ANP1105B - Carnegie
Notes - Topic 4.1,2,3: Blood, The Cardiovascular System, and Blood Vessels + Hemodynamics

4.1. Blood

4.1.1. Describe the composition of blood (plasma & formed elements)

4.1.1.1. List the physical characteristics of blood and the types of formed elements found in blood

Blood Components I

- Only FLUID tissue in body (formed elements suspended in plasma)
    - Formed elements:
        - Erythrocytes or Red Blood Cells
            - Everything but with a nucleus, and even ejects most organelles later in life cycle
        - Leucocytes or White Blood Cells
            - Lmao?
        - Platelets
            - Minimal organelles and chemicals
            - Supports blood clotting

Blood Components II

- Plasma
    - 55% of whole blood
    - Least dense component
- Buffy Coat
    - < 1% of whole blood
    - Leukocytes and platelets
- Erythrocytes
    - 45% of whole blood (hematocrit)
    - Most dense component

Physical characteristics

- Color is scarlet (oxygen-rich) to dark red (oxygen-poor)
    - State of oxygenation of hemoglobin
- More dense, more viscous than water
- pH = 7.35 to 7.45
    - Blood pH is regulated, below 7.3 would be in acidosis for the human body, over 7.5 body would be in alkalosis
- 8% body weight (5-6 L in males, 4 to 5 L in females)

4.1.1.2. List and briefly describe the 3 main functions associated with blood and the circulatory system

Functions

- 1. Distribution
    - Oxygen and nutrients: carries them to tissues
    - Metabolic wastes: urea to kidneys, CO2
    - Hormones
- 2. Regulation
    - Body temperature: distribution, conservation, dissipation
    - pH in body tissues
    - Adequate fluid volume
- 3. Protection
    - Platelets. Plasma proteins, blood clotting
    - Antibodies, complements WBCs

4.1.1.3. List the physical characteristics of plasma

Blood Plasma

- Straw-colored
- 90% water and many solutes, with electrolytes outnumbering the other solutes
- Plasma proteins
    - Produced in liver (except gamma-globulins)
    - Functional proteins which remain in blood
        - *Albumin*
            - 60% of all plasma proteins
            - Carrier of various molecules, important blood buffer; major osmotic protein
            - Blood constantly adjusted to keep its composition, pH within normal range

4.1.2. Erythrocytes: describe their structure, function and life cycle

4.1.2.1. Describe the functional anatomy of an erythrocyte; show the structural organization of the hemoglobin molecule

Erythrocytes (RBCs) and Structural Organization of Hemoglobin

Red Blood Cells (RBCs)

- ~7.5 μm in diameter; biconcave discs (no nucleus)
- "bags of hemoglobin"
    - Other proteins maintain plasma membrane, and regulate cell shape
        - *Spectrin* protein helps maintain cell shape
- Function
    - RBCs transport O2 from lungs to tissues
    - Also transport 20% of CO2 back to lungs
- Specialized Characteristics that Optimize Function:
    - i) Small size & biconcave shape, large SA to V ratio
    - ii) >97% non-water composition is hemoglobin
    - iii) No mitochondria; generate ATP anaerobically
- Viscosity
    - Directly related to RBC count in blood
    - Rate of blood flow inversely affected by RBC count

Hemoglobin (Hb)

- Globin = 4 polypeptide chains (2α & 2β) (tetramer)
    - 4 Fe-containing central heme groups
    - Each Fe can reversibly bind one molecule of oxygen
        - 4 per Hb molecule
        - Each RBC contains 250 million Hb molecules!!
- Hb contained in Erythrocytes
    - Keeps it from fragmenting and being lost
    - Keeps it from contributing directly to osmotic pressure & blood viscosity
        - When in cell, it does not contribute to the osmolarity of the blood
- oxyHb a different shape and colour than deoxyHb
- O2 combines with heme group
- CO2 combines with globin part called *carbaminohemoglobin*

4.1.2.2. Describe the process of erythropoiesis, its regulation and the dietary requirements associated with the daily production of erythrocytes; outline the life cycle of an erythrocyte

Define Erythropoiesis

- Hematopoiesis = production of blood cells
    - Erythropoiesis = production of red blood cells (RBCs)

Hematopoietic Stem Cells

- Stem cell for all formed elements, residing in the *red bone marrow*
    - Cells become committed to a particular pathway
        - Sometimes called *hemocytoblasts*

Erythropoiesis Phases

- Begins when a hematopoietic stem cell descendant called the *myeloid stem cell* transforms into a *proerythroblas*t
    - Phase 1: Ribosome Synthesis
        - Proerythrxxoblasts give rise to *basophilic erythroblasts* that produce huge numbers of ribosomes, all the while dividing many times
    - Phase 2: Hemoglobin Accumulation
        - Hemoglobin is synthesized and iron accumulates
        - The basophilic erythroblast transforms into a polychromatic erythroblast and then a orthochromatic erythroblast
    - Phase 3: Ejection of Nucleus
        - When having accumulated most of its hemoglobin, it ejects most of its organelles, and the nucleus degenerates and is pinched off
        - Result is the reticulocyte, still containing a scant network of ribosomes

Regulation of Erythropoiesis

- Balance between RBC production and destruction
    - Too few erythrocytes leads to *tissue hypoxia* (oxygen deprivation) and anemia
    - Too many leads to *undesirable viscosity* of the blood and polycythemia
        - New cells are produced at a rate of *more than 2 million per second*
            - This process is controlled hormonally and by adequate supplies of iron, amino acids, and certain B vitamins

Hormonal Controls

- Erythropoietin (EPO)
    - A glycoprotein hormone produced in the kidney and liver
        - Always some EPO in the blood; additional is released if hypoxia is occurring, due to
            - i) hemorrhage/excess RBC destruction
            - ii) high altitude or pneumonia or high demand
            - iii) insufficient Hb per RBC (as in iron deficiency)
    - Monitoring Demand for EPO
        - Occurring hypoxia in certain kidney cells oxygen-sensitive enzymes are unable to break down and degrade *hypoxia-inducing factor* (HIF)
            - HIF accumulates, accelerating the synthesis and release of EPO

Dietary Requirements

- Absorption of dietary iron controlled by body's storage levels
    - Approximately 65% of iron already in hemoglobin
        - Rest is stored in liver, spleen, and bone marrow
            - Stored as *ferritin* or *hemosiderin* as Fe^{2+} and Fe^{3+} are toxic
            - Iron transported in blood loosely bound to *transferrin*
        - Small loss of iron daily in feces, urine, or sweat
            - Avg daily loss =1.7 mg (♀), 0.9 mg (♂)
        - Essentials
            - Vitamin B12 & folic acid are essential to DNA synthesis

Fate and Destruction of Erythrocytes

- Mature erythrocytes become rigid and fragile with time, Hb begins to degenerate
- Usual useful lifespan lasts 100 to 120 days
    - Becomes trapped and fragments in smaller circulatory channels, particularly those of the spleen, thus *spleen = RBC graveyard*
        - Macrophages engulf and destroy aging RBCs
            - Heme is split off from the globin
                - Globin amino acids are partly recycled
            - Iron core is salvaged, stored for reuse
                - Heme is degraded into *bilirubin*, which is then released and binds to *albumin* for transport
                    - Liver cells pick up bilirubin and secrete it into intestine, then metabolized into *urobilinogen*
                        - Degraded pigment leaves as brown pigment called *stercobilin* in feces.

4.1.2.3. Define: anemia, polycythemia and give an example of a situation that can result in each of these conditions

Anemia

- Symptoms include being tired, pale, short of breath, chilly
    - Caused by:
        - i) Insufficient numbers of RBCs
        - ii) Decreases in Hb content
        - iii) Abnormal Hb (E.g. Sickle Cell Anemia)

Polycythemia

- The abnormal excess of erythrocytes in the blood that increases blood viscosity
    - i) Polycythemia vera
        - Bone marrow cancer characterized by dizziness and an exceptionally high RBC count; 8-11 million cells / μL, hematocrit can be as high as 80%, severely impairing circulation
    - ii) Secondary polycythemia
        - When less oxygen is available or EPO production increases, usually appearing in those at high altitudes
        - RBC count of 6-8 million cells / μL are common in such people
    - iii) Artificial polycythemia
        - Known as blood doping, where blood is drawn and stored and increased EPO response increases RBC count in body, then blood is reinfused to induce temporary polycythemia
        - Risks of stroke and heart failure due to high hematocrit and viscosity

4.1.3. Hemostasis: list the principal steps and justify the role of platelets in this process

4.1.3.1. Define platelet (thrombocyte) and summarize the main steps in platelet production

Platelets

- Cytoplasmic fragments of megakaryocytes, anucleate, containing purple staining granules, which themselves contain clotting factors & enzymes.
    - Lifespan of approximately 10 days
    - 250,000-500,000 platelets / μL blood

Developmental Pathway of Platelets

- Platelet formation regulated by thrombopoietin
- Hematopoietic stem cells are the original stem cell
- Megakaryoblast Stage I → Megakaryocyte → Stage II/III → Megakaryocyte Stage IV
    - Extends lengths into bloodflow, pinches off fragments of platelets

4.1.3.2. Define Hemostasis; list the 3 key events involved in the process and give a description of the physiological and biochemical processes occurring during each of these 3 events.

Hemostasis

- 3 Key Events
    - A. Vascular Spasms
    - B. Platelet Plug Formation
    - C. Coagulation

A. Vascular Spasms

- Vasoconstriction of vessel in response to damage
    - Triggered by damage, chemicals from endothelial cells & platelets, pain reflexes
        - Spasm response is valuable as it can significantly reduce blood loss

B. Platelet Plug Formation

- Platelets aggregate (stick together), forming a plug that temporarily seals the break
    - Platelets do not stick to each other or to the smooth endothelial linings of blood vessels
        - Intact endothelial cells release nitric oxide and a prostaglandin called prostacyclin (PGI_2), preventing aggregation in undamaged tissue
    - Exposure of collagen of damaged tissue stimulates platelets to swell, becoming spiky & sticky

- Large plasma protein called von Willebrand factor stabilizes bound platelets by forming a bridge between collagen and platelets
    - In addition, they release chemical messengers
        - ADP
            - Potent aggregating agent
            - Causes more platelets to stick to the area
        - Serotonin and thromboxane A_2
            - Enhances vascular spasms and platelet aggregation

4.1.3.3. Differentiate between the intrinsic and extrinsic pathways for the formation of prothrombin activator in terms of conditions under which each pathway would occur and the relative speed of each pathway

C. Coagulation

- Also known as blood clotting, where blood is transformed from a liquid to a gel, involving a series of substances called clotting factors or procoagulants
    - 3 Phases:
        - i) Prothrombin activator formed (RDS)
            - Two Pathways
                - Intrinsic pathway
                    - Clotting of blood outside the body or in slightly damaged vessel
                        - Slower pathway to factor X and PA
                - Extrinsic pathway
                    - Clotting of blood associated with body and blood vessel damage
                        - Release of Tissue Factor (TF)
                        - Faster pathway to factor X and PA
                            - However, limited capacity to finish the process
        - ii) Prothrombin to thrombin
            - Prothrombin activator converts into the active enzyme thrombin
        - iii) Fibrinogen molecules
            - Thrombin catalyzes the transformation of the clotting factor fibrinogen into fibrin
                - Fibrin polymerize into long insoluble strands of fibrin
                    - The fibrin strands glue the platelets together that make up the fibrin mesh
    - Note: Calcium very important and essential to blood clotting

4.1.4. Describe briefly the processes of clot retraction and fibrinolysis

Clot Retraction and Repair

- Platelet-induced process called *clot retraction* further stabilizes the clot with 30-60 min
    - They contract using contractile proteins (containing actin & myosin), exerting pull on surrounding fibrin strands
    - *Serum* squeezed from clot & ruptured edges of blood vessels pulled closer
        - Serum is plasma without the clotting factors
    - *Platelet-derived growth factor* (PDGF) released from platelets stimulates smooth muscle cells and fibroblasts to divide and rebuild the vessel wall
        - Fibroblasts form a CT patch in the injured area
            - Endothelial cells multiply to fill gap in lining (stimulated by *vascular endothelial growth factor* (VEGF))

Fibrinolysis

- Removal of clot when no longer needed
- Key fibrin-digesting enzyme is *plasmin* (precursor = plasminogen)
    - Plasminogen is activated by tPA (tissue plasminogen activator)
        - tPA is released by endothelial cells
    - Also activated by released factor XII and thrombin
- Begins within 2 days & continues until clot is dissolved

4.1.4.1. Distinguish between pro- and anti-coagulants, giving examples of each, and demonstrate an understanding of their relative roles in regulating Hemostasis in damaged and undamaged blood vessels.

Factors Limiting Clot Growth/Formation

- 2 Homeostatic Mechanisms prevent clots from becoming too large
    - i) Swift removal of coagulation factors
    - ii) Inhibition of activated clotting factors

Procoagulants

- Clot formation requires procoagulation factors at certain concentrations
- Clot will form when there are more procoagulants than anticoagulants and vice versa
    - i) Normally flowing blood washes away procoagulants
        - ii) As thrombin forms, adsorbed onto fibrin threads (limits clot size)
            - iii) *Antithrombin III* (in plasma) inactivates any escaping thrombin
                - iv) Antithrombin III & *protein C* (produced in liver) inactivate many intrinsic pathway procoagulants
                    - v) *Heparin* (contained basophils & mast cells) enhances activity of antithrombin III
                        - vi) Smooth endothelial lining of undamaged blood vessels (also endothelial-derived heparin & prostacyclin)

Anticoagulants

- As long as the endothelium is smooth and intact, platelets are prevented from clinging and piling up by anticoagulants
    - Antithrombotic substances - nitric oxide and prostacyclin - secreted by the endothelial cells normally prevent platelet adhesion
        - Additionally, vitamin E quinone is also a potent anticoagulant

4.1.4.2. Define: thrombus, embolus, thrombocytopenia

Thromboembolic conditions

- Undesirable intravascular clot formation
    - *Thrombus*:
        - Clot that develops & persists in an unbroken blood vessel - can block critical blood circulation to those tissues
    - *Embolus*:
        - A thrombus which has broken free, can get stuck in a vessel of small diameter (eg: pulmonary or cerebral emboli)

Anticoagulant Drugs

- Drugs such as synthetic tPA, streptokinase to dissolve clots
    - Aspirin:
        - Aspirin inhibits the production of prostaglandin and thromboxanes
            - Acts as an anticoagulant, blocking platelet aggregation, etc.

Bleeding Disorders

- Interference with normal clotting
    - Thrombocytopenia, liver disorders, hemophilias, etc.
        - *Thrombocytopenia*
            - Not enough platelets, causes spontaneous bleeding from small blood vessels all over the body, widespread hemorrhage
                - Platelet count < 50,000/µl
                - Whole blood transfusions provide temporary relief
        - *Impaired Liver Function*
            - Lacking certain procoagulants in the intrinsic pathway
                - E.g. hepatitis, cirrhosis
                    - (Liver is source of procoagulants)
                    - Liver disease also associated with reduced bile production; bile needed to absorb vitamin K
                        - Vitamin K need for clotting
        - *Hemophilias*
            - Hereditary bleeding disorders (X-linked conditions)
            - Both sex-linked conditions
            - Require transfusions/injections of purified clotting factors
                - Hemophilia A: Deficiency in factor VIII
                - Hemophilia B: Deficiency in factor IX

4.1.5. Differentiate among the different blood types and explain the basis of transfusion reactions

4.1.5.1. Define the components of the ABO and Rh blood group systems; describe a transfusion reaction using the terms agglutination and hemolysis

ABO Blood Groups

- The ABO blood groups are based on the presence or absence of two agglutinogens, type A and type B.
- Depending on which of these a person inherits, his or her ABO blood group will be one of the following blood types: A, B, AB, or O
    - The O blood group, which has neither agglutinogen, is the most common ABO group in North America
    - The AB blood group is the least prevalent
- Unique to this group is the presence of preformed antibodies called agglutinins
    - The agglutinins act against RBCs carrying ABO antigens not present on a person's own red blood cells

Rh Blood Groups

- There are 52 Rh agglutinogens, each of which is called an Rh factor
    - Only five, the C, D, E, c, and e antigens, are fairly common
        - Named Rh system, because one Rh antigen (agglutinogen D) was first identified in rhesus monkeys, then discovered in humans
    - About 85% of Americans are Rh+ (Rh positive), meaning that their RBCs carry the D antigen
        - As a rule, a person's ABO and Rh groups are reported together, for example O+, A+, and so on
    - Unlike the ABO system antibodies, anti-Rh antibodies do not spontaneously form in the blood of Rh- (Rh negative) individuals
        - If an Rh- person receive Rh+ blood, the immune system becomes sensitized and begins begins producing anti-Rh antibodies soon after transfusion

Transfusion Reactions

- Occurs when mismatched blood is infused, in which the recipient's plasma antibodies attack the donor's red blood cells
    - Agglutinations of foreign red blood cells, clogs small blood vessels throughout the body, then the clumped RBCs begin to rupture or are destroyed by phagocytes
        - Hb is released into the bloodstream
        - Known as hemolysis

Overall result

- i) Blocked flow to tissues
- ii) Reduced O2 -carrying ability of blood
- iii) Hb precipitates/clogs kidney tubules, can lead to possible kidney failure and death

4.2. The Heart

4.2.1. Describe the internal and external anatomy of the heart

4.2.1.1. Describe the size, location and orientation of the heart in the thoracic cavity

Internal Anatomy

- The heart is a transport system pump
    - Contains hollow blood vessels for delivery
    - Enclosed in the *mediastinum* of thorax
        - Mediastinum
            - The medial cavity of the thorax
        - Extends obliquely for 12-14 cm from second rib to fifth intercostal space
        - 2/3 of mass on left side
        - Right side lying on diaphragm
    - Towards the right shoulder = broad, flat base
        - *Apex points toward left hip*

External Anatomy

- 3 layers; pericardium, myocardium endocardium

1. Pericardium (outer layer)

- Double-walled fibroserous sac
    - *Fibrous pericardium*
        - Tough, dense connective tissue layer
            - Protects heart
            - Anchors heart to surrounding tissue
            - Prevents overfilling of heart
    - *Serous pericardium (2 layers)*
        - Thin, slippery, two-layered serous membrane which forms a closed sac around the heart
            - I. Parietal layer
                - Outer layer of serous pericardium
                - Adheres completely to the fibrous pericardium
            - II. Visceral layer
                - Inner layer of the serous pericardium
                - Covers and protects great vessels and the heart
            - Between them lies the *pericardial cavity*
                - Filled with fluid
                - Allows for a friction free environment

2. Myocardium (middle layer)
- Cardiac muscle, *myocardium* is the bulk of the heart
- Branching cardiac muscle cells arranged into bundles and the connective tissue wrappings of these bundles:
    - Reinforce myocardium internally and anchor cardiac muscle fibers
    - Provide additional support for great vessels and valves
    - Direct spread of action potentials across heart to specific pathways

3. Endocardium (inner layer)
- Layer of endothelium and CT layer on inner myocardial surface
    - Continuous with endothelium of vessels leavings and entering heart
        - Lines chambers of the heart
        - Forms surface of valves
        - Protects valves and chambers of the heart

4.2.1.3. Locate the following on diagrams that show both the external and internal anatomy of the heart: left & right atria and ventricles, aortic arch, superior and inferior venae cavae, pulmonary trunk, left & right arteries and veins, coronary sinus, atrioventricular groove, anterior-posterior interventricular sulcus, pectinate muscles, fossa ovalis, trabeculae carneae, papillary muscles

Chambers
- Includes 4 chambers:
    - Right and left atriums
    - Right and left ventricles
- The internal partition that divides the heart longitudinally is called the *interatrial septum* and the partition that divides the ventricles is called the *interventricular septum*

Superior Atria

- Atrium
    - Small, thin-walled receiving chamber, only needed to carry blood to ventricles
    - Deoxygenated: systemic blood enters *right atrium* via:
        - i. *Superior vena cava*
            - Systemic from:
                - Head, neck, upper limbs, thorax
        - ii. *Inferior vena cava*
            - Systemic from:
                - Thorax, abdomen, pelvis, lower limbs
        - iii. *Coronary sinus*
            - Systemic from:
                - From myocardium
    - Oxygenated: system blood enters *left atrium* via:
        - 4 pulmonary veins
            - 2 pulmonary veins from the right lung
            - 2 pulmonary veins from the left lung

Ventricles: Discharging chamber

- "Pumps of the heart"
- Walls much thicker (especially left ventricle)
    - *Right Ventricle*
        - Pumps blood to pulmonary trunk
    - *Left Ventricle*
        - Pumps blood to aorta
- Internals walls have muscle bundles:
    - *Trabeculae carneae*
        - Irregular ridges of muscles
        - Marks the internal walls of the ventricular chambers
    - *Papillary muscles*
        - Guy wires that anchor the valve flaps in their *closed* position

Heart Valves

- Blood flow is *unidirectional*; enforced by 4 heart valves
- Chordae tendineae and papillary muscles
    - Guy wires that anchor the valve flaps in their *closed* position

Atrioventricular Valves

- Paired between atria and the ventricles
    - i) *Tricuspid valve*
        - Right atrium to right ventricle
    - ii) *Bicuspid valve*
        - Left atrium to left ventricle

Semilunar Valves

- Paried, from ventricles to either pulmonary or systemic circuits
    - i) *Pulmonary valve*
        - Right ventricle to pulmonary artery
    - ii) *Aortic valve*
        - Left ventricle to aorta

Disorders and Workload on the Heart

- Valvular Insufficiency
    - Doesn't close completely
- Stenosis
    - Doesn't open completely

Aortic Arch

- The **aortic arch** is the portion of the main artery that bends between the ascending and descending **aorta**.
- It leaves the heart and ascends, then descends back to create the **arch.**

Superior and Inferior Venae Cavae

- The superior and inferior venae cavae are the veins in the body that carries deoxygenated blood to the right atrium of the heart.
    - Superior vena cava
        - Systemic from upper body, thorax
    - Inferior vena cava
        - Systemic from thorax, lower body

Pulmonary Trunk

- The pulmonary trunk is a major vessel of the human heart that *originates from the right ventricle*, pumping deoxygenated blood to the lungs.
    - It branches into the right and left pulmonary arteries, which lead to the lungs.

Left and Right Arteries and Veins

- Left arteries and veins
    - Arteries: aorta and aortic arch, left coronary arteries
    - Veins: left pulmonary veins from left lung
- Right arteries and veins
    - Arteries: pulmonary arteries, left coronary arteries
    - Veins: superior and inferior vena cava

Coronary Sinus

- Venous blood is collected by the *cardiac veins*, whose paths join to form an enlarged vessel called the *coronary sinus.*

Grooves

- Atrioventricular Groove
    - Also known as the coronary sulcus, it encircles the junction of atria and ventricles like a crown (*corona = crown*).
- Anterior-posterior Interventricular Groove
    - Cradles the anterior/posterior coronary arteries
        - Marks the anterior/posterior position of the septum separating the right and left ventricles.

Pectinate Muscles

- Bundles of muscle tissue that form ridges in the *anterior right atrium's walls*
- In the *left atrium*, pectinate muscles are only found in the *auricle*.

Fossa Ovalis

- A depression in the right atrium of the heart, *at the level of the interatrial septum*, the wall between right and left atrium.
- The *fossa ovalis* is the remnant of a thin fibrous sheet that *covered the foramen ovale* during fetal development.

Trabeculae Carneae

- Irregular ridges of muscles
- Marks the internal walls of the ventricular chambers

Papillary Muscles

- Guy wires that anchor the valve flaps in their *closed* position

4.2.2. Trace the pathway followed by the blood in both the pulmonary and systemic circuits

4.2.2.1. Trace the pathway followed by a red blood cell from its entry into the heart via the inferior vena cava to its exit from the heart via the aorta; this pathway should include all of the valves in the order in which they are encountered

Pathway in the Heart

- SVC, IVC and CS empty into right atrium
    - Right atrium empties into right ventricle through tricuspid valve
        - Right ventricle empties into the pulmonary trunk through semilunar valve
            - Lungs
                - Pulmonary veins empty into left atrium
                    - Left atrium empties into left ventricle through bicuspid (mitral) valve
                        - Left ventricle empties into the aorta through the aortic semilunar valve

4.2.2.2. Distinguish between the pathways followed for the pulmonary and systemic circuits in terms of oxygenation of the blood, workload and its effect on the structure of the ventricular wall

Pulmonary and Systemic Circuits

- Equal volumes are pumped into pulmonary and systemic circuits
- However, 2 ventricles have unequal workloads
    - i) Pulmonary circuit (right ventricle)
        - Short, low-pressure circulation
        - Deoxygenated
    - ii) Systemic circuit (left ventricle)
        - Long pathway, with 5x more resistance
        - Oxygenated

Coronary Circulation

- Shortest, but one of the most important circulations in body
- Right & left coronary arteries from base of aorta;
    - Encircles heart in coronary sulcus (atrioventricular groove)

4.2.3. Describe the organization of the coronary circulation

4.2.3.1. Identify the main arterial and venous components of the coronary circulation and indicate those areas of the heart which they supply or drain

Coronary Circulation

- *Shortest*, but one of the most important circulations in body
- *Right & left coronary arteries from base of aorta*; encircle heart in coronary sulcus (atrioventricular groove)

Coronary venous supply.

Begins with capillaries:

- Venous blood is collected by the *cardiac veins*
- Cardiac veins join to form an enlarged vessel called the *coronary sinus*
    - Coronary Sinus
        - Empties the blood into the right atrium
        - The coronary sinus can be obviously seen in the posterior aspect of the heart
        - Coronary Sinus is composed of 3 tributaries:
            - 1. *Great cardiac vein*
                - Found in the anterior interventricular sulcus
            - 2. *Middle cardiac vein*
                - Found in the posterior interventricular sulcus
            - 3. *Small cardiac vein*
                - Runs along the heart's right inferior margin
            - Anterior cardiac veins
                - Several anterior cardiac veins empty directly into the right atrium anteriorly

Diseases of coronary vessels

- Angina pectoris
    - Chest pains caused by lack of blood delivery to the myocardium
    - Myocardial cells are weakened by lack of O2 but do not die
- Myocardial infarction
    - Aka heart attack
    - Myocardial cells die. Damaged tissue replaced with fibrous CT

4.2.3.2. Define anastomosis and justify the presence of anastomoses in the coronary circulation

Anastomosis

- *The joining together of blood vessels to provide alternate channels* in the same organ
    - Vascular anastomoses for between arteries, veins, and between arterioles and venules, when a given artery begins to be occluded.

4.2.4. Compare the physiological properties of cardiac muscle cells with those of skeletal muscle cells

4.2.4.1. Compare and contrast cardiac versus skeletal muscle in terms of morphology, function, energy requirements and metabolism

Cardiac Muscle	Skeletal Muscle
shorter, fatter *single or double nuclei* *intercalated disks (desmosomes, gap junctions) = interdependence* *functional syncytium* *20-40% of volume is mitochondria* *myofibril diameters vary & much branching gives indistinct striations* *fewer T-tubules; less elaborate Ca^{++} delivery* *less developed sarcoplasmic reticulum* *almost exclusively aerobic metabolism* *abundance of fuel type determines fuel used*	longer, cylindrical multinucleate structural independence; motor unit grouping functional independence 2-5% of volume is mitochondria uniform myofibrils give distinct striations many T-tubules; complex Ca^{++} delivery complex sarcoplasmic reticulum readily uses anaerobic metabolism intensity determines fuel type used

4.2.4.2 describe intercalated discs and relate 2 aspects of their structure to the support of cardiac function

Intercalated Discs

- *Contains anchoring desmosomes and gap junctions*
    - i) Desmosomes
        - Prevent adjacent cells from separating during contraction/strong cell-cell adhesion during contraction
    - ii) Gap junctions
        - Allows ions to pass from cell to cell transmitting current across the entire heart
        - Electric coupling of cardiac cells therefore myocardium behaves as a single coordinated unit (*functional syncytium*).

4.2.5. Compare the electrical properties of contractile cardiac muscle cells with those of autorhythmic cardiac muscle cells

Contractile cardiac muscle cells

- Responsible for the heart's pumping activity
- Heart contraction stimulated by action potentials
    - Action potential = signal

Autorhythmic cardiac muscle cells

- Special noncontractile cells, called *pacemaker cells*
- Spontaneously depolarize
- Muscle twitch = response of Action Potential

4.2.5.1. Trace a cardiac muscle cell action potential and identify the ion movements and resultant changes in membrane potential that are responsible for phase 0 to phase 4 of this tracing

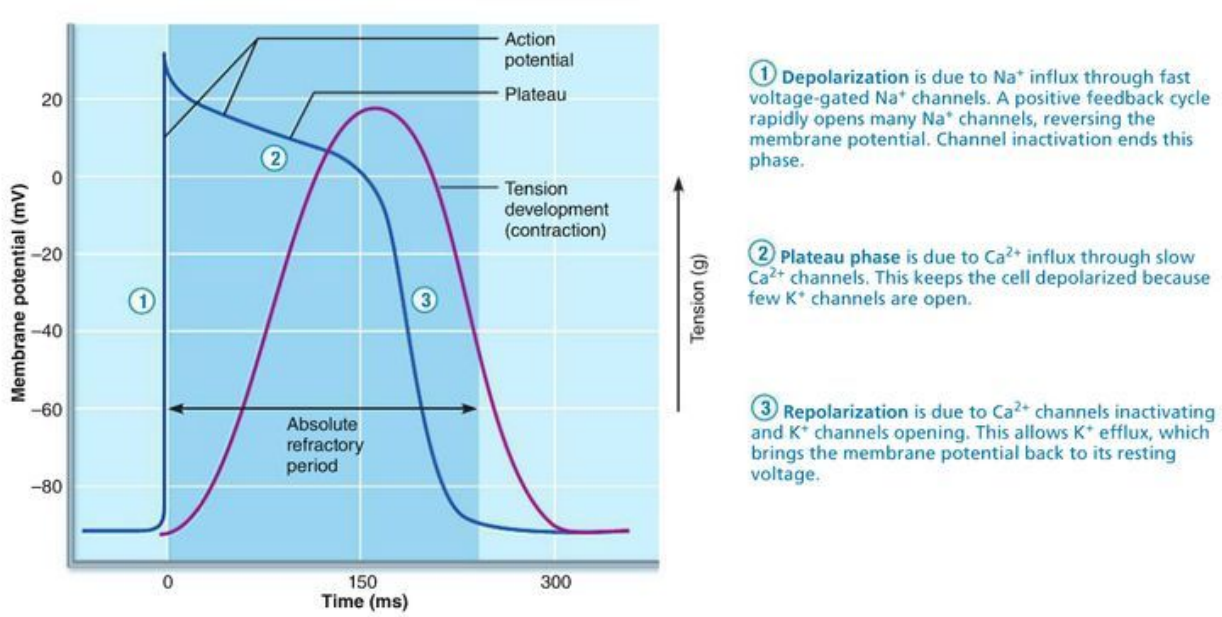


Figure 18.13 The action potential of contractile cardiac muscle cells. Relationship between the action potential, period of contraction, and absolute refractory period in a single ventricular cell.

Action Potential of Contractile Cardiac Muscles

- 1. Depolarization
  - Due to *Na+ influx* through *fast voltage-gated Na+ channels*.
  - A positive feedback cycle rapidly opens many Na+ channels, reversing the membrane potential.
  - Channel inactivation ends this phase.
- 2. Plateau Phase
  - Due to *Ca++ influx* through slow *Ca++ channels*.
  - This keeps cell depolarized because few K+ channels are open.
- 3. Repolarization
  - Due to *Ca++ channels inactivating* and *K+ channels opening*.
  - This allows *K+ efflux*, which brings the membrane potential back to its resting voltage.

4.2.5.2. Relate each of the following characteristics of cardiac muscle to the ability of the heart to function as a pump: all-or-none law; autorhythmicity of some cardiac muscle cells, duration of the absolute refractory period

Special Characteristics of Cardiac Muscles

- I. *Stimulation:*
  - *Autorhythmicity of (1%) cardiac cells*
- II. The heart contracts as a unit
  - All or none law
- III. Influx of Ca2+ from ECF trigger Ca2+ release in the SR
- IV. *Absolute refractory period*
  - *250 ms* in heart vs 1-2 ms for skeletal muscle
  - Period during AP when another AP cannot be triggered
  - *Skeletal Muscles*
    - Absolute refractory period is much shorter than contraction
      - Multiple contractions can occur and summate (tetanic contractions)
  - *Cardiac Muscles*
    - Absolute refractory period must be longer and not be tetanic
      - *Heart must relax and fill to be a pump*
      - Allows for individual contractions
- V. *Heart relies almost exclusively on aerobic respiration*

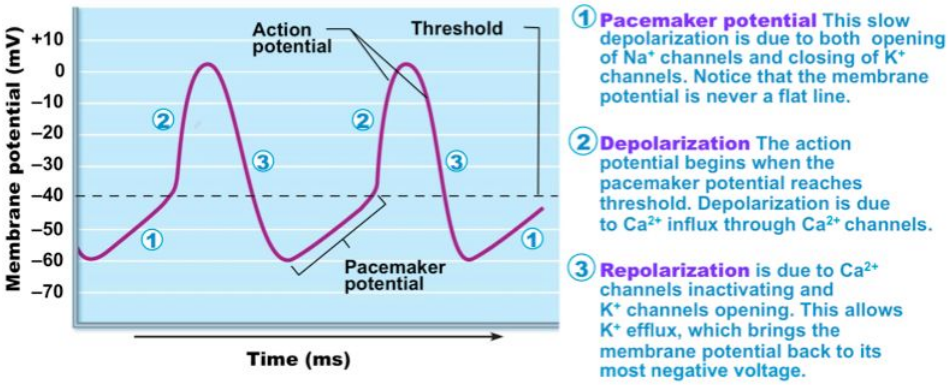
Note:

- Absolute refractory period almost = muscle twitch, allows heart to fill again
- Heart needs to be stimulated in just one location; whole organ responds
- Activation of contraction basically as in skeletal muscle

4.2.5.3 Define "autorhythmic cell; describe cardiac autorhythmic cell properties that allow them to spontaneously depolarize

Autorhythmic Cell

- Autorhythmic cardiac pacemaker cells have the ability to depolarize spontaneously and thus pace the heart. They are part of the *intrinsic conduction system*.
    - Pacemaker cells have an *unstable resting potential* that continuously depolarizes, drifting slowly towards threshold.
        - Called *pacemaker potentials* or *prepotentials*
            - Initiates the action potentials that spread down throughout the heart to trigger its rhythmic contractions



- 1. Pacemaker potential
    - Slow depolarization due to different channels
        - Na+ channels open
        - K+ channels close
- 2. Depolarization
    - Pacemaker reaches threshold → AP begins
        - Ca++ influx through Ca++ channels depolarizes
- 3. Repolarization
    - Ca++ channels inactivate
    - K+ channels open
        - K+ efflux = membrane potential back to most negative voltage

4.2.5.4. Define "sinus rhythm" and indicate why the SA node is the pacemaker of the heart

Sinus Rhythm

- The Sinoatrial Node (SA Node) typically generates impulses about 75 times every minute.
- Why the SA Node is the Pacemaker:
    - The SA Node sets the pace for the whole heart because no other region of the conduction system or myocardium has a faster depolarization rate.

4.2.6. Explain how the intrinsic conduction system of the heart allows it to function as a pump

4.2.6.1. Trace the pathway followed by a cardiac action potential from the SA node to the Purkinje fibers

Intrinsic Conduction System

- Sets the basic rhythm of the beating heart.
- It consists of autorhythmic cardiac cells that initiate and distribute impulses (action potentials) throughout the heart.

Pathway

- Cardiac pacemaker cells are found in the *sinoatrial (SA)* and *atrioventricular (AV)* nodes. Purkinje fibers can sometimes act as pacemakers.
    - 1. SA node
        - Located in the right atrial wall, just below the entrance of the superior vena cava
        - SA node sets the pace for the whole heart
            - Fastest depolarization rate
                - Therefore *sinus rhythm* determines heart rate
    - 2. AV node
        - SA node depolarizes via *internodal pathway* to the AV node
        - Located below the interatrial septum, before the tricuspid valve
        - *Impulse pauses for 0.1 seconds*
            - Allows atria to respond and complete contraction before ventricles contract
    - 3. AV bundle
        - Found in the superior part of the interventricular septum
        - AV bundle is the *only* electrical connection between adjacent atria and ventricles
        - *Fibrous cardiac skeleton is nonconducting and insulates* the rest of the AV junction
    - 4. Right and left bundle branches
        - AV bundle splits into right and left bundle branches
            - Bundle branches course along the interventricular septum toward the *heart apex*
    - 5. Subendocardial conducting network
        - *Purkinje fibers*
        - Depolarization (nerve impulses) on ventricles of the the heart
            - Causes contractions and pumping of the blood either to the lungs or the body

4.2.6.2. Indicate the site of the bottleneck in this pathway and its relevance to the ability of the heart to function as a pump

Bottleneck

- From atrium to ventricles
    - Only one pathway from atria to ventricle
        - 1. Atria contracts first to fill ventricles
        - 2. Ventricles contracts and pushes blood out
    - *0.22 sec (220 msec) from initiation at SA node to depolarization of last of ventricular cells*

4.2.6.3. Delineate the extrinsic innervation of the heart and contrast the influences of the parasympathetic versus the sympathetic nervous systems on heart rate

Extrinsic Innervation of the heart

- Rate of SA node depolarization regulated by autonomic nervous system
    - Parasympathetic NS
        - *Decreases diastolic depolarization rate*
        - Slows the heart ("the breaks")
        - Under resting conditions, tonic parasympathetic output have a *dampening* (less strong/reduced) effect on heart rate.
    - Sympathetic NS
        - *Increases depolarization and repolarization rates*
        - Increases the heart rate and force of heartbeat ("the accelerator")
- Bradycardia
    - Slow/decrease heart rate
- Tachycardia
    - Fast/increased heart rate
- Sinus rhythm
    - SA node sets the pace of the whole heart
        - Determines heart rate. The Sinoatrial Node (SA Node) typically generates impulses about 75 times every minute.

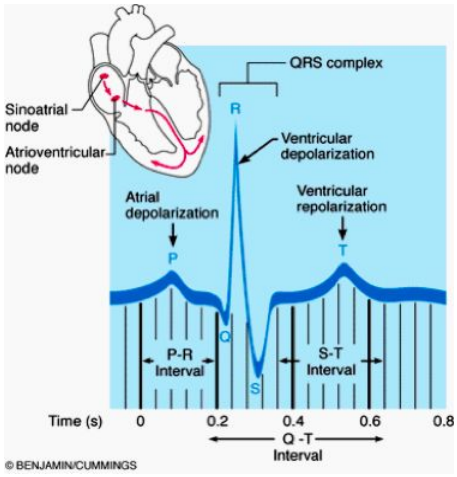
4.2.7. Explain what is an ECG tracing and the nature of the information it is providing

Electrocardiogram (ECG)

- Records electrical changes during heart activity.
- Relies on conductile activity of body fluids.

4.2.7.1. Identify the P wave, QRS complex & T wave on a normal electrocardiogram (ECG) tracing

4.2.7.2. Specify the electrical information conveyed by each component of an ECG tracing and the inferences that are made regarding cardiac muscle contraction



The P wave, QRS complex and T wave.

- i) *P-wave = atrial depolarization*
  - Initiated by the SA node
  - Atrial repolarization is not detected
- ii) *QRS complex = ventricular depolarization*
  - Proceeds in ventricular contraction
  - Begins at apex
- iii) *T-wave = ventricular repolarization*
  - Slower than depolarization
  - Lower amplitude
  - Begins at apex

Note:

- ECG records only voltage (current flow) and time; shows only electrical events, but from these can deduce contractile events

4.2.7.3. Show how the ECG tracing would be altered in the event of a nonfunctional SA node, second degree heart block and ventricular fibrillation

Normal and Abnormal Activation of the Heart

a) Sinus rhythm
- Contains P wave, QRS complex and T wave

b) Nonfunctional SA node
- No P wave present

c) 2nd degree heart block
- More P waves
  - Because AV node fails to conduct some SA node impulses.

d) Ventricular fibrillation
- Quivering heart

4.2.8. Explain the events occurring during each phase of the cardiac cycle

4.2.8.1. Describe the pressure changes that are responsible for valve opening and closing and link these pressure changes with resultant volume changes during the cardiac cycle

The Cardiac Cycle

- The cycle
    - *Atrial systole + diastole → ventricular systole + diastole*
        - **Systole**
            - **Contraction of heart**, pumps blood OUT
        - **Diastole**
            - **Relaxation of heart**, filling of blood IN
    - Start = mid to late diastole
        - 1. *Period of ventricular filling*
            - Pressures are low, however $P_{atria} > P_{ventricles}$
            - AV valves are open
            - SL valves are closed
        - *After 70% ventricular filling, AV valves begin to close*
            - P wave and atrial systole begins
            - Atrial pressure increases and final 30% of blood enters ventricles
                - End diastolic volume (EDV)
    - Ventricular Systole (QRS and T)
        - *Ventricles begins to contract*
            - 2a. Increase pressure *closes AV valves*
                - Periods of isovolumetric contractions
            - 2b. Increased pressure *opens SL valves*
                - Ventricular ejection phase
                    - (Aortic pressure up to 120 mmHg)
    - Isovolumetric Relaxation: Early Diastole
        - 3. *Ventricles relax*
            - Pressure decreases rapidly
                - *Backflow of aortic/pulmonary blood closes SL valves* (*dicrotic notch*). Ventricles a closed system
                    - Known as isovolumetric relaxation
- Time Needed for Cardiac Cycle Phases
    - 75 beats per minute. *Thus each cycle = 0.8 seconds*
            - Atrial systole = 0.1 sec
            - Ventricular systole = 0.3 sec
            - Quiescent period = 0.4 sec

4.2.8.2. Demonstrate your understanding of the following terms when outlining a single cardiac cycle: systole, diastole, isovolumetric contraction, isovolumetric relaxation, dicrotic notch

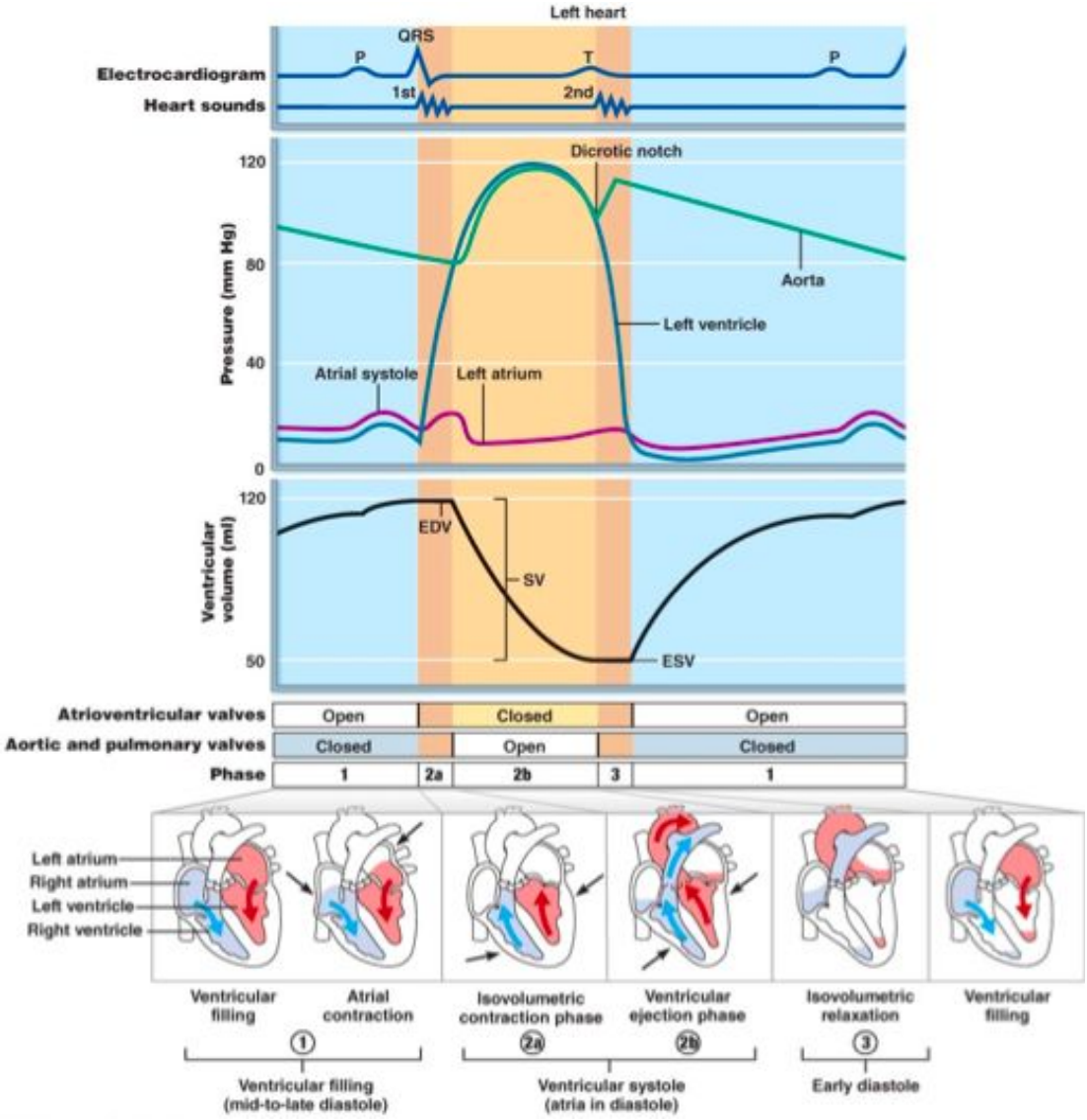


*Diagram in reference to notes above.

In summary:

- 1. *Ventricular filling*
    - Atria empty into ventricles
- 2. *Ventricular systole*
    - 2a. Isovolumetric contraction phase
    - 2b. Ventricular ejection phase
- 3. *Ventricular relaxation*
    - Note that chambers are not fully emptied

4.2.8.3. Indicate the physiological significance of the first and second heart sounds

Heart Sounds

- 2 distinguishable sounds
    - First heart sounds
        - *Closure of AV valves = beginning of ventricular systole*
    - Second heart sounds
        - *Closure of SL valves = end of ventricular systole*
- Heart sounds due to vibrations of heart/chest due to valve closure

4.2.8.4. Describe 2 physiological causes for heart murmurs

Heart Murmurs

- Due to *valvular obstruction*
    - High velocity jet of blood through narrow opening
    - Higher pitched sound
- Due to *valvular insufficiency*
    - Leakage of blood back
    - Causes sounds when there should be silence

4.2.9. Define cardiac output in terms of heart rate and stroke volume

4.2.9.1. Be aware of the average cardiac output for a resting, healthy male

4.2.9.2. Express stroke volume as a function of end diastolic and end systolic volumes

Define Cardiac Output

- Amount of blood pumped from *left ventricle into the aorta per minute*
    - Average Cardiac Output (CO) for resting, healthy male is 5L/min
- Calculation
    - Stroke Volume SV = EDV - ESV
        - CO = Heart Rate HR x Stroke Volume SV
            - *CO = cardiac output*
            - *HR = heart rate*
            - *SV = stroke volume*

4.2.9.3. Indicate the influences of exercise on heart rate and stroke volume

Influences of exercise: CO and increase 4-5 times in a fit person, can increase 7 times in a runner

4.2.10. Describe in detail the mechanisms for the regulation of heart rate and stroke volume

4.2.10.1. Delineate the effects of each of the following on the rate of SA node depolarization: autonomic nervous system (which branch dominant under resting conditions?), adrenal medulla-derived epinephrine, plasma electrolytes (Ca++, Na+ , K+ , H+), body temperature

Mechanisms for the Regulation of HR and SV

- Heart rate is determined by rate of spontaneous depolarization of SA node:
    - *Autonomic fibers innervating SA node*
    - *Circulating hormones (eg: epinephrine)*
    - *Plasma electrolyte concentration (Ca++, Na+ , K+ , H+)*
    - *Body temperature (useful in surgery)*
- Norepinephrine
    - *Increases rate of spontaneous depolarization heart rate is increased*
- ACh
    - *Decreases rate of spontaneous depolarization*
        - (hyperpolarizes pacemaker cells)
- Resting conditions
    - Parasympathetic is dominant (vagal tone)

4.2.10.2. Apply the Frank Starling Law of the Heart to the intrinsic regulation of stroke volume (define preload)

Frank Starling Law of the Heart

- *Preload = Frank Starling Law*
    - *Within defined limits, the heart will pump whatever volume of blood it receives*
    - Over a fairly wide range, there is a *proportional relationship between EDV and stroke volume*
    - Cardiac muscle has optimal length for contraction (= length-tension relationship); resting = shorter than optimal length!
    - Each ventricle regulated independently and beat-to-beat: FS mechanism ensures that each ventricle pumps same volume over a period of time

4.2.10.3. Define afterload and describe its influence on stroke volume

Afterload

- *Pressure that ventricles must overcome to force open valves & eject blood from heart*
    - Healthy: ~80 mm in aorta; 10 mm in pulmonary trunk »» not a major determinant of SV
    - Hypertension reduces ability of ventricles to eject blood

4.2.10.4. Describe two types of extrinsic influences on stroke volume

Extrinsic Influences on Stroke Volume

- Factors outside heart which change vigour of contraction without changing EDV = change in contractility
- Not due to greater initial fiber length but involves change in strength of contraction due to increased Ca++ influx
    - (i) *sympathetic stimulation:* increases rate of contraction & relaxation
    - (ii) *drugs such as digoxin*: increase heart contractility
    - (iii) *parasympathetic ns*: antagonizes sympathetic stimulation

4.3. Blood vessels and hemodynamics

4.3.1. Compare and contrast the structure of the walls of arteries, capillaries and veins

4.3.1.1. Define arteries and veins in terms of direction of blood flow

Arteries, Capillaries, and Veins

- *Arteries carry blood away from the heart*
    - Branch, diverge, or fork
- *Veins carry blood toward the heart*
    - Join, merge, and converge
- *Only capillaries directly serve cells*
    - Only ones to have intimate contact with tissue cells

4.3.1.2. From inside to outside, list the 3 tunics of blood vessels and briefly describe their structural composition; indicate what blood vessels would have fewer than these 3 layers in their walls

Structure of Blood Vessel Walls

- The walls of all blood vessels, except the very smallest, have three distinct layers, or *tunics*, that surround the a central blood containing space, the *lumen*.
    - ***Tunica intima***
        - Innermost tunic
        - Contains the endothelium, the ***simple squamous epithelium***
            - In vessels larger than 1 mm in diameter, a ***subendothelial layer*** supports the endothelium.
    - ***Tunica media***
        - Middle tunic
        - Circularly arranged ***smooth muscle cells*** and ***sheets of elastin***.
        - The activity of the smooth muscle is regulated by ***sympathetic vasomotor nerve fibers*** of the *autonomic nervous system (**ANS**)*.
            - Regulation causes either ***vasoconstriction*** or ***vasodilation***.
                - Critical in regulating circulatory dynamics.
    - ***Tunica externa***
        - Outermost tunic
        - Infiltrated with ***nerve fibers***, ***lymphatic vessels***, and in larger veins a ***network of elastic fibers***.
        - Composed largely of loosely woven ***collagen fibers*** that:
            - Protect and reinforce the vessel
            - Anchor it to surrounding structures
        - In larger vessels:
            - Contains a system of **tiny blood vessels** called the ***vasa vasorum***
                - *Nourishes the external tissues of the wall*
                    - Internal tissues are nourished directly

4.3.2. Compare the 3 types of arterial vessels

4.3.2.1. Distinguish between elastic (conducting) and muscular (distributing) arteries

4.3.2.2. Define and briefly describe the anatomy of arterioles

3 Types of Arterial Vessels

- *1.* ***Elastic (Conducting) Arteries***
    - Thick-walled, large-diameter arteries near heart
    - *Highest proportion of elastin smooth* out pressure fluctuations;
        - Recoil helps maintain pressure & flow of blood
- *2.* ***Muscular (Distributing) Arteries***
    - Delivers blood to specific organs (0.3mm-1 cm diameter)
    - More *smooth muscle* vs. *elastin*
        - Active in vasoconstriction and less capable of stretching
- *3.* ***Arterioles***
    - *Tunica media* of primarily smooth muscle
    - A *single layer* in smallest arterioles
    - Arterioles determine which capillary beds flushed, minute-to-minute
        - *10 um to 0.3 mm in diameter*

4.3.3. Define "microcirculation" and compare the 3 types of capillaries in terms of structure, permeability and localization

4.3.3.1. Define/describe the following terms/structures: microcirculation, vascular shunt, terminal arteriole, metarteriole, thoroughfare channel, precapillary sphincter, postcapillary venule

4.3.3.2. List the 3 types of capillaries and give examples of tissues in which you would expect to find each type of capillary

Microcirculation

- Flow of blood from an arteriole to a venule through a ***capillary bed***
    - i) ***Vascular shunt***
        - Metarteriole + thoroughfare channel
    - ii) ***True capillaries***
        - Actual exchange vessels (10-100 per capillary bed)
- *Precapillary sphincter* surrounds root of each true capillary

Capillaries

- ***Walls only a thin tunica intima***
    - Length = *~1 mm; lumen diam = 8-10 um*
    - Function = *exchange*

3 Types of Capillaries

- 1. ***Continuous capillaries***
    - *Skin & muscle*, uninterrupted lining intercellular clefts allow limited passage of fluids, small solutes
- 2. ***Fenestrated capillaries***
    - Similar but endothelial cells riddled with *pores* (*fenestrations*) increased permeability to fluids/small solutes
    - *Small intestine, endocrine organs, kidney*
- 3. ***Sinusoidal capillaries***
    - Highly modified, *leaky capillaries*
    - *Liver, bone marrow, lymphoid tissues, endocrine organs*
    - Large, irregular lumens & usually fenestrated; fewer tight junctions & *large intercellular clefts* for passage of *proteins, RBCs*.

4.3.4. Describe the structure and functions of the venules and veins

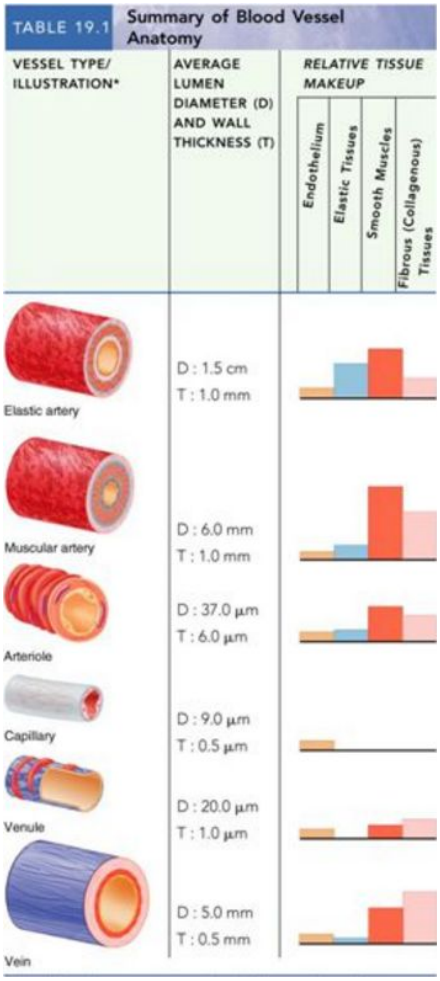
Venules

- Capillaries unite to form ***venules***
    - 8-100 um diameter
    - *Smallest venules*
        - Composed of ***endothelium and a few fibroblasts***
        - Extremely porous (capillary-like)
    - *Larger venules*
        - ***One or two layers of smooth muscle***
        - Has sparse tunica media & thin tunica externa

Veins

- Venules join to form ***veins***
    - Composed of 3 tunics but ***walls are thinner*** & ***lumens are larger***
    - Relatively *little elastin or smooth muscle in tunica media*;
        - Tunica externa is heaviest, thickest layer
    - Called capacitance vessels or blood reservoirs
        - *Up to 65% of blood in veins at any one time*

4.3.4.1. Contrast the typical anatomy of the wall of a vein with that of an artery



Contrasting Wall Anatomy of Arteries vs. Veins

- Refer to Table 19.1

Arterial Walls Consisting of:

- Elastic arteries
- Muscular arteries
- Arterioles

Venous Walls Consisting of:

- Capillaries
- Venules
- Veins

4.3.4.2. Describe 2 structural adaptations of veins that promote blood return to the heart

Structural Adaptations That Promote Blood Return

- ***Large Diameter Lumens***
  - Offers relatively little resistance to blood flow
- ***Venous Valves***
  - Prevents blood from flowing backwards
  - Also compensates for low venous pressure
    - Formed from:
      - Folds of the tunica intima
      - Resembles semilunar valves of the heart
  - Abundantly found in lower limbs, where gravity opposes blood flow

Venous Blood Pressure

- Steady and changes very little during cardiac cycle
- Pressure gradients in vein (from venules to venae cavae) is 15 mmHg
- Factors Aiding Venous Return
    - i) ***Respiratory pump***
        - As we inhale, abdominal pressure increases squeezing local veins, forcing blood toward the heart
            - Pressure in chest decreases, thoracic veins expand and speed blood entry into right atrium
    - ii) ***Muscular pump***
        - If you move around, contraction of skeletal muscle pushes vessels slightly towards the heart
    - iii) ***Sympathetic Venoconstriction***
        - Reduces volume of blood in veins (capacitance vessels)
            - Layer of smooth muscle around veins constrict, venous volume reduces and blood pushed toward the heart

4.3.4.3. Outline the role of the respiratory system in promoting venous return

Respiratory Factors Aiding Venous Return

- Respiratory pump
    - As it passes by abdominal area, breathing will help through changes in the thoracic area

4.3.5. Illustrate the changes in blood pressure throughout the various vessels of the circulatory system

4.3.5.1. Define blood flow, blood pressure, resistance, peripheral resistance

Define Blood Flow

- The volume of blood flowing through a vessel, an organ, or the entire circulation given a period of units (*ml/min*).
    - Considering the entire vascular system, ***CO = Blood Flow***
        - Relatively constant as well under resting conditions
        - Individual organ blood flow may vary according to their needs
    - *Blood Flow = Difference in BP / Peripheral Resistance*
        - Noted in short form as:
            - $\mathbf{BF = BP_1 - BP_2 / R}$

Define Blood Pressure (BP)

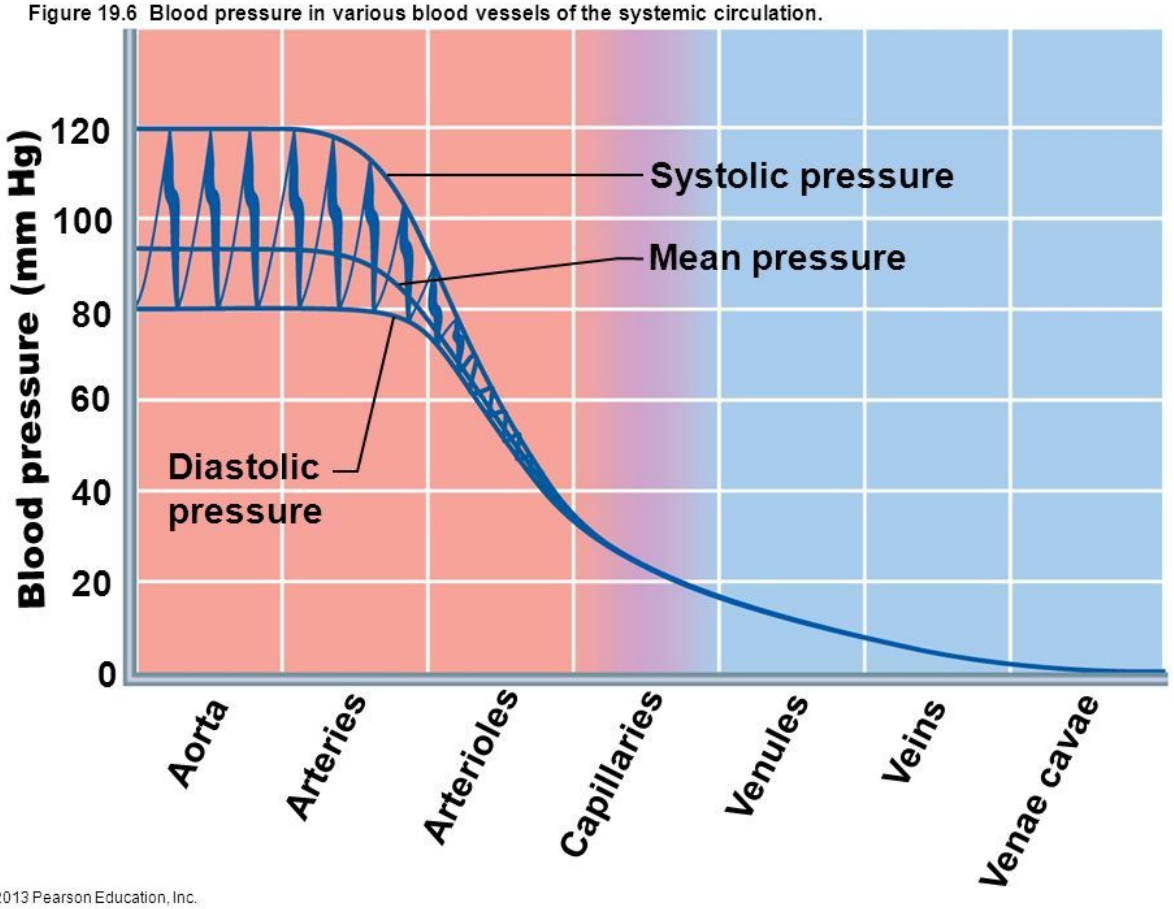
- The force per unit area exerted on a vessel wall by the contained blood, expressed in units of millimeters of mercury (mm Hg).
    - The term blood pressure means systemic arterial blood pressure in the largest arteries near the heart (i.e. avg Aortic BP = 90 mm Hg)
        - The pressure gradient, or differences, drives the movement of blood
            - Flows from area of high pressure to area of low pressure

Define Resistance

- Opposition to flow and is a measure of the amount of friction blood encounters as it passes through the vessels.
    - *Peripheral resistance*
        - Most friction is encountered in the peripheral (systemic) circulation.
        - Thus generally the term used is peripheral resistance.
    - *Resistance is a major determinant of blood flow*
        - Change in blood vessel diameter can increase resistance to the 4th power

4.3.5.2. Plot changes in blood pressure as blood travels through the circulatory system from the aorta to the vena cava

Figure 19.6 Blood pressure in various blood vessels of the systemic circulation.



4.3.6. Explain the factors that affect resistance and justify the importance of arterioles in the control of peripheral resistance

Factors that Affect Resistance

- Measures total of frictional forces that impede flow
    - Flow & resistance are inversely related (Resistance $\propto 1/r^4$)
    - Resistance is influenced by: blood viscosity, vessel length/diameter
        - i) *Blood viscosity*:
            - Due to formed elements, plasma proteins
        - ii) *Total blood vessel length*:
            - More length = more resistance, vice versa
                - (e.g. extra adipose tissue)
        - iii) *Blood vessel diameter*:
            - Can be regulated; fluid not touching walls moves faster

4.3.6.2. Justify the association between arterioles and the largest drop in blood pressure

Importance of Arterioles

- Arterioles offer the greatest resistance to blood flow
    - However, as long as a pressure gradient exists, blood continues to flow.

4.3.7. Describe the role of elastic arteries in promoting continuous blood flow throughout systole and diastole

Arterial Blood Pressure

- ***Reflects 2 Factors***
    - 1. How much elastic arteries close to the heart can stretch
    - 2. The volume of blood forced into them at any time
        - Blood pressure is pulsatile, it rises and falls in the elastic arteries

4.3.8. Define systolic and diastolic arterial pressure, pulse pressure and mean arterial pressure

4.3.8.1. Express pulse pressure in terms of systolic and diastolic pressure

Pulse Pressure

- Expressed as **Pulse pressure = Systolic BP - Diastolic BP**
    - Indicates vigor of contraction of ventricle
    - Also provides info on elasticity of aorta & major arteries

4.3.8.2. Express mean arterial pressure (MAP) in terms of diastolic pressure and pulse pressure

Mean Arterial Pressure (MAP)

- Expressed as **MAP = Diastolic pressure + 1/3 Pulse pressure**
    - *MAP is the pressure that propels blood to tissues during the cardiac cycle*
        - Not mean of systolic & diastolic pressures; ventricular diastole is longer than ventricular systole (0.5 sec vs 0.3 sec)
    - MAP & pulse pressure decrease with distance from heart; by end of arterial tree, blood flow is steady & pulse pressure has disappeared

4.3.9. Identify and justify the value for mean capillary blood pressure

4.3.9.1. Be aware of blood pressure in capillary beds

4.3.9.2. Indicate 2 reasons why capillary beds are low pressure systems

Capillary Blood Pressure

- Blood pressure has dropped to ~35 mm Hg entering capillaries, by the end of capillaries, pressure is 17 mm Hg
    - Low pressure in capillaries desirable because
        - i) capillaries are fragile and high pressures would rupture them
        - ii) capillaries extremely permeable; lots of exchange at low BP

4.3.10. Express blood pressure in terms of cardiac output and peripheral resistance

Expressing Cardiac Output (CO) and Peripheral Resistance

- Main factors influencing blood pressure are:
    - Cardiac output, peripheral resistance, and blood volume
        - ***BP = CO x PR***

Cardiac output

- How much volume pushing into per unit/time
    - Increase in stroke volume and heart rate = increased CO
        - Also recall: ***CO = HR x SV***

Peripheral Resistance

- More blood in the middle of vessel, results in easier flow
    - Decrease diameter of vessels, increase blood viscosity/blood vessel length = increased peripheral resistance

4.3.10.1. Define pulse; explain how pulse and arterial blood pressure are measured

Define Pulse

- The throbbing pulsation in an artery (*pulse*) during systole as ventricular contraction forces blood into elastic arteries, expanding them; ***Systolic BP - Diastolic BP***
- Measured by pushing surface artery against firm tissue (*usually radial artery pulse*)
    - *Pressure Point*
        - These points are compressed to stop blood flow into distal tissues during hemorrhage

4.3.10.2. Define hypotension and hypertension

Hypotension

- Low BP: only concern is inadequate blood flow to tissues

Hypertension

- Sustained increase in either Systolic BP (>140 mmHg) or Diastolic BP (>90 mmHg)

4.3.11. Describe the short-term neural and chemical mechanisms for the regulation of blood pressure

Short-term Regulation: Neural Controls

- Alters Cardiac Output (CO) and Peripheral Resistance (PR)
- Neural Controls of PR directed at two main goals:
    - i) *Maintaining adequate MAP by altering blood vessel diameter*
        - Under conditions of low blood volume:
            - Vessels constrict to allow maximum blood flow to vital organs
    - ii) *Altering blood distribution to respond to specific demands of various organs*
        - i.e. during exercise blood is shunted away from GI tract
- Neural controls operate via reflex arcs involved *baroreceptors*,
    - These integrate with *the Cardiovascular Centre in the medulla oblongata* and travel via autonomic fibers to the heart and vascular smooth muscle
- Occasionally, *chemoreceptors* influence neural control mechanism

4.3.11.1. Define vasomotor tone; describe the location and role of the vasomotor centre in the short-term regulation of blood pressure

The Cardiovascular Centre

- *Cardiovascular Centre* composed of *cardiac centers* and *vasomotor center,* all found as several clusters of sympathetic neurons in the medulla oblongata
    - *Vasomotor Centre*
        - Controls diameter of blood vessels
        - Transmits impulses at a fairly steady state along sympathetic efferents called *vasomotor fibers*
        - Responds to:
            - i) *Baroreceptors*
            - ii) *Chemoreceptors* (CO_2 , O_2 , H^+)
            - iii) *Higher brain centres or hormones*
    - *Vasomotor Tone*
        - Constant input
            - Arterioles are almost always in a state of moderate constriction, called vasomotor tone
    - Increased sympathetic activity produces generalized vasoconstriction and raise BP
    - Decreased sympathetic activity relaxes vascular muscle and lowers BP

4.3.11.2. Outline the roles of Baroreceptors and various chemical signals in the short-term regulation of blood pressure

Baroreceptors Reflexes

- Stretch receptors, respond to MAP rise or fall
    - Rapidly responding baroreceptors protect the circulation against short-term abnormal changes in BP
- Located in *carotid sinus, aortic arch*, and other large arteries of neck and thorax
    - When stretched, it sends rapid stream of impulse to CV center
        - Inhibit the vasomotor and cardioacceleratory centers (stimulates cardioinhibitory center). Result is a decrease in BP.
            - *Vasodilation*
                - Decreased output of vasomotor centre allor arterioles and veins to dilate
                    - *Arteriolar vasodilation* reduces peripheral resistance (MAP decreases)
                    - *Venodilation* shifts blood to venous reservoirs (decreases venous return and CO)
            - *Decreased CO*
                - Impulse to cardiac center inhibits sympathetic activity and stimulate PNS (reduces HR and contractile force)
                    - CO and MAP decreases
    - In the opposite situation, a decline in MAP initiates reflex vasoconstriction and increases CO, bringing BP up
        - CO and PR are regulated in tandem to minimize changes in BP

Chemoreceptor Reflexes

- Chemoreceptors respond to sudden changes when *carbon dioxide levels rise*, or *the pH falls*, or *oxygen content of the blood drops sharply*
    - Chemoreceptors in *aortic arch* and *large arteries* of the neck transmit impulses to the *cardioacceleratory center*, in response to chemical stimuli
        - Increases cardiac output (CO)
    - Chemoreceptors also activate the *vasomotor center*, which causes reflex vasoconstriction
        - The rise in BP that follows the response speeds the return of blood to the *heart and lungs*
    - The most prominent chemoreceptors are the *carotid* and *aortic bodies* located close by the baroreceptors

Hormones and the Short-term Regulation

- I. Adrenal Medulla hormones
    - NE/E and fight or flight response
        - (a) generalized vasoconstriction (except skeletal/cardiac muscle)
        - (b) increases CO
        - (c) nicotine mimics effects of catecholamines
- II. Angiotensin II
    - Renin-angiotensin system; decreased renal perfusion
        - (a) intense generalized vasoconstriction to increase systemic bp
        - (b) release of aldosterone, ADH
- III. Atrial Natriuretic Peptide (ANP)
    - Produced by atria of heart
        - (a) causes blood volume & blood pressure to decrease.
        - (b) generalized vasodilation
- IV. Antidiuretic hormone (ADH)
    - Source from hypothalamus/posterior pituitary
        - (a) stimulates kidneys to conserve water (eg: severe hemorrhage) – long term effect
        - (b) not usually important in short term unless bp drops very low – then much more ADH is released and high levels can cause vasoconstriction

4.3.11.3. Briefly indicate the roles of higher brain centres in the short-term regulation of blood pressure

Higher Brain Centres in Short-Term Regulation

- Higher Brain centre include ***cerebral cortex*** and ***hypothalamus***
    - Relay messages to medullary centers to modify arterial pressure
    - Ex. Fight-or-flight response mediated by the hypothalamus
        - Hypothalamus mediates redistribution of blood flow

4.3.12. Briefly summarize the role of the kidneys in the long-term regulation of blood pressure

Role of the Kidneys in Long-term Regulation of Blood Pressure

- Baroreceptors adapt to prolonged/ chronic high/low blood pressure
    - ***Kidneys restore BP by adjusting blood volume***
    - Anything that changes blood volume will change blood pressure
    - If blood volume is increased, kidneys will excrete more salt & water

- The Kidneys
    - 1. ***Direct Action:***
        - *Increased blood volume/pressure* = i***ncreased rate of filtrate formation → insufficient time to reclaim water → increased volume of urine***
    - 2. ***Indirect Action:***
        - *Renin-angiotensin system* - ***MAP decreases → kidney cells release renin → cascade of reactions to yield angiotensin II*** (potent vasoconstrictor) → increased blood pressure to restore renal perfusion
    - ***Notes:***
        - ***Angiotensin II stimulates secretion of aldosterone*** (adrenal cortex)
            - This increases renal reabsorption of Na+ (& water if ADH present)
            - Increased secretion of ADH (post pituitary) promotes water reabsorption

4.3.13. Define and explain the mechanisms of autoregulation with regard to local blood flow

4.3.13.1. Define "resting vascular tone" and explain how this normal physiological mechanism permits redistribution of blood flow among various tissues and organs

Mechanisms of Autoregulation with regard to Local Blood Flow

- Blood flow to each organ regulated to meet needs
- *Resting vascular tone:*
    - In resting state, smooth muscles in walls of arterioles somewhat contracted by sympathetic nervous system
        - Can increase flow by vasodilation
            - Immediate adjustments to changes in local conditions
                - R varies 1/r4
- Organs regulate individual blood flow by varying resistance of arterioles

4.3.13.2. Describe briefly the metabolic and myogenic local regulation of blood flow

Metabolic Local Regulation

- Blood flow is too low to meet tissue metabolic needs, O2 declines, metabolic products accumulate
    - This increases CO2 levels, H+, K+, heat, inflammatory chemicals
    - End Result: immediate increased perfusion of "needy" tissue
        - ***Reactive Hyperemia***
            - ***Dramatically increased blood flow*** into tissue that occur after the blood supply to area has been temporarily blood

- ***Active Hyperemia***
    - ***Muscles active***, ***blood flow increases*** in direct proportion to their greater *metabolic* activity

Myogenic Local Regulation

- Vascular smooth muscles prevent fluctuations in systemic BP problems by responding directly to passive stretch
    - Increased tone, which resists the stretch and causes vasoconstriction

4.3.14. Explain the forces that act to influence capillary exchange

Forces that act to Influence Capillary Exchange (Pt.1)

- *Velocity:* ***1/(Cross-sectional area)***
    - Slowest in the capillaries
    - Beneficial for exchange between blood and tissue cells
- *Volume:*
    - Individual branches have smaller lumens, but combined, the volume of blood they hold is more than the aorta
- *Vasomotion:*
    - Intermittent flow of blood through capillary bed is due to vasomotion
        - ***Vasomotion is the opening and closing of precapillary sphincters***

Forces that act to Influence Capillary Exchange (Pt.2)

- Capillaries
    - Major point of communication between interstitial fluid & blood
        - i) Most cells in body within 0.02 mm of a capillary »» diffusion works
        - ii) Capillary walls only 1 cell thick: mix of diffusional, osmotic & hydrostatic forces
- Precapillary Sphincter
    - Cuff of smooth muscle at beginning of capillary; capillary walls themselves have no smooth muscle
- ***Vasomotion***
    - ***Contraction and relaxation of precapillary sphincter***
        - Sporadic flow through each capillary

4.3.14.2. Describe the 3 types of exchange occurring in capillary beds; your description should demonstrate understanding of the hydrostatic and oncotic forces acting at the arterial versus the venous ends of capillaries

Capillary Exchange Mechanisms - 3 Types

- 1. ***Vesicle Transport***
    - *For relatively large, lipid-insoluble molecules* (eg: insulin)
        - Shuttling via endocytosis, and then exocytosis
        - Also antibody molecules from maternal to fetal circulation
- 2. ***Diffusion***
    - *Primary mechanism for dissolved solutes & gases* -
        - (eg: O2 , CO2 , glucose • follow gradients)
        - Heat moves via convection down a thermal gradient
        - Water-filled pores or through bilayer
            - (Na+, K+, Cl-, glucose)
            - (O2 , CO2 , urea)
        - Pores <1% capillary SA;
            - Lipid-soluble substances have 100X more SA
- 3. ***Bulk Flow***
    - *At the arterial end of the capillary*
        - Capillary
            - Hydrostatic pressure in capillary "pushes" fluid OUT
                - ***35 mm Hg***
            - Osmotic pressure "pulls" fluid IN
                - 26 mm Hg
        - Interstitial Fluid
            - Hydrostatic pressure in capillary "pushes" fluid IN
                - 0 mm Hg
            - Osmotic pressure "pulls" fluid OUT
                - 1 mm Hg
    - *At the venous end of the capillary*
        - Capillary
            - Hydrostatic pressure in capillary "pushes" fluid OUT
            - Pressure dropped because of the resistance in capillaries
                - ***17 mm Hg***
            - Osmotic pressure "pulls" fluid IN
                - 26 mm Hg
        - Interstitial Fluid
            - Hydrostatic pressure in capillary "pushes" fluid IN
                - 0 mm Hg
            - Osmotic pressure "pulls" fluid OUT
                - 1 mm Hg
    - Net Filtration Pressure ***(NFP) = (HPc + OPif) - (HPif + OPc)***

4.4 The Blood Vessels - Anatomy

Arteries of the Head and Neck

- Brachiocephalic trunk
    - Branching off the aorta
- Subclavian
    - Below the collarbone
- Carotid Arteries
    - Common carotid
        - Branches into:
            - Internal carotid
            - External carotid
- Vertebral
    - Inside the vertebrae
- Facial
    - Branches throughout the face
- Superficial Temporal
    - Near the temple of the skull

Arteries of the Upper Limb

- Brachiocephalic trunk
    - Branching off the aorta
- Right subclavian
    - Under the right collarbone, same for left as well
- Axillary
    - Near armpit or joint between arm and torso
- Anterior Circumflex
    - Around upper humerus
- Brachial
    - Down lower humerus
- Deep Artery of Arm
    - Guess they ran out of names
- Lower Arm Arteries
    - Radial
    - Ulnar

Arteries of the Abdomen

- **The Celiac Trunk**
    - Branches into:
        - **Common Hepatic Artery**
            - Leads to the Liver, hence “hepatic.”
                - **Hepatic Artery Proper**
                    - Branches off the common
        - **Gastroduodenal Artery**
            - Near the duodenum of the stomach and intestines
                - **Right Gastroepiploic Artery**
                    - Continues from the gastroduodenal
                        - **Left Gastroepiploic Artery**
                            - Continues the right gastroepiploic
        - Gastric Arteries
            - **Left**
            - **Right**
        - Splenic Artery
            - **Artery leads to the spleen organ**
- **Abdominal Aorta**
    - Continues down the lower abdomen

Arteries of the Lower Limb

- **Common Iliac**
    - Branches into:
        - **Internal**
        - **External**
    - Down the Limb:
        - **Lateral femoral circumflex**
            - Outer leg
        - **Femoral**
            - Descends down along the femur
        - **Popliteal**
            - Near the knee joint
        - **Tibial**
            - **Anterior**
            - **Posterior**
        - **Fibular**
            - Near the fibula

Veins of the Head and Neck

- **Superior Vena Cava**
    - Leading to Right Atrium
- **Brachiocephalic**
    - Leading to the superior vena cava
- **Subclavian**
    - Under the collarbone
- **Jugular Veins**
    - **Internal and External**
- **Vertebral**
    - Inside the vertebrae
- **Facial**
    - The face lmao
- **Ophthalmic**
    - From the eye leading to the facial veins
- **Superficial Temporal**
    - Near the temple of the skull

Veins of the Upper Limb

- **Brachiocephalic**
    - Leading to the superior vena cava
- **Subclavian**
    - Under the collarbone
- **Axillary**
    - Near armpit or joint between arm and torso
- **Cephalic**
    - Along the upper humerus (facing outer)
- **Basilic**
    - Along the upper humerus (facing inner)
- **Brachial**
    - Lower humerus
- **Median cubital**
    - Near the elbow joint, crosses between cephalic and basilic
- **Median antebrachial**
    - Leads into the basilic
- **Lower Arm Veins**
    - **Radial**
    - **Ulnar**

Veins of the Hepatic Portal Circulation

- **Inferior Vena Cava**
    - Leads up into the right atrium
- **Hepatic Portal Vein**
    - Leads into the inferior vena cava
- **Splenic Vein**
    - Coming back from the spleen and into the the hepatic portal vein
- **Right Gastroepiploic Vein**
    - Around bottom of stomach leading into the hepatic portal vein
- **Inferior Mesenteric Vein**
    - Parallel with superior mesenteric, connects with splenic vein (left)
- **Superior Mesenteric Vein**
    - Parallel with inferior mesenteric, directly connects with hepatic portal vein

Veins of the Lower Limb

- **Inferior Vena Cava**
    - Leads up into the right atrium
- **Common Iliac**
    - "Inferior" veins leading into the common
        - **Internal**
        - **External**
- **Femoral**
    - Along the femur
- **Great saphenous**
    - Inner upper leg, connects with femoral into the common iliac
- **Popliteal**
    - Near the knee joint
- **Small saphenous**
    - Outer lower leg, leads into the popliteal vein
- **Fibular**
    - Along the fibula
- **Anterior Tibial**
    - Along the tibia