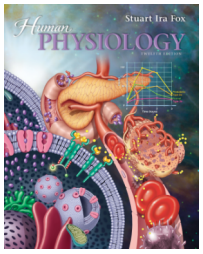
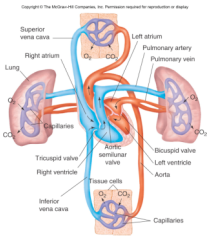


Chapter 13

Blood, Heart, and Circulation

Lecture PowerPoint

I. Functions and Components of the Circulatory System



Circulatory System Functions

- Transportation
  - Respiratory gases, nutrients, and wastes
- Regulation
  - Hormonal and temperature
- Protection
  - Clotting and immune

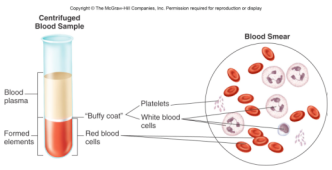
Circulatory System Components

- Cardiovascular system
  - Heart: four-chambered pump
  - Blood vessels: arteries, arterioles, capillaries, venules, and veins
- Lymphatic system
  - Lymphatic vessels, lymphoid tissues, lymphatic organs (spleen, thymus, tonsils, lymph nodes)

II. Composition of the Blood

Composition of the Blood

1. Plasma: fluid part of blood
   - Plasma proteins
   - Serum



Composition of the Blood

1. Plasma: fluid part of blood
   - Plasma proteins
     - Albumin: creates osmotic pressure to help draw water from tissues into capillaries to maintain blood volume and pressure
     - Globulins: some carry lipids
   - Gamma globulins: antibodies
     - Fibrinogen: helps in clotting after becoming fibrin

Composition of the Blood

2. Erythrocytes
   - Carry oxygen
   - Lack nuclei and mitochondria
   - Have a 120-day life span
   - Contain hemoglobin and transferrin

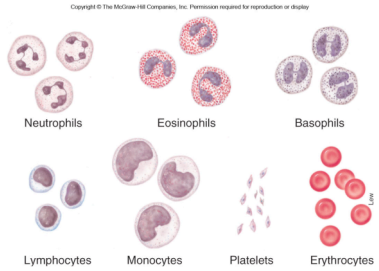
Composition of the Blood

Reginald J. Poole/Polaroid International Instant Photomicrography Competition

Composition of the Blood

3. Leukocytes
   - Have nuclei and mitochondria
     - Granular leukocytes: neutrophils, eosinophils, and basophils
     - Aggranular leukocytes: monocytes and lymphocytes

Composition of the Blood



Composition of the Blood

4. Platelets (thrombocytes)
   - Smallest formed element
   - Lack nuclei
   - Very short-lived (5–9 days)
   - Clot blood
   - Need fibrinogen

Formed Elements in the Blood

Table 13.2 | Formed Elements of the Blood

Component	Description	Number Present	Function
Erythrocyte (red blood cell)	Biconcave disc without nucleus; contains hemoglobin; survives 100 to 120 days	4,000,000 to 6,000,000 / mm³	Transports oxygen and carbon dioxide
Leukocytes (white blood cells)		5,000 to 10,000 / mm³	Aid in defense against infections by microorganisms
Granulocytes	About twice the size of red blood cells; cytoplasmic granules present; survive 12 hours to 3 days		
1. Neutrophil	Nucleus with 2 to 5 lobes; cytoplasmic granules stain slightly pink	54% to 62% of white cells present	Phagocytic
2. Eosinophil	Nucleus bilobed; cytoplasmic granules stain red in eosin stain	1% to 3% of white cells present	Helps to detoxify foreign substances; secretes enzymes that dissolve clots; fights parasitic infections
3. Basophil	Nucleus lobed; cytoplasmic granules stain blue in hematoxylin stain	Less than 1% of white cells present	Releases anticoagulant heparin
Agranulocytes	Cytoplasmic granules not visible; survive 100 to 300 days (some much longer)		
1. Monocyte	2 to 3 times larger than red blood cell; nuclear shape varies from round to lobed	3% to 9% of white cells present	Phagocytic
2. Lymphocyte	Only slightly larger than red blood cell; nucleus nearly fits cell	25% to 33% of white cells present	Provides specific immune response (including antibodies)
Platelet (thrombocyte)	Cytoplasmic fragment; survives 5 to 9 days	130,000 to 400,000 / mm³	Enables clotting; releases serotonin, which causes vasoconstriction

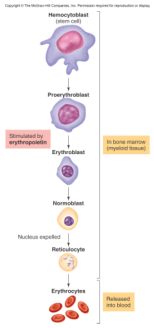
Hematopoiesis

- Process of blood cell formation
  - Leukopoiesis: white blood cells
    - Red bone marrow and lymphoid tissues
    - Cytokine regulation

Hematopoiesis

- Process of blood cell formation:
  - Erythropoiesis: RBCs
    - Erythropoietin
    - Secreted by kidneys
    - Low oxygen levels
    - Initiates erythropoietin
  - Hepcidin
    - Secreted by liver
    - Regulates iron metabolism

Hematopoiesis



Red Blood Cell Antigens and Blood Typing

- Antigens: found on the surface of cells to help immune system recognize self cells
- Antibodies: secreted by lymphocytes in response to foreign cells
- ABO system: antigens on erythrocyte cell surfaces
  - Possibilities:
    - Type A = Has the A antigen
    - Type B = Has the B antigen
    - Type AB = Has *both* the A and B antigens
    - Type O = Has *neither* the A nor the B antigen

Red Blood Cell Antigens and Blood Typing

- In a transfusion reaction, a person has antibodies against antigens he does not have.

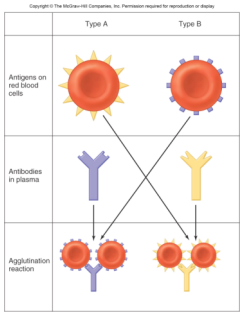
Table 13.3 | The ABO System of Red Blood Cell Antigens

Genotype	Antigen on RBCs	Antibody in Plasma
$I^A I^A$; $I^A i$	A	Anti-B
$I^B I^B$; $I^B i$	B	Anti-A
ii	O	Anti-A and anti-B
$I^A I^B$	AB	Neither anti-A nor anti-B

Red Blood Cell Antigens and Blood Typing

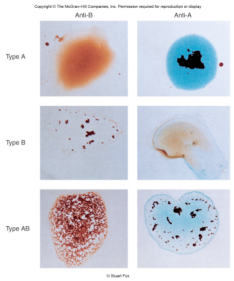
- Transfusion reaction: If a person receives the wrong blood type, antibodies bind to erythrocytes and cause agglutination.

Red Blood Cell Antigens and Blood Typing



Red Blood Cell Antigens and Blood Typing

- Agglutination can be used for blood typing.



Red Blood Cell Antigens and Blood Typing

- Rh factor
  - Antigen D
  - Rh-positive or Rh-negative
  - Issues in pregnancy: An Rh^- mother exposed to Rh^+ fetal blood produces antibodies. This may cause erythroblastosis fetalis in future pregnancies as antibodies cross the placenta and attack fetal RBCs.

Blood Clotting

- Hemostasis: cessation of bleeding when a blood vessel is damaged
- Damage exposes collagen fibers to blood, producing:
  1. Vasoconstriction
  2. Formation of platelet plug
  3. Formation of fibrin protein web

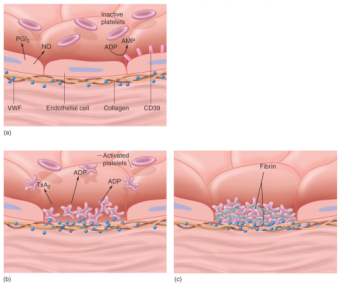
Blood Clotting: Vessel Walls

- Intact endothelium secretes prostacyclin and nitric oxide, which:
  1. Vasodilate
  2. Inhibit platelet aggregation
- and CD39, which:
  1. Breaks down ADP into AMP and P_i to inhibit platelet aggregation further

Blood Clotting: Platelets

- Damaged endothelium exposes collagen:
  1. Platelets bind to collagen.
  2. Von Willebrand factor holds them there.
  3. Platelets recruit more platelets and form a platelet plug by secreting:
     - ADP (sticky platelets)
     - Serotonin (vasoconstriction)
     - Thromboxane A (sticky platelets and vasoconstriction)

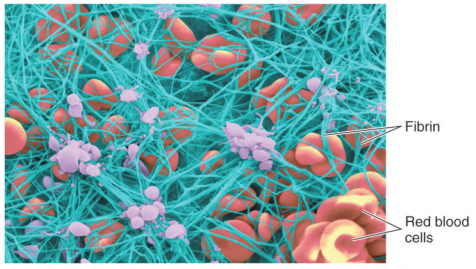
Blood Clotting: Platelets



Blood Clotting: Fibrin

- Fibrinogen is converted to fibrin via one of two pathways:
  1. Intrinsic: Activated by exposure to collagen. Factor VII activates a cascade of other blood factors.

Blood Clotting: Fibrin



From Nature Volume 413, Issue 6855, 4 October 2001, cover. Photo by Dr. John W. Weisel, University of Pennsylvania

Blood Clotting: Fibrin

Table 13.4 | The Plasma Clotting Factors

Factor	Name	Function	Pathway
I	Fibrinogen	Converted to fibrin	Common
II	Prothrombin	Converted to thrombin (enzyme)	Common
III	Tissue thromboplastin	Cofactor	Extrinsic
IV	Calcium ions (Ca^{2+})	Cofactor	Intrinsic, extrinsic, and common
V	Proaccelerin	Cofactor	Common
VII*	Proconvertin	Enzyme	Extrinsic
VIII	Antihemophilic factor	Cofactor	Intrinsic
IX	Plasma thromboplastin component; Christmas factor	Enzyme	Intrinsic
X	Stuart-Prower factor	Enzyme	Common
XI	Plasma thromboplastin antecedent	Enzyme	Intrinsic
XII	Hageman factor	Enzyme	Intrinsic
XIII	Fibrin stabilizing factor	Enzyme	Common

*Factor VI is no longer referenced; it is now believed to be the same substance as activated factor V.

Blood Clotting: Fibrin

- Next, calcium and phospholipids (from the platelets) convert prothrombin to the active enzyme thrombin, which converts fibrinogen to fibrin.

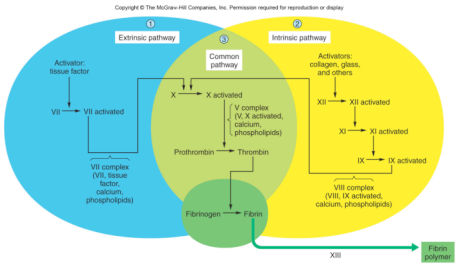
Blood Clotting: Fibrin

- Fibrinogen is converted to fibrin via one of two pathways:

2. Extrinsic: Initiated by tissue factor (factor III). This is a more direct pathway.

- Vitamin K is needed for both pathways.

Blood Clotting: Fibrin



Blood Clotting

Table 13.5 | Some Acquired and Inherited Clotting Disorders and a Listing of Anticoagulant Drugs

Category	Cause of Disorder	Comments
Acquired clotting disorders	Vitamin K deficiency	Inadequate formation of prothrombin and other clotting factors in the liver
Inherited clotting disorders	Hemophilia A (defective factor $VIII_{AHF}$)	Recessive trait carried on X chromosome; results in delayed formation of fibrin
	Von Willebrand's disease (defective factor $VIII_{vWF}$)	Dominant trait carried on autosomal chromosome; impaired ability of platelets to adhere to collagen in subendothelial connective tissue
	Hemophilia B (defective factor IX); also called Christmas disease	Recessive trait carried on X chromosome; results in delayed formation of fibrin
Anticoagulants		
Aspirin	Inhibits prostaglandin production, resulting in a defective platelet release reaction	
Coumarin	Inhibits activation of vitamin K	
Heparin	Inhibits activity of thrombin	
Citrate	Combines with Ca^{2+}, and thus inhibits the activity of many clotting factors	

Anticoagulants

- Clotting can be prevented with certain drugs:
  - Calcium chelators (sodium citrate or EDTA)
  - Heparin: blocks thrombin
  - Coumarin: inhibits vitamin K

III. Structure of the Heart

Structure of the Heart

- Right atrium: receives deoxygenated blood from the body
- Left atrium: receives oxygenated blood from the lungs
- Right ventricle: pumps deoxygenated blood to the lungs
- Left ventricle: pumps oxygenated blood to the body

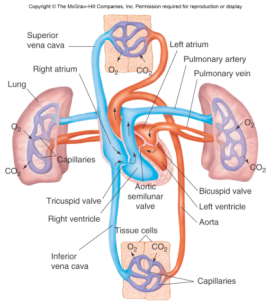
Structure of the Heart

- Fibrous skeleton:
  - Separates atria from ventricles. The atria therefore work as one unit, while the ventricles work as a separate unit.
  - Forms the annuli fibrosi, which hold in heart valves

Pulmonary and Systemic Circulations

- Pulmonary: between heart and lungs
  - Blood pumps to lungs via pulmonary arteries.
  - Blood returns to heart via pulmonary veins.
- Systemic: between heart and body tissues
  - Blood pumps to body tissues via aorta.
  - Blood returns to heart via superior and inferior venae cavae.

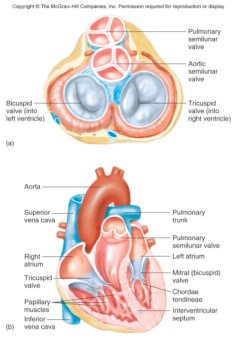
Pulmonary and Systemic Circulations



Valves of the Heart

- Atrioventricular valves: located between the atria and the ventricles
  - Tricuspid: between right atrium and ventricle
  - Bicuspid: between left atrium and ventricle
- Semilunar valves: located between the ventricles and arteries leaving the heart
  - Pulmonary: between right ventricle and pulmonary trunk
  - Aortic: between left ventricle and aorta

Valves of the Heart



Heart Sounds

- Produced by closing valves
  - "*Lub*" = closing of AV valves
    - Occurs at ventricular systole
  - "*Dub*" = closing of semilunar valves
    - Occurs at ventricular diastole

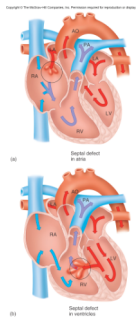
Heart Murmur

- Abnormal heart sounds produced by abnormal blood flow through heart.
  - Many caused by defective heart valves.
- Mitral stenosis: Mitral valve calcifies and impairs flow between left atrium and ventricle.
  - May result in pulmonary hypertension.

Heart Murmur

- Incompetent valves: do not close properly
  - May be due to damaged papillary muscles
- Septal defects: holes in interventricular or interatrial septum
  - Blood crosses sides.

Heart Murmur

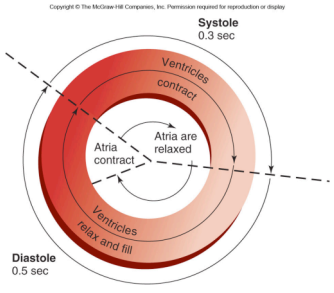


IV. Cardiac Cycle

Cardiac Cycle

- Repeating pattern of contraction and relaxation of the heart.
  - Systole: contraction of heart muscles
  - Diastole: relaxation of heart muscles

Cardiac Cycle



Cardiac Cycle

1. Ventricles begin contraction, pressure rises, and AV valves close (*lub*).

1. Pressure builds, semilunar valves open, and blood is ejected into arteries.

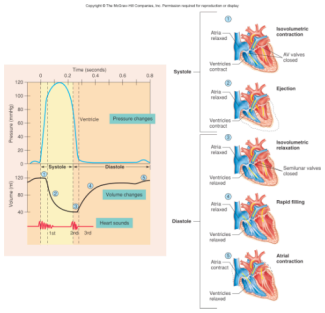
1. Pressure in ventricles falls; semilunar valves close (*dub*).

Cardiac Cycle

4. Pressure in ventricles falls below that of atria, and AV valve opens. Ventricles fill.

5. Atria contract, sending last of blood to ventricles

Cardiac Cycle and Pressures



V. Electrical Activity of the Heart and the Electrocardiogram

Electrical Activity of the Heart

- Cardiac muscle cells are interconnected by gap junctions called intercalated discs.
  - Once stimulation is applied, it flows from cell to cell.
  - The area of the heart that contracts from one stimulation event is called a myocardium.
  - The atria and ventricles are separated electrically by the fibrous skeleton.

Electrical Activity of the Heart

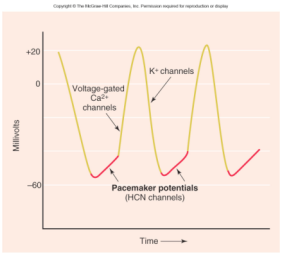
- Sinoatrial node: “pacemaker”; located in right atrium
  - Pacemaker potential: slow, spontaneous depolarization

Electrical Activity of the Heart

– At −40mV, voltage-gated Ca^{2+} channels open, triggering action potential and contraction.

– Repolarization occurs with the opening of voltage-gated K^+ channels.

Electrical Activity of the Heart



Electrical Activity of the Heart

- Pacemaker cells in the sinoatrial node depolarize spontaneously, but the rate at which they do so can be modulated:
  - – Epinephrine and norepinephrine increase the production of cAMP, which keeps Na^+ channels open.
    - Speeds heart rate.
  - – Parasympathetic neurons secrete acetylcholine, which opens K^+ channels.
    - Slows heart rate.

Electrical Activity of the Heart

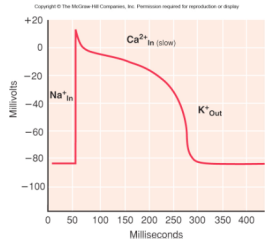
- Myocardial action potentials
  - – Cardiac muscle cells have a resting potential of −90mV.
  - – They are depolarized to threshold by action potentials from the SA node.

Electrical Activity of the Heart

– Voltage-gated Na^+ channels open, and membrane potential plateaus at 15mV for 200–300 msec.
  - Due to balance between slow influx of Ca^{2+} and efflux of K^+

– More K^+ are opened, and repolarization occurs.

Electrical Activity of the Heart



Electrical Activity of the Heart

– Action potentials spread via intercalated discs (gap junctions).

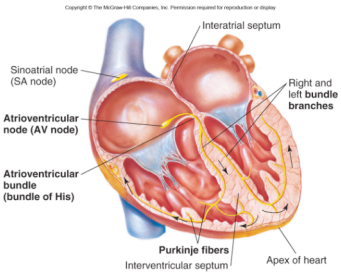
– AV node at base of right atrium and bundle of His conduct stimulation to ventricles.

Electrical Activity of the Heart

– In the interventricular septum, the bundle of His divides into bundle branches.

– Branch bundles become Purkinje fibers, which stimulate ventricular contraction.

Electrical Activity of the Heart



Conduction of Impulses

– Action potentials from the SA node spread rapidly.
  • 0.8–1.0 meters/second
– At the AV node, things slow down.
  • 0.03–0.05 m/sec
  • This accounts for half of the time delay between atrial and ventricular contraction.
– The speed picks up in the bundle of His, reaching 5 m/sec in the Purkinje fibers.
– Ventricles contract 0.1–0.2 seconds after atria.

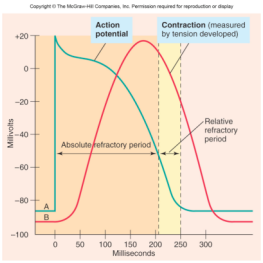
Action Potentials in the Sinoatrial (SA) Node

Begin

Refractory Periods

- Because the atria and ventricles contract as single units, they cannot sustain a contraction.
- Because the action potential of cardiac cells is long, they also have long refractory periods before they can contract again.

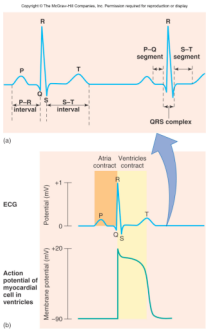
Refractory Periods



Electrocardiogram

- This instrument records the electrical activity of the heart by picking up the movement of ions in body tissues in response to this activity.

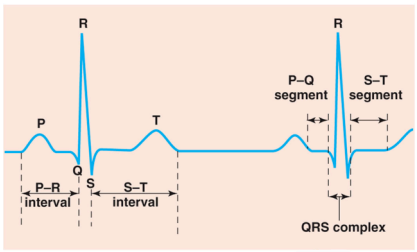
Electrocardiogram



Electrocardiogram

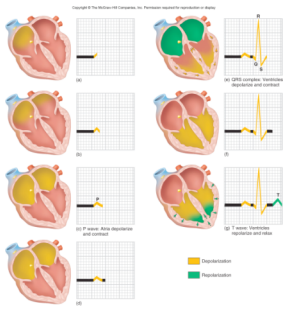
- P wave: atrial depolarization
- QRS wave: ventricular depolarization
- S-T segment: plateau phase
- T wave: ventricular repolarization

Electrocardiogram



(a)

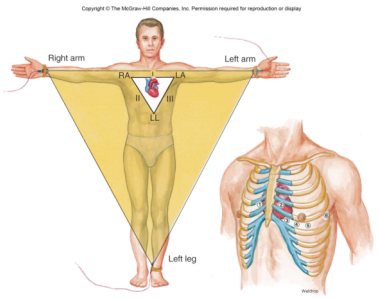
Electrocardiogram



Electrocardiogram

- Bipolar limb leads record voltage between electrodes placed on wrists and legs.
  - Lead I: between right arm and right leg
  - Lead II: between right arm and left leg
  - Lead III: between left arm and left leg

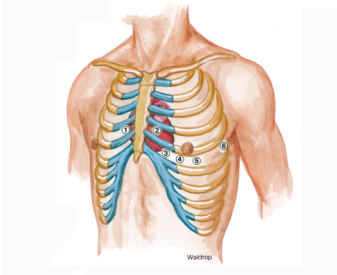
Electrocardiogram



Electrocardiogram

- Unipolar leads record voltage between a single electrode on the body and one built into the machine (ground).
  - Limb leads go on the right arm (AVR), left arm (AVL), and left leg (AVF).
  - There are six chest leads.

Electrocardiogram



Electrocardiogram

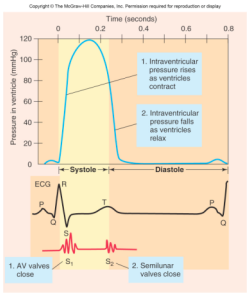
Table 13.7 | Electrocardiograph (ECG) Leads

Name of Lead	Placement of Electrodes
Bipolar Limb Leads	
I	Right arm and left arm
II	Right arm and left leg
III	Left arm and left leg
Unipolar Limb Leads	
AVR	Right arm
AVL	Left arm
AVF	Left leg
Unipolar Chest Leads	
V_1	4th intercostal space to the right of the sternum
V_2	4th intercostal space to the left of the sternum
V_3	5th intercostal space to the left of the sternum
V_4	5th intercostal space in line with the middle of the clavicle (collarbone)
V_5	5th intercostal space to the left of V_4
V_6	5th intercostal space in line with the middle of the axilla (underarm)

ECG and Heart Sounds

- *Lub* occurs after the QRS wave.
- *Dub* occurs at the beginning of the T wave.

ECG and Heart Sounds

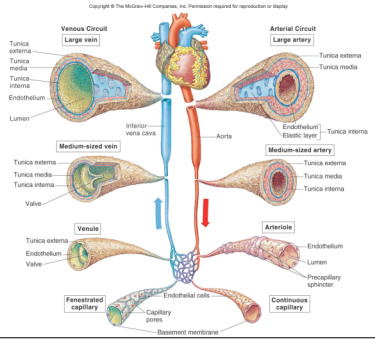


VI. Blood Vessels

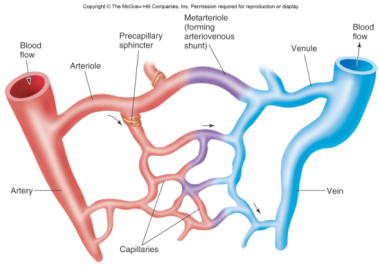
Blood Vessels

- Arteries
- Arterioles
- Capillaries
- Venules
- Veins

Blood Vessels



Blood Vessels



Arteries and Veins

- The walls of arteries and veins have three tunics, or coats:
  - Tunica intima: inner layer; composed of simple squamous endothelium on a basement membrane and connective tissue
  - Tunica media: middle layer; composed of smooth muscle tissue
  - Tunica externa: outer layer; composed of connective tissue

Arteries

- Elastic arteries: closer to the heart; allow stretch as blood is pumped into them and recoil when ventricles relax
- Muscular arteries: farther from the heart; have more smooth muscle in proportion to diameter; also have more resistance due to smaller lumina
- Arterioles: 20–30 μm in diameter.

Capillaries

- Smallest blood vessel: 7–10 μm in diameter
- Single layer of simple squamous epithelium tissue in wall
- Where gases and nutrients are exchanged between the blood and tissues
- Blood flow to capillaries is regulated by:
  - Vasoconstriction and vasodilation of arterioles
  - Precapillary sphincters

Types of Capillaries

1. Continuous capillaries: Adjacent cells are close together; found in muscles, adipose tissue, and central nervous system (add to blood-brain barrier)
2. Fenestrated capillaries: have pores in vessel wall; found in kidneys, intestines, and endocrine glands
3. Discontinuous: have gaps between cells; found in bone marrow, liver, and spleen; allow the passage of proteins

Veins

- Lower pressure (2 mmHg compared to 100 mmHg average arterial pressure)
- Help return blood to the heart:

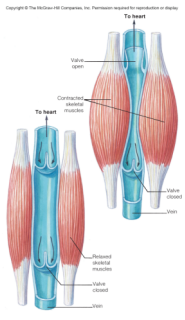
1. Skeletal muscle pumps: Muscles surrounding the veins help pump blood.

Veins

2. Venous valves: Ensure one-directional flow of blood

3. Breathing: Flattening of the diaphragm at inhalation increases abdominal cavity pressure in relation to thoracic pressure and moves blood toward heart.

Veins



VII. Atherosclerosis and Cardiac Arrhythmias

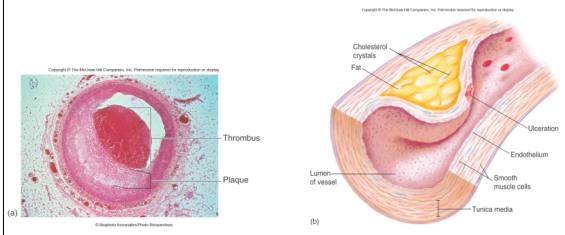
Atherosclerosis

- Contributes to 50% of the deaths due to heart attack and stroke
  - Plaques protrude into the lumen and reduce blood flow.

Atherosclerosis

- Plaques form in response to damage done to the endothelium of a blood vessel.
- Caused by:
  - Smoking, high blood pressure, diabetes, high cholesterol

Atherosclerosis



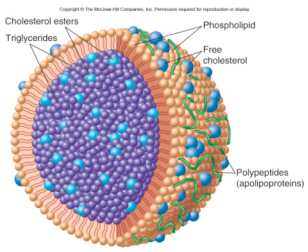
Developing Atherosclerosis

- Lipid-filled macrophages and lymphocytes assemble at the site of damage within the tunica intima.
- Next, layers of smooth muscle are added.
- Finally, a cap of connective tissue covers the layers of smooth muscle, lipids, and cellular debris.

Cholesterol and Lipoproteins

- Low-density lipoproteins (LDLs) carry cholesterol to arteries.
  - People who consume or produce a lot of cholesterol have more LDLs.
  - This high LDL level is associated with increased development of atherosclerosis

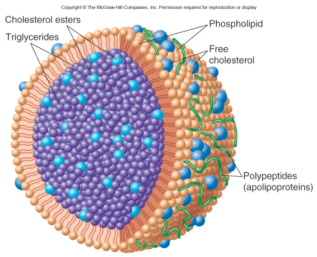
Cholesterol and Lipoproteins



Cholesterol and Lipoproteins

- High-density lipoproteins (HDLs) carry cholesterol away from the arteries to the liver for metabolism.
  - This takes cholesterol away from the macrophages in developing plaques.
  - Statin drugs (e.g., Lipitor) increase HDL levels.

Cholesterol and Lipoproteins



Inflammation in Atherosclerosis

- Atherosclerosis is now believed to be an inflammatory disease.
  - C-reactive protein (a measure of inflammation) is a better predictor for atherosclerosis than LDL levels.
  - Antioxidants may be future treatments for this condition.

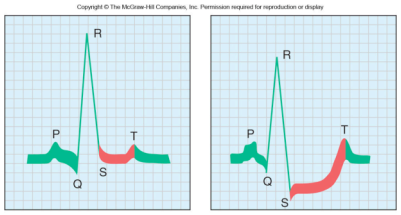
Ischemic Heart Disease

- Ischemia is a condition characterized by inadequate oxygen due to reduced blood flow.
  - Atherosclerosis is the most common cause.
  - Associated with increased production of lactic acid and resulting pain, called angina pectoris.
  - Eventually, necrosis of some areas of the heart occurs, leading to a myocardial infarction (heart attack).

Detecting Ischemia

- Depression of the S-T segment of an electrocardiogram
- Plasma concentration of blood enzymes
  - Creatine phosphokinase, lactate dehydrogenase, troponin I, and troponin T

Detecting Ischemia



Normal Ischemia

Heart Arrhythmias

- Abnormal heart rhythms
  - Bradycardia: slow heart rate, below 60 bpm
  - Tachycardia: fast heart rate, above 100 bpm
    - These heart rhythms are normal if the person is active, but not normal at rest.
    - Abnormal tachycardia can occur due to drugs or fast ectopic pacemakers.

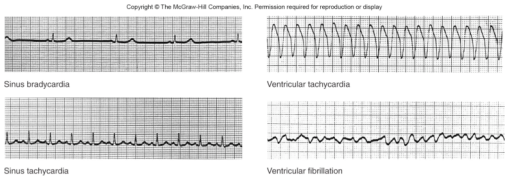
Heart Arrhythmias

- Ventricular tachycardia occurs when pacemakers in the ventricles make them contract out of synch with the atria.
- This condition is very dangerous and can lead to ventricular fibrillation and sudden death.

Flutter and Fibrillation

- Flutter: extremely fast (200–300 bpm) but coordinated contractions
- Fibrillation: uncoordinated pumping between the atria and ventricles

Flutter and Fibrillation



Sinus bradycardia

Ventricular tachycardia

Sinus tachycardia

Ventricular fibrillation

Types of Fibrillation

- Atrial fibrillation:
  - Can result from atrial flutter
  - Atrial muscles cannot effectively contract.
  - AV node can't keep pace with speed of atrial contractions, but some stimulation is passed on.
  - Only reduces cardiac output by 15%
  - Associated with increased risk of stroke and heart failure

Types of Fibrillation

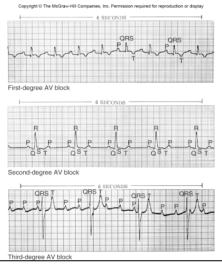
- Ventricular fibrillation:
  - Ventricles can't pump blood, and victim dies without CPR and/or electrical defibrillation to reset the heart rhythm.

AV Node Block

- Damage to the AV node can be seen in changes in the P-R interval of an ECG.
  - First degree: Impulse conduction exceeds 0.2 secs.
  - Second degree: Not every electrical wave can pass to ventricles

AV Node Block

- Third degree/complete: No stimulation gets through. A pacemaker in the Purkinje fibers takes over, but this is slow (20–40 bpm).

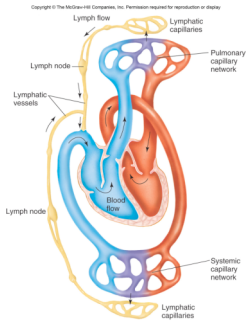


VIII. Lymphatic System

Functions of the Lymphatic System

- Transports excess interstitial fluid (lymph) from tissues to the veins
- Produces and houses lymphocytes for the immune response
- Transports absorbed fats from intestines to blood

Functions of the Lymphatic System



Vessels of the Lymphatic System

- Lymphatic capillaries: smallest; found within most organs
  - Interstitial fluids, proteins, microorganisms, and fats can enter.
- Lymph ducts: formed from merging capillaries
  - Similar in structure to veins
  - Lymph is filtered through lymph nodes

Vessels of the Lymphatic System

- Thoracic trunk and right lymphatic trunk
  - From merging lymphatic ducts
  - Deliver lymph into right and left subclavian veins

Organs of the Lymphatic System

- Tonsils, thymus, spleen
  - Sites for lymphocyte production

Organs of the Lymphatic System