Cardiovascular system-I

Cardiac Physiology

• Basics of cardiovascular system and heart function is transport of blood

1. Heart is the pump establishes a pressure gradient (flow occurs from greater → lesser pressure)
2. Blood vessels are passage ways
3. Heart is a double pump

1. Pulmonary circuit heart → lungs and back (at lungs, picks up O2, releases CO2)/ right side

2. Systemic circuit heart → body tissues and back (at tissues, picks up CO2, releases O2) / left side

Valves prevent backflow of blood

1. AV valves attached by chordae tendinae to papillary muscles so that they open in one direction only
2. Semilunar valves are shaped like cups, this structure prevents them from opening backward- fibrous skeleton

1. Provides attachment for valves and muscle
2. separates atria from ventricles (important so they contract at different times)

Heart wall is 3-layered

1. Endocardium (epithelial lining)
2. Myocardium (muscle)
3. Epicardium (thin fibrous connective tissue layer)

Pericardial sac

Fibrous covering continuous with epicardium

a. anchors heart

b. filled with fluid to prevent friction

• Electrical activity of heart

- Auto rhythmic cells

1. Specialized cells that initiate and conduct APs
2. Display pacemaker activity (no resting potential, changes in potential due to voltage-gated Na+, K+ and Ca2+ channels)

a. decreased flow of K+ out and increased inward flow of Na+ through "funny" channels results in slow depolarization

b. near threshold, voltage-gated transient Ca2+ channels open and bring membrane to threshold (Ca2+ flows in)

c. at threshold voltage-gated long-lasting Ca2+ channels open, more Ca2+ flows in (this is the AP)

d. at peak of depolarization, voltage-gated K+ channels open and repolarization occurs

3. locations

a. SA node (sinoatrial)

(1) Right atrium

(2) Fastest rate of auto-rhythmicity, it's the pacemaker of the heart (under usual conditions initiates APs)

(3) Interatrial pathway extends to left atrium (spreads AP, atria contract)

(4) Internodal pathway extends to next node

b. AV node (atrioventricular)

(1) Electrical connection between atria and ventricles

(2) Signal slightly delayed (.1 sec) to allow atria to finish contracting – more efficient blood pumping

c. AV bundle (bundle of His)
(1) Branch into ventricles

d. Purkinje fibers
(1) Branch throughout ventricular myocardium (ventricles contract) - Contractile cells

1. APs spread from cell to cell- adjacent cells joined by intercalated discs
(1) Desmosomes resist mechanical stress
(2) Gap junctions allow spread of electrical signals

2. Cardiac muscle APs
a. cell depolarized by auto-rhythmic activity
b. voltage-gated Na+ channels open, Na+ → in, cell depolarized to +30 mV
c. at the peak of depolarization, Na+ channels close, voltage-gated slow Ca2+ channels open (Ca2+ flows in results in plateau, the channels are a "slow" version of the long lasting Ca2+ channels in auto-rhythmic cells)
d. at the end of the plateau, Ca2+ channels close, voltage-gated K+ channels open (K+ → out, repolarization)

3. excitation-contraction coupling
a. AP travels down T tubules, voltage-gated Ca2+ channels open, Ca2+ → in from ECF
b. Ca2+ influx triggers further release of Ca2+ from sarcoplasmic reticulum
c. Ca2+ binds with troponin-tropomyosin complex, cross bridge cycling occurs
d. Ca2+ actively pumped back to ECF and SR
e. extent of cross bridge cycling depends on amount of Ca2+ that enters cytosol (unlike in skeletal muscle, where enough Ca2+ for maximum contraction is always released)
4. long contractions due to lots of Ca2+ from ECF and SR
5. long refractory period
a. due to inactivation of Na+ channels during plateau
b. tetanus does not occur (no summation)
c. keeps cardiac functioning efficient

• Cardiac cycle
- systole (contraction) and diastole (relaxation) occur in atria and ventricles - most often refers to ventricles
1. diastole
a. AV valves open
b. blood fills ventricles (amount at end of diastole is called end-diastolic volume, EDV is about 135 ml)
c. atria contract
2. systole
a. ventricles contract, closing AV valves
b. semilunar valves open
c. blood ejected (amount of blood still in ventricles is end-systolic volume, ESV is about 65 ml)

• Cardiac output (CO)
- CO is the volume of blood pumped by each ventricle in one minute (left and right normally equal)
CO = heart rate (beats/min) x stroke volume (ml/beat)
1. typically about 5 liters/min at rest (entire blood volume)
2. can increase to 20-25 l/min. difference between CO at rest and maximum CO is cardiac reserve

Factors influencing heart rate (HR)

1. parasympathetic effects (ACh, decrease HR)
a. primarily supplies atria (SA and AV nodes)
b. acts on SA node
(1) increases PK+ by slowing K+ channel closure, resulting in hyperpolarization, takes longer to reach threshold
c. also increases PK+ at AV node, lengthening delay
d. acts on atrial contractile cells, weakening contraction
(1) shortens the plateau phase, by decreasing Ca2+ influx
e. little effect on strength of ventricular contraction

2. sympathetic effects (NE and E, increase HR)
a. acts on SA node
(1) decreases PK+ by speeding up inactivation of K+ channels, resulting in "hypo polarization", threshold reached more quickly
b. reduces delay at AV node, probably by enhancing influx of Ca2+
c. speeds spread of AP throughout nodal system by enhancing Ca2+ influx

Factors influencing stroke volume (SV)
1. intrinsic control
a. resting cardiac muscle is at less than optimal length - stretching fibers by increasing EDV (increasing venous return) results in a more forceful contraction (increases SV)
b. important to match SV to venous return
(1) Automatically equalizes flow through pulmonary and systemic circuits (blood does not "back up")
2. increasing contractility (increasing SV)
a. sympathetic stimulation increases Ca2+ influx (atria and ventricles) resulting in greater cross bridge cycling and more forceful contraction
(1) also enhances venous return by constricting veins, squeezing more blood toward heart

• Coronary circulation
- Heart receives O2 and nutrients from coronary arteries branching off the aorta (coronary veins empty into right atrium)
1. Most blood flow occurs during diastole
2. Uses oxidative phosphorylation(uses mostly free fatty acids, but can use glucose)
3. During exercise, increased demands for O2 met by vasodilation (dilation of blood vessels)
a. adenosine (formed from breaking down ATP) released from muscle cells
(1) During O2 deficit
(2) During increased activity (using more ATP)
(3) Induces dilation of vessels (smooth muscle relaxes)

• Homeostatic imbalances
- Heart failure (heart can't keep up with demands of body)
1. Two main reasons
a. damage from heart attack or impaired circulation to cardiac muscle
b. prolonged pumping against increased afterload (stenotic semilunar valve or chronically elevated blood pressure)
2. Contractility of heart is decreased
a. SV decreased for a given EDV (Frank-Starling curve shifts down to right)

b. body compensates with increased sympathetic activity and retaining salt and water to expand blood volume and increase EDV
c. eventually body can't compensate
(1) Backward failure - blood pools in venous system (congestive heart failure)
(2) Forward failure - inadequate supplies to tissues
(3) left-sided failure worse
backward - fluid accumulates in lungs (pulmonary edema), forward – kidney function depressed and they retain even more water and salt

Atherosclerosis and its effects on the heart (called coronary artery disease when it occurs in coronary vessels)
1. Complications of disease are leading cause of death in US
2. Can lead to myocardial ischemia (insufficient O2 to heart)

Factors causing ischemia:
a. vascular spasm - decreased O2 triggers platelet activating factor (PAF) release from vessels, causing spastic constriction, further decreasing O2 to heart
b. atherosclerotic plaques - accumulation of lipid and overgrown smooth muscle reduce blood flow, in later stages Ca2+ accumulates ("hardening of the arteries")
c. thromboembolism - plaque breaks through lining of blood vessels and platelets form abnormal clots (thrombus) if clot breaks free (embolus) it can block small vessels (complete blockage causes myocardial infarction - heart attack)
3. Transient ischemia causes angina pectoris (chest pain)
a. usually during physical or emotional stress
b. may be due to accumulation of lactic acid as heart makes ATP anaerobically
4. risk factors - genetics, obesity, old age, smoking, high blood pressure, diabetes, lack of exercise, nervous tension, high blood cholesterol levels
5. Specific indicators of risk
a. high blood levels of homocysteine (promotes smooth muscle growth and causes oxidation)
b. high blood levels of C-reactive protein (an indicator of inflammation)
6. Cholesterol
a. carried in blood as lipoprotein complexes
b. low density lipoproteins (LDL) transport to cells ("bad cholesterol")
c. high density lipoproteins (HDL) transport to liver and some excreted from body ("good cholesterol")
d. cholesterol needed for cell membranes, hormones, bile salts - but high levels of LDL associated with atherosclerosis

Blood Vessels and Blood Pressure

- Exchanges between blood and tissue cells take place through the interstitial fluid
- all organs receive fresh blood (amount to each organ adjusted based on need)
- the blood is constantly "reconditioned" so its composition is relatively constant
1. Reconditioning organs receive a high proportion of cardiac output (digestive system, kidneys)
- Organization "vascular tree"
1. Arteries (carries blood from heart toward tissues)
2. Arterioles (adjusts blood flow to tissues)
3. Capillaries (exchanges made)
4. Venules (carries blood to veins)
5. Veins (carries blood from tissues toward heart)
- flow rate (volume of blood passing through a particular segment of vascular tree per unit time)

1. Directly proportional to pressure gradient
2. Inversely proportional to resistance (hindrance to flow from friction)
*a. vessel radius - smaller vessels → more resistance
b. viscosity of blood - thicker blood → more resistance
c. length of vessel - longer vessel → more resistance

• Arteries
- Fast transport
1. Large
- Pressure reservoir
1. Walls contain endothelial lining surrounded by smooth muscle and connective tissue fibers (collagen and elastin), which allow walls to stretch to contain pumped blood
2. When the heart is relaxing the arteries recoil and keep the blood flowing
- Arterial pressure fluctuates
1. Blood pressure is the force exerted by blood on vessel walls
a. depends on blood volume and distensibility of vessel
b. systolic pressure is the maximum pressure during systole (should be <120 mmHg)
c. diastolic pressure is the pressure during diastole (should be <80 mmHg)
d. systolic - diastolic = pulse pressure (the pressure felt in arteries near the body surface)
2. Mean arterial pressure is the main driving force for blood flow to tissues
MAP = diastolic pressure + 1/3 pulse pressure

• Arterioles
- major resistance vessels (small radii)
- radii adjusted by smooth muscle
1. Vasoconstriction and vasodilation (narrowing and enlarging)
2. Normally partially constricted (vascular tone)
a. myogenic activity
b. sympathetic innervation
- local control of arteriolar radius matches blood flow to tissue needs

1. Chemical influences

a. metabolic factors causing vasodilation
(1) Decreased O2
(2) Increased CO2
(3) increased acid (from CO2 and lactic acid)
(4) Increased K+ (APs outpacing Na+-K+ pump in brain or skeletal muscle)
(5) Increased osmolarity (more solutes formed during times of elevated metabolism)
(6) release of adenosine (in cardiac muscle)
(7) Release of prostaglandins (not well understood)

b. local metabolic factors probably act by causing release of chemical mediators from endothelial cells (called vasoactive mediators), e.g.,
(1) endothelial-derived relaxing factor (EDRF), also known as nitric oxide (NO) inhibits Ca2+ influx in smooth muscle - vasodilator
(2) Endothelin – vasoconstrictor

2. Physical influences
a. application of heat (vasodilation) or cold (vasoconstriction)
b. myogenic responses to stretch (vasoactive substances probably contribute)
(1) Tone increases in response to increased stretch (resists stretch) -important to keep flow to tissues constant as MAP changes (pressure autoregulation)
(2) Tone decreases in response to decreased stretch - important in restoring flow to previously deprived tissue (reactive hyperemia)
- extrinsic control of arteriolar radius helps regulate arterial BP
1. Sympathetic activity produces generalized vasoconstriction, increasing resistance and BP (don't vaso-constrict brain)
MAP = CO x total peripheral resistance
a. NE at α receptors causes vasoconstriction
b. E at β2 receptors causes vasodilation (heart, skeletal muscles)
2. Other hormones
a. vasopressin - important in fluid balance, vasoconstrictor
b. angiotensin II - important in fluid balance, vasoconstrictor
3. **local control mechanisms** can override

• Capillaries
- Responsible for exchanges between plasma and interstitial fluid (solute exchange mainly by diffusion)
1. thin-walled, narrow vessels
2. Highly branched
3. Blood flows slowly through individual vessels
4. Lipid soluble substances pass through cells (O2, CO2)
5. Water soluble substances pass through pores (ions, glucose, amino acids)
6. Some vesicular transport (hormones)
7. Degree of "leakiness" may change due to actin-myosin in capillary cells- precapillary sphincters
1. Rings of smooth muscle can block flow through capillaries in less active tissues
a. sensitive to local metabolic changes
- fluid shifts and bulk flow
1. important in distribution of fluids between plasma and interstitial fluid
a. fluid (not proteins) pushed out through pores at arteriolar end (ultrafiltration)
(1) Capillary blood pressure exceeds plasma-colloid osmotic pressure (oncotic pressure - force drawing water toward plasma proteins)
b. fluid reabsorbed at venular end
(1) Capillary BP lower than plasma-colloid osmotic pressure
2. and, ultrafiltration occurs in open capillaries, reabsorption in closed capillaries
3. Fluid shifts occur as needed
a. loss of blood, shifts to plasma
b. excess fluid in blood, shifts to interstitial fluid
c. keeps plasma volume relatively constant (temporary)
- extra fluid picked up by lymph vessels (initial lymphatics) in capillary beds
1. Large valve-like openings allow in fluid and any leaked proteins (lymph)
2. Around larger lymph vessels, surrounding smooth muscle pushes fluid to larger and larger vessels, which contain one-way valves
3. Skeletal muscles help squeeze lymph through
4. Eventually empty into thoracic veins
- Edema (accumulation of excess interstitial fluid, reduces exchange between blood and cells)
1. low plasma proteins

a. more fluid filtered out, less reabsorbed
b. kidney or liver disease, diet deficient in protein, burns
2. increased permeability of capillaries
a. loss of proteins
b. injuries, allergic responses
3. Increased venous pressure
a. also increased capillary pressure
b. congestive heart failure, pregnancy
4. Blocked lymph vessels
a. lymph node removal, parasite

• Veins
- Transport back to heart- blood reservoir
1. stretchable with little recoil
2. Venous storage decreases effective circulating volume
a. can be altered based on need

Factors influencing venous return
1. Sympathetic activity
a. vasoconstriction drives more blood toward heart
b. still low resistance vessels (large radius)
2. Skeletal muscle activity
a. acts as pump
3. Valves
a. one-way valves every few centimeters allow flow toward heart only
4. Respiratory activity
a. acts as pump due to decreased pressure in thoracic cavity
5. Cardiac suction
a. blood "sucked in" as ventricles relax

• Blood Pressure
- MAP is main driving force
1. high enough to get blood to tissues
2. not too high or extra work for heart, increased risk of vascular damage
- short term regulation (seconds)
1. baroreceptor reflex
a. pressure sensors in carotid sinus and aortic arch sense changes in MAP and pulse pressure
(1) rate of firing increases with increasing pressure, decreases with decreasing pressure
b. integrating center is cardiovascular control center in medulla of brain stem
(1) Adjusts sympathetic/parasympathetic activity
- long term regulation (minutes to days)
1. Adjustments in total blood volume via salt/water balance - urinary system and thirst
(Volume receptors in left atrium, osmoreceptors in hypothalamus)

Other contributing factors
1. Chemoreceptors in carotid and aortic arteries
a. sense low O2 and high acid
(1) Increase respiratory activity but also increase BP (signals CV center)
2. Cerebral cortex - hypothalamic pathway influence emotional/behavioral responses

3. Exercise
a. may be unidentified "exercise centers"
4. Hypothalamic temperature regulation
a. overrides baroreceptor reflex for skin vessels
5. Vasoactive substances from endothelial cells
6. Neurotransmitter effects in brain (poorly understood)

Hypertension
1. BP above 140/90 (high-normal is 135/85)
2. Cause identified in about 10% of cases (secondary hypertension)
a. include atherosclerosis, endocrine disorders, nervous system defects

3. Primary hypertension causes may include...
a. kidney salt regulation
b. excessive salt intake
c. diet low in fruit, vegetables, dairy (low in K+ and Ca2+)
d. defects in Na+-K+ pumps
e. abnormal local vasoactive substances
f. excess vasopressin

4. Baroreceptors reset at higher level

5. stresses heart and blood vessels
a. congestive heart failure from increased afterload
b. rupture of vessels - stroke, heart attack
c. damage to vessels may cause accumulation of lipids and lead to atherosclerosis
d. kidney failure due to damaged vessels
e. loss of vision from damaged vessels

Hypotension
1. BP below 100/60
2. Transient
a. standing up - gravity decreases venous return
b. in some people emotional stress decreases sympathetic activity (may be adaptive)
3. When blood flow to tissues inadequate its called circulatory shock
a. many causes
(1) Loss of blood volume (hemorrhage, diarrhea)
(2) Weakened heart
(3) Vasodilation (septic or anaphylactic)
(4) Loss of sympathetic tone (extreme pain as in crushing injury)
b. may become irreversible