ANP1105 Final Review - Based off of Lectures

85%: Blood Vessels, Lymphatic & Respiratory, 15%: Cumulative Midterms #1 & #2

Lecture 15: Blood Vessels Part 1

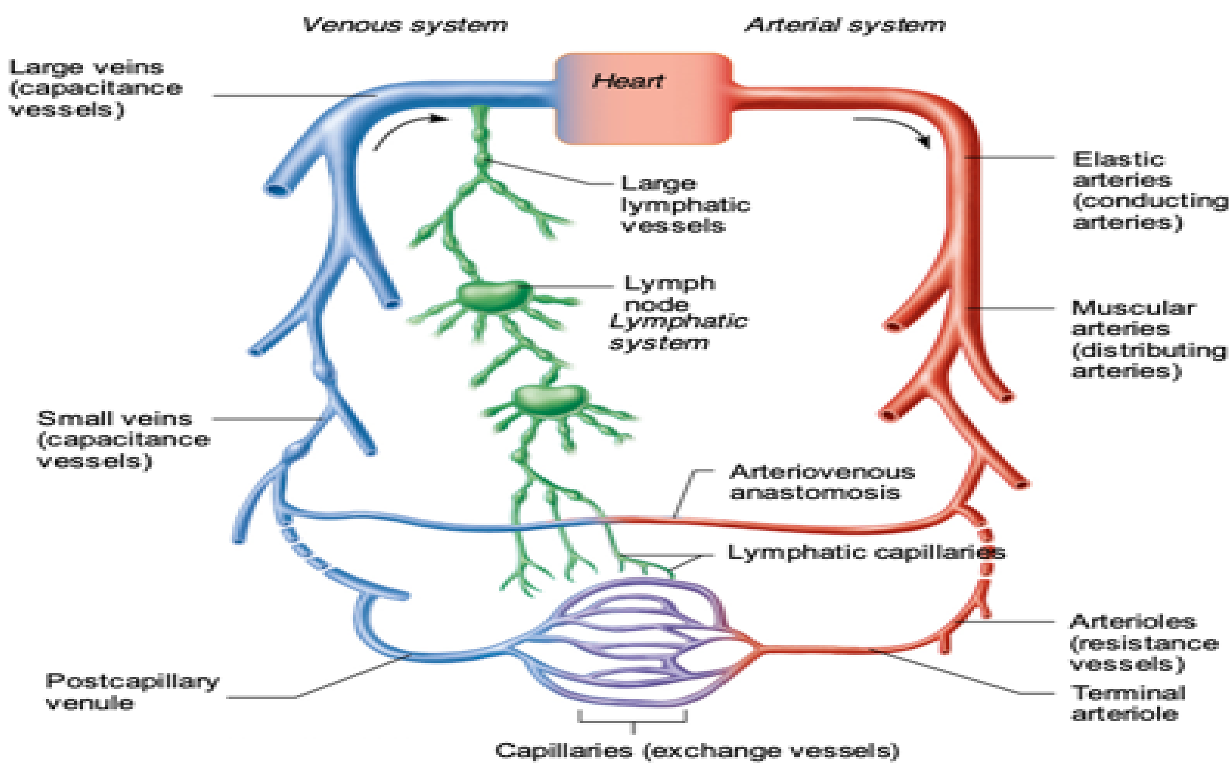
- [ ] ***4.3. Blood vessels and hemodynamics:***
- [ ] ***4.3.1.*** *Compare and contrast the structure of the walls of arteries, capillaries and veins*
- [ ] ***4.3.2.*** *Compare the 3 types of arterial vessels*
- [ ] ***4.3.3.*** *Define microcirculation and compare the 3 types of capillaries*
- [ ] ***4.3.4.*** *Describe the structure and functions of the venules and veins*
- [ ] ***4.3.5.*** *Define blood flow, blood pressure, resistance, peripheral resistance*

Chapter 19

https://www.youtube.com/watch?v=v43ej5lCeBo

Components of Blood Vessels

- Blood Vessels: delivery system of dynamic structures that begins and ends at the heart
    - Works with the lymphatic system to circulate fluid
- Arteries: Carry blood away from the heart; oxygenated except for pulmonary circulation and umbilical vessels of fetus
- Capillaries: direct contact with tissue cells; directly serve cellular needs
- Veins: carry blood toward the heart; deoxygenated except for pulmonary circulation and umbilical vessels of the fetus

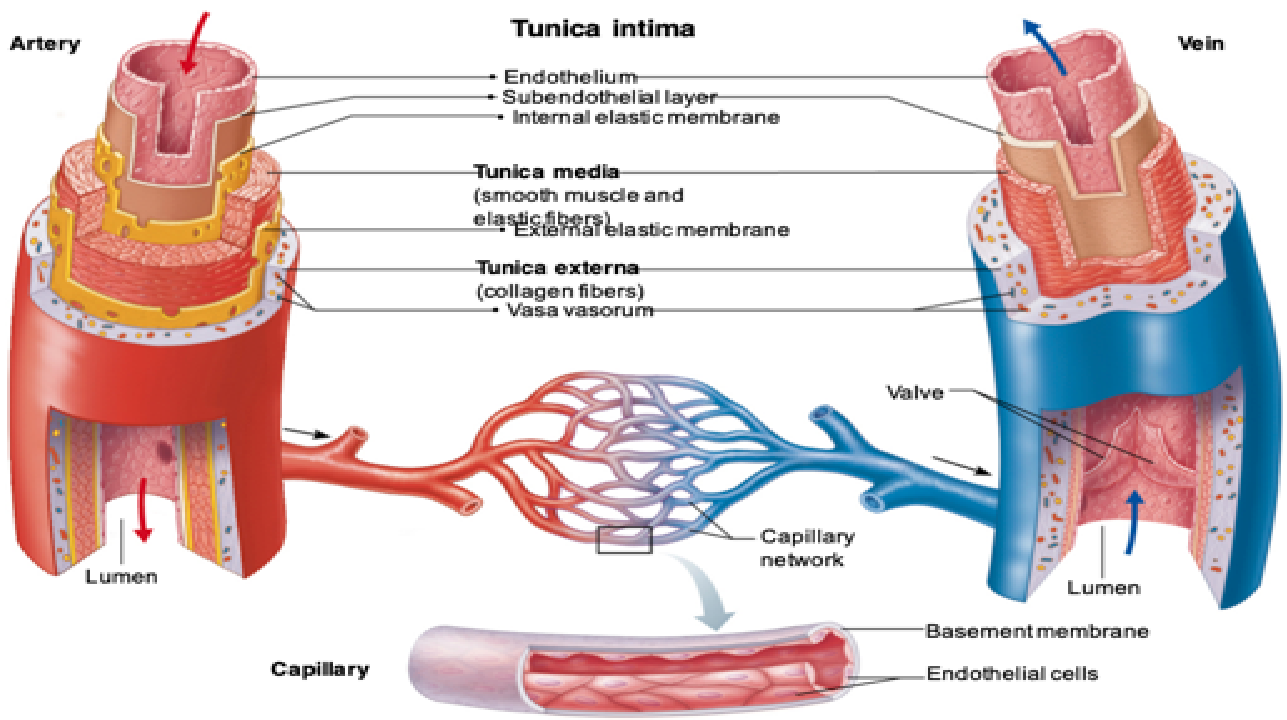


Relative Proportion of Blood Volume Throughout the Cardiovascular System

- 5% capillaries
- 8% heart
- 12% pulmonary blood vessels
- 15% systemic arteries and arterioles
- 60% systemic veins and venules
    - Supply all of the body except the lungs, are distensible, contain a large proportion of the blood volume and so are called capacitance vessels or blood reservoirs

Different Types of Blood Vessels

- All vessels consist of a lumen, central blood-containing space, surrounded by a wall - blood vessels are tubes
- Walls of all vessels, except capillaries, have 3 layers/ tunics:
    1. Tunica Intima
    2. Tunica Media
    3. Tunica Externa
- Capillaries are different because they don't have 3 layers, they are just endothelium with sparse basal lamina.



- <u>Vasa vasorum:</u> conceptually similar to the coronary blood supply

Different Types of Arteries & Veins

- Arteries
    - Elastic, Muscular, Arteriole

- Capillaries
- Veins
    - Venule, Vein

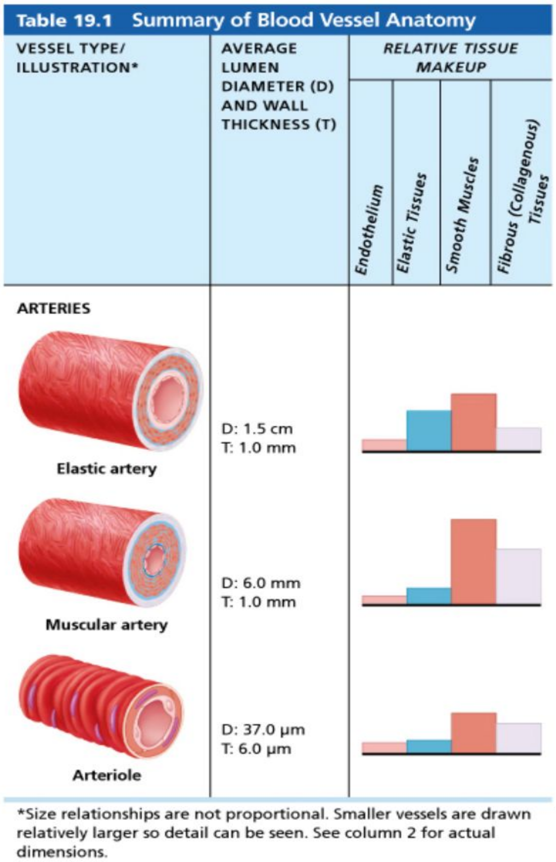


Table 19.1 Summary of Blood Vessel Anatomy

VESSEL TYPE/ ILLUSTRATION*	AVERAGE LUMEN DIAMETER (D) AND WALL THICKNESS (T)	RELATIVE TISSUE MAKEUP			
		Endothelium	Elastic Tissues	Smooth Muscles	Fibrous (Collagenous) Tissues
ARTERIES					
Elastic artery	D: 1.5 cm T: 1.0 mm				
Muscular artery	D: 6.0 mm T: 1.0 mm				
Arteriole	D: 37.0 µm T: 6.0 µm				

*Size relationships are not proportional. Smaller vessels are drawn relatively larger so detail can be seen. See column 2 for actual dimensions.

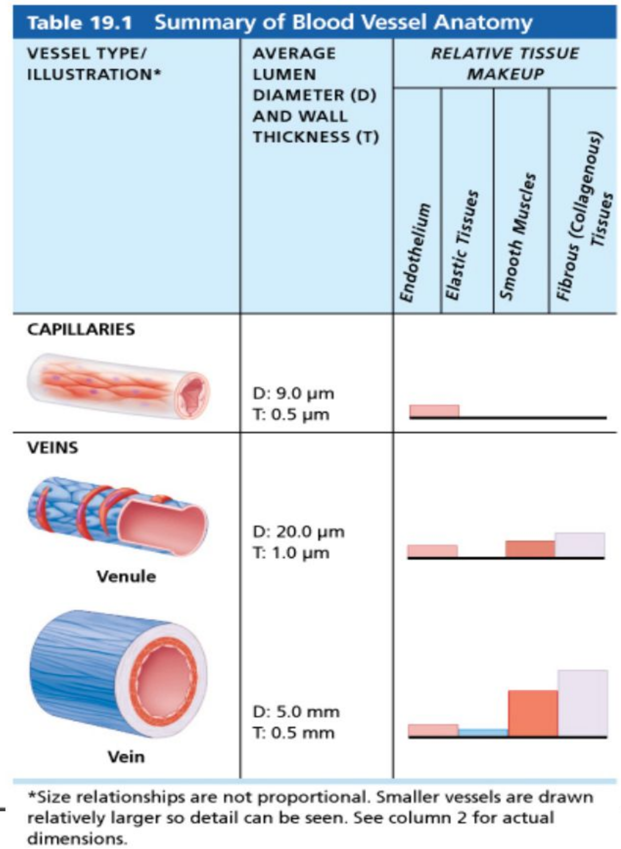


Table 19.1 Summary of Blood Vessel Anatomy

VESSEL TYPE/ ILLUSTRATION*	AVERAGE LUMEN DIAMETER (D) AND WALL THICKNESS (T)	RELATIVE TISSUE MAKEUP			
		Endothelium	Elastic Tissues	Smooth Muscles	Fibrous (Collagenous) Tissues
CAPILLARIES	D: 9.0 µm T: 0.5 µm				
VEINS					
Venule	D: 20.0 µm T: 1.0 µm				
Vein	D: 5.0 mm T: 0.5 mm				

*Size relationships are not proportional. Smaller vessels are drawn relatively larger so detail can be seen. See column 2 for actual dimensions.

Arteries

- Arteries are divided into 3 groups, based on size and function

1. <u>Elastic Arteries</u>

- Thick walled with large, low-resistance lumen
    - Aorta and its major branches: also called conducting arteries because they conduct blood from heart to medium sized vessels
- Elastin found in all 3 tunics, mostly in the tunica media
- Contain substantial smooth muscle, but inactive in vasoconstriction
- Act as pressure reservoirs that expand and recoil as blood is ejected from heart
    - Allows for continuous blood flow downstream even between heartbeats

2. <u>Muscular Arteries</u>

- Arise from elastic arteries
- Also called distributing arteries because they deliver blood to body organs
    - Diameters range from pinky-finger size to pencil-lead size
- Account for most of the named arteries
- Have thickest tunica media with more smooth muscle, but less elastic tissue
    - Tunica media sandwiched between elastic membranes

- Active in vasoconstriction

3. Arterioles

- Smallest of all arteries
    - Larger arterioles contain all 3 tunics
    - Smaller arterioles are mostly single layer of smooth muscle surrounding endothelial cells
- Control flow into capillary beds via vasodilation and vasoconstriction of smooth muscle
    - Vasodilation: the dilation of blood vessels, which decreases blood pressure.
    - Vasoconstriction: the constriction of blood vessels, which increases blood pressure.
- Also called resistance arteries because changing diameters change resistance to blood flow
- Lead to capillary beds

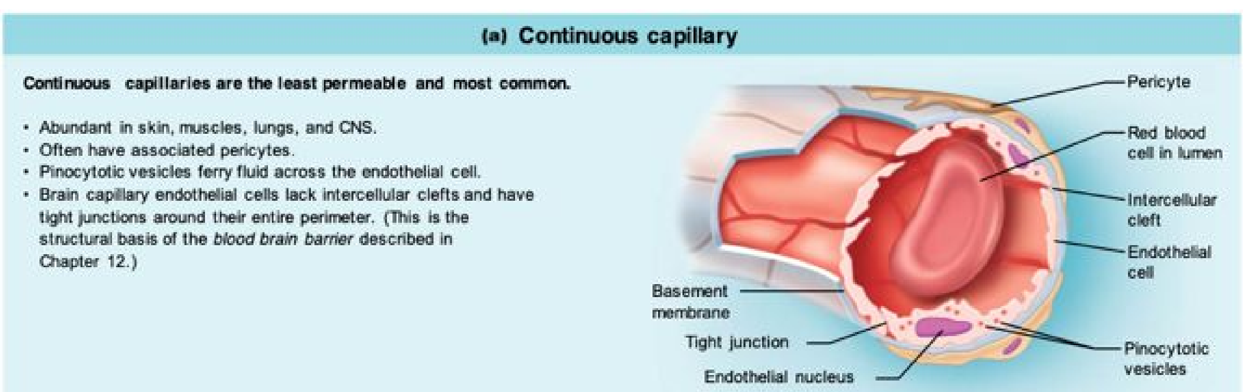
Elastic Arteries → Muscular Arteries → Arterioles

Capillaries

- Microscopic vessels; diameters so small only single RBC can pass through at a time
- Walls just as thin as tunica intima; in smallest vessels one cell forms the entire circumference
    - Pericytes: spider-shaped stem cells help stabilize capillary walls, control permeability, and play a role in vessel repair
        - Supply almost every cell, except for cartilage, epithelia, cornea and lens of eye
        - Exchange of gases, nutrients, wastes, hormones etc between blood and interstitial fluid (relates to lymphatic system)
- All capillary endothelial cells are joined by tight junctions with gaps called intercellular clefts
    - Allow passage of fluids and small solutes
- There are 3 types of capillaries

1. Continuous capillaries

- Least permeable; found in skin, muscles, nervous system



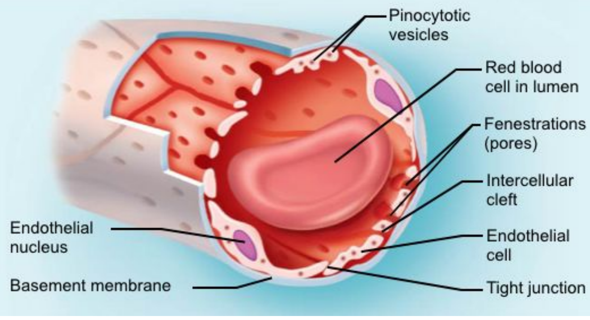
2. Fenestrated capillaries

- Medium permeable; found in areas of filtration such as the kidney or gut

(b) Fenestrated capillary

Fenestrated capillaries have large fenestrations (pores) that increase permeability.

- Occur in areas of active filtration (e.g., kidney) or absorption (e.g., small intestine), and areas of endocrine hormone secretion.
- Fenestrations are Swiss cheese–like holes that tunnel *through* endothelial cells.
- Fenestrations are usually covered by a very thin diaphragm made of extracellular glycoproteins. This diaphragm has little effect on solute and fluid movement.
- In some digestive tract organs, the number of fenestrations in capillaries increases during active absorption of nutrients.



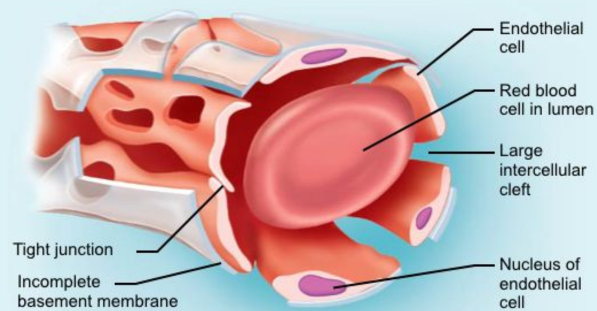
3. <u>Sinusoidal capillaries</u>

- Most permeable; found in liver, bone marrow, parts of kidney

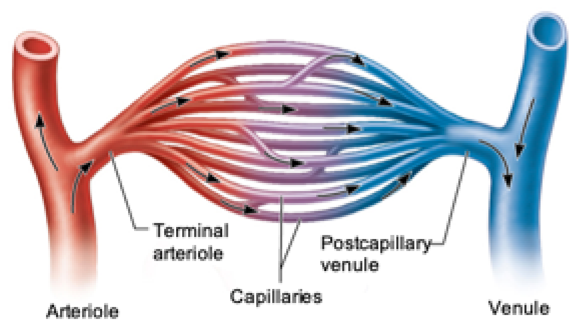
(c) Sinusoid capillary

Sinusoid capillaries are the most permeable and occur in limited locations.

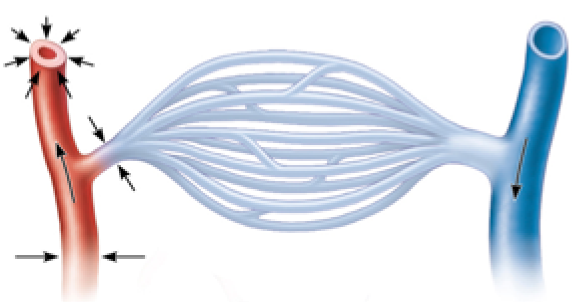
- Occur in liver, bone marrow, spleen, and adrenal medulla.
- Have large intercellular clefts as well as fenestrations; few tight junctions.
- Have incomplete basement membranes.
- Are irregularly shaped and have larger lumens than other capillaries.
- Allow large molecules and even cells to pass across their walls.
- Blood flows *slowly* through their tortuous channels.
- Macrophages may extend processes through the clefts to catch "prey" or, in liver, form part of the sinusoid wall.



- <u>Capillary beds</u>: where arterioles and venules meet



(a) Arterioles dilated—blood flows through capillaries.



(b) Arterioles constricted—no blood flows through capillaries.

- Capillaries found in serous membranes of intestinal mesenteries have 2 additional features
    - Vascular shunt: channel that directly connects arteriole with venule (bypasses true capillaries) consists of metarteriole and thoroughfare channel
    - Precapillary sphincter: cuff of smooth muscle surrounding each true capillary that branches off metarteriole; acts as valve regulating blood flow into capillary bed
        - Controlled by local chemical conditions (not innervated)

Veins

- Vein: carry blood toward the heart
    - Formation begins when capillary beds unite in postcapillary venules and merge into larger and larger veins
- Have all tunics, but thinner walls with large lumens compared to corresponding arteries
- Tunica media is thin, but tunica externa is thick
- Contain collagen fibers and elastic networks
- Larger lumen and thin walls make veins good storage vessels
- Called capacitance vessels (blood reservoirs) because they contain up to 65% of blood supply
- Venules
    - Capillaries unite to form postcapillary venules
        - Consist of endothelium and a few pericytes
        - Very porous; allow fluids and WBCs into tissues
    - Larger venules have one or two layers of smooth muscle cells formed when venules converge

Regulation of Flow Through Arteries and Veins

- Blood pressure lower than in arteries, so adaptations ensure return of blood to heart
    1. Large-diameter lumens - offer little resistance
    2. Venous valves - prevents backflow of blood, most abundant in veins of limbs
- Muscles help blood flow through veins by contraction and relaxation

Problems with Blood Vessels

- Varicose veins: dilated painful veins due to incompentent (leaky) valves
    - Factors that contribute include heredity and conditions that hinder venous return such as; prolonged standing in one position, obesity, pregnancy, blood pools in lower limbs weakening valves; affects more than 15% of adults
    - Elevated venous pressure can cause varicose veins - such as; straining to deliver a bay or have bowel movement raises in intra-abdominal pressure, resulting in varicosities in anal verins called hemorrhoids

Anastomoses

- Vascular anastomoses: interconnections of blood vessels

- Arterial anastomoses: provide alternate pathway (collateral channels) to ensure continuous flow, even if one artery is blocked
    - Common in joints, abdominal organs, brain, and heart; none in retina, kidneys, spleen
- Venous anastomoses: so abundant that occluded veins rarely block blood flow

Lecture 16: Blood Vessels Part 2

- ❑ ***4.3.5.*** *Define blood flow, blood pressure, resistance, peripheral resistance*
- ❑ ***4.3.6.*** *Illustrate the changes in blood pressure throughout the various vessels of the circulatory system*
- ❑ ***4.3.7.*** *Explain the factors that affect resistance and justify the importance of arterioles in the control of peripheral resistance*
- ❑ ***4.3.8.*** *Define systolic and diastolic arterial pressure, pulse pressure and mean arterial pressure*
- ❑ ***4.3.9.*** *Identify and justify the value for mean capillary blood pressure*
- ❑ ***4.3.10.*** *Express blood pressure in terms of cardiac output and peripheral resistance*
- ❑ ***4.3.11.*** *Describe the short-term neural and chemical mechanisms for the regulation of blood pressure*

Chapter 19 –Special attention to pg. 716-717, Figure 19.10
and pg. 719-721, also refer back to formula and description on page 715
http://www.interactive-biology.com/7073/peripheral-resistance-blood-flow/
https://www.youtube.com/watch?v=OHh9-gk3oEQ

Blood Vessel Physiology

- Blood flow: volume of blood flowing through vessel, organ, or entire circulation in a given period
- Blood pressure (BP): force per unit area exerted on the wall of blood vessel by blood
- Resistance (peripheral resistance): opposition to flow

Resistance

- We can define 3 things that impact resistance
1. Blood viscosity: higher viscosity, more resistance
2. Vessel length: longer, more resistance
3. Vessel diameter: thinner, more resistance
    a. Greatest influence in the body
    b. Small-diameter arterioles are major determinants of peripheral resistance

Quantitative Analysis of Blood Flow

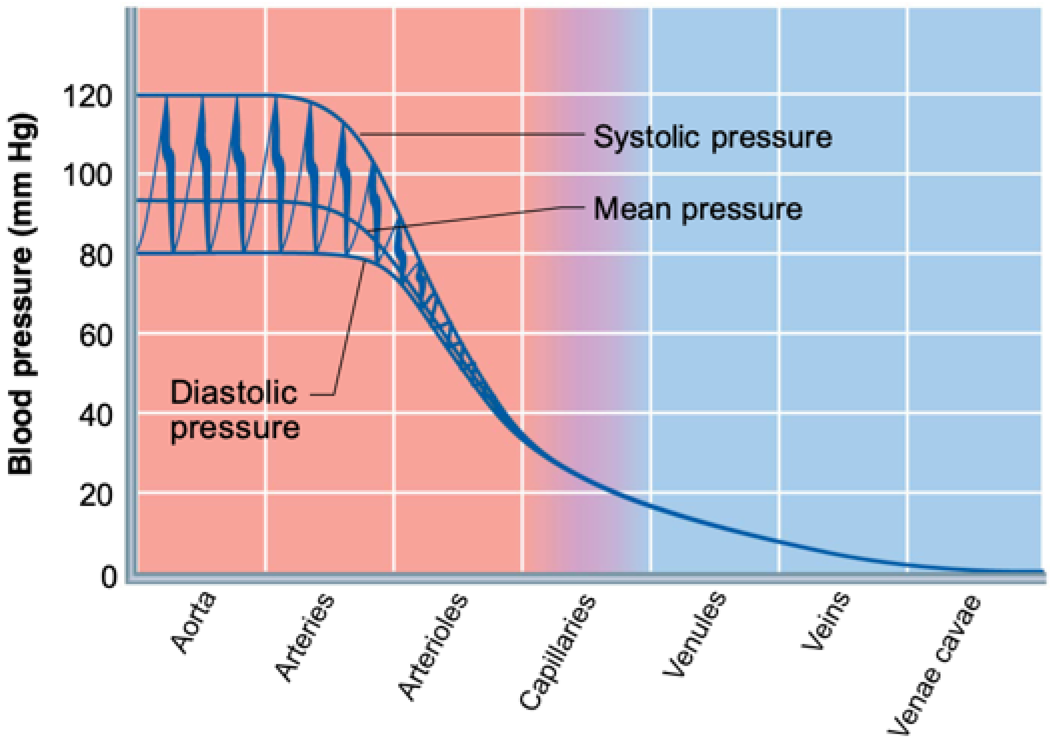
- Blood Flow (F) is directly proportional to blood pressure gradient (ΔP)
    - If ΔP increases, blood flow speeds up
- Blood flow is inversely proportional to peripheral resistance (R)

- If R increases, blood flow decreases

$$F = \Delta P / R$$

- R is more important in influencing local blood flow because it is easily changed by altering blood vessel diameter
- Pumping action of heart generate blood flow
- Pressure results when flow is opposed by resistance
- Systemic pressure is highest in aorta and declines throughout pathway
    - Steepest drop occurs in arterioles

Mean Pressure Throughout Circulatory System



Regulation of Blood Pressure in the Arteries

- Determined by 2 factors

1. Elasticity (compliance or distensibility) of arteries close to heart
2. Volume of blood forced into them at any time

- Blood pressure near heart is pulsatile
    - Rises and falls with each heartbeat
- Mean arterial pressure (MAP)
    - Pressure that propels blood tissues
        - Pulse pressure phases out near end of arterial tree
        - Flow is nonpulsatile with a steady MAP pressure
- Heart spends more time in diastole, so not just a simple average of diastole and systole
- Sample calculation for MAP
    - It is calculated by adding the pressure +⅓ pulse pressure

BP = 120/80 (systolic/diastolic)
Pulse Pressure = 120 - 80 = 40
So MAP = 80 + (⅓) x 40 = 80 + ~13 = 93 mm Hg

Measuring Blood Pressure

- <u>What is a pulse:</u> Throbbing in artery during systole as ventricular contraction forces blood into the elastic arteries and expands them.
- Measuring blood pressure: systemic arterial BP is measured indirectly by auscultatory methods using a sphygmomanometer

1. Wrap cuff around arm superior to elbow
2. Increase pressure in cuff until it exceeds systolic pressure in brachial artery
3. Pressure is released slowly and examiner listens for sounds of Korotkoff with a stethoscope

- Ideal blood pressure results
    - Systolic pressure: Normally less than 120 mm Hg
        - Pressure when sounds first occur as blood starts to spurt through artery
    - Diastolic pressure: Normally less than 80 mm Hg
        - Pressure when sounds disappear because artery no longer constricted; blood flowing freely

Regulation of Blood Pressure in the Capillaries

- Ranges from 35 mm Hg at the beginning of capillary bed to ~17 mm Hg at the end of the bed
- Low capillary pressure is desirable because:

1. High BP would rupture fragile, thin-walled capillaries
2. Most capillaries are very permeable, so low pressure forces filtrate into interstitial spaces

Regulation of Blood Pressure in the Veins

- Changes little during cardiac cycle
- Small pressure gradient, only about 15 mm Hg
    - If vein is cut, low pressure of venous system causes blood to flow out smoothly
    - If artery is cut, blood spurts out because pressure is higher
- Low pressure is due to cumulative effects of peripheral resistance
- Low pressure of venous side requires adaptations to help with venous return

Linking Blood Pressure to Cardiac Output

- 3 main factors regulating blood pressure

1. Cardiac output (CO)
2. Peripheral resistance (PR)
3. Blood volume

- Blood pressure varies directly with CO, PR, and blood volume

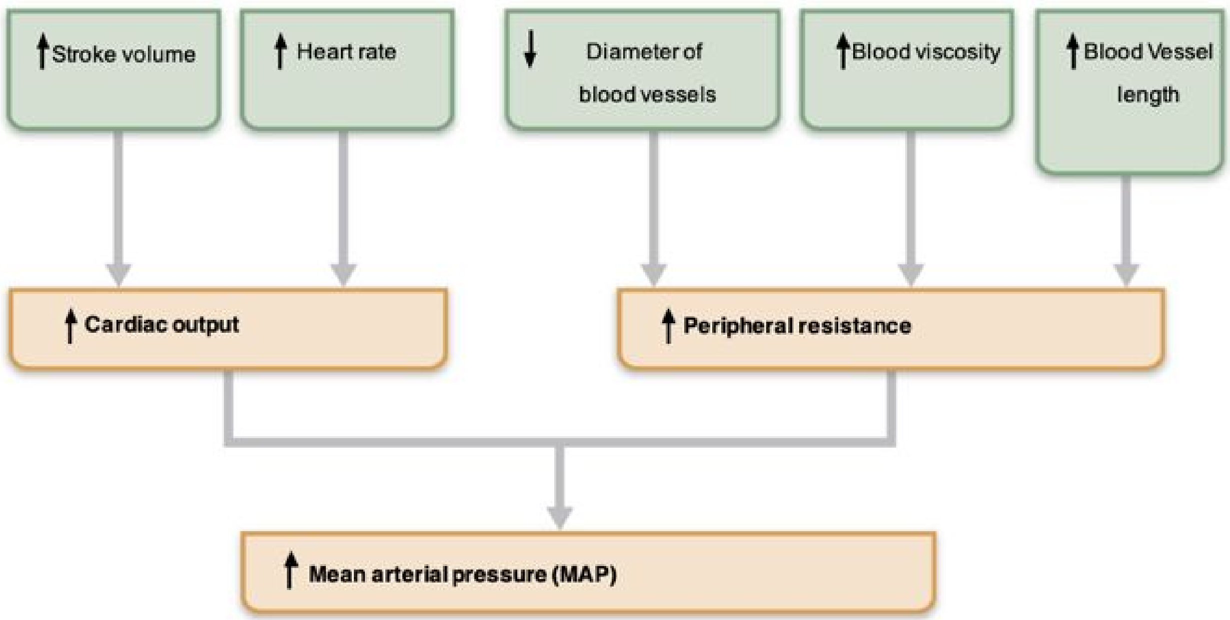
Cardiac Output = Flow

*Remember → $F = \Delta P/R$

But if CO = F then…

CO = ΔP/R which can be rearranged to → ΔP = CO x R

- This math shows that blood pressure (MAO) is directly proportional to CO and PR
    - Changes in 1 variable are quickly compensated for by changes in other variables

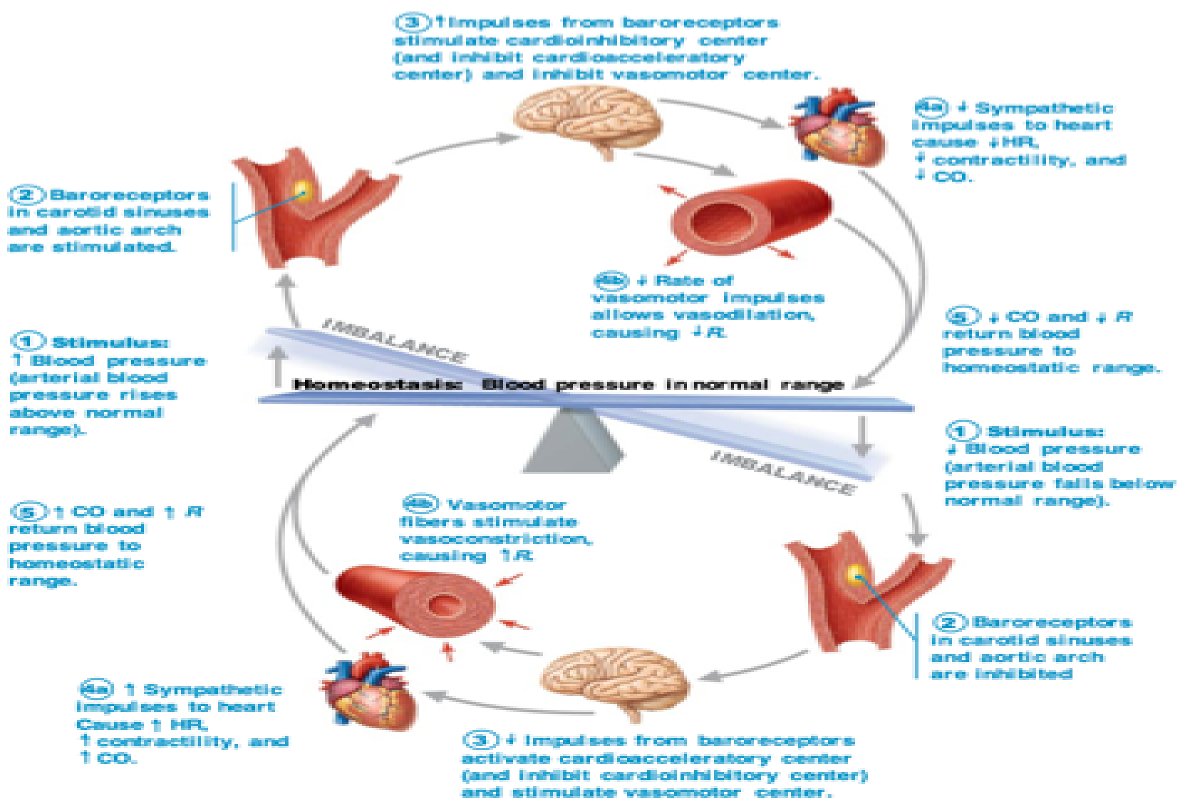


Regulation of Blood Pressure

1. <u>Short-Term Regulation: Neural Controls</u>

- Neural mechanisms can control blood pressure by regulating; Resistance & Cardiac Output
- Basic idea behind resistance; MAP is maintained by alerting blood vessel diameter, which alters resistance
    - Example: If blood volume drops, all vessels constrict (except those to heart and brain)
    - Can alter blood distribution to organs in response to specific demands
- Resistance and cardiac output regulated via some of the same/overlapping pathways
- Role of cardiovascular center in resistance
    - <u>Cardiovascular center:</u> composed of clusters of sympathetic and parasympathetic neurons in medulla and consists of:
        - <u>Cardiac centers:</u> cardioinhibitory and cardioacceleratory centers
        - <u>Vasomotor center</u>: sends steady impulses via sympathetic efferents called vasomotor fibers to blood vessels
            - Causes continuous moderate constriction called vasomotor tone
            - Vasomotor centre receives input from baroreceptors, chemoreceptors, and higher brain centers

- Special role: Baroreceptors: stretch receptors in the carotid sinuses
    - If MAP is high:
        - Increased blood pressure forces baroreceptors to give negative input to vasomotor center
        - Inhibits vasomotor and cardioacceleratory centers
        - Stimulates cardioinhibitory center
        - Results in decreased blood pressure
    - If MAP is low:
        - Reflex vasoconstriction is initiated that increases CO and blood pressure
        - Example: upon standing, BP falls and triggers:
            - Carotid sinus reflex: baroreceptors that monitor BP to ensure enough blood to brain
            - Aortic reflex (also baroreceptors) maintains BP in systemic circuit



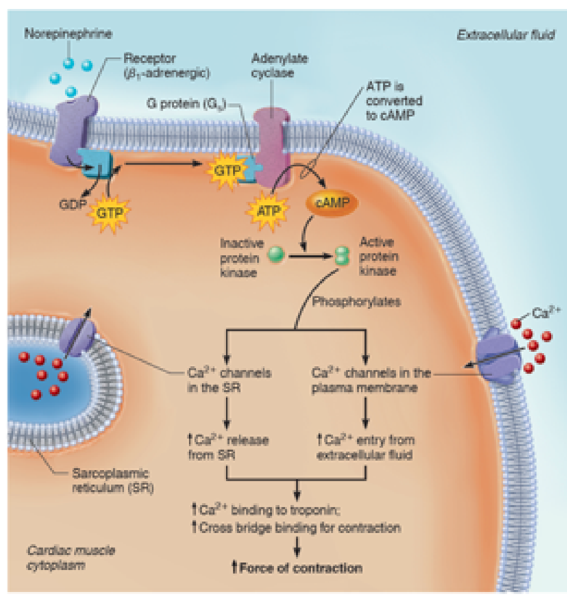
- Chemoreceptor reflexes
    - Aortic arch and large arteries of neck detect increase in CO_2, or drop in pH or O_2
    - Cause increased blood pressure by:
        - Signaling cardioacceleratory center to increase CO
        - Signaling vasomotor center to increase vasoconstriction
        - Point is to get blood to the lungs
- Higher brain centers

    - Control via hypothalamus and cerebral cortex - integrated by the medulla oblongata
    - EX: fight or flight response can increase blood pressure
- Neural control - Higher brain centres
    - Hypothalamus mediates redistribution of blood flow during exercise and changes in body temperature
    - Hypothalamus increases blood pressure during stress
    - Reflexes that regulate BP are found in medulla
    - Hypothalamus and cerebral cortex can modify arterial pressure via relays to medulla

2. <u>Short-Term Regulation: Hormonal Controls</u>

- What is a hormone: A regulatory substance produced in an organism and transported in tissue fluids such as blood or sap to stimulate specific cells or tissues into action.
    - EX: Lipid, amino acid, peptide hormones
    - Hormones regulate BP in short term via changes in peripheral resistance or long term via changes in blood volume
- <u>Adrenal medulla hormones (released during stress)</u> **-** Epinephrine and norepinephrine from adrenal gland increase CO and vasoconstriction – increases blood pressure (increased blood to lungs)
- <u>ADH (anti-diruretic hormone; hypothalamus)</u> -not usually a short term hormone but high levels can cause vasoconstriction
- <u>Atrial natriuretic peptide (ANP)</u> decreases BP by antagonizing aldosterone, causing decreased blood volume (long term) but also generalized vasodilation (short term)
- <u>Angiotensin II</u> stimulates vasoconstriction in short term (but perhaps better characterized as part of long-term system)
- Regulation of stroke volume by contractility:

(Nor)Epinephrine Increases Heart Contractility Via a Cyclic AMP Second Messenger System



- Short term effects: effects will be on the arterioles and the heart

- Long term effects: effects on the kidney to control blood volume

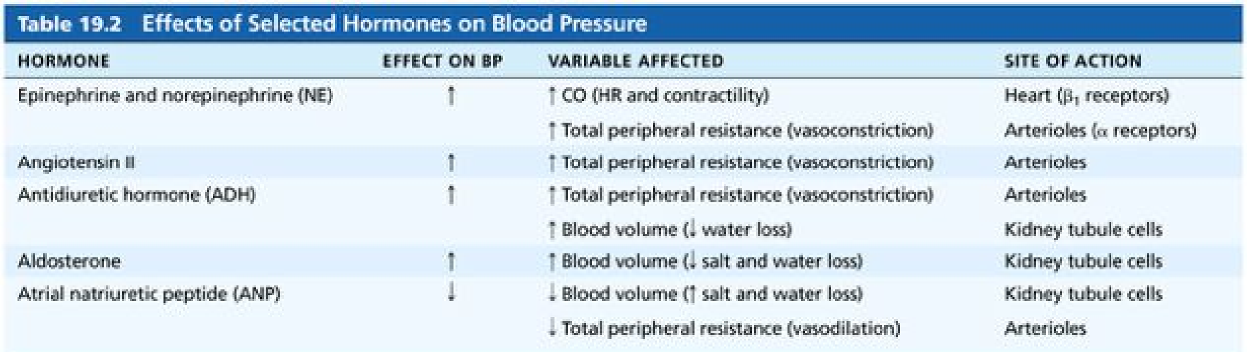


Table 19.2 Effects of Selected Hormones on Blood Pressure

HORMONE	EFFECT ON BP	VARIABLE AFFECTED	SITE OF ACTION
Epinephrine and norepinephrine (NE)	↑	↑ CO (HR and contractility)	Heart (β_1 receptors)
		↑ Total peripheral resistance (vasoconstriction)	Arterioles (α receptors)
Angiotensin II	↑	↑ Total peripheral resistance (vasoconstriction)	Arterioles
Antidiuretic hormone (ADH)	↑	↑ Total peripheral resistance (vasoconstriction)	Arterioles
		↑ Blood volume (↓ water loss)	Kidney tubule cells
Aldosterone	↑	↑ Blood volume (↓ salt and water loss)	Kidney tubule cells
Atrial natriuretic peptide (ANP)	↓	↓ Blood volume (↑ salt and water loss)	Kidney tubule cells
		↓ Total peripheral resistance (vasodilation)	Arterioles

Lecture 17: Blood Vessels Part 3

- ❑ *4.3.12. Describe the role of the kidneys in the long-term regulation of blood pressure*
- ❑ *4.3.13. Define and explain the mechanisms of autoregulation with regard to local blood flow*
- ❑ *4.3.14. Explain the forces that act to influence capillary exchange*
- ❑ *4.3.15. Identify the principal arteries and veins of the cardiovascular system: You will be responsible for arteries and vein up to the level of the wrist and ankle, to each organ and to the brain (to and including the circle of Willis).*

Chapter 19 - Focus; pg. 721, 725-727, 730-733

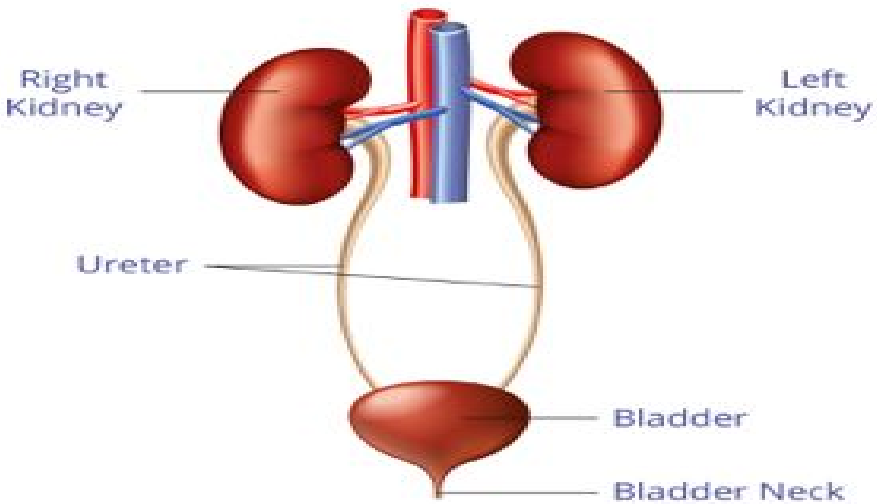
https://www.youtube.com/watch?v=bQX3uDfigpo

https://www.youtube.com/watch?v=-qY17G_n-WA

Regulation of Blood Pressure (Continued)

3. Long-Term Regulation: Hormonal & Renal Controls

- Baroreceptors quickly adapt to chronic high or low BP so are ineffective for long-term regulation
- Long-term mechanisms control BP by altering blood volume via kidneys
- Kidneys regulate arterial blood pressure by:
  - Direct renal mechanism
  - Indirect renal mechanism (renin-angiotensin-aldosterone)
- Direct Regulation; Direct Renal Mechanism
  - Alters blood volume independently of hormones
    - Increased BP or blood volume causes elimination of more urine, thus reducing BP
    - Decreased BP or blood volume causes kidneys to conserve water, and BP rises

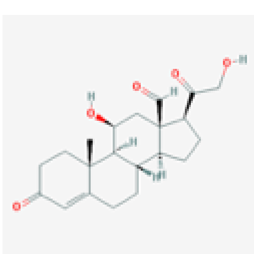


- Indirect Regulation; The Renin-angiotensin-aldosterone mechanism
  - Decreased arterial blood pressure causes release of renin from kidneys (adrenal gland)
  - Renin enters blood and catalyzes conversion of angiotensinogen from liver to angiotensin I
  - Angiotensin-converting enzyme, especially from lungs, converts angiotensin I to angiotensin II

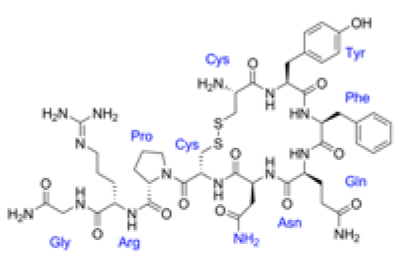
Decreased BP → Renin ↘

Angiotensinogen → Angiotensin I —ACE→ **Angiotensin II**

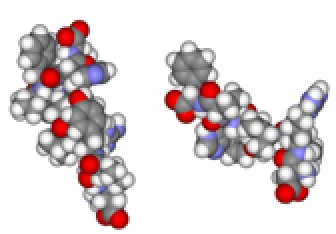
- Angiotensin II acts in four ways to stabilize blood pressure:
  - Stimulates **aldosterone** secretion - salt and water retention
  - Causes ADH release from posterior pituitary
  - Triggers hypothalamic thirst center to drink more water
  - Acts as a potent vasoconstrictor, directly increasing blood pressure



Aldosterone

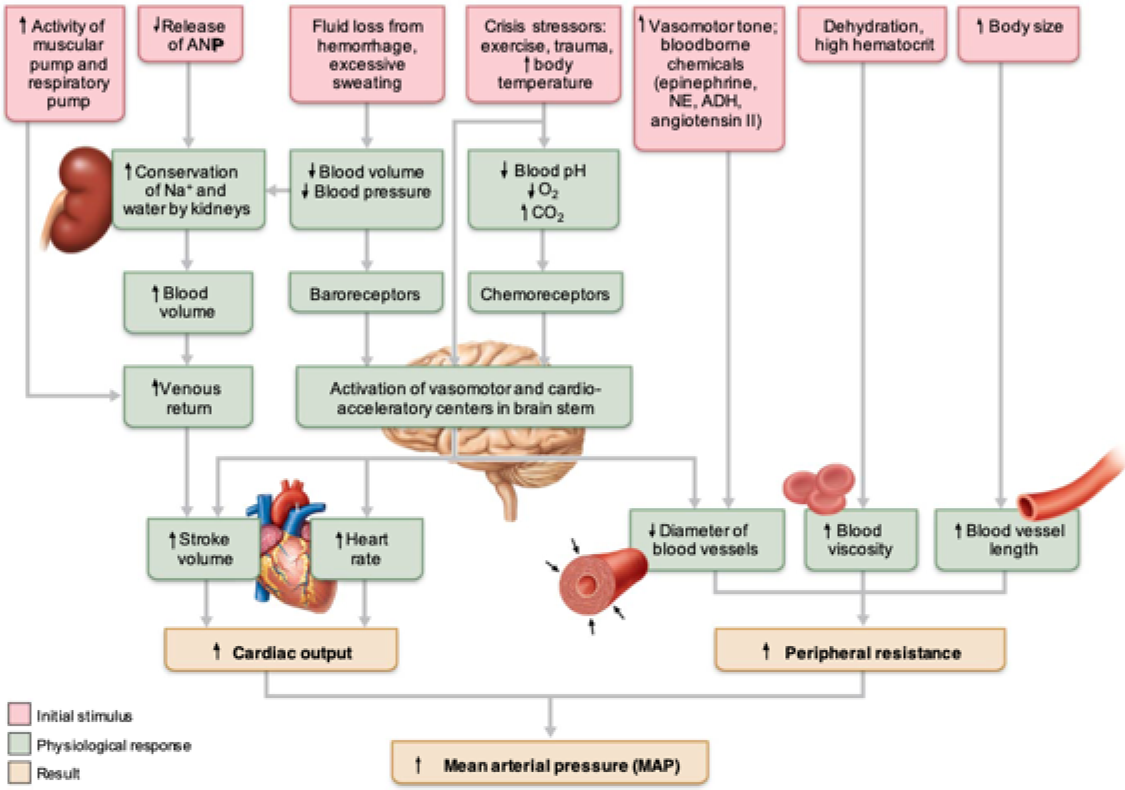


ADH



Angiotensin

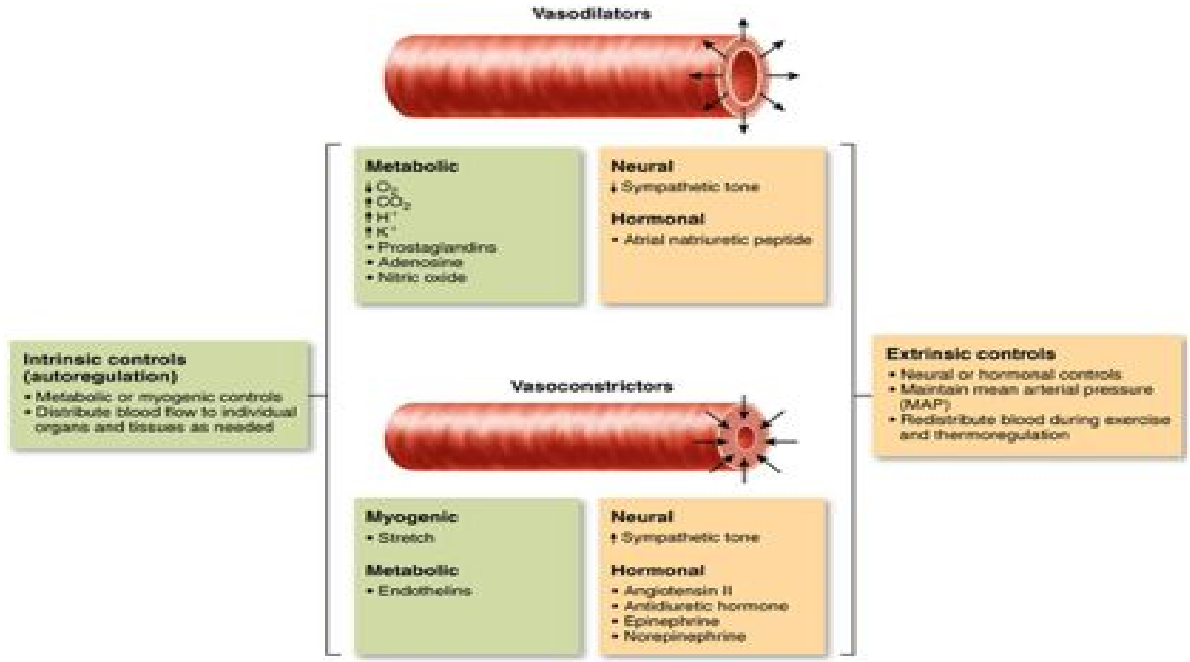
Factors That Increase MAP



- Loss of homeostasis
    - Hypertension
        - Sustained elevated arterial pressure of 140/90 mm Hg or higher
        - Prehypertension if values elevated but not yet in hypertension range
            - May be transient adaptations during fever, physical exertion, and emotional upset
            - Often persistent in obese people
        - Prolonged hypertension is major cause of heart failure, vascular disease, renal failure, and stroke
            - Heart must work harder; myocardium enlarges, weakens, and becomes flabby
            - Also accelerates atherosclerosis
    - Hypotension
        - Low blood pressure below 90/60 mm Hg
        - Usually not a concern unless it causes inadequate blood flow to tissues
        - Often associated with long life and lack of cardiovascular illness
- Controlling flow at the level of individual tissues
    - <u>Tissue perfusion:</u> blood flow through body tissues; involved in:

1. Delivery of O_2 and nutrients to, and removal of wastes from, tissue cells
2. Gas exchange (lungs)

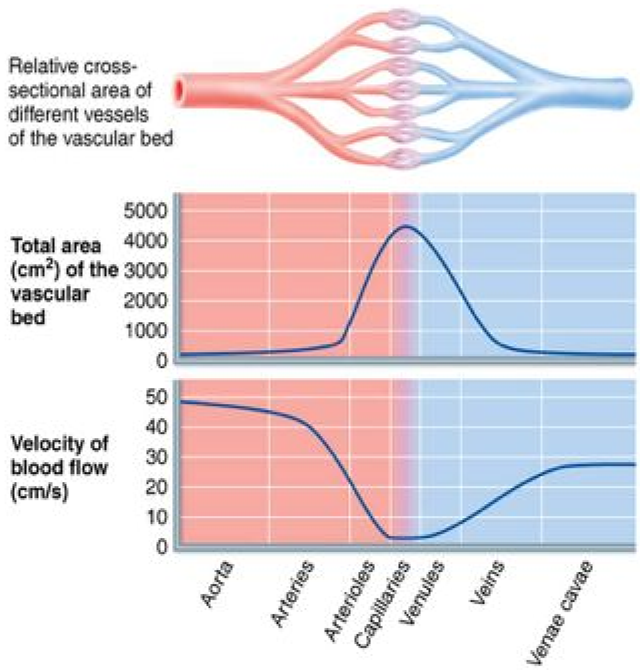
3. Absorption of nutrients (digestive tract)
4. Urine formation (kidneys)
    - Rate of flow is precisely regulated to provide proper function to a given tissue or organ
    - How do we control tissue profusion
        - Extrinsic: whole body
        - Intrinsic: local
- There are 2 types of intrinsic mechanisms both determine final autoregulatory response
    - Metabolic controls
        - Increase in tissue metabolic activities results in:
            - Declining levels of O_2
            - Increasing levels of metabolic products (H^+, K^+, adenosine, and prostaglandins)
            - Cause direct relaxation of arterioles and relaxation of precapillary sphincters
            - Cause release of nitric oxide (NO), a powerful vasodilator, by endothelial cells
        - Balanced by constricting chemicals:
            - Endothelins, also released from endothelium, are potent vasoconstrictors
            - NO and endothelins are usually balanced unless blood flow is inadequate, in which case NO wins control, causing vasodilation
- Myogenic controls
    - Take home message: local vascular smooth muscle responds to changes in MAP to keep perfusion constant to avoid damage to tissue
        - Increased stretch: increased MAP stretches vessel wall more than normal
            - Response: Smooth muscle responds by constricting, causing decreased blood flow to tissue
        - Reduced stretch: decreased MAP causes less stretch than normal
            - Response: Smooth muscle responds by dilating, causing increased blood flow to tissue



- Extrinsic and intrinsic can compete with eachother;
  - Blood flow varies with fiber type and activity
  - At rest, myogenic and neural mechanisms predominate; maintain flow at ~1L /min
  - Active or exercise hyperemia: during muscle activity, blood flow increases in direct proportion to metabolic activity
    - Local controls override sympathetic vasoconstriction; flow can increase 10×
    -

Introduction to Capillary Exchange

- Velocity of flow fastest in aorta, slowest in capillaries, then increases again in veins
- Speed is inversely related to total cross-sectional area
  - Capillaries have largest area so slowest flow
  - Slow capillary flow allows adequate time for exchange between blood and tissues



- Transport of gasses and solutes from blood to interstitial fluid
    1. Diffuse directly through endothelial membranes

       Example: lipid-soluble molecules such as respiratory gases

    2. Pass through clefts

       Example: water-soluble solutes

    3. Pass through fenestrations

       Example: water-soluble solutes

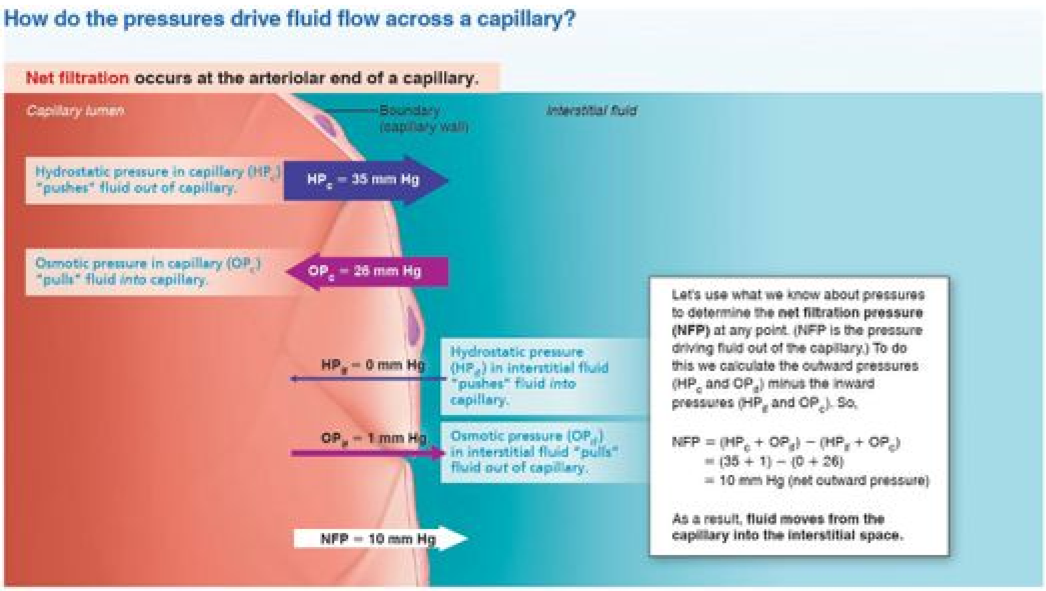
    4. Active transport via pinocytotic vesicles

       Example: larger molecules such as proteins

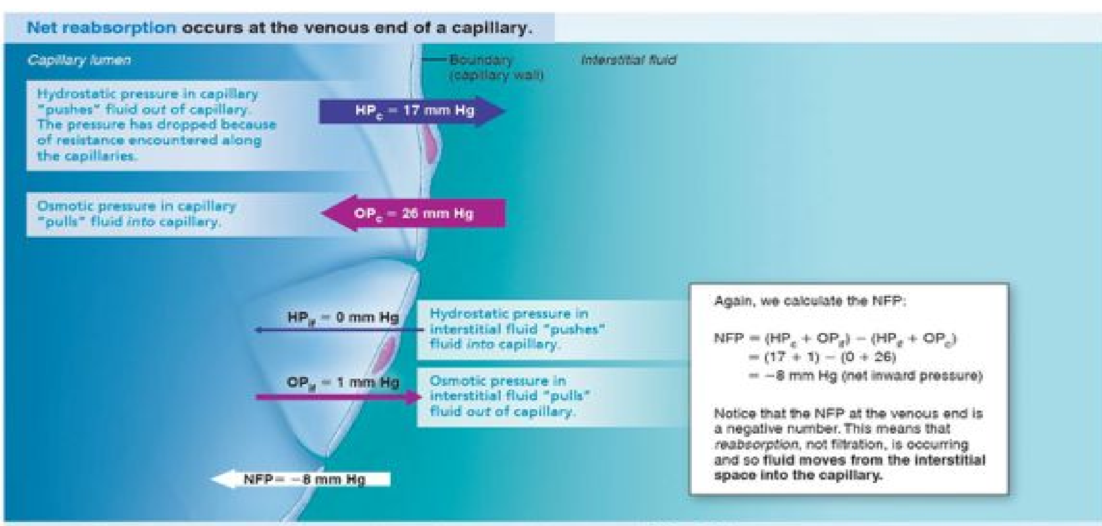
- Bulk fluid flow
    - **Fluid** is forced out clefts of capillaries at arterial end, and most returns to blood at venous end
        - Extremely important in determining relative fluid volumes in blood and interstitial space
    - Bulk fluid flow across capillary walls causes continuous mixing of fluid between plasma and interstitial fluid; maintains interstitial environment.
    - Direction and amount of fluid flow depend on two opposing forces
        - Hydrostatic pressures - force on vessel wall (see notes) (called HP)

- Colloid osmotic pressures – sucking pressure generated by non-diffusable proteins in vessels (called OP)
- Net filtration pressure
  - comprises all forces acting on capillary bed
    - $NFP = (HP_c + OP_{if}) - (HP_{if} + OP_c)$
  - Net fluid flow out at arterial end (*filtration*)
  - Net fluid flow in at venous end (*reabsorption*)
  - More fluid leaves at arterial end than is returned at venous end
  - Where: IF= Interstitial fluid (outside capillaries), C= capillaries

- Arteriole End; In



- Venous End; Out



When bulk flow goes wrong, *edema* can result (see Homeostatic Imbalance 19.2, p. 734).

Major Arteries: (Pages 739-758 in textbook)

- Common Hepatic artery
- Circle of Willis
- Descending aorta
- Radial Artery
- Ulnar Artery
- Internal Thoracic artery
- Radial
- Ulnar
- Femoral Artery
- Iliac artery (common and internal)
- Ascending aorta
- Renal Artery
- Subclavian Artery
- Brachial Artery
- Mesenteric artery
- Fibular vein
- Dural venous sinuses
- Hepatic veins
- Renal vein
- Femoral vein
- Superior vena cava
- Inferior vena cava
- Internal jugular vein
- Exterior jugular vein

Lecture 18: Lymphatic

- ❑ *5.1. Describe the structure and main functions of the vessels and organs of the lymphatic system*
- ❑ *5.2. Explain the origin of lymph as well as its transport*

Chapter 20, Figure 20.3, Table 20.1 NOT chapter 21

https://www.youtube.com/watch?v=I7orwMgTQ5I

Lymphatic Basics

- Lymphatic system returns fluids leaked from blood vessels back to blood; consists of three parts
- Network of lymphatic vessels (lymphatics)
- *Lymph*: fluid in vessels
- *Lymph nodes*: cleanse lymph
- Lymphoid organs and tissues provide structural basis of immune system by housing phagocytic cells and lymphocytes
  - Structures include spleen, thymus, tonsils, lymph nodes, other lymphoid tissues

-

Function of the Lymphatic System

- Lymphatic system returns interstitial fluid and leaked plasma proteins back to blood via:
    - Lymphatic vessels (lymphatics): elaborate network of drainage vessels
    - Circulates ~ 3L interstitial fluid per day
    - Once interstitial fluid enters lymphatics, it is called lymph

Specialized Capillaries

- Lymphatic vessels offer a one-way system, ensuring lymph flows only toward heart
- Lymph vessels (lymphatics) include lymphatic capillaries and larger lymphatic vessels
- Lymphatic capillaries
    - Blind-ended vessels that weave between tissue cells and blood capillaries
    - Absent from bone and teeth
- Similar to blood capillaries, but more permeable
- Can take up larger molecules and particles that blood capillaries cannot
    - Example: proteins, cell debris, pathogens, and cancer cells
    - Can act as route for pathogens or cancer cells to travel throughout body
- Increased permeability due to two specialized structures

1. Endothelial cells overlap loosely to form one-way *minivalves*
2. Minivalves are anchored by collagen filaments to matrix, so increases in ECF volume opens minivalves even more
    - Decreases in ECF cause minivalves to close

Broader Lymphatic System

- Larger lymphatic vessels
- Lymph capillaries drain into increasingly larger vessels called collecting lymphatic vessels
- Consist of collecting vessels, trunks, and ducts
- Have structures and tunics similar to veins, except
    - Have thinner walls, with more internal valves
    - Anastomose more frequently
- <u>Right lymphatic</u> duct drains right upper arm and right side of head and thorax
- <u>Thoracic duct</u> drains rest of body
    - In about half of individuals, starts out as an enlarged sac, cisterna chyli
- **Lymph system is a low-pressure system like venous system**
- Lymph is propelled by same mechanisms:
    - Milking action of skeletal muscle
    - Pressure changes in thorax during breathing
    - Valves to prevent backflow
    - Pulsations of nearby arteries
    - Contractions of smooth muscle in walls of lymphatics

- Physical activity increases flow of lymph; immobilization of area keeps needed inflammatory material in area for faster healing

Link to Homeostasis

- *Lymphangitis*: condition in which lymphatic vessels appear as painful red lines under the skin
    - Caused by inflammation of larger lymphatic vessels that contain vaso vasora
        - Vaso vasora become congested with blood. Larger lymphatics, like blood vessels, receive their nutrients from branching vasa vasorum
- *Lymphedema*: severe localized edema
- Caused by anything that prevents normal return of lymph to blood
    - Examples: tumors blocking lymphatics or removal of lymphatics during cancer surgery
    - Lymphedema may improve if some lymphatic pathways remain and enlarge
- *Buboes*: inflamed, swollen, tender lymph nodes that result when nodes are overwhelmed by what they are trying to destroy
    - Condition often referred to as swollen "glands"
    - Buboes are sometimes pus-filled
    - *Bubonic plague* was named after chief clinical feature of this disease

Lymphatic System is an Immune Organ

- Lymphoid cells consist of (1) immune system cells found in lymphoid tissue and (2) supporting cells that form lymphoid tissue structures
    - Immune system cells
        - Lymphocytes:
            - T cells (T lymphocytes)
            - B cells (B lymphocytes)
    - Macrophages and dendritic cells (partners of lymphocytes)
    - Reticular cells produce reticular fibers called stroma in lymphoid organs
        - Stroma: network-like support that acts as scaffolding for immune cells

Focus on Immune Cells

- B and T cells
    - T cells and B cells protect against antigens (anything the body perceives as foreign)
        - Examples: bacteria, toxins, viruses, defective RBCs, cancer cells
    - T cells: manage immune response, and some also attack and destroy infected cells
    - B cells: produce plasma cells, which secrete antibodies
        - Antibodies mark antigens for destruction by phagocytosis or other means
    - Macrophages phagocytize foreign substances and help activate T cells

- ○ Dendritic cells capture antigens and deliver them to lymph nodes; also help activate T cells

What Does Lymphoid Tissue Do?

- Main functions of lymphoid tissue
    - Houses and provides proliferation sites for lymphocytes
    - Offers surveillance vantage points for lymphocytes and macrophages
    - Largely composed of reticular connective tissue, a type of loose connective tissue
    - Macrophages live on reticular fibers
    - Spaces between fibers offer a place for lymphocytes to occupy when they return from patrolling body
- 2 main types of lymphoid tissues
    - Diffuse lymphoid tissue: loose arrangement of lymphoid cells and some reticular fibers
    - Follicles: solid, spherical bodies consisting of tightly packed lymphoid cells and reticular fibers
- Lymphoid organs are grouped into 2 functional categories
    - Primary lymphoid organs: areas where T and B cells mature—*red bone marrow* and *thymus*
    - Secondary lymphoid organs: areas where mature lymphocytes first encounter their antigen and become activated

Lymph Nodes

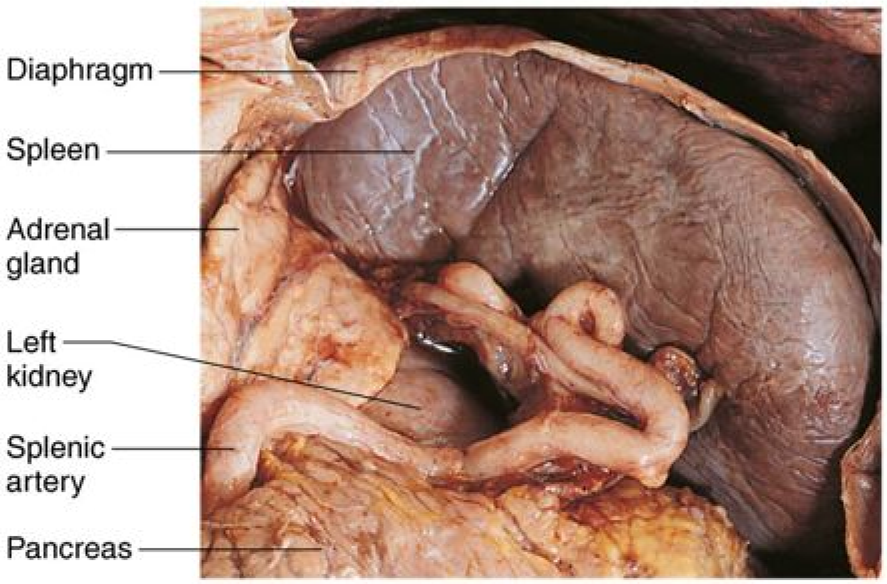
- 2 main functions

1. Cleansing the lymph: act as lymph "filters"
    a. Macrophages remove and destroy microorganisms and debris that enter lymph
    b. Prevent unwanted substances from being delivered to blood
2. Immune system activation: offer a place for lymphocytes to become activated and mount an attack against antigens

- ● Lymph nodes: principal secondary lymphoid organs of body
- ● Hundreds of nodes are found throughout body
    a. Most are embedded deep in connective tissue in clusters along lymphatic vessels
    b. Some are nearer to body surface in inguinal, axillary, and cervical regions of body where collecting vessels converge into trunks
- Structure
- ● Cortex
- ● B cells at centre
- ● Transient stop for T cells
- ● Medulla – B/Plasma cells and T cells
- ● Sinuses - macrophages

Spleen

- Spleen is blood-rich organ about size of fist, located in left side of abdominal cavity, just below stomach
- Served by *splenic artery* and *vein*
- Functions:
  - Site of lymphocyte proliferation and immune surveillance and response
  - Cleanses blood of aged blood cells and platelets; macrophages remove debris



(c) Photograph of the spleen in its normal position in the abdominal cavity, anterior view.

- Three additional functions of spleen:

1. Stores breakdown products of RBCs (e.g., iron) for later reuse
2. Stores blood platelets and monocytes for release into blood when needed
3. May be site of fetal erythrocyte production

- Spleen Anatomy
  - White pulp: site where immune function occurs
    - Contains mostly lymphocytes on reticular fibers
  - Red pulp: site where old blood cells and bloodborne pathogens are destroyed
    - Rich in RBCs and macrophages that engulf them
- The spleen has a thin capsule, so direct blow or severe infection may cause it to rupture, spilling blood into peritoneal cavity
- *Splenectomy*: surgical removal of ruptured spleen
  - You can live without a spleen
  - Once standard treatment to prevent hemorrhage and shock, but has been discovered spleen can often repair itself
    - Frequency of emergency splenectomies has decreased dramatically

- Mucosa-associated lymphoid tissue (MALT)
    - Lymphoid tissues in mucous membranes throughout body
- Protects from pathogens trying to enter body
- Found in mucosa of respiratory tract, genitourinary organs, and digestive tract; largest collections of MALT found in
    - Tonsils
    - Peyer's patches
    - Appendix
- Simplest lymphoid organs
- Form ring of lymphatic tissue around pharynx; appear as swellings of mucosa
- Named according to location
    - Palatine tonsils: at posterior end of oral cavity
    - Lingual tonsil: lumpy collection of follicles at base of tongue
    - Pharyngeal tonsil: also called *adenoids*; located in posterior wall of nasopharynx
    - Tubal tonsils: surround openings of auditory tubes into pharynx
- Peyer's patches: clusters of lymphoid follicles in wall of distal portion of small intestine
    - Structurally similar to tonsils
    - Location aids in functions
        1. Destroy bacteria, preventing them from breaching intestinal wall
        2. Generate "memory" lymphocytes
- Appendix: offshoot of first part of large intestine
    - Contains a large number of lymphoid follicles
    - Location aids in functions (like Peyer's patches)
        1. Destroy bacteria, preventing them from breaching intestinal wall
        2. Generate "memory" lymphocytes
- Thymus
    - Thymus: bilobed lymphoid organ found in inferior neck
    - Functions as lymphoid organ where T cells mature

Lecture 19: Respiration Part 1

- ❑ ***6.1.*** *Describe the structures of each one of the components of the conduction and respiratory zones*
- ❑ ***6.2.*** *Describe the gross structure of the lungs & the pleural coverings*
- ❑ ***6.3.*** *Define & explain the following: intrapulmonary, intrapleural & transpleural pressures*

Chapter 22 - Focus on Pg. 828-835, Figures; 22.2, 22.9, 22.14, 22.15, Table 22.2

https://www.youtube.com/watch?v=bHZsvBdUC2I

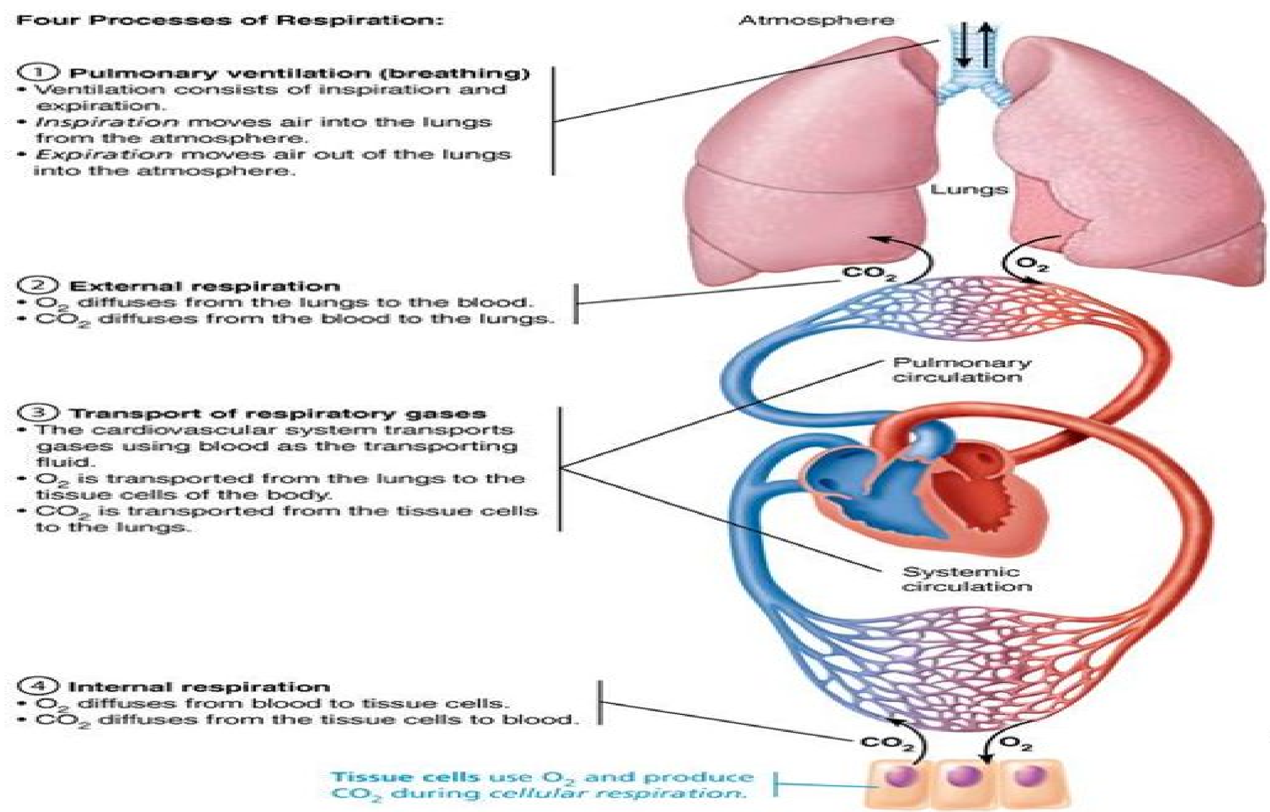
Major Functions of the Respiratory System

1. Supply body with O_2 for *cellular respiration* and dispose ofCO_2, a waste product of *cellular respiration*
    a. Respiratory and circulatory system are closely coupled

2. Also functions in olfaction and speech

The 4 Processes of Respiration

- Respiratory system
  - 1. Pulmonary ventilation (breathing): movement of air into and out of lungs
  - 2. External respiration: exchange of O_2 and CO_2 between lungs and blood
- Circulatory system
  - 3. Transport of O_2 and CO_2in blood
  - 4. Internal respiration: exchange of O_2 and CO_2between systemic blood vessels and tissues

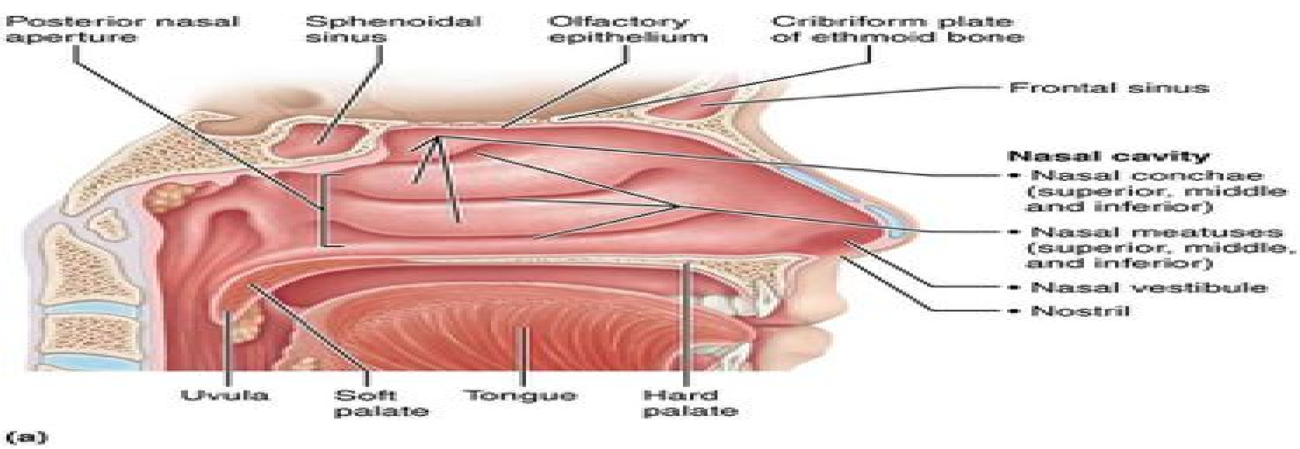


Upper Respiratory System

- The Nose and Paranasal Sinuses
  - Nose is only external portion of respiratory system
  - Functions of nose
  1. Provides an airway for respiration
  2. Moistens and warms entering air
  3. Filters and cleans inspired air
  4. Serves as resonating chamber for speech

5. Houses olfactory receptors

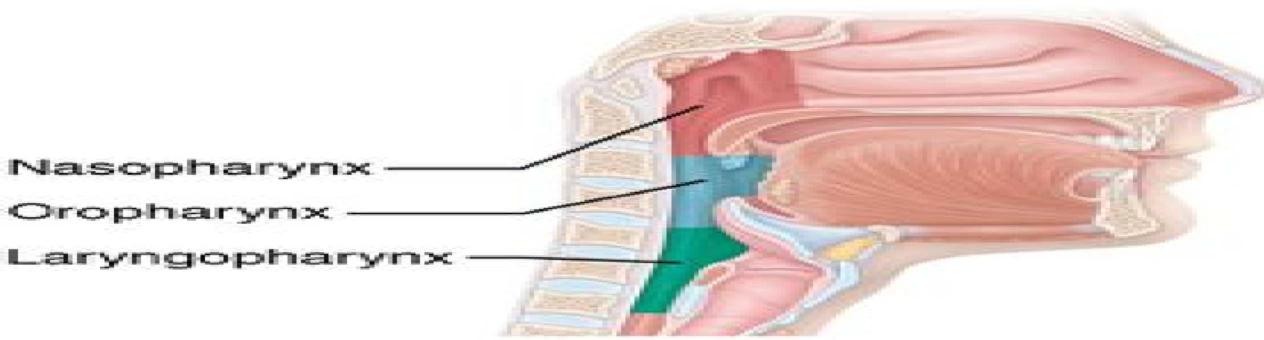
- Divided into two regions: external nose and nasal cavity
    - Mucus and serous secretions also contain lysozyme and defensins
    - Ciliated cells sweep contaminated mucus posteriorly towards throat
    - Inspired air is warmed by plexuses of capillaries and veins in nasal cavity
    - Nasal mucosa contains many sensory nerve endings that can cause sneezing to force particles out of cavity
- Four Functions of the Conchae
    1. Increase mucosal area
    2. Enhance air turbulence
    3. During inhalation, conchae and nasal mucosa:
        a. Filter, heat, and moisten air
    4. During exhalation these structures:
        a. Reclaim heat and moisture
- Paranasal Sinuses
    - Form ring around nasal cavities
    - Located in frontal, sphenoid, ethmoid, and maxillary bones
    - Functions
        - Lighten skull
        - Secrete mucus
        - Help to warm and moisten air



- Link to Homeostasis
    - *Rhinitis:*
        - Inflammation of nasal mucosa
        - Nasal mucosa is continuous with mucosa of respiratory tract, so infections spread from nose to throat to chest
        - Can also spread to tear ducts and paranasal sinuses, causing blockage of sinus passageways, resulting in sinusitis (inflamed sinuses)
            - Can lead to absorption of air resulting in sinus headache
- Pharynx

- Funnel-shaped muscular tube that runs from base of skull to vertebra C_6
    - Connects nasal cavity and mouth to larynx and esophagus
    - Composed of skeletal muscle
- Three regions;

1. Nasopharynx
2. Oropharynx
3. Laryngopharynx



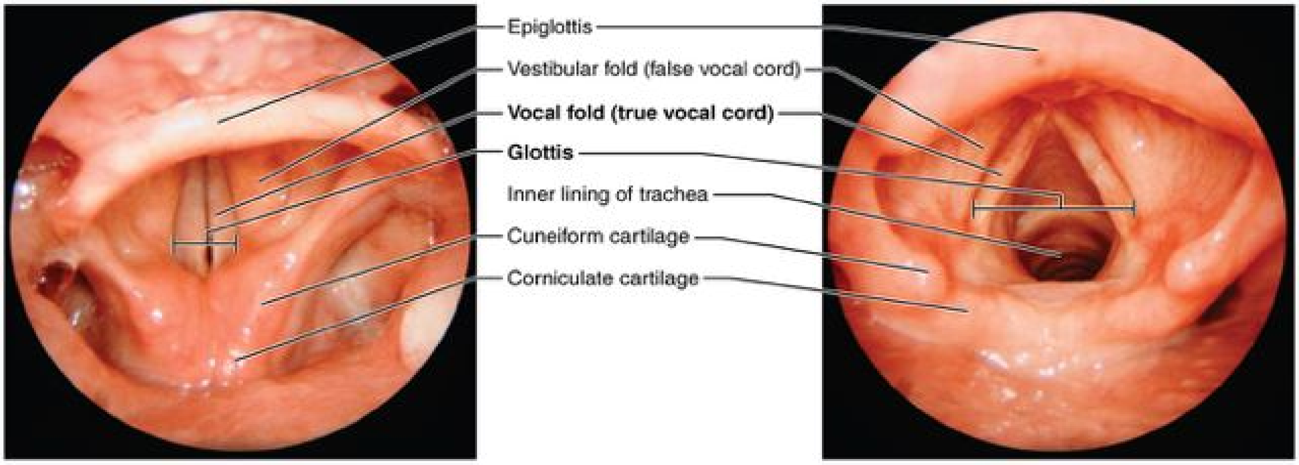
(a) Regions of the pharynx

- Nasopharynx
    - Air passageway posterior to nasal cavity
    - Lining contains ciliated pseudostratified columnar epithelium
    - Soft palate and uvula close nasopharynx during swallowing
- Oropharynx
    - Passageway for food and air from level of soft palate to epiglottis
    - Lining consists of stratified squamous epithelium (protective)
- Laryngopharnyx
    - Passageway for food and air
    - Posterior to upright epiglottis
    - Extends to larynx, where it is continuous with esophagus
    - Lined with stratified squamous epithelium (protective)

Lower Respiratory System (Conducting and Respiratory)

- Larnyx
    - Larynx (voice box) extends from 3rd to 6th cervical vertebra and attaches to hyoid bone
- Opens into laryngopharynx and is continuous with trachea
- Three functions of larynx:
    1. Provides *patent (OPEN)* airway
    2. Routes air and food into proper channels
    3. Voice production

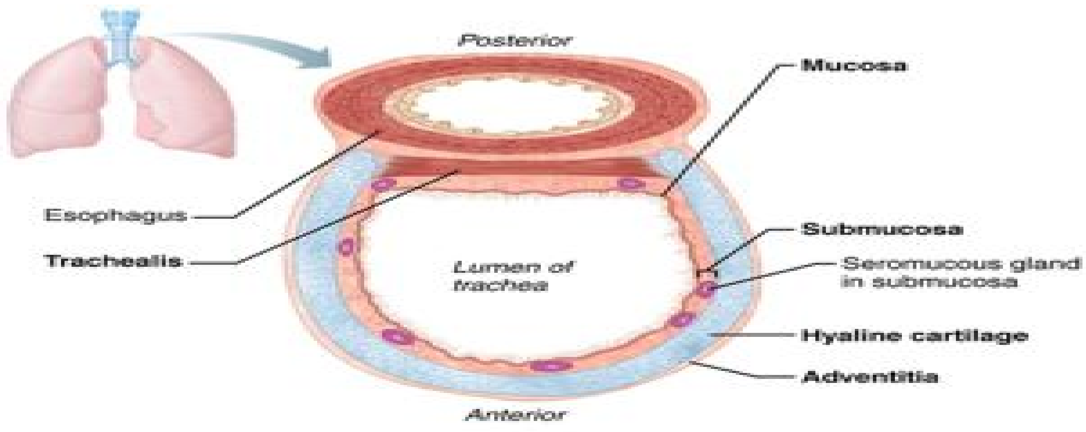
- Houses vocal folds



(a) Vocal folds in closed position; closed glottis

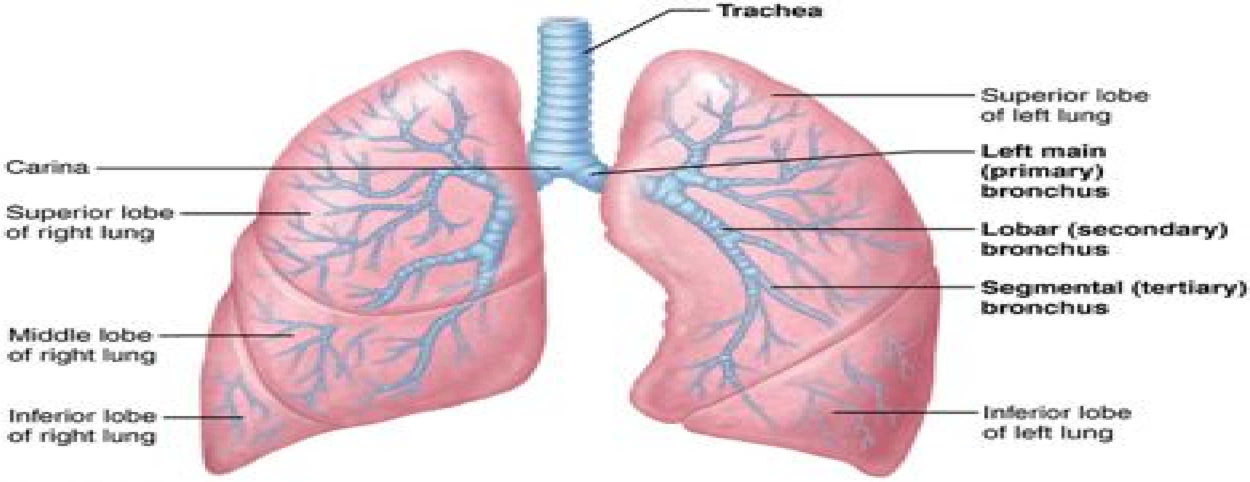
(b) Vocal folds in open position; open glottis

- Link to Homeostasis - Larynx
    - Laryngitis: inflammation of the vocal folds that causes the vocal folds to swell, interfering with vibrations
        - Results in changes to vocal tone, causing hoarseness; in severe cases, speaking is limited to a whisper
        - Laryngitis is most often caused by viral infections but may also be due to overuse of the voice, very dry air, bacterial infections, tumors on the vocal folds, or inhalation of irritating chemicals
- The Trachea
    - “windpipe” extends from larynx into mediastinum, where it divides into two main bronchi
    - It is about 4 inches long, 3/4 inch in diameter, and very flexible
- Structure of the Trachea
    - Mucosa: ciliated pseudostratified epithelium with goblet cells
    - Submucosa: connective tissue with seromucous glands supported by 16–20 C-shaped cartilage rings that prevent collapse of trachea
    - Adventitia: outermost layer made of connective tissue



(a) Cross section of the trachea and esophagus

- Bronchi
  - Trachea divides to form **right and left main** (**primary**) **bronchi**
  - Each main bronchus then branches into **lobar** (**secondary**) **bronchi**
    - Three on right and two on left
    - Each lobar bronchus supplies one lobe

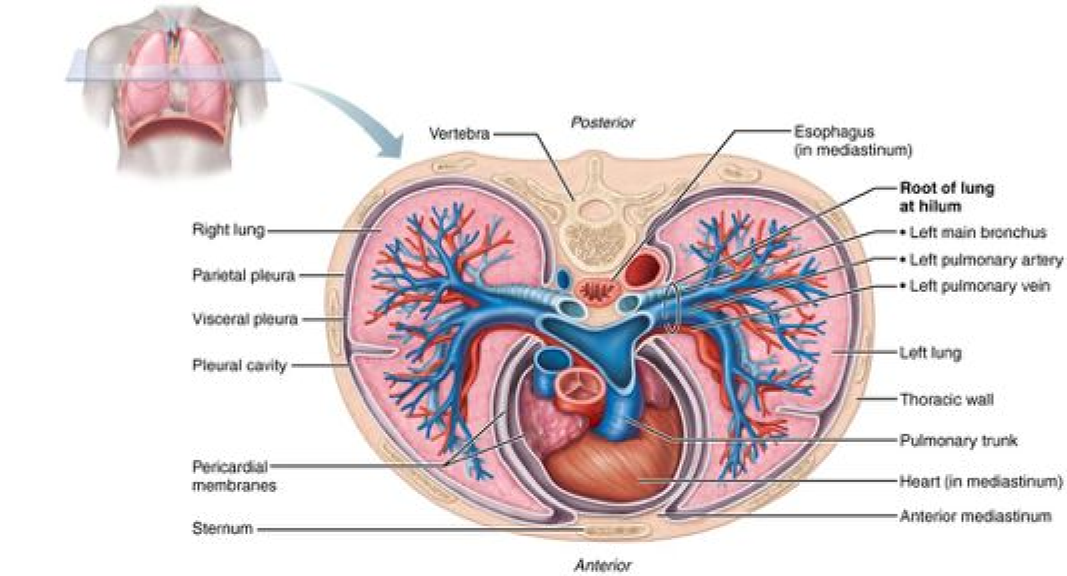


- Each lobar bronchus branches into segmental (tertiary) bronchi
  - Segmental bronchi divide repeatedly
- Branches become smaller and smaller
  - Bronchioles: less than 1 mm in diameter
  - Terminal bronchioles: smallest of all branches
    - Less than 0.5 mm in diameter
- Changes in Structure from Bronchi to Bronchioles
  - Support structures change
    - Cartilage rings become irregular plates

        - In bronchioles, elastic fibers replace cartilage altogether

- Epithelium type changes
    - Pseudostratified columnar gives way to cuboidal
    - Cilia and goblet cells become more sparse

- Smooth muscle increases
    - Allows bronchioles to provide substantial resistance to air passage
    - (CONTROL OVER AIR FLOW)
- Alveoli
    - Respiratory zone begins where terminal bronchioles feed into respiratory bronchioles, which lead into alveolar ducts and finally into alveolar sacs (saccules)
        - Alveolar sacs contain clusters of alveoli
            - ~300 million alveoli make up most of lung volume
            - Sites of actual gas exchange
    - Respiratory membrane
    - Blood air barrier that consists of alveolar and capillary walls along with their fused basement membranes
        - Very thin (~0.5 μm); allows gas exchange across membrane by simple diffusion
    - Alveolar walls consist of:
        - Single layer of squamous epithelium (type I alveolar cells)
        - Scattered cuboidal type II alveolar cells secrete surfactant and antimicrobial proteins
        - Pores equalize pressure
- Lungs
    - Lungs occupy all of the thoracic cavity except for mediastinum
    - <u>Root:</u> site of vascular and bronchial attachment to mediastinum
    - <u>Apex:</u> superior tip, deep to clavicle
    - <u>Base:</u> inferior surface that rests on diaphragm
    - <u>Hilum:</u> found on mediastinal surface, it is the site for entry/exit of blood vessels, bronchi, lymphatic vessels, and nerves
    - Left lung: separated into superior and inferior lobes by oblique fissure
        - Smaller than right because of position of heart
            - <u>Cardiac notch:</u> concavity for heart to fit into
    - Right lung: separated into superior, middle, and inferior lobes
        - Superior and middle lobes separated by *horizontal fissure*
        - Middle and inferior lobes separated by oblique fissure



(c) Transverse section through the thorax, viewed from above. Lungs, pleural membranes, and major organs in the mediastinum are shown.

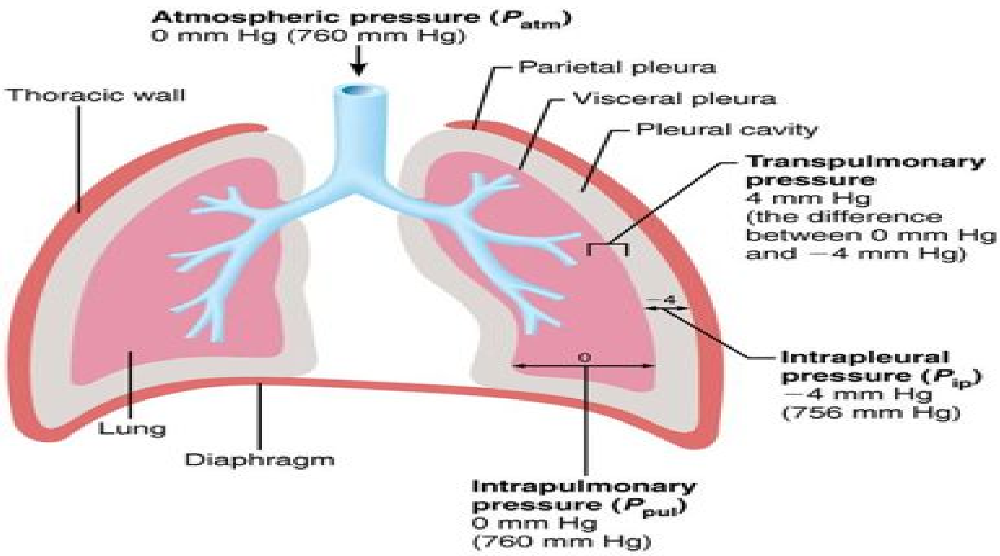
- Subdivisions of Lungs
    - Each lobe further divided into bronchopulmonary segments
        - 10 on right and 8–10 on left
        - Separated by connective tissue septa
        - Each segment is served by its own artery, vein, and bronchus
            - If one segment is diseased, it can be individually removed
- Pulmonary circulation
    - Pulmonary arteries deliver systemic venous blood from heart to lungs for oxygenation
        - Branch profusely to feed into pulmonary capillary networks
    - Pulmonary veins carry oxygenated blood from respiratory zones back to heart
    - Low-pressure, high-volume system
    - Lung capillary endothelium contains many enzymes that act on different substances in blood
        - Example: *angiotensin-converting enzyme* activates blood pressure hormone (ACE)
- Bronchial Circulation
    - Bronchial arteries provide oxygenated blood to lung tissue
        - Arise from aorta and enter lungs at hilum
        - Part of systemic circulation, so are high pressure, low volume
        - Supply all lung tissue except alveoli
    - Bronchial veins anastomose with pulmonary veins
        - Pulmonary veins carry most venous blood back to heart
- Innervation of the lungs
    - Parasympathetic - Constriction
    - Sympathetic - Dilation
- Pleura

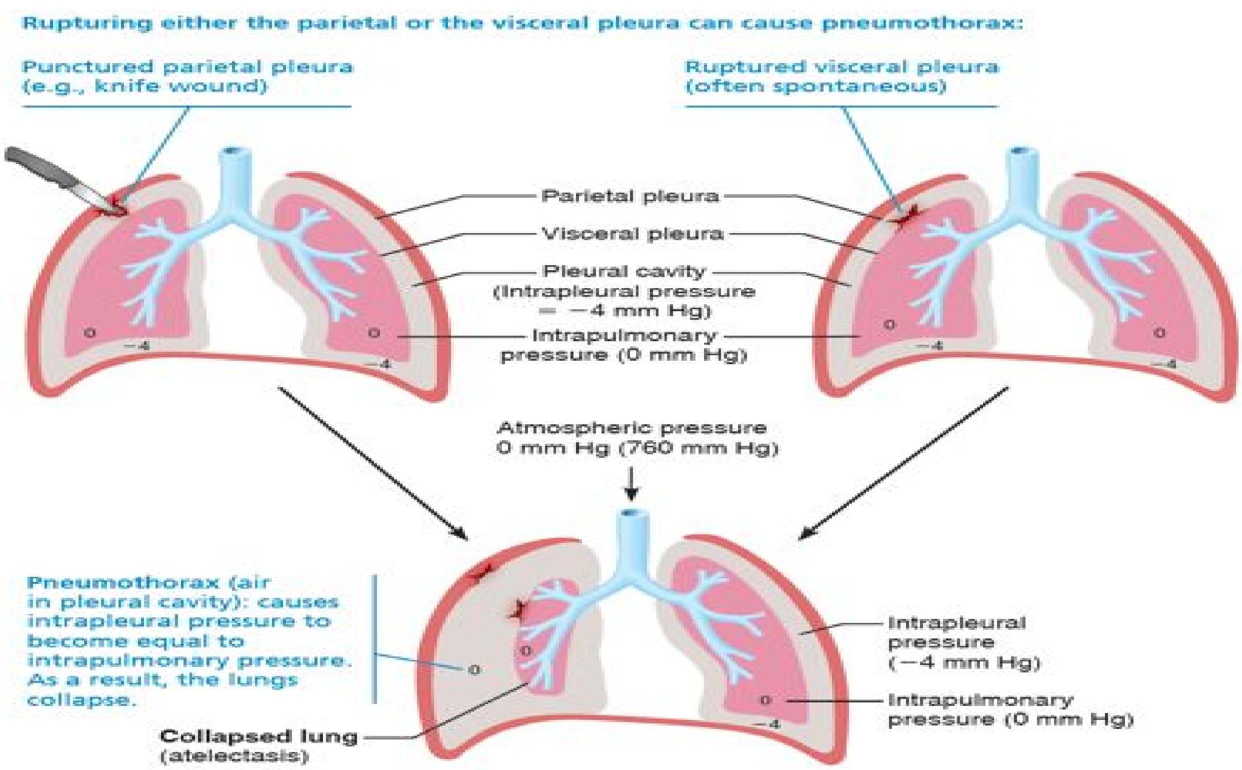
  - Pleurae: thin, double-layered serosal membrane that divides thoracic cavity into two pleural compartments and mediastinum
  - Parietal pleura: membrane on thoracic wall, superior face of diaphragm, around heart, and between lungs
  - Visceral pleura: membrane on external lung surface
  - Pleural fluid fills slitlike pleural cavity between two pleurae
    - Provides lubrication and surface tension that assists in expansion and recoil of lungs

Breathing Mechanics

- Pulmonary ventilation consists of two phases
  - Inspiration: gases flow into lungs
  - Expiration: gases exit lungs
- Atmospheric pressure (P_{atm})
  - Pressure exerted by air surrounding the body
  - 760 mm Hg at sea level = 1 atmosphere
- Respiratory pressures described relative to P_{atm}
  - Negative respiratory pressure: less than P_{atm}
  - Positive respiratory pressure: greater than P_{atm}
  - Zero respiratory pressure: equal to P_{atm}
- Intrapulmonary pressure (Ppul)
  - Pressure in alveoli
    - Also called *intra-alveolar pressure*
  - Fluctuates with breathing
  - Always eventually equalizes with P_{atm}
- Intrapleural pressure (Pip)
  - Pressure in pleural cavity
  - Fluctuates with breathing
  - Always a negative pressure ($<P_{atm}$ and $<P_{pul}$)
    - Usually always 4 mm Hg less than P_{pul}
  - Two inward forces promote lung collapse
    - Lungs' natural tendency to recoil
      - Because of elasticity, lungs try to assume smallest size
    - Surface tension of alveolar fluid
      - Surface tension pulls on alveoli to reduce alveolar size
  - One outward force tends to enlarge lungs
      - Elasticity of chest wall pulls thorax outward
  - Negative P_{ip} is affected by these opposing forces but is maintained by strong adhesive force between parietal and visceral pleurae
- Transpulmonary Pressure (Ppul - Pip)
    - Pressure that keeps lung spaces open
      - Keeps lungs from collapsing

- Greater transpulmonary pressure, the larger the lungs will be
- Lungs will collapse if:
  - $P_{ip} = P_{pul}$ or
  - $P_{ip} = P_{atm}$
  - Negative P_{ip} must be maintained to keep lungs inflated





Lecture 20: Respiration Part 2

- ❏ *6.4. Explain the roles of the diaphragm & accessory muscles during inspiration & expiration (quiet & forced)*
- ❏ *6.5. Explain the 3 factors that influence pulmonary ventilation*
- ❏ *6.6. Describe how lung volumes & capacities are measured; indicate their physiological significance*
- ❏ *6.7. Define dead space and indicated its importance in minute and alveolar ventilation*
- ❏ *6.8. Explain the mechanisms underlying the non-respiratory air movements*
- ❏ *6.9. State Dalton's Law and use it to describe the composition of atmospheric and alveolar air*
- ❏ *6.10. Explain the factors that influence the movement of gases at the air-liquid interface*

Chapter 22 - 836 - 846, Focus on Figures 22.17, 22.19
https://www.youtube.com/watch?v=GD-HPx_ZG8I

Loss of Homeostasis - Regulation of Air Pressures

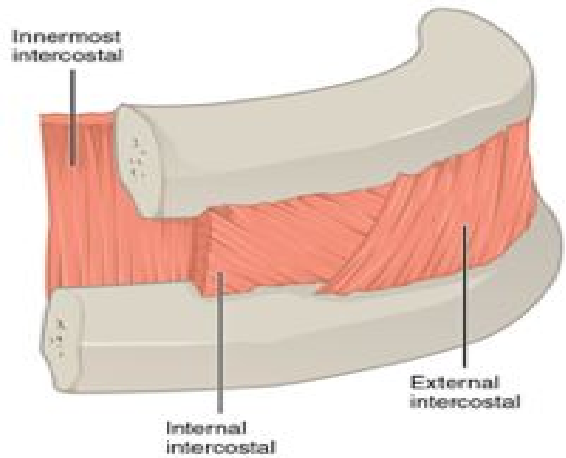
- Atelectasis: lung collapse due to
- Plugged bronchioles, which cause collapse of alveoli, or
- Pneumothorax, air in pleural cavity
    - Can occur from either wound in parietal pleura or rupture of visceral pleura
    - Treated by removing air with chest tubes
    - When pleurae heal, lung reinflates
- If pressures in various compartments are not properly maintained, then lungs can collapse
- in most cases this is a reversible process
- Pulmonary Ventilation
    - Consists of inspiration and expiration
    - Mechanical process that depends on volume changes in thoracic cavity
        - Volume changes lead to pressure changes
        - Pressure changes lead to flow of gases to equalize pressure

Boyle's Law

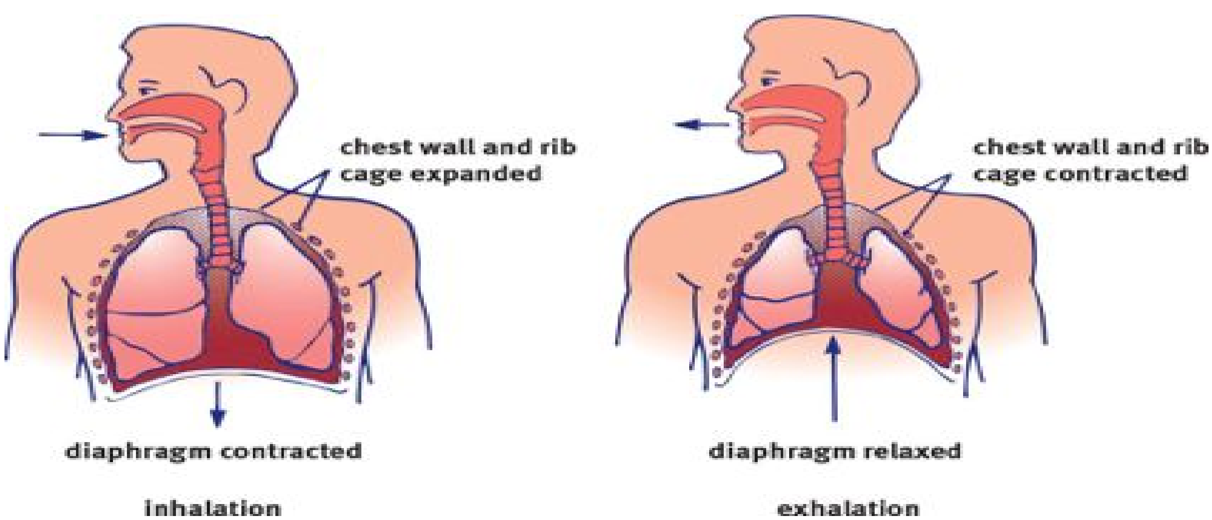
- Boyle's law: relationship between pressure and volume of a gas
    - Gases always fill the container they are in
        - If amount of gas is the same and container size is reduced, pressure will increase
    - So pressure (P) varies inversely with volume (V)
    - Mathematically:
        - $P_1V_1 = P_2V_2$

Role of the diaphragm and intercostals

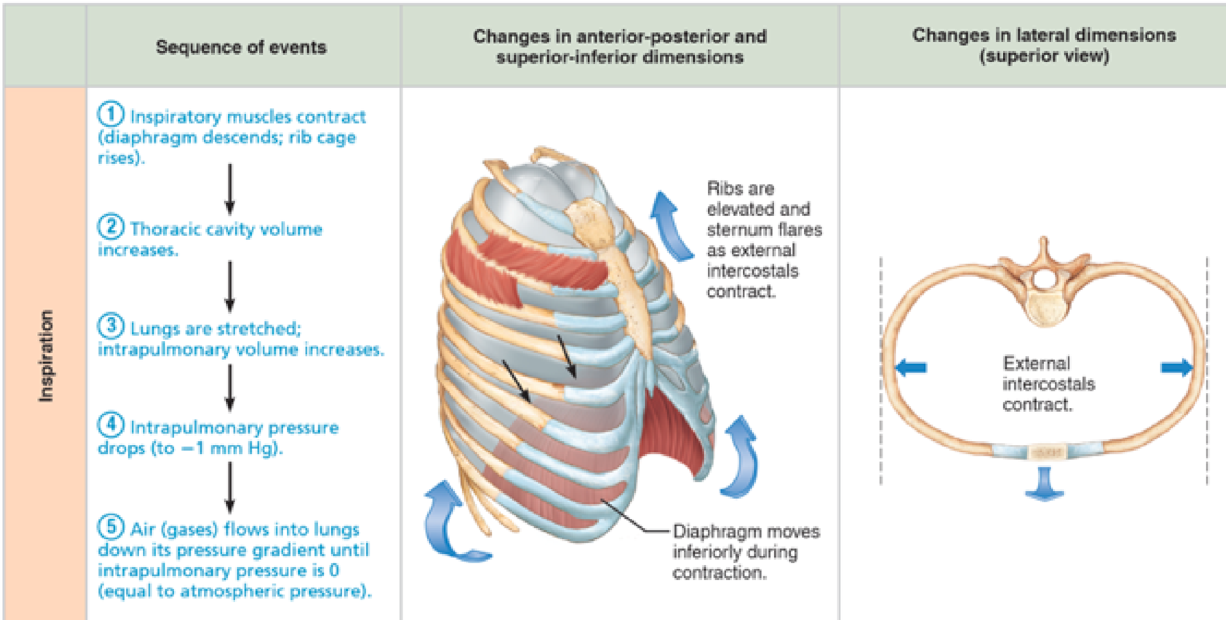
- Action of the diaphragm: when dome-shaped diaphragm contracts, it moves inferiorly and flattens out
    - Results in increase in thoracic volume
- Action of intercostal muscles: when external intercostals contract, rib cage is lifted up and out, much like when handle on a bucket is raised (outward as it moves upward)
    - Results in increase in thoracic volume



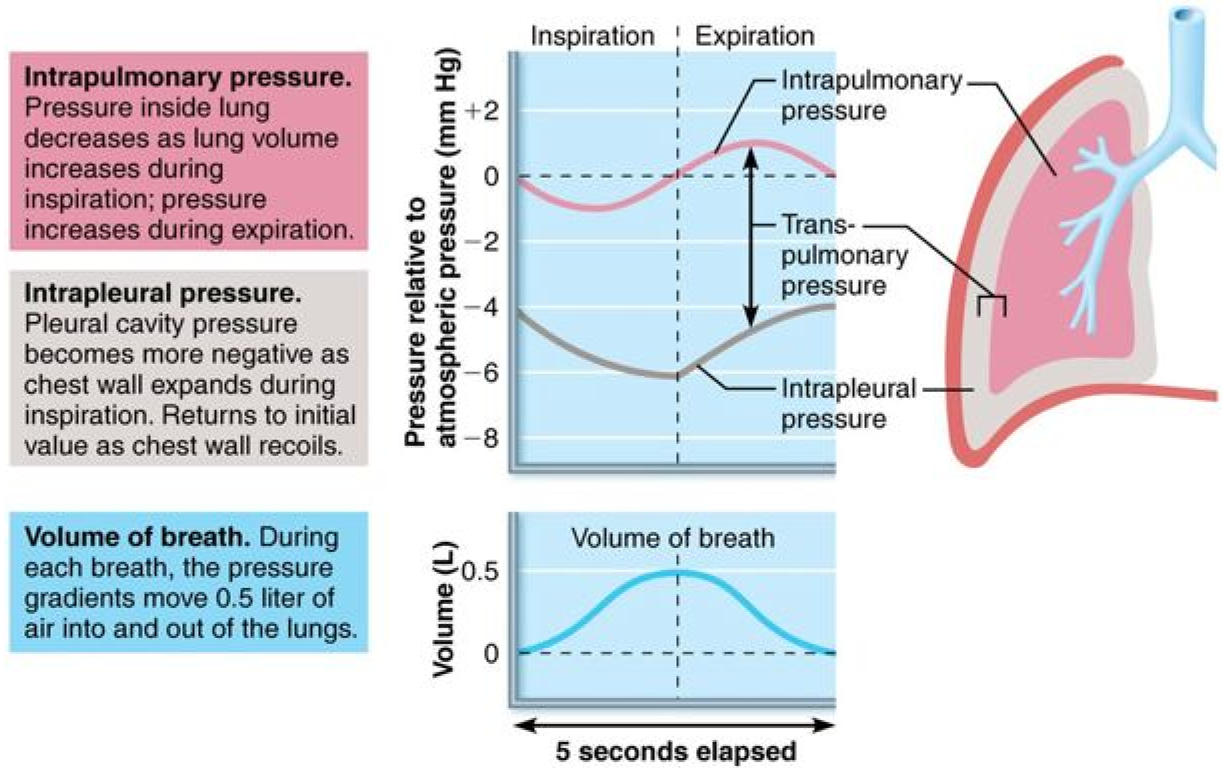
1. As thoracic cavity volume increases, lungs are stretched as they are pulled out with thoracic cage
2. Causes intrapulmonary pressure to drop by 1 mm Hg $P_{pul} < P_{atm}$
3. Because of difference between atmospheric and intrapulmonary pressure, air flows into lungs, down its pressure gradient, until $P_{pul} = P_{atm}$
4. During same period, P_{ip} lowers to about 6 mm Hg less than P_{atm}



Summary Figure Inspiration



- Expiration
    - Quiet expiration normally is passive process
        - Inspiratory muscles relax, thoracic cavity volume decreases, and lungs recoil
        - Volume decrease causes intrapulmonary pressure (P_{pul}) to increase by +1 mm Hg
        - P_{pul} > Patm so air flows out of lungs down its pressure gradient until $P_{pul} = P_{atm}$
- Forced expiration
    - Forced expiration is an active process that uses oblique and transverse abdominal muscles, as well as internal intercostal muscles
    - Forced (deep) inspirations can occur during vigorous exercise or in people with pulmonary disease
    - Accessory muscles are also activated
        - Scalenes, sternocleidomastoid, and pectoralis minor
            - Erector spinae muscles of back also help to straighten thoracic curvature
        - Act to further increase thoracic cage size, creating a larger pressure gradient so more air is drawn in
- Pressure changes during inspiration and expiration

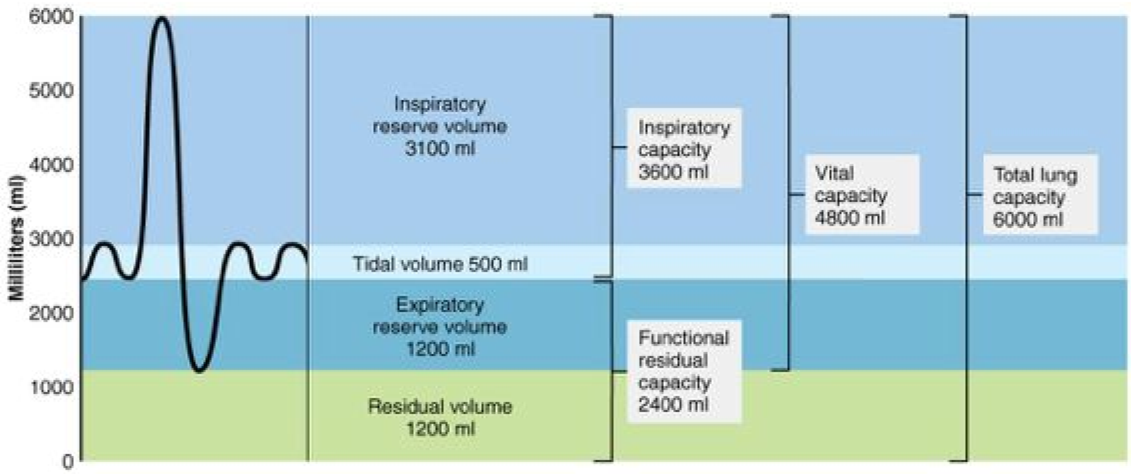


Air Passage and Ventilation

- Three physical factors influence the ease of air passage and the amount of energy required for ventilation
  - Airway resistance
  - Alveolar surface tension
  - Lung compliance
- Airway Resistance
  - Friction: major *non-elastic* source of resistance to gas flow; occurs in airways
  - $F = \Delta P / R$
  - Relationship between flow (F), pressure (P), and resistance (R):
    - ΔP – pressure gradient between atmosphere and alveoli (2 mm Hg or less during normal quiet breathing)
      - 2 mm Hg difference sufficient to move 500 ml of air
  - Gas flow changes inversely with resistance
  - Resistance in respiratory tree is usually insignificant for two reasons:
  1. Diameters of airways in first part of conducting zone are huge
  2. Progressive branching of airways as they get smaller leads to an increase in total cross-sectional area
     a. Any resistance usually occurs in medium-sized bronchi
     b. Resistance disappears at terminal bronchioles, where diffusion is what drives gas movement

- Alveolar Surface Tension
    - Surface tension: the attraction of liquid molecules to one another at a gas-liquid interface
        - Tends to draw liquid molecules closer together and reduce contact with dissimilar gas molecules
        - Water, which has very high surface tension, coats alveolar walls in a thin film
        - Tends to cause alveoli to shrink to smallest size
    - Surfactant is body's detergent-like lipid and protein complex that helps reduce surface tension of alveolar fluid
        - Prevents alveolar collapse
        - Produced by type II alveolar cells
    - Homeostasis
        - Insufficient quantity of surfactant in premature infants causes **infant respiratory distress syndrome (IRDS)**
        - Increased surface tension results in collapse of alveoli after each breath
        - Alveoli must be completely reinflated during each inspiration
        - Uses a tremendous amount of energy
        - Increased surface tension results in collapse of alveoli after each breath
        - 1 % of newborns
        - Common in premature babies
            - Fetal lungs do produce adequate amounts of surfactant until last two months of development
        - Treatment includes surfactant treatment and ventilation
- Lung compliance
    - Lung compliance: measure of change in lung volume that occurs with given change in transpulmonary pressure
        - Measure of how much "stretch" the lung has
    - Normally high because of
        - Distensibility of lung tissue
        - Surfactant, which decreases alveolar surface tension
    - Higher lung compliance means it is easier to expand lungs
    - Measuring ventilation
    - Several respiratory volumes can be used to assess respiratory status
    - Respiratory volumes can be combined to calculate respiratory capacities, which can give information on a person's respiratory status
    - Respiratory volumes and capacities are usually abnormal in people with pulmonary disorders
    - Spirometer: original, cumbersome clinical tool used to measure patient's respiratory volumes
    - Electronic measuring devices used today

- Tidal volume (TV): amount of air moved into and out of lung with each breath
    - Averages ~500ml
- Inspiratory reserve volume (IRV): amount of air that can be inspired forcibly beyond the tidal volume (2100–3200 ml)
- Expiratory reserve volume (ERV): amount of air that can be forcibly expelled from lungs (1000–1200 ml)
- Residual volume (RV): amount of air that always remains in lungs
    - Needed to keep alveoli open



(a) Spirographic record for a male

- Inspiratory capacity (IC): sum of TV + IRV
- Functional residual capacity (FRC): sum of RV + ERV
- Vital capacity (VC): sum of TV + IRV + ERV
- Total lung capacity (TLC): sum of all lung volumes (TV + IRV+ ERV + RV)

Importance of Spirometry

- Spirometry can distinguish between:
    - Obstructive pulmonary disease: increased airway resistance (example: bronchitis, asthma)
        - TLC, FRC, RV may increase because of hyperinflation of lungs
    - Restrictive disease: reduced TLC due to disease (example: tuberculosis) or exposure to environmental agents (example: fibrosis)
        - VC, TLC, FRC, RV decline because lung expansion is compromised
- Pulmonary functions tests can measure *rate* of gas movement
    - Forced vital capacity (FVC): amount of gas forcibly expelled after taking deep breath
    - Forced expiratory volume (FEV): amount of gas expelled during specific time interval of FVC
        - FEV_1: amount of air expelled in 1st second

            - Healthy individuals can expel 80% of FVC in 1st second
            - Patients with obstructive disease exhale less than 80% in 1st second, whereas those with restrictive disease exhale 80% or more even with reduced FVC

- Dead Space
    - Anatomical dead space: does not contribute to gas exchange
        - Consists of air that remains in passageways
            - ~150 ml out of 500 ml TV
    - Alveolar dead space: space occupied by nonfunctional alveoli
        - Can be due to collapse or obstruction
    - Total dead space: sum of anatomical and alveolar dead space
    - dead space measured by metabolic changes in CO_2
- Dead space - Why does it matter in Physiology?
    - Well there are two types of ventilations we can measure: Minute ventilation: total amount of gas that flows into or out of respiratory tract in 1 minute
        - Normal at rest = ~ 6 L/min
        - Normal with exercise = up to 200 L/min
        - Only rough estimate of respiratory efficiency
    - Alveolar ventilation rate (AVR): flow of gases into and out of alveoli during a particular time
        - Better indicator of effective ventilation - AND THIS TAKES INTO ACCOUNT THE DEAD SPACE = (Tidal Volume – deadspace)/(mls/breath) * frequency/(breaths/minute)
    - Significant increases in AVR are brought about by increasing TV rather than frequency
    - Rapid, shallow breathing can actually decrease AVR

Table 22.3 Effects of Breathing Rate and Depth on Alveolar Ventilation of Three Hypothetical Patients

BREATHING PATTERN OF HYPOTHETICAL PATIENT	DEAD SPACE VOLUME (DSV)	TIDAL VOLUME (TV)	RESPIRATORY RATE*	MINUTE VENTILATION (MVR)	ALVEOLAR VENTILATION (AVR)	% EFFECTIVE VENTILATION (AVR/MVR)
I—Normal rate and depth	150 ml	500 ml	20/min	10,000 ml/min	7000 ml/min	70%
II—Slow, deep breathing	150 ml	1000 ml	10/min	10,000 ml/min	8500 ml/min	85%
III—Rapid, shallow breathing	150 ml	250 ml	40/min	10,000 ml/min	4000 ml/min	40%

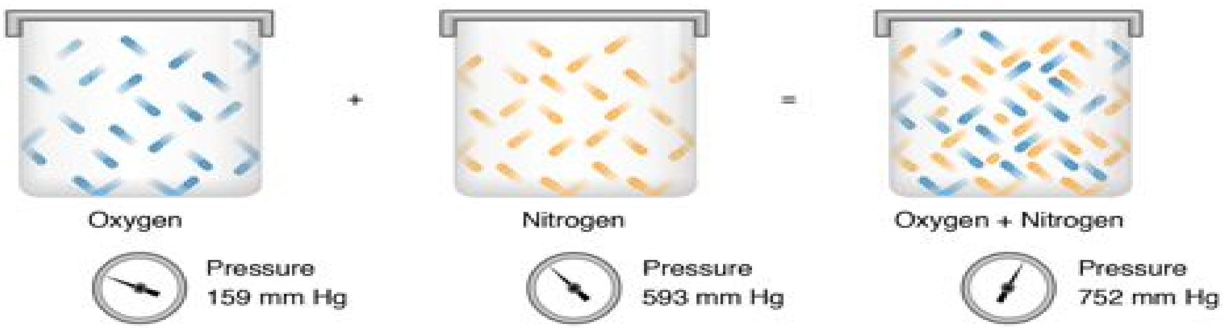
*Respiratory rate values are artificially adjusted to provide equivalent minute ventilation as a baseline for comparing alveolar ventilation.

Non-Respiratory Air Movements

- Many processes can move air into or out of lungs besides breathing
- May modify normal respiratory rhythm
- Most result from reflex action, although some are voluntary
- Examples: coughing, sneezing, crying, laughing, hiccups, and yawns

Gas Exchange

- Gas exchange occurs between lungs and blood as well as blood and tissues
- External respiration: diffusion of gases between blood and lungs
- Internal respiration: diffusion of gases between blood and tissues
- Both processes are subject to:
    - Basic properties of gases
    - Composition of alveolar gas
- Dalton's law of partial pressures
    - Total pressure exerted by mixture of gases is equal to sum of pressures exerted by each gas
    - Partial pressure
        - Pressure exerted by each gas in mixture
        - Directly proportional to its percentage in mixture



What is Air?

- Alveoli contain more CO_2 and water vapor than atmospheric air because of:
    - Gas exchanges in lungs (O_2 diffuses out of lung, and CO_2 diffuses into lung)
    - Humidification of air by conducting passages
    - Mixing of alveolar gas with each breath
        - Newly inspired air mixes with air that was left in passageways between breaths

Table 22.4 Comparison of Gas Partial Pressures and Approximate Percentages in the Atmosphere and in the Alveoli

	ATMOSPHERE (SEA LEVEL)		ALVEOLI	
GAS	APPROXIMATE PERCENTAGE	PARTIAL PRESSURE (mm Hg)	APPROXIMATE PERCENTAGE	PARTIAL PRESSURE (mm Hg)
N_2	78.6	597	74.9	569
O_2	20.9	159	13.7	104
CO_2	0.04	0.3	5.2	40
H_2O	0.46	3.7	6.2	47
	100.0%	760	100.0%	760

Dissolving Gases

- Henry's law
  - For gas mixtures in contact with liquids:
    - Each gas will dissolve in the liquid in proportion to its partial pressure
    -
    - Amount of each gas dissolved also depends on:
      - *Solubility*: CO_2 is 20× more soluble in water than O_2, and little N_2 will dissolve
      - Temperature: as temperature of liquid rises, solubility decreases
      - Example application: Hyperbaric chambers

External Respiration

- Exchange is influenced by:

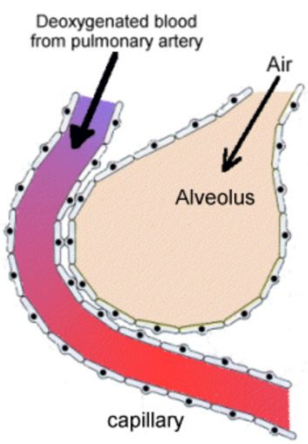
1. Partial pressure gradients and gas solubilities
2. Thickness and surface area of respiratory membrane
3. Ventilation-perfusion coupling: matching of alveolar ventilation with pulmomary blood perfusion

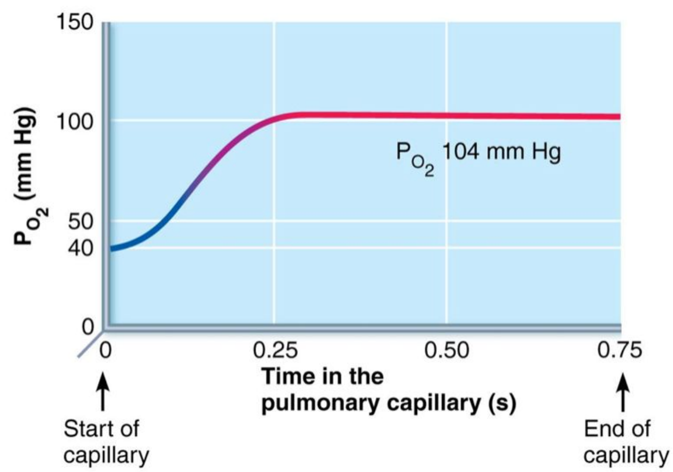
1. Partial pressures:

O_2	CO_2

Steep partial pressure gradient for O_2 exists between blood and lungs
• Venous blood P_{O_2} = 40 mm Hg
• **Alveolar P_{O_2}** = 104 mm Hg
  • Drives oxygen flow into blood
  • Equilibrium is reached across respiratory membrane in ~0.25 seconds, but it takes red blood cell ~0.75 seconds to travel from start to end of pulmonary capillary
	Partial pressure gradient for CO_2 is less steep
	• Venous blood P_{CO_2} = 45 mm Hg
	• Alveolar P_{CO_2} = 40 mm Hg
	• Though gradient is not as steep, CO_2 still diffuses in equal amounts with oxygen
	  • Reason is that CO_2 is 20× more soluble in plasma and alveolar fluid than oxygen

1. Partial pressures:





*Rapid transfer of oxygen at higher pressure differentials

2. Thickness and surface area of the respiratory membrane:

- Respiratory membranes are very thin
  - 0.5 to 1 μm thick
- Large total surface area of the alveoli is 40× the surface area of the skin

Surface = 70 M^2 = ½ tennis court

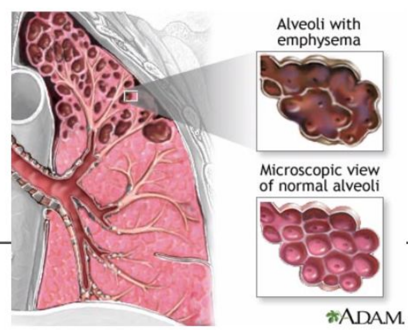
2. Thickness and surface area of the respiratory membrane:

Link to Homeostasis:

Situation 1 – lungs become waterlogged **(pneumonia)**

- - Thickness of respiratory membrane increases dramatically if lungs become waterlogged
- Tissues suffer from oxygen deprivation

Situation 2 – **Emphysema –** Alveoli walls break down, surface area decreases



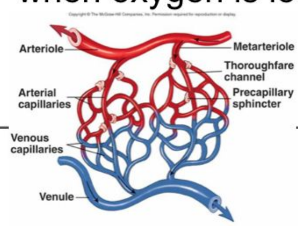
uOttawa

3. Coupling of ventilation and perfusion:

- **Perfusion**: blood flow reaching alveoli
- **Ventilation**: amount of gas reaching alveoli
- Ventilation and perfusion rates must be matched for optimal, efficient gas exchange
- Both are controlled by local autoregulatory mechanisms
  - P_{O_2} controls perfusion by changing arteriolar diameter
  - P_{CO_2} controls ventilation by changing bronchiolar diameter

3. Coupling of ventilation and perfusion:

- **Influence of local P_{O_2} on perfusion**
  - Changes in P_{O_2} in alveoli cause changes in diameters of arterioles
    - Where alveolar O_2 is high, arterioles dilate
    - Where alveolar O_2 is low, arterioles constrict
    - Directs blood to go to alveoli, where oxygen is high, so blood can pick up more oxygen
  - Opposite mechanism seen in systemic arterioles that dilate when oxygen is low and constrict when high



3. Coupling of ventilation and perfusion:

- **Influence of local P_{CO_2} on perfusion**
  - Changes in P_{CO_2} in alveoli cause changes in diameters of bronchioles
    - Where alveolar CO_2 is high, bronchioles dilate
    - Where alveolar CO_2 is low, bronchioles constrict
    - Allows elimination of CO_2 more rapidly

---

3. Coupling of ventilation and perfusion:

Balancing ventilation and perfusion

- Changing diameters of local arterioles and bronchioles synchronizes ventilation-perfusion
- Ventilation-perfusion is never balanced for all alveoli because:
  1. Regional variations may be present, due to effect of gravity on blood and air flow
  2. Occasionally, alveolar ducts plugged with mucus cause unventilated areas

Lecture 21: Respiration Part 3

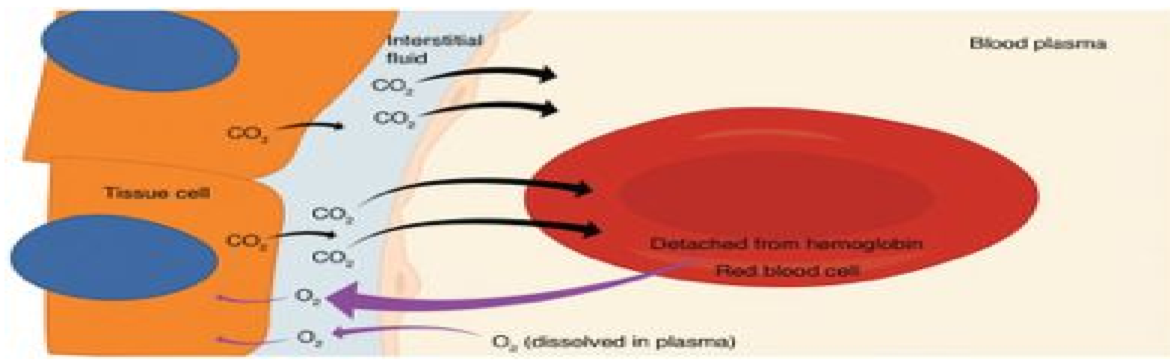
- ❑ ***6.11.*** *List and describe 3 factors that influence the exchange of air and carbon dioxide (lungs)*
- ❑ ***** Note we left off here as part of 6.10 – 6.10 from last lecture also includes 6.11***
- ❑ ***6.12.*** *Describe the partial pressure gradients that drive oxygen and carbon dioxide movement (tissues)*
- ❑ ***6.13.*** *Describe completely the transport of oxygen in the blood*
- ❑ ***6.14.*** *Explain the sigmoidal nature of the oxygen-hemoglobin dissociation curve*
- ❑ ***6.15.*** *Describe completely the 3 ways in which carbon dioxide is transported in the blood*
- ❑ ***6.16.*** *Explain the Bohr and Haldane effects*

Chapter 22, pg. 847-852, Focus on Figure 22.1

https://www.youtube.com/watch?v=WXOBJEXxNEo

Internal Respiration

- Internal respiration involves capillary gas exchange in body tissues
- Partial pressures and diffusion gradients are reversed compared to external respiration
    - Tissue P_{O2} is always lower than in arterial blood P_{O2} (40 vs. 100 mm Hg), so oxygen moves from blood to tissues
    - Tissue P_{CO2} is always higher than arterial blood P_{CO2} (45 vs. 40 mm Hg), so CO_2 moves from tissues into blood
    - Venous blood returning to heart has P_{O2} of 40 mm Hg and P_{CO2} of 45 mm Hg



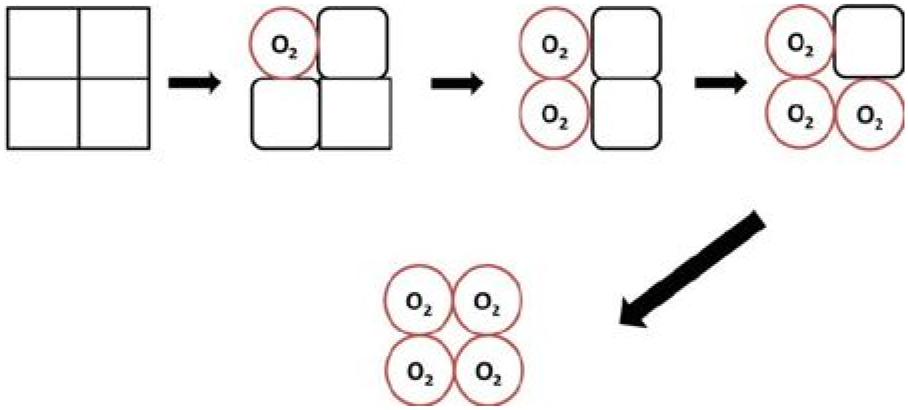
How Does Oxygen Travel in the Blood?

- Most oxygen is attached to hemoglobin in RBCs
- Molecular O_2 is carried in blood in two ways:
    1. 1.5% is dissolved in plasma
    2. 98.5% is loosely bound to each Fe of hemoglobin (Hb) in RBCs
- Association of oxygen and hemoglobin
    - Each Hb molecule is composed of four polypeptide chains, each with a iron-containing heme group
        - So each Hb can transport four (4) oxygen molecules
    - Oxyhemoglobin (HbO_2): hemoglobin-O_2 combination
    - Reduced hemoglobin (deoxyhemoglobin) (HHb): hemoglobin that has released O_2

$$HHb + O_2 \underset{\text{Tissues}}{\overset{\text{Lungs}}{\rightleftharpoons}} HbO_2 + H^+$$

- <u>Fully saturated (100%):</u> all four heme groups carry O_2
- <u>Partially saturated:</u> when only one to three hemes carry O_2
- BUT WAIT: Loading and unloading of O_2 is facilitated by a change in shape of Hb
    - As O_2 binds, Hb changes shape, increasing its affinity for O_2 increases

- Reverse is also true: As O_2 is released, Hb shape change causes a decrease in affinity for O_2



How Does Pressure Impact Oxygen Transport

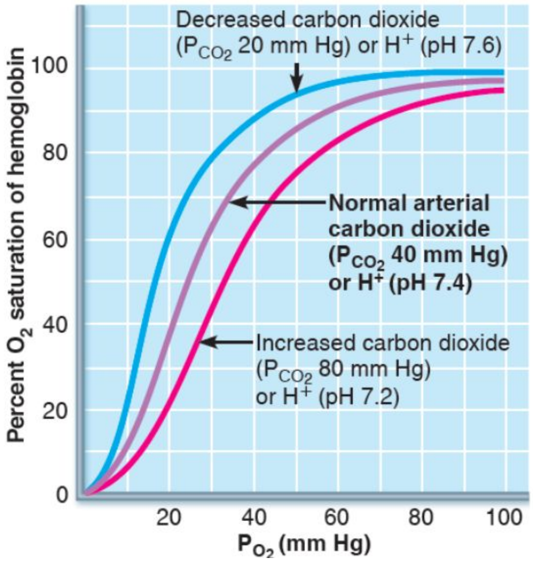
- Percent of Hb saturation can be plotted against P_{O2} concentrations
    - Resulting graph is not linear, but an S-shaped curve
    - Referred to as an *oxygen-hemoglobin* dissociation curve
- Cooperative binding - common in biochemistry

How Does Pressure Impact Hemoglobin Saturation in Arteries & Veins

- Influence of P_{O2} on hemoglobin saturation
    - In SYSTEMIC arterial blood:
        - P_{O2} is ~100 mm Hg
        - Hb is 98% saturated
    - In SYSTEMIC venous blood:
        - P_{O2} is 40 mm Hg
        - Hb is still 75% saturated
        - Venous reserve: oxygen remaining in venous blood that can still be used

Other Factors that Influence Oxygen Association

1. Temperature
2. Blood pH
3. P_{CO2}
4. Concentration of BPG



Same trend for other factors:

- pH (increased H+)
- CO_2
- Bisphosphoglycerate (BPG)

As cells metabolize glucose they:

1. **produce BPG**
2. **Consume oxygen to result in**
   Increases in A) P_{CO_2} and B) H^+ in capillary blood

Again – like temperature, <u>all of this happening in the tissues</u>

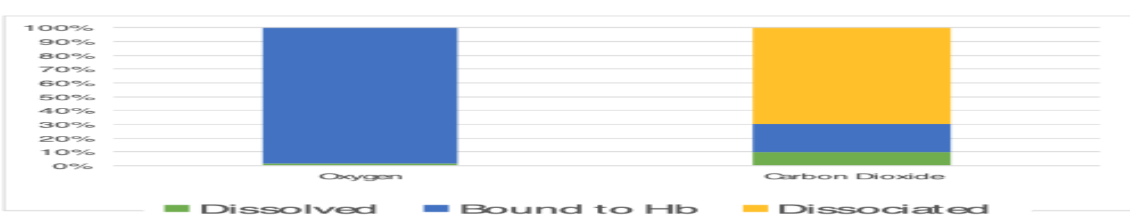
Consequences of Local Regulation of Hb in the Tissues

- Declining blood pH (acidosis) and increasing P_{CO2} cause Hb-O_2 bond to weaken
  - Referred to as Bohr effect allows for oxygen unloading
- To restate:
  - Bohr effect refers to the fact that Hb-oxygen bond is weakened when coming into contact with carbon dioxide or hydrogen ions associated with metabolic activity.
  - It ensures increased release of oxygen at metabolically activity tissues.

Carbon Dioxide Transport in Blood

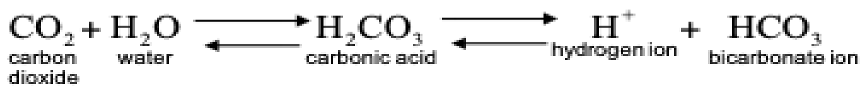
- CO_2 is transported in blood in three forms:
  1. Dissolved in plasma (7 to 10%) as P_{CO2}
  2. Chemically bound to hemoglobin (just over 20%).
     a. CO_2 is bound to the *globin* part of hemoglobin
     b. Referred to ass carbaminohemoglobin
  3. As bicarbonate ions in plasma (about 70%). (HCO_3^-) in plasma
- Formation of bicarbonate involves CO_2 combining with water to form carbonic acid (H_2CO_3), which quickly dissociates into bicarbonate and H^+

$$\underset{\text{carbon dioxide}}{CO_2} + \underset{\text{water}}{H_2O} \rightleftharpoons \underset{\text{carbonic acid}}{H_2CO_3} \rightleftharpoons \underset{\text{hydrogen ion}}{H^+} + \underset{\text{bicarbonate ion}}{HCO_3^-}$$



- Why is so much CO2 converted to bicarbonate?
    - The enzyme carbonic anhydrase reversibly and rapidly catalyzes this reaction in RBCs
    - In systemic capillaries, after HCO_3^- is created, it quickly diffuses from RBCs into plasma
        - Outrush of HCO_3^- from RBCs is balanced as Cl^- moves into RBCs from plasma
            - Referred to as chloride shift
    - In pulmonary capillaries, the processes occur in reverse
        - HCO_3^- moves into RBCs while Cl^- moves out of RBCs back into plasma
        - HCO_3^- binds with H^+ to form H_2CO_3
        - H_2CO_3 is split by carbonic anhydrase into CO_2 and water
        - CO_2 diffuses into alveoli
- Haldane Effect
    - Amount of CO_2 transported is affected by P_{O2}
    - The lower the P_{O2} and hemoglobin O_2 saturation, the more CO_2 can be carried in blood
    - Reduced hemoglobin buffers H^+ and forms carbaminohemoglobin more easily
    - Process encourages CO_2 exchange at tissues and at lungs
        - At tissues, as more CO_2 enters blood, more oxygen dissociates from hemoglobin (Bohr effect)
            - As HbO_2 releases O_2, it more readily forms bonds with CO_2 to form carbaminohemoglobin
    - Who is John Haldane? An interesting guy…
        - Experimented on himself
        - Investigated poison gases used in WWI First respirator
        - In the late 1890s introduced idea of using small animals in coal mines to detect harmful gases such as carbon monoxide
- Link to Homeostasis
    - <u>Hypoxia:</u> inadequate O_2 delivery to tissues; can result in *cyanosis* and is classified by cause:
    - <u>Anemic hypoxia</u>: too few RBCs or abnormal or too little Hb
    - <u>Ischemic hypoxia:</u> impaired or blocked blood circulation
    - <u>Histotoxic hypoxia:</u> cells unable to use O_2, as in metabolic poisons (ex: cyanide)
    - <u>Hypoxemic hypoxia:</u> abnormal ventilation; pulmonary disease, low levels of oxygen in air
    - <u>Carbon monoxide poisoning:</u> especially from fire; Hb has a 200◊ greater affinity for carbon monoxide than oxygen
        - Victims have headaches and can become flushed
- Influence of CO2 on Blood pH
    - <u>Carbonic acid–bicarbonate buffer system:</u> helps blood resist changes in pH

- If H^+ concentration in blood rises, excess H^+ is removed by combining with HCO_3^- to form H_2CO_3, which dissociates into CO_2 and H_2O
- If H^+ concentration begins to drop, H_2CO_3 dissociates, releasing H^+
- HCO_3^- is considered the *alkaline reserve* of carbonic acid-bicarbonate buffer system



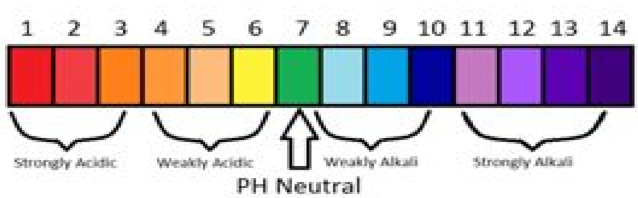
Lecture 22: Respiration Part 4

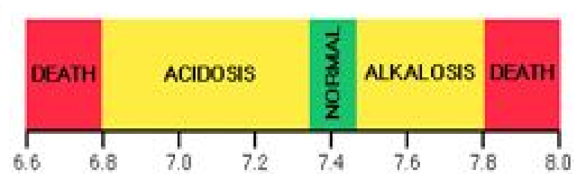
- ❑ ***6.17.*** *Associate carbon dioxide levels with blood pH; explain how respiration can regulate blood pH*
- ❑ ***6.18.*** *Describe how respiration is controlled by the nervous system*
- ❑ ***6.19***. *Indicate the effects of the following factors on respiration: Hering Breuer reflex, hypothalamus, cortex*
- ❑ ***6.20.*** *List the 3 principal chemical factors that influence respiration and explain their mechanisms of action*
- ❑ ***6.21.*** *Discuss the mechanisms controlling respiration during intense exercise*

Chapter 22; Pg. 853-857, Figure 22.27, Figure 22.28
https://www.youtube.com/watch?v=9j6BpanhpKY

Respiration and Blood pH

- Changes in respiratory rate and depth affect blood pH
  - Slow, shallow breathing causes an increase in CO_2 in blood, resulting in a drop in pH
  - Rapid, deep breathing causes a decrease in CO_2 in blood, resulting in a rise in pH
- Changes in ventilation can help adjust pH when disturbances are caused by metabolic factors
  - Breathing plays a major role in acid-base balance of body





Overall Neural Controls for Respiration

- Neural controls involve neurons in reticular formation of medulla and pons
- Medullary respiratory centers
  - Clustered neurons in two areas of medulla are most important:

        - Ventral respiratory group
        - Dorsal respiratory group
- Recall; Medulla is an active area of regulation

Neural Controls

- Ventral respiratory group
    - Rhythm-generating and integrative center
        - Recent evidence suggests forced expiration may involve a separate group of neurons than passive respiration
    - Consists of network of neurons in brain stem that extends from spinal cord to pons-medulla junction
    - <u>Sets eupnea</u>: normal respiratory rate and rhythm (12–15 breaths/minute)
    - Its inspiratory neurons excite inspiratory muscles via phrenic (diaphragm) and intercostal nerves (external intercostals)
    - Expiratory neurons inhibit inspiratory neurons
    - Depth is determined by how actively respiratory center stimulates respiratory muscles
        - The greater the stimulation, the greater the number of motor units excited, increasing depth of inspiration
    - Rate is determined by how long center is active
    - Both are modified by changing body demands
- Dorsal respiratory group (DRG)
    - Network of neurons located near root of cranial nerve IX
    - Group integrates input from peripheral stretch and chemoreceptors, then sends information to VRG neurons
    - Not much known about this group of neurons
- Pontine respiratory centers
    - Neurons in this center influence and modify activity of VRG
    - Act to smooth out transition between inspiration and expiration and vice versa
    - Transmit impulses to VRG that modify and fine-tune breathing rhythms during vocalization, sleep, exercise
    - Lesions in this area of brain lead to *apneustic breathing*, where patient takes prolonged inspirations
- Generation of the respiratory rhythm
    - Origin of breathing rhythm is not yet fully understood
    - One hypothesis: *pacemaker neurons* in VRG control intrinsic rhythmicity
    - Most widely accepted hypothesis: reciprocal inhibition of two sets of interconnected pacemaker neurons in medulla generates rhythm
        - Each neuron set controls the other to ensure rhythm

Control of Respiration

- Control of respiration by 3 things

1. Chemicals (CO_2, O_2, H+)
2. Higher brain centres
3. Reflexes

Control of Respiration by Chemical Factors

- Chemicals - 3 Main Chemical Factors
    - Chemical factors
        - Most important of all factors affecting depth and rate of inspiration
        - Changing levels of P_{CO2}, P_{O2}, and pH are most important
        - Levels of these chemicals are sensed by:
            - Central chemoreceptors: located throughout brain stem
            - Peripheral chemoreceptors: found in aortic arch and carotid arteries
    - Influence of P_{CO2}
        - Most potent and most closely controlled
        - If blood P_{CO2} levels rise (**hypercapnia**), CO_2 accumulates in brain and joins with water to become carbonic acid
            - Carbonic acid dissociates, releasing H^+, causing a drop in pH (increased acidity)
            - Increased H^+ stimulates central chemoreceptors of brain stem, which synapse with respiratory regulatory centers
            - Respiratory centers increase depth and rate of breathing, which act to lower blood P_{CO2}, and pH rises to normal levels
            - If blood P_{CO2} levels decrease, respiration becomes slow and shallow
    - Hyperventilation
        - Hyperventilation: increased depth and rate of breathing that exceeds body's need to remove CO_2
        - May be caused by anxiety attacks
        - Leads to decreased blood CO_2 levels (hypocapnia)
        - Causes cerebral vasoconstriction and cerebral ischemia, resulting in dizziness, fainting
        - Early symptoms include tingling and + muscle spasms
        - Treatment: breathing into paper bag increases CO_2 levels being inspired
    - Influence of P_{O2}
        - Peripheral chemoreceptors in aortic and carotid bodies sense arterial O_2 levels
        - Declining P_{O2} normally has only Requires substantial drop in arterial P_{O2} (below 60 mm Hg) to stimulate increased ventilation
        - slight effect on ventilation because of huge O_2 reservoir bound to Hb

        - When excited, chemoreceptors cause respiratory centers to increase ventilation
    - Influence of Arterial pH
        - pH can modify respiratory rate and rhythm even if CO_2 and O_2 levels are normal
        - Mediated by peripheral chemoreceptors
        - Decreased pH may reflect CO_2 retention, accumulation of lactic acid, or excess ketone bodies
        - Respiratory system controls attempt to raise pH by increasing respiratory rate and depth
    - Summary of Chemical Factors
        - Rising CO_2 levels are most powerful respiratory stimulant
        1. Normally, blood P_{O2} affects breathing only indirectly by influencing peripheral chemoreceptor sensitivity to changes in P_{CO2}
        2. When arterial P_{O2} falls below 60 mm Hg, it becomes major stimulus for respiration (via peripheral chemoreceptors)
        3. Changes in arterial pH resulting from CO_2 retention or metabolic factors act indirectly through peripheral chemoreceptors

Control of Respiration by Higher Brain Centres

1. Hypothalamic controls: act through limbic system to modify rate and depth of respiration

- Example: breath holding that occurs in anger or gasping with pain

2. Cortical controls: direct signals from cerebral motor cortex that bypass medullary controls

- Example: voluntary breath holding at least until brain stem reinstates breathing when blood CO_2 becomes critical

Control of Respiration by Reflexes

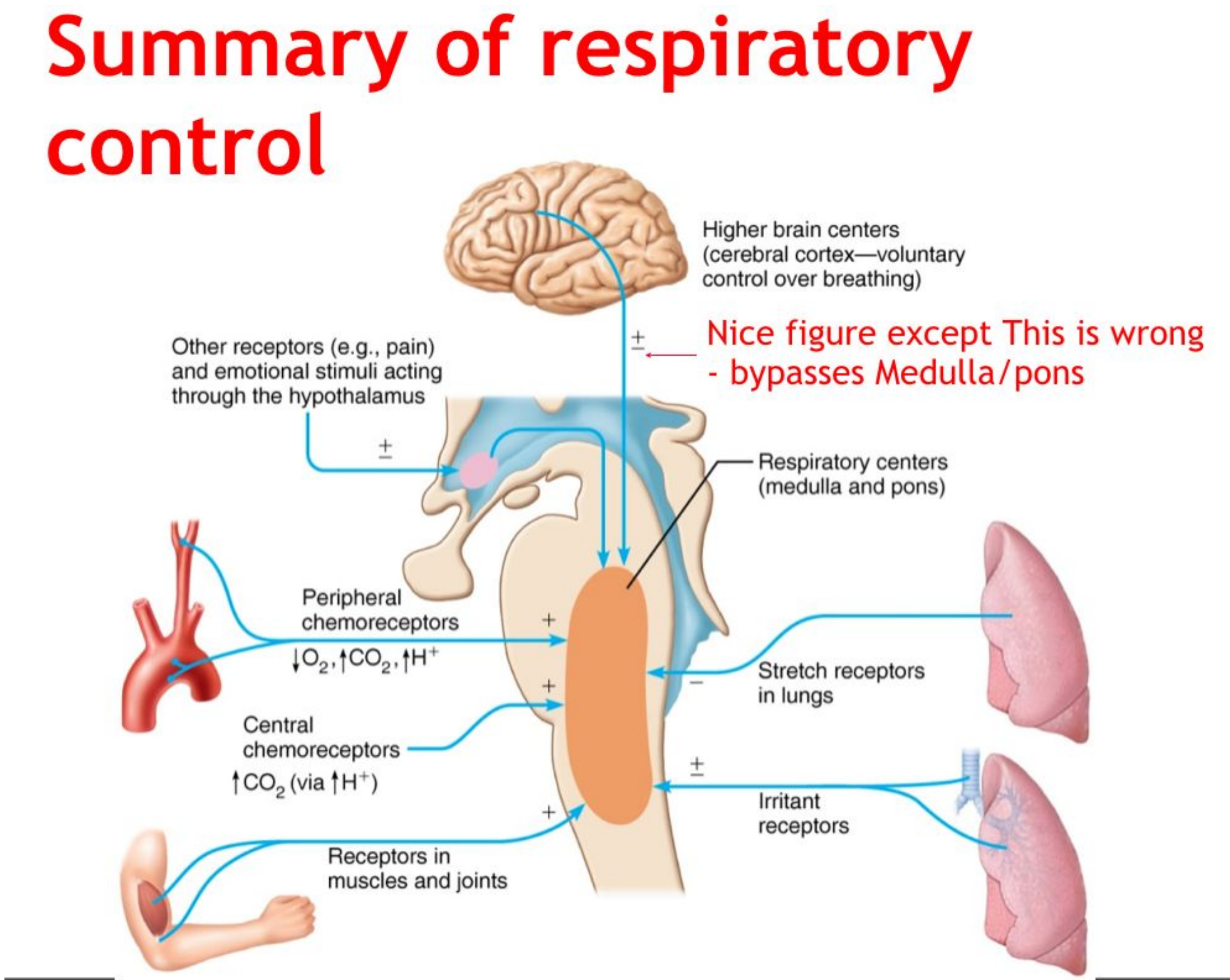
1. Pulmonary irritant reflexes

- Receptors in bronchioles respond to irritants such as dust, accumulated mucus, or noxious fumes
    - Receptors communicate with respiratory centers via vagal nerve afferents
- Promote reflexive constriction of air passages
- Same irritant triggers a cough in trachea or bronchi or a sneeze in nasal cavity

2. Inflation reflex

- Hering-Breuer reflex (inflation reflex)
    - Stretch receptors in pleurae and airways are stimulated by lung inflation

- Send inhibitory signals to medullary respiratory centers to end inhalation and allow expiration
- May act as protective response more than as a normal regulatory mechanism



Respiration Adaptations During Exercise

- During exercise, adjustments geared to both intensity and duration must be made
- Hyperpnea: increased ventilation in response to metabolic needs
    - Ventilation can increase 10 to 20 fold
- Ventilation increases abruptly, increases gradually, then reaches steady state; when exercise stops, there is a small, abrupt decline in ventilation, followed by a gradual decrease
- P_{CO2}, P_{O2}, and pH remain surprisingly constant during exercise
- Abrupt increase in ventilation that occurs as exercise begins involves three neural factors:

1. Psychological stimuli: anticipation of exercise
2. Simultaneous cortical motor activation of skeletal muscles and respiratory centers
3. Excitatory impulses to respiratory centers from proprioceptors in moving muscles, tendons, joints

- There is very little change in oxygen levels or CO_2 in the arterial blood during exercise due to the efficient coupling to use in muscle.