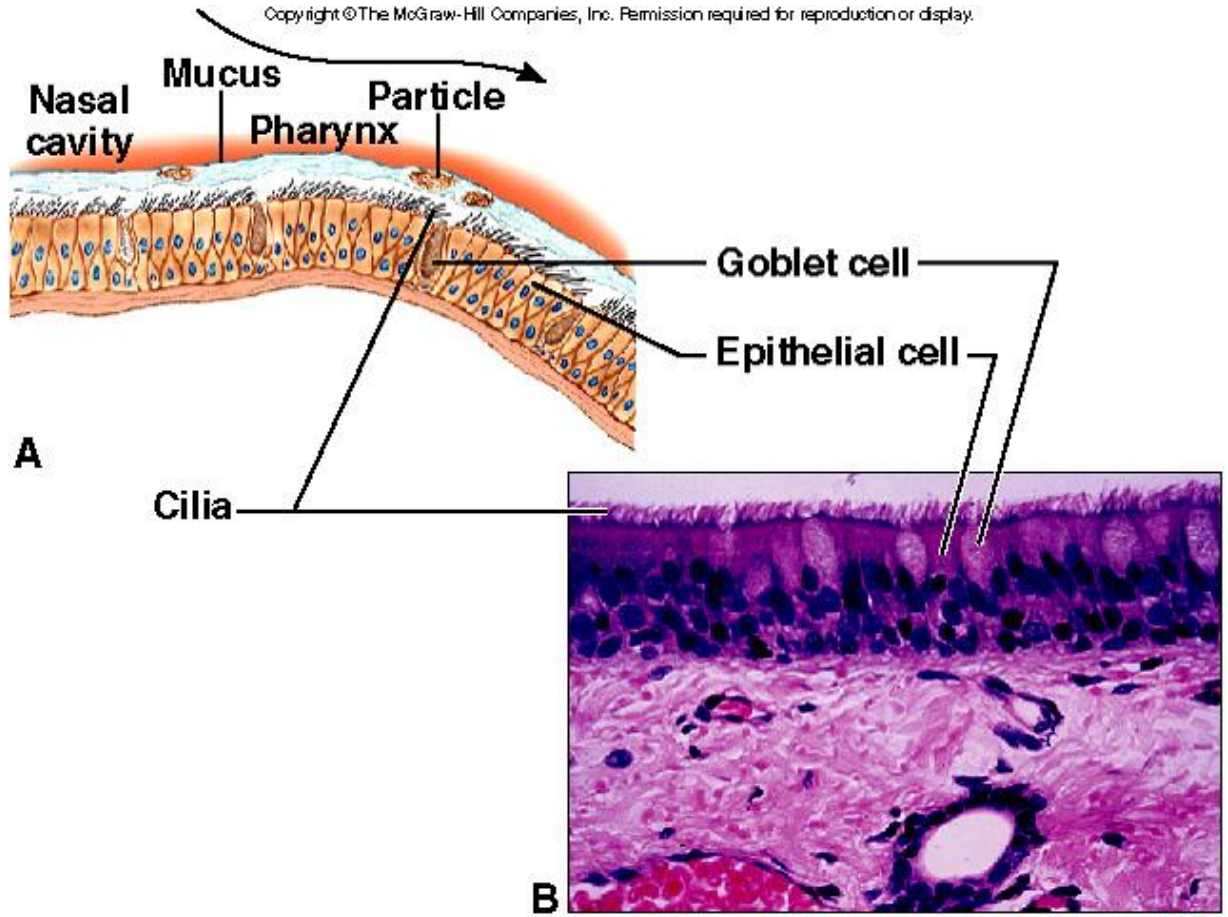


- The nasal cavity is a space posterior to the nose that is divided medially by the nasal septum
- Nasal conchae divide the cavity into passageways that are lined with mucous membrane, and help increase the surface area available to warm and filter incoming air
- Particles trapped in the mucus are carried to the pharynx by ciliary action, swallowed, and carried to the stomach where gastric juice destroys any microorganisms in the mucus

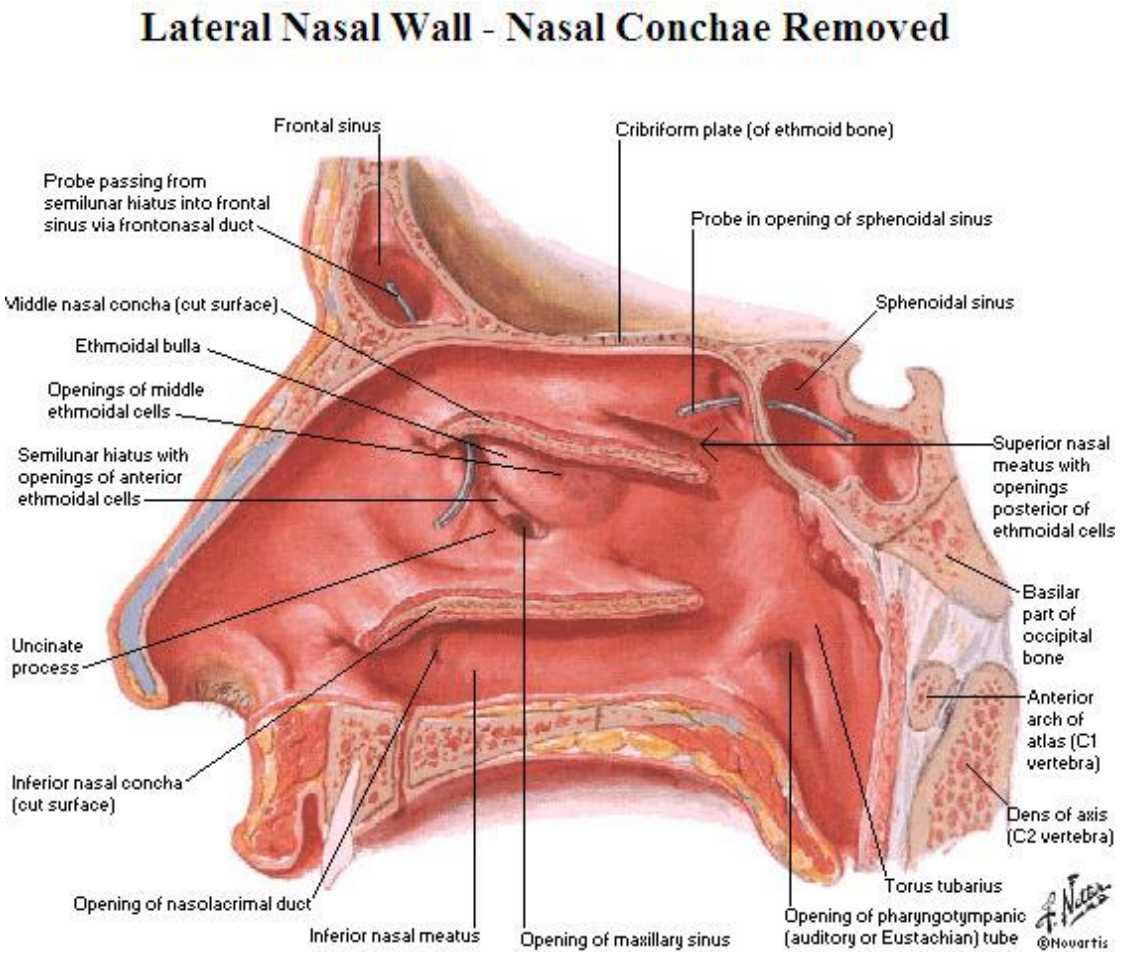
Nasal Conchae



Nasal Mucosa

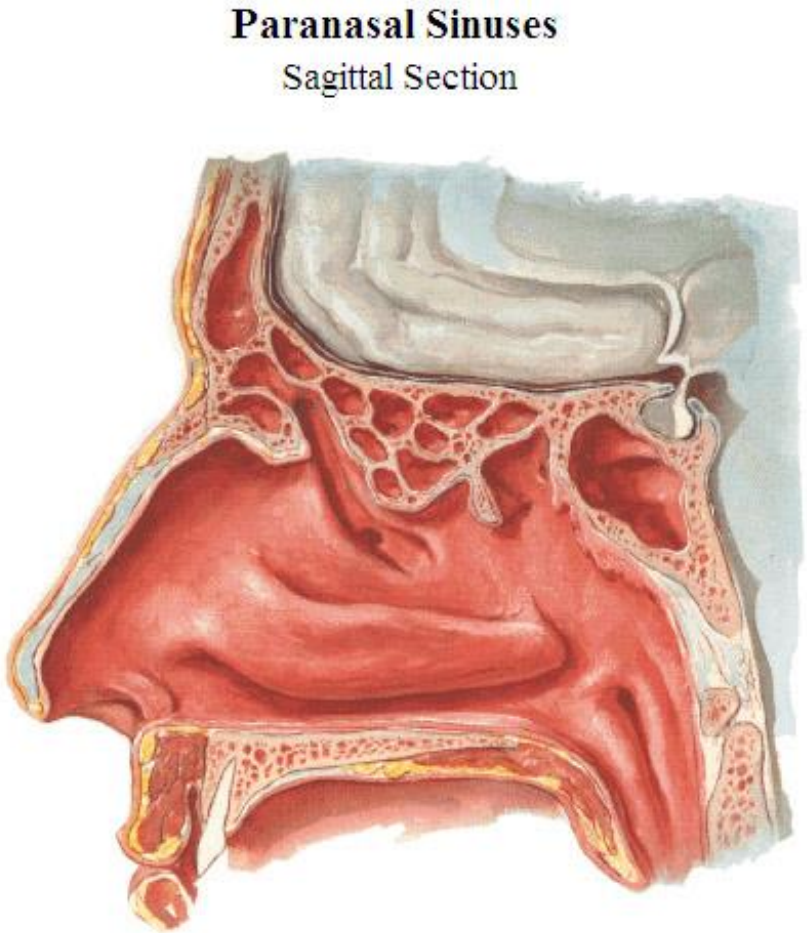


Paranasal Sinuses



- Sinuses are air-filled spaces within the maxillary, frontal, ethmoid, and sphenoid bones of the skull
- These spaces open to the nasal cavity and are lined with mucus membrane that is continuous with that lining the nasal cavity
- The sinuses reduce the weight of the skull and serve as a resonant chamber to affect the quality of the voice

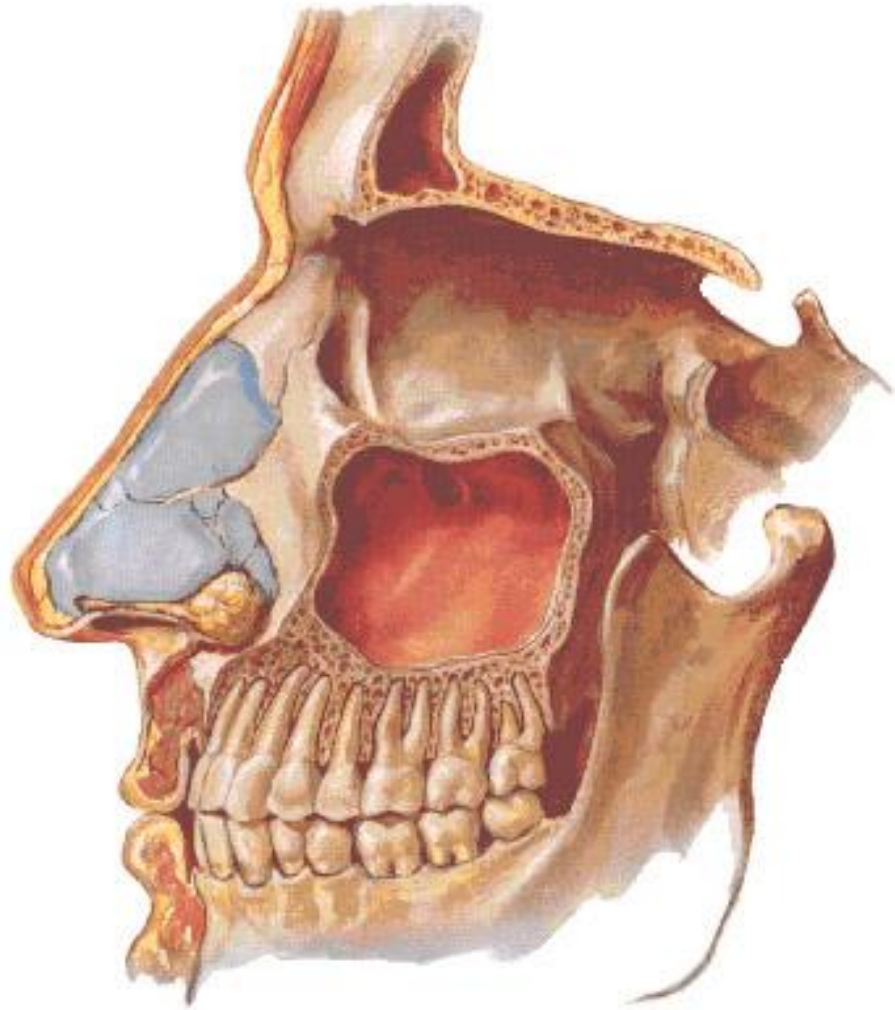
Paranasal Sinuses



- Consists of
  - Frontal sinus
  - Ethmoid Sinus
  - Maxillary Sinus
  - Sphenoid Sinus

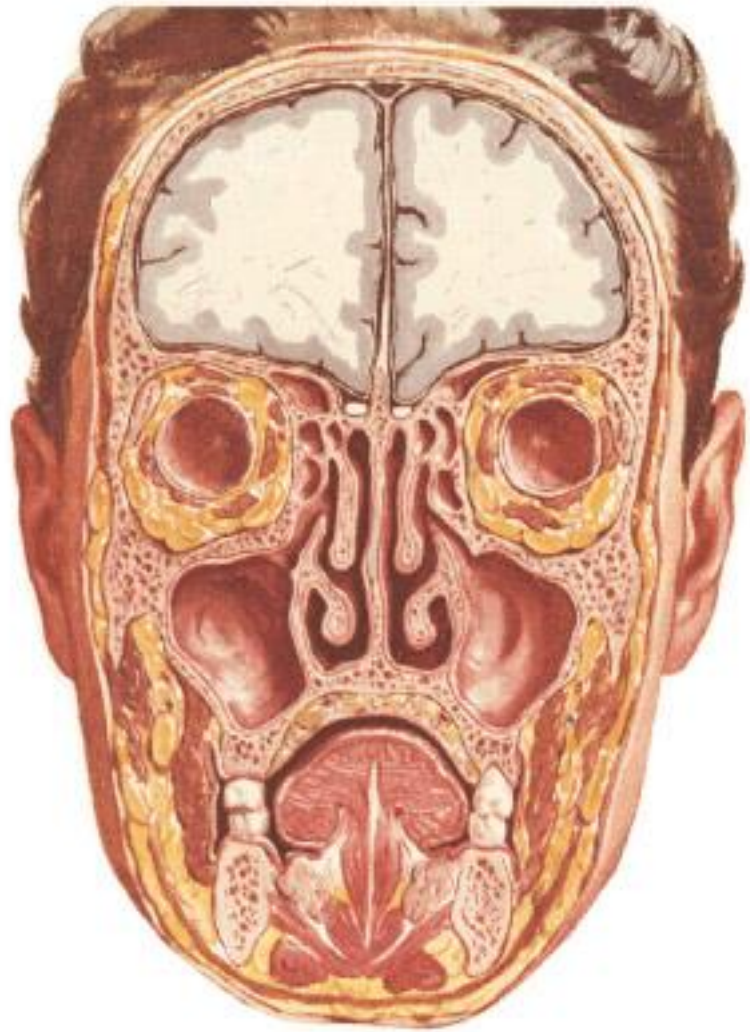
Paranasal Sinuses

Lateral Dissection



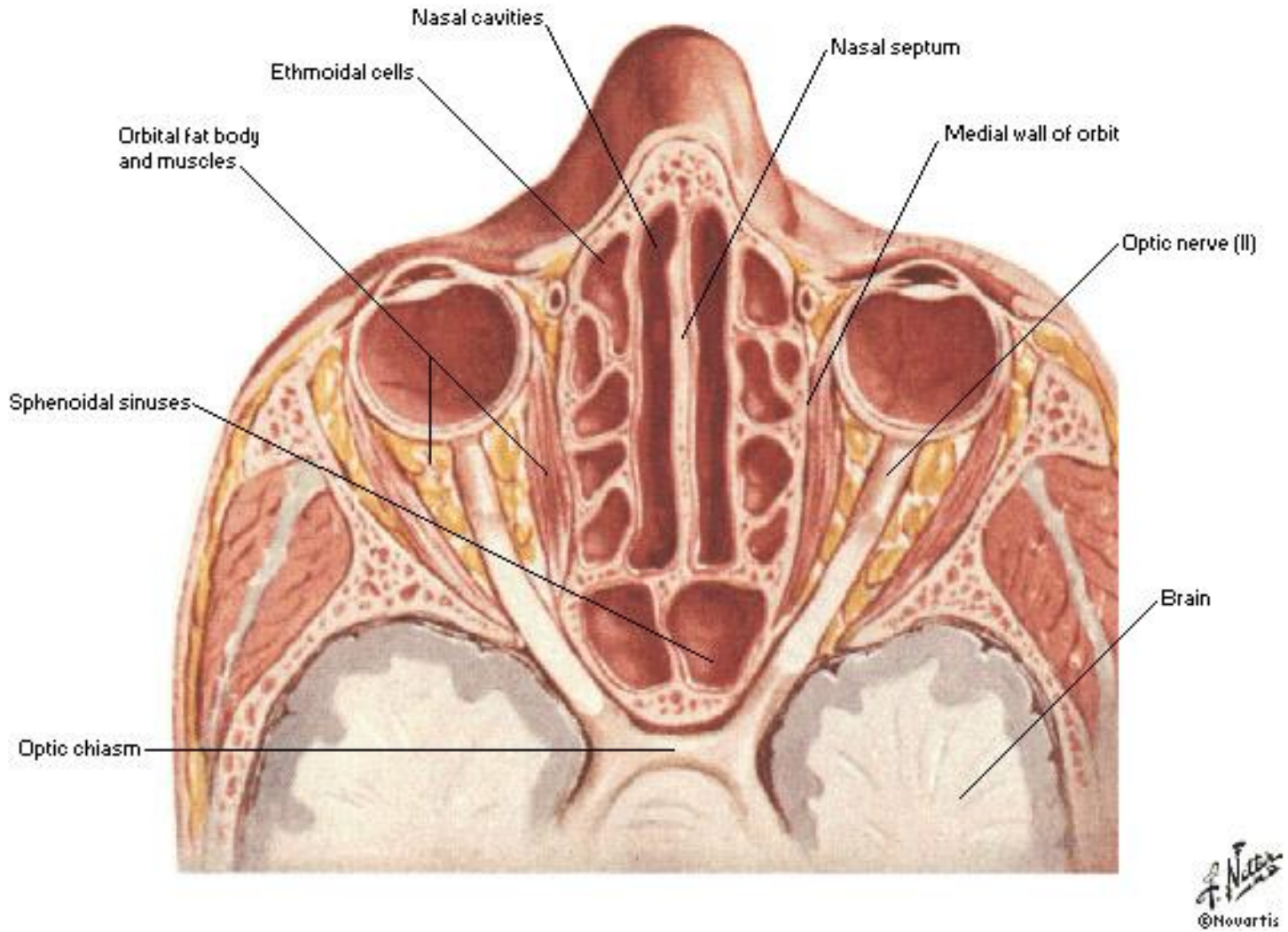
Paranasal Sinuses

Coronal Section



Paranasal Sinuses

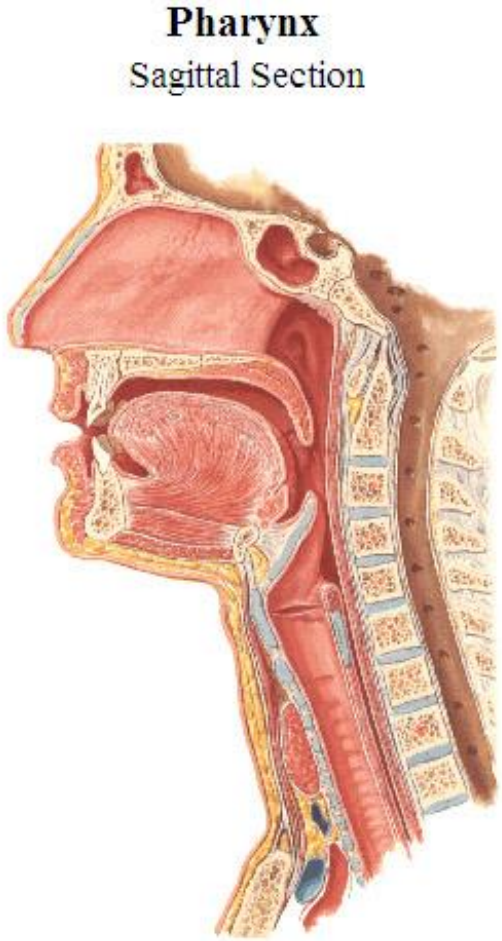
Horizontal Section



Respiratory System Anatomy Review

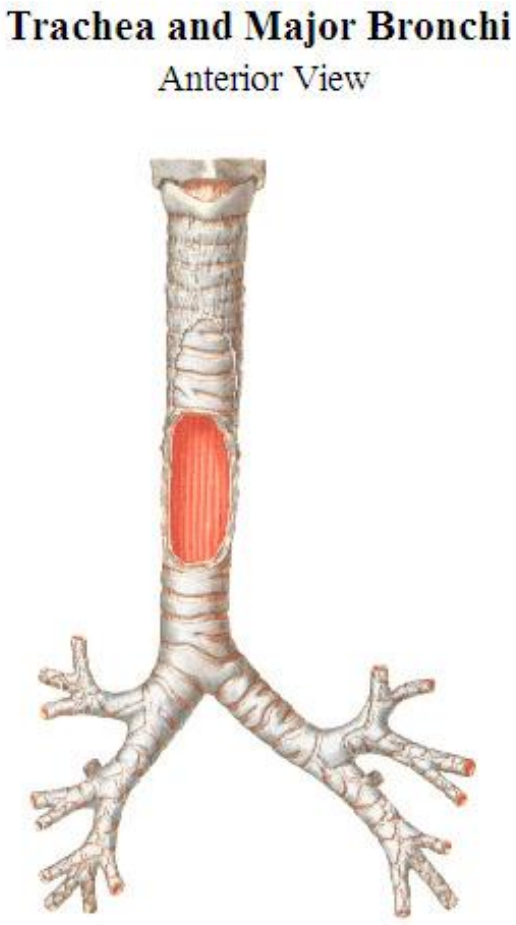
Respiratory Tract and Lungs

The Pharynx and Larynx



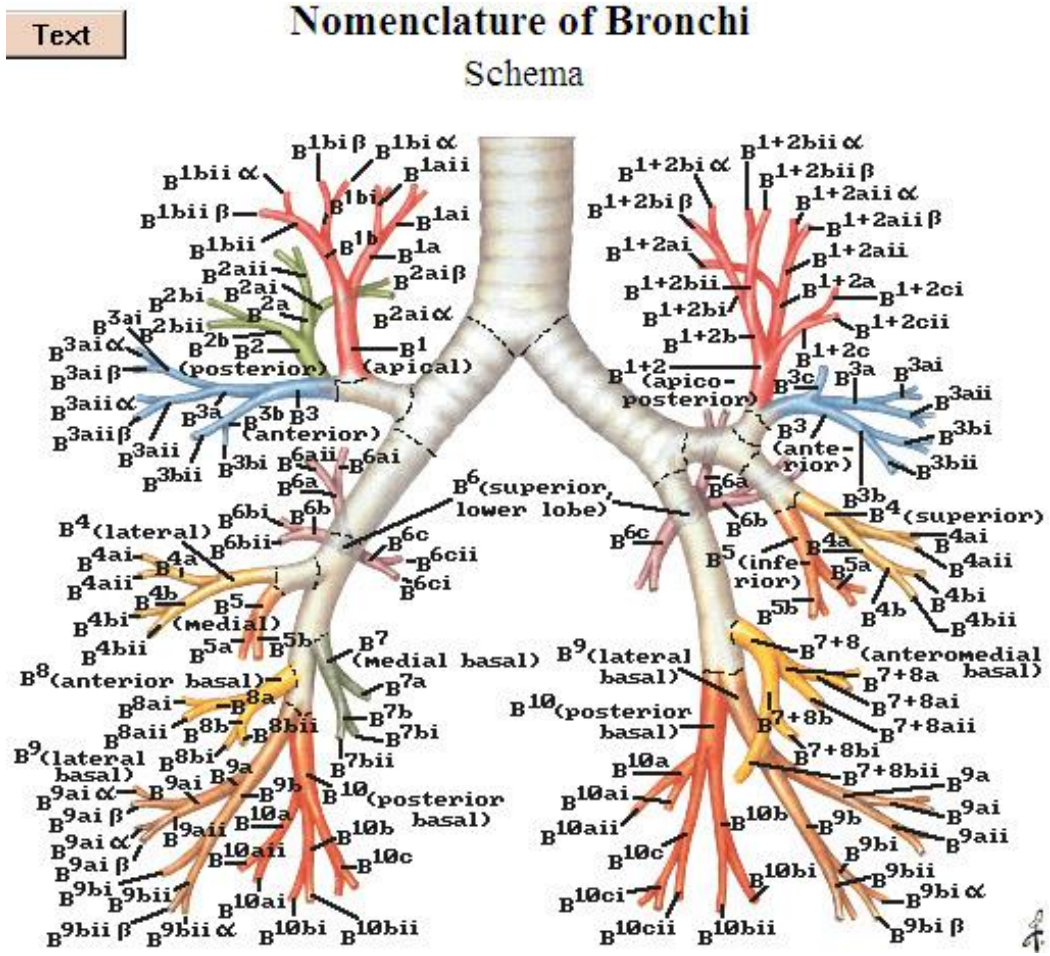
- The pharynx is a common passageway for air and food.
- The larynx is an enlargement in the airway superior to the trachea and inferior to the pharynx. It helps keep particles from entering the trachea and also houses the vocal cords
- Both are lined with squamous epithelium, provided mechanical support. Also, mucosa is rich in lymphoid tissue

The Trachea and Bronchi



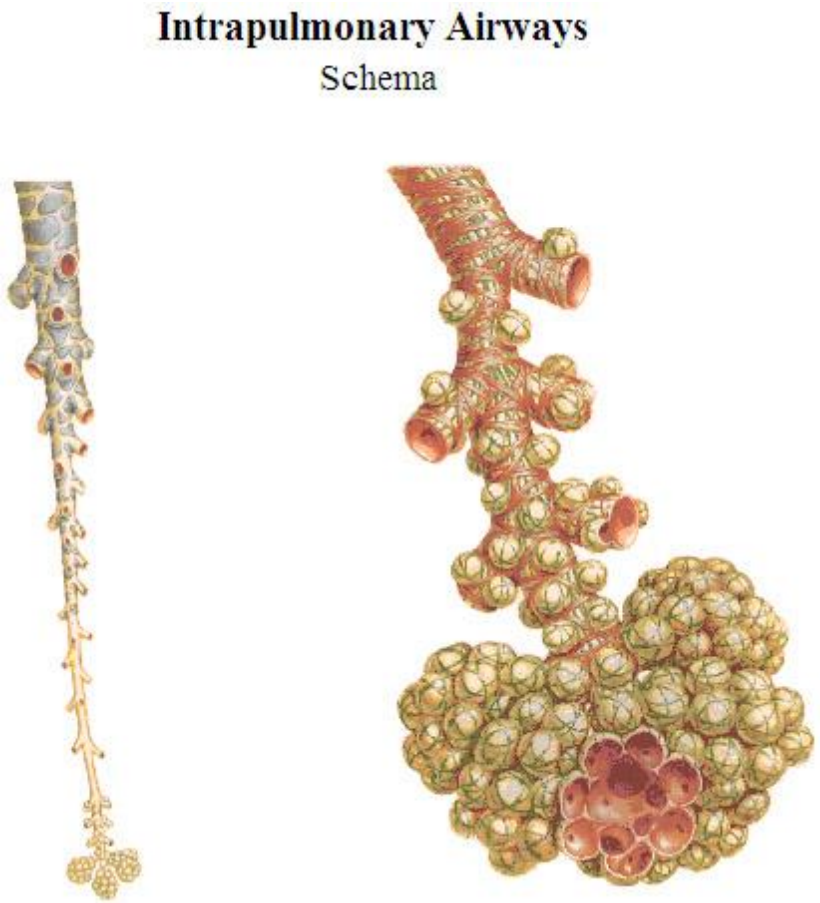
- The trachea extends downward anterior to the esophagus and into the thoracic cavity, where it splits into right and left bronchi.
- The trachea and bronchi are lined with ciliated cuboid epithelium and mucous membrane with many goblet cells that serve to trap incoming particles.
- Under pathological conditions, transitions into squamous cells.
- Most lung cancers originate in bronchi.

The Bronchial Tree



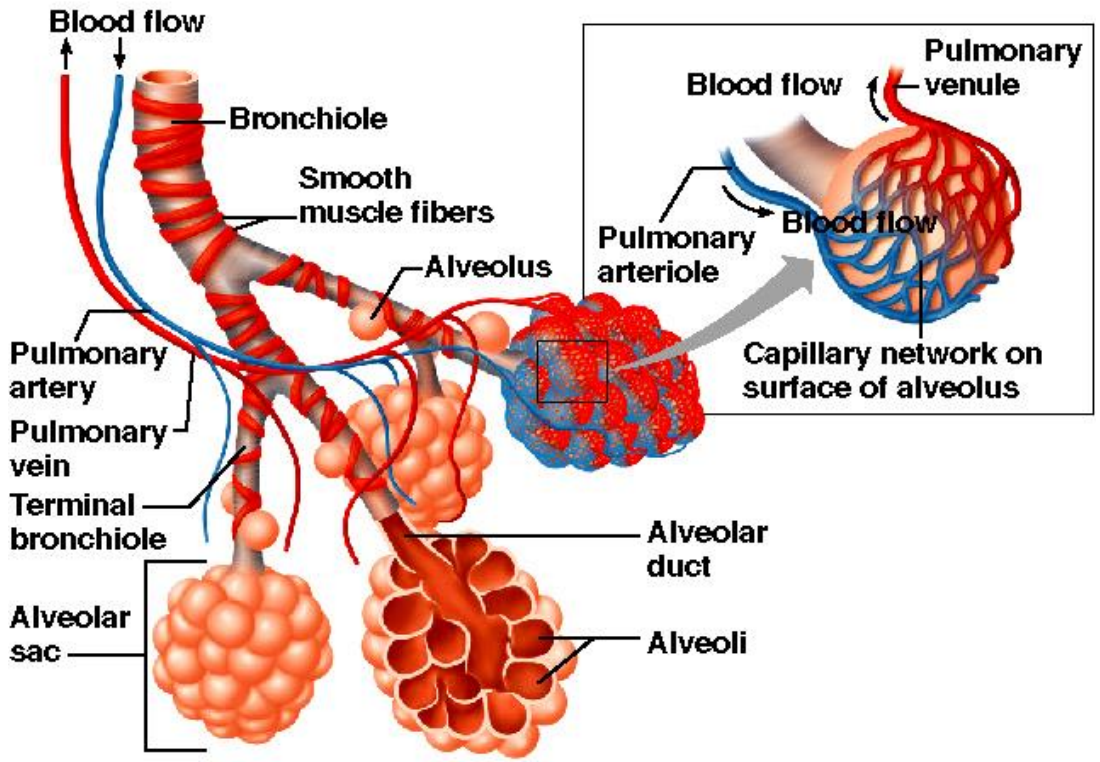
- The bronchial tree consists of branched tubes leading from the trachea to the alveoli
- The bronchi are held open by cartilage. This becomes increasing more regulated by smooth muscles with the bronchioles.

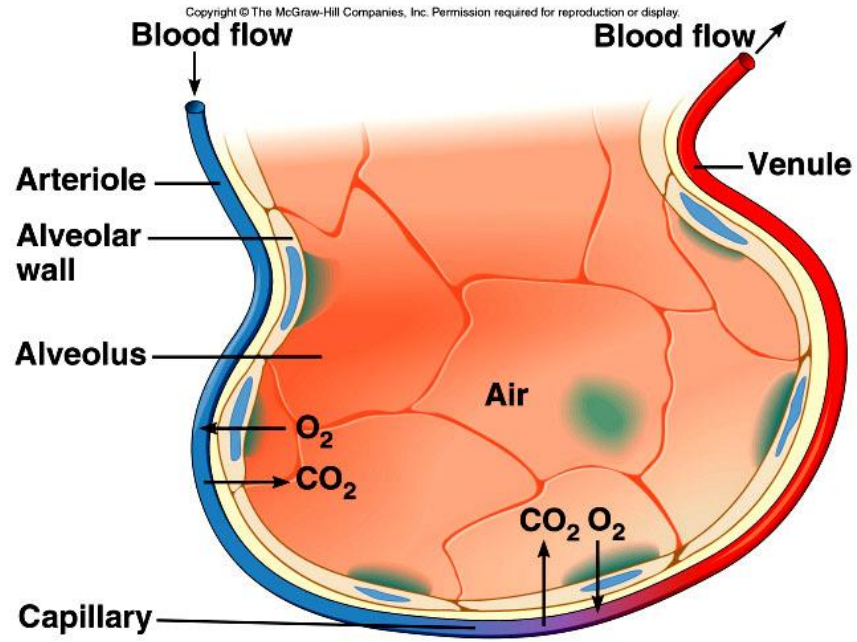
Alveoli



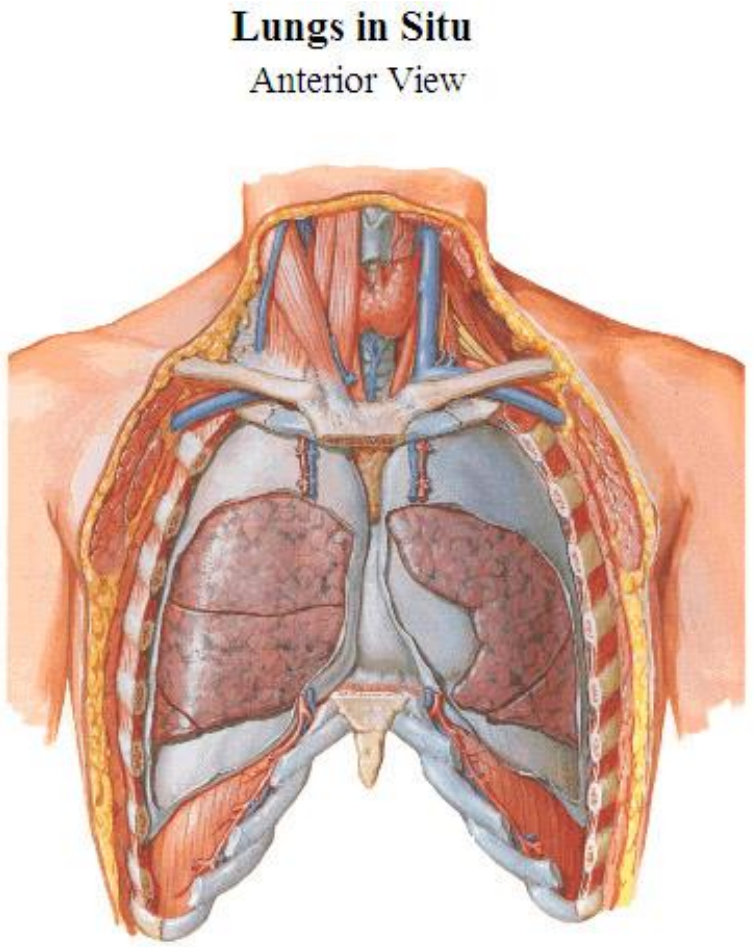
- The alveoli are the terminal portion of the bronchial tree which is in close proximity to the capillaries. External respiration occurs between the alveoli and the capillaries.

Gas Exchange Between Alveoli and Capillaries



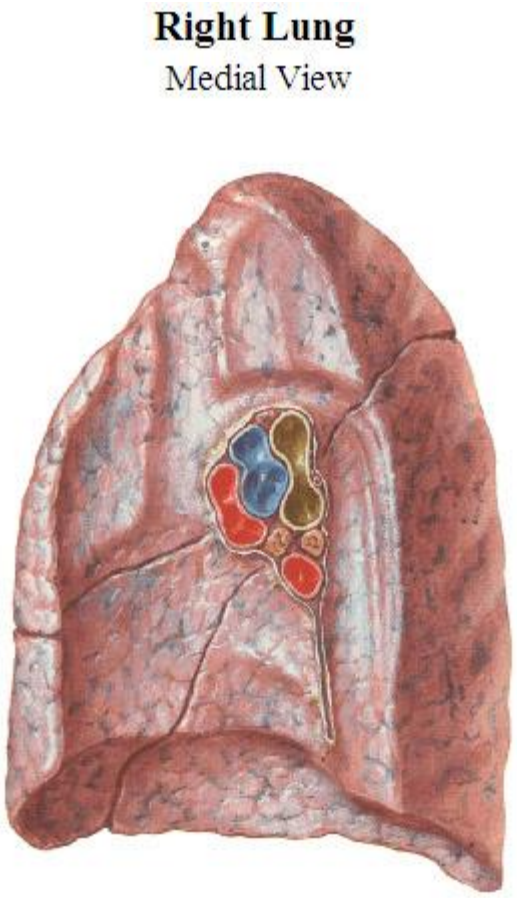


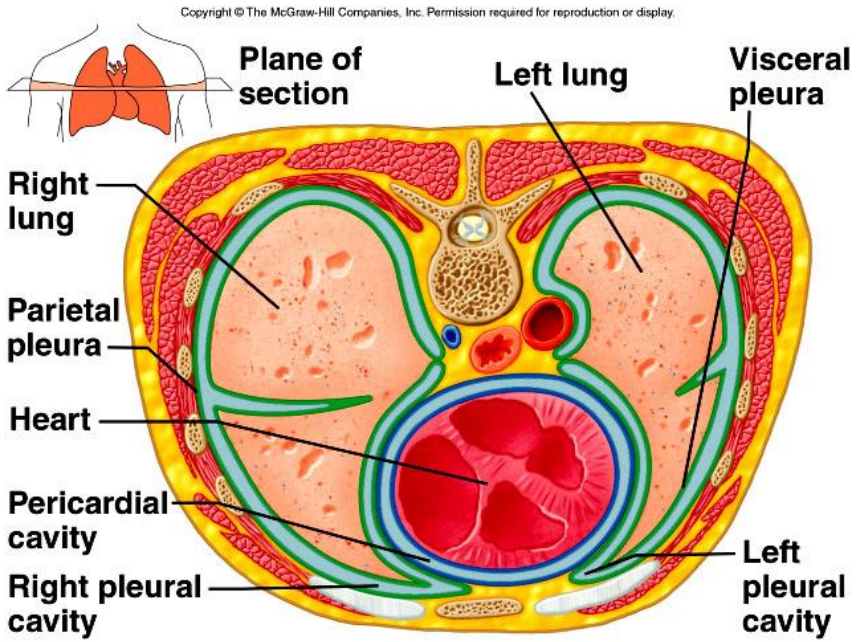
Lungs



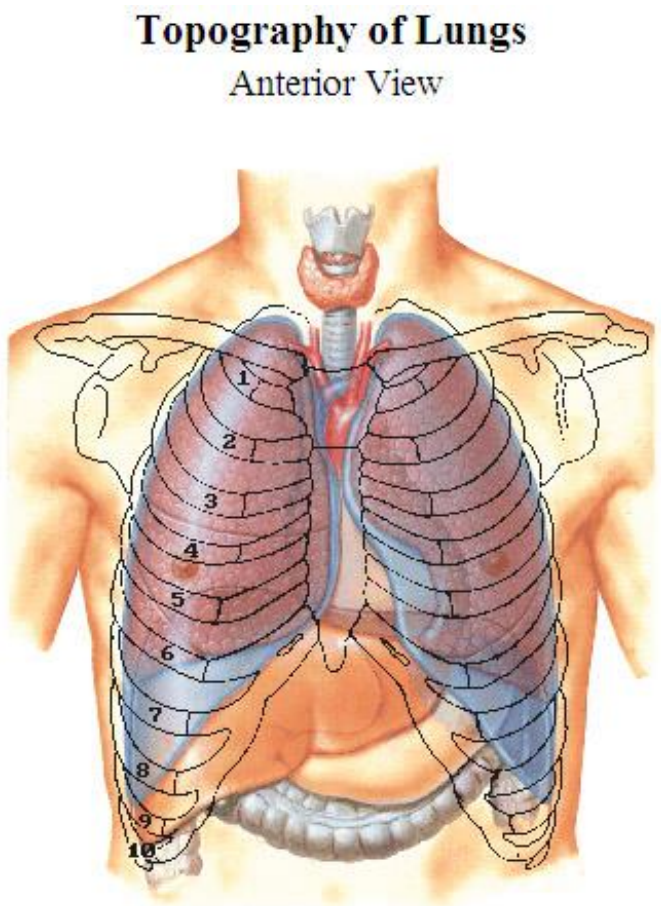
- The right and left soft, spongy, cone-shaped lungs are separated medially by the mediastinum and are enclosed by the diaphragm and thoracic cage. The bronchus and large blood vessels enter each lung.
- The lungs are surrounded by the pleura. The visceral pleura is attached to the lung, and the parietal pleura lines the thoracic cavity; serous fluid lubricates the "pleura cavity" between these two membranes
- The right lung has three lobes, the left has two
- Each lobe is composed of lobules that contain air passages, alveoli, nerves, blood vessels, lymphatic vessels, and connective tissues

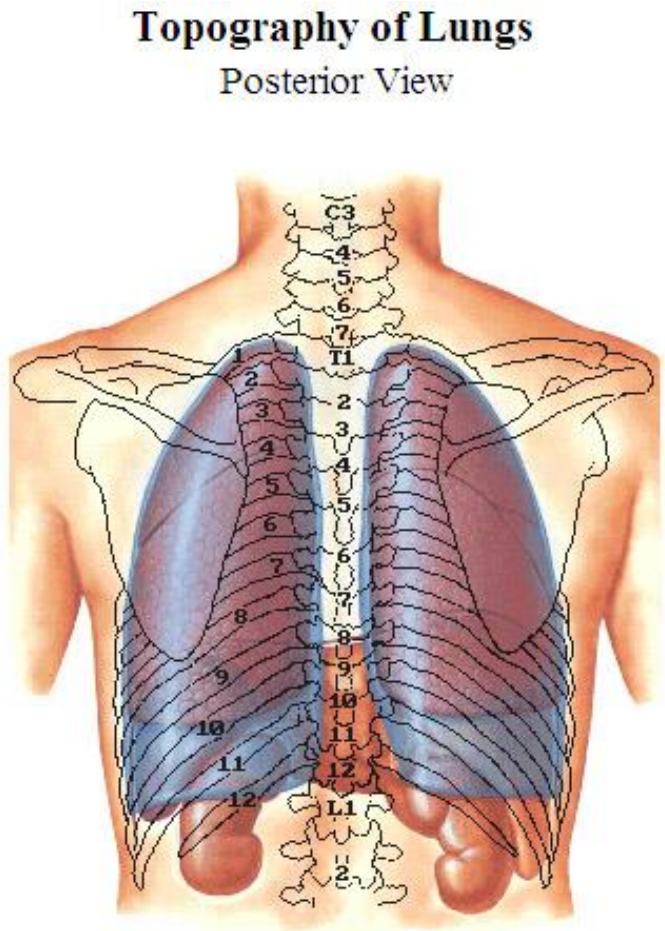
Hilum of Lungs



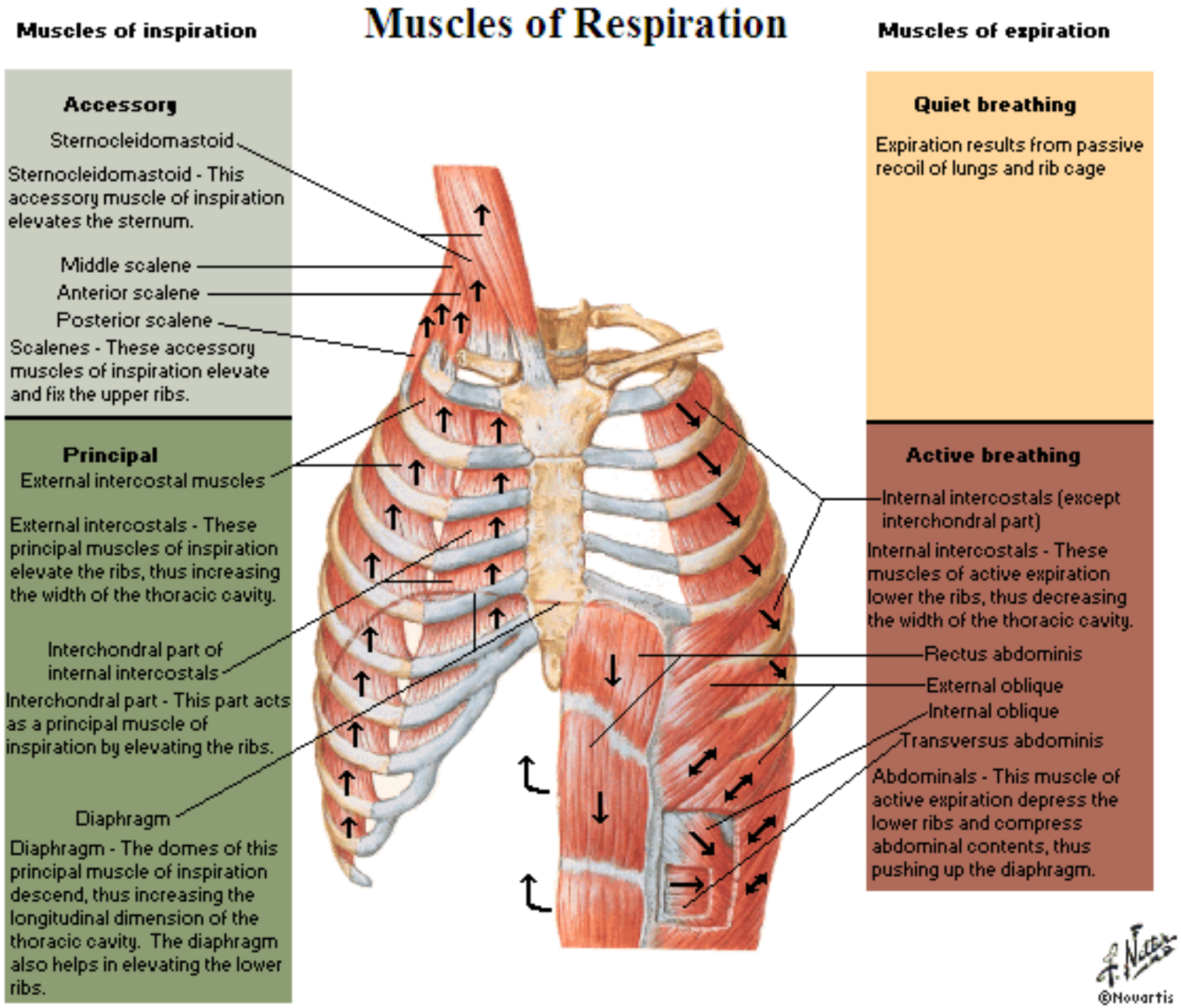


Lung Topography





Muscles of Respiration



Respiratory System

Pathophysiology

Respiratory System Pathophysiology

- The respiratory system may be affected by the following:
  - Infectious diseases
  - Immune diseases
  - Environmentally induced diseases
  - Circulatory diseases
  - Tumors

Respiratory System

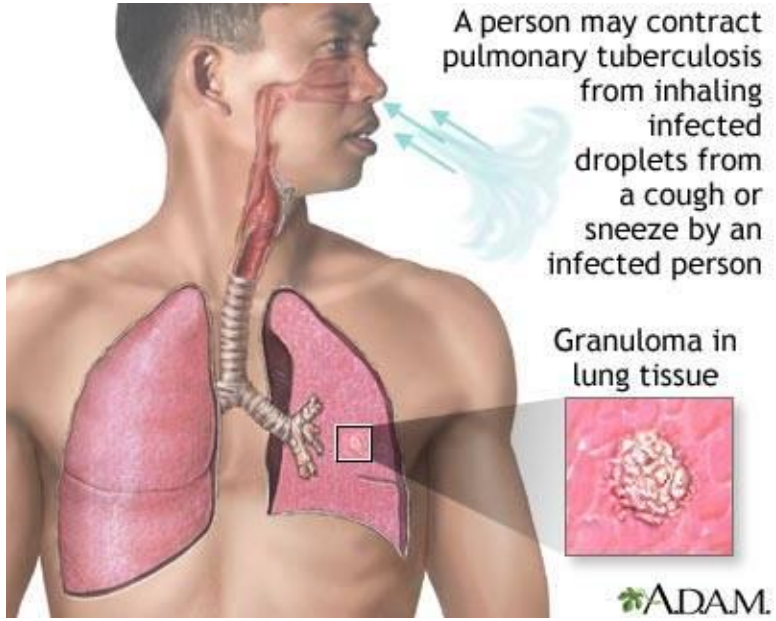
Infectious Disease, Allergens, Pollutants

Respiratory System
Infectious Disease – Upper Respiratory Infections (URI)

- URI are important cause of disease. These can project downward to the bronchi and lungs
- Respiratory system is open-ended and in contact with the environment.
- URI or common colds are a very common cause of respiratory disease. Characterized by acute inflammation involving the nose, paranasal sinuses, throat, and/or larynx.
- Can extend down into the trachea and bronchi. In a small number of patients, may be complicated by pneumonia

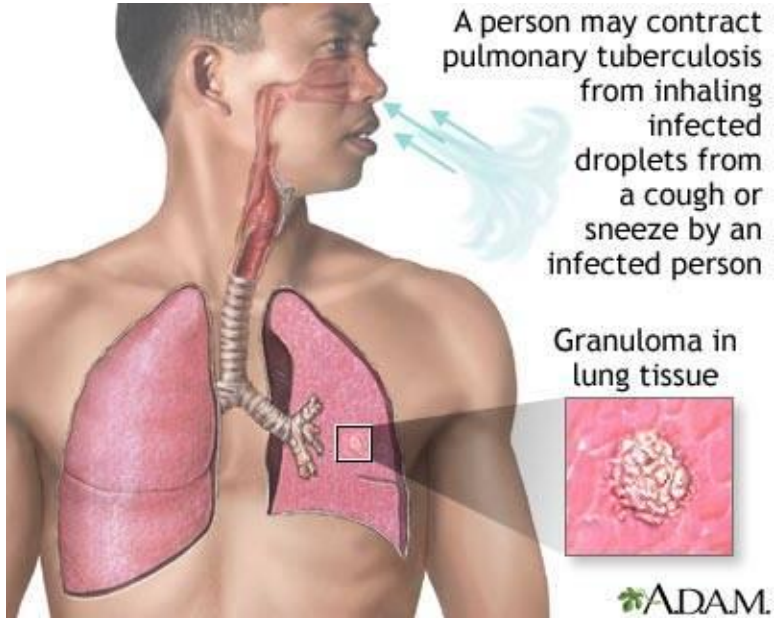
Respiratory System
Infectious Disease - Tuberculosis

- Tuberculosis is a chronic bacterial infectious disease caused by *M. tuberculosis.* In the lungs, this bacteria elicits formation of a granuloma composed of lymphocytes and macrophages. Macrophages fuse, surround the bacteria, and calcify. This is referred to as a Ghon complex.
- The body is protected, but the bacteria is still alive and can cause secondary TB infection. The necrotic central portion of the graduloma resembles cottage cheese and is called casseous necrosis.



Respiratory System
Infectious Disease - Tuberculosis

- Secondary TB infection occurs when the bacteria breaks free (often associated with a weakened immune system). Bacteria can spread in the lungs and granulomas create cavities which are a cause of hemoptysis.
- Can spread to pleura (cause pleurisy) and essentially any organ.



Respiratory System
Infectious Disease - Tuberculosis

- Primary TB presents with mostly unspecific symptoms. Secondary TB includes nonproductive cough, low-grade fever, malaise, night sweats, and weight loss. Hemoptysis occurs later.
- PPD is test. This is very similar to TB. When it is injected on the arm, a patient with TB will have an instant reaction. Chest x-rays are essential for diagnosis.
- Usually, TB is treatable with antibiotics.

Respiratory System
Allergens and Immune Diseases

- Respiratory system is exposed to many allergens inhaled in air.
- Allergic rhinitis and bronchial asthma are the most immune disorders affecting the respiratory system.
  - Allergic rhinitis (hay fever), mostly caused by pollen. It is an IgG mediated allergic reaction causing release of histamine from mast cells.
  - Asthma is caused by bronchial spasm

Respiratory System
Airborne Pollutants

- Inhaled air contains pollutants, airborne particles, and gases, which may cause disease
- Pneumoconioses are lung diseases caused by inhalation of mineral dusts, fumes, and various organic and inorganic particulate matter. Most of these diseases are occupational.
- Silicosis and asbestosis are most important. Other pollutants listed on table 8-4.

Respiratory Diseases

Chronic Obstructive Pulmonary Disease (COPD)

Respiratory System
Chronic Obstructive Pulmonary Disease (COPD)

- COPD is a term used for diseases which are characterized by chronic airway obstruction.
- Includes chronic bronchitis and emphysema
  - Chronic bronchitis presents with chronic cough and sputum production with thickening of the bronchial passages
  - Emphysema destroys the lung parenchyma and causes enlargement of the air spaces with destruction of the alveoli
  - The two can be a combined form of COPD, usually the end result to smoking

Respiratory System
Chronic Obstructive Pulmonary Disease (COPD)

- Etiology is usually smoking and/or other environment and industrial pollutants
- Smoking increases mucus production and bronchial inflammation. Metaplastic changes reduces the mucociliary elevator, entrapping irritants and bacteria. Neutrophils release enzymes which dissolve proteins. Nicotine blocks inhibitors to these proteases which then dissolve the alveoli.
- Other factors contribute (especially to those who smoke), such as:
  - Environmental toxins, multiple lung infections in children, genetics

Respiratory System
Chronic Obstructive Pulmonary Disease (COPD)

- Patients with COPD are customarily divided into two groups:
  - Those with predominantly bronchitis (blue bloaters)
  - Those with predominantly emphysema (pink puffers)

Respiratory System
Chronic Obstructive Pulmonary Disease (COPD)

- Those with predominantly bronchitis (blue bloaters)
  - Bronchiolar obstruction and non-ventilated alveoli causes hypoxia, which can become very pronounced during coughing episodes causing cyanosis (blue). Inflammation causes fibrosis and pulmonary hypertension and chronic cor pulmonale. Right ventricular failure results in peripheral venous stagnation (bloating)

Respiratory System
Chronic Obstructive Pulmonary Disease (COPD)

- Those with predominantly emphysema (pink puffers)
  - Patients do not have (or have less) bronchial obstruction and no irritation causing coughing. They need to breathe rapidly to make up for reduced respiratory surface area. However, they can prevent cyanosis (and stay pink). The chest is overexpanded (barrel-chested). They often hunch forward to engage the secondary breathing muscles.

Respiratory Disease and Carcinogens

- Malignant tumors of the respiratory system are common. Lung carcinomas are the most important of these and usually originate in the bronchi.
- Smoking is a major cause. Genetics and other carcinogens also contribute.

Respiratory Disease and Carcinogens

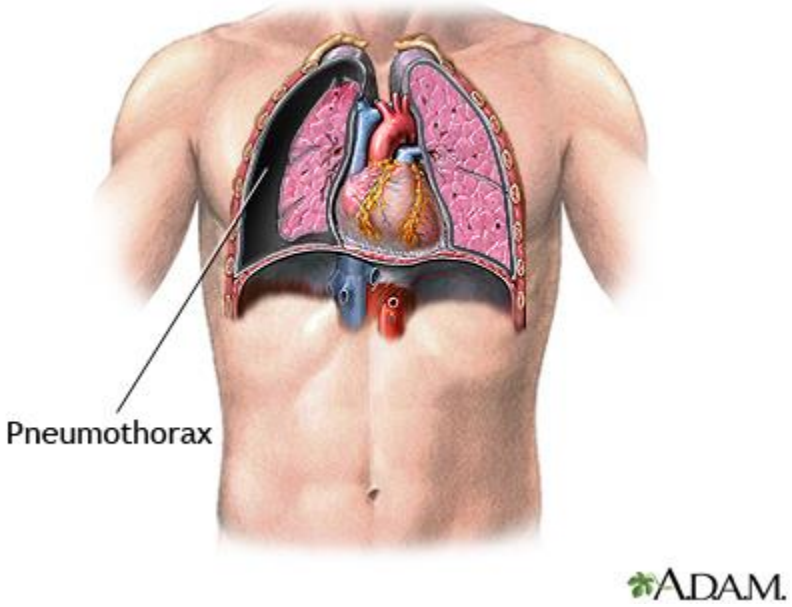
- Signs and symptoms of lung cancer
  - 10-15% asymptomatic
  - 1/3rd will present will symptoms pertaining to the chest including:
    - Bronchial irritation, coughing most likely, wheezing, dyspnea
    - Hemoptysis
    - Atelectasis (collapse of all or part of lung characterized by air in the alveoli).
    - Pleura effusion
    - Chest pain
    - Dysphagia
  - Systemic conditions similar to other tumors
    - Weight loss, cachexia, anorexia, general malaise
  - Distant metastases
  - Paraneoplastic syndrome

Respiratory Disease and Carcinogens

- Mesiothelioma is a form of cancer almost always due to exposure to asbestos
- Fiber in the alveoli are taken up by macrophages which, inflammation causes fibrosis of pleura and plaque formation which stimulates production of mesotheliomas

Respiratory System
Pleural Disease – Pneumothorax

- The pleura of the lungs includes the parietal pleura, the visceral pleura and the pleura cavity. There is a negative pressure in this cavity which keeps the lungs expanded. If this pressure is lost, the lungs will collapse towards the hilum.
- A pneumothorax involves an entry of air into the pleural cavity. Typically occurs with a stab to the chest, broken ribs, or rupture of emphysematous lung tissue



Respiratory System
Pleural Disease – Pleural Effusion

- A pleural effusion (or hydrothorax) involves an accumulation of fluid in the pleural cavity.
- This may be caused by inflammation, which is a hallmark of pleuritic (resulting from pneumonia).
- This may also be caused heart failure or generalized edema.