Bio217: Pathophysiology Class Notes
Professor Linda Falkow

Unit VI: Blood and Cardiovascular System Disorders

Chapter 19: Structure & Function of the Hematologic System
Chapter 20: Alterations of Hematologic Function
Chapter 22: Structure & Function of CV & Lymphatic Systems
Chapter 23: Alterations of Cardiovascular Function

Components of the Hematologic System

- Main functions
  - Delivery of substances needed for cell metabolism
  - Removal of wastes
  - Defense against microorganisms and injury
  - Maintain acid-base balance

Components of the Hematologic System

- Composition of blood (~6 quarts)
  - Plasma
    - 55% to 60% of the blood volume
    - Organic and inorganic elements
  - Plasma proteins
    - Albumins
      - Function as carriers and control the plasma oncotic pressure
    - Globulins
      - Carrier proteins and immunoglobulins (antibodies)
    - Fibrinogen

Components of the Hematologic System

- Composition of blood
  - Cellular components (~45%)
    - **Erythrocytes** (red blood cells)
      - Carry O_2 and remove CO_2
      - 120-day life cycle
    - **Leukocytes** (white blood cells)
      - Defend the body against infection and remove debris
      - Granulocytes (neutrophils, eosinophils, basophils)
      - Agranulocytes (monocytes and lymphocytes)
    - **Platelets**
      - Disk-shaped cytoplasmic fragments
      - Essential for blood clotting

Composition of Whole Blood

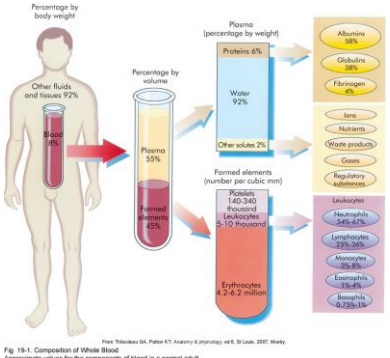


Fig. 19-1. Composition of Whole Blood
Approximate values for the components of blood in a normal adult.

Blood Cells

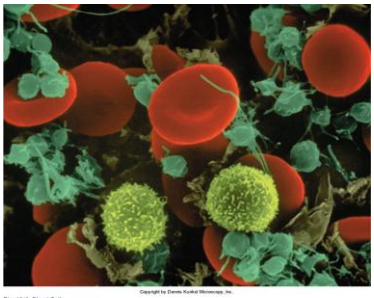
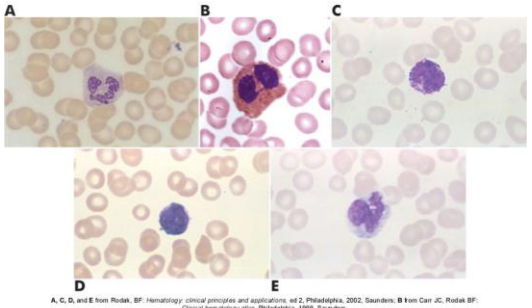


Fig. 19-2. Blood Cells
Leukocytes are spherical and have irregular surfaces with numerous extending pili. Leukocytes are the cotton candy–like cells in yellow. Erythrocytes are flattened spheres with a depressed center.

Leukocytes



A, C, D, and E from Rodak, BF: *Hematology: clinical principles and applications*, ed 2, Philadelphia, 2002, Saunders; B from Carr JC, Rodak BF: *Clinical hematology atlas*, Philadelphia, 1999, Saunders.

Fig. 19-3. Leukocytes
An example of leukocytes in human blood smear. **A**, Neutrophil. **B**, Eosinophil. **C**, Basophil with obscured nucleus. **D**, Typical monocyte showing vacuolated cytoplasm and cerebriform nucleus. **E**, Lymphocyte.

Evaluation of the Hematologic System

- Tests of bone marrow function
  - Bone marrow aspiration
  - Bone marrow biopsy
  - Measurement of bone marrow iron stores
  - Differential cell count
- Blood tests
  - Large variety of tests

Concept Check

- 1. Which is not a component of plasma?
  - A. Colloids
  - B. Electrolytes
  - C. Glucose
  - D. Platelets
- 2. Which is the most abundant protein in blood?
  - A. Fibrinogen
  - B. Albumins
  - C. Globulins
  - D. Hormones
- 3. The purpose of EPO:
  - A. Decrease maturation of RBCs
  - B. Detect hypoxia
  - C. Control RBC production
  - D. Control platelet size

- 4. About how many times more RBCs than WBCs are there in a mm^3 of blood?
  - A. 15
  - B. 90
  - C. 100
  - D. 1000
- 5. Which of the following are agranulocytes?
  - A. Mast cell
  - B. Lymphocyte
  - C. Monocyte
  - D. Reticulocyte
  - E. B and C are correct

Alterations of Hematologic Function
Chapter 20

- **Anemia** = reduced number of erythrocytes or Hb
  - Impaired erythrocyte production
  - Acute or chronic blood loss
  - Increased erythrocyte destruction
  - Classifications
    - **Size**
      - Identified by terms that end in "-cytic"
      - Macrocytic, microcytic, normocytic
    - **Hemoglobin content**
      - Identified by terms that end in "-chromic"
      - Normochromic and hypochromic

Anemia

- Physiologic manifestation
  - Reduced oxygen-carrying capacity
- Variable symptoms depending on severity and body's ability to compensate
- Classic anemia symptoms
  - Fatigue, weakness, dyspnea, and pallor

Macrocytic-Normochromic Anemias

- **Pernicious anemia (PA)**
  - Caused by a lack of intrinsic factor (**IF)** (parietal cells in stomach)
  - Results in vitamin B_{12} deficiency
  - Loss of appetite, abdominal pain, beefy red tongue (atrophic glossitis), icterus, and splenic enlargement
  - PA associated with incr. alcohol intake, hot tea, smoking
  - Treatment: Vit. B_{12} throughout life

Microcytic-Hypochromic Anemias

- **Iron deficiency anemia (IDA)**
  - Most common type of anemia worldwide
  - Due to:
    - Inadequate dietary intake of iron
    - Pregnancy
    - Blood loss (2-4ml/day- ulcer, hiatal hernia, colitis, menorrhagia)
    - Iron malabsorption (chronic diarrhea, celiac disease)
  - Progression of iron deficiency causes:
    - Brittle, thin, coarsely ridged, and spoon-shaped nails (koilonychia)
    - Red, sore, and painful tongue (glossitis)

Microcytic-Hypochromic Anemias

- Pathophysiology
  - Iron use in body for Hb and storage for future Hb
  - Iron is recycled and it is important to maintain a balance.
  - Blood loss → disrupts the balance
  - Normal Hb = ~12-18g/dl
  - When Hb levels drop to7-8g/dl patients seek medical attention
- Treatment
  - Determine source of blood loss
  - Iron replacement therapy

Alterations of Leukocyte Function

- Quantitative disorders
  - Increases or decreases in cell numbers
  - Bone marrow disorders or premature destruction of cells
  - Response to infectious microorganism invasion
- Qualitative disorders
  - Disruption of cellular function

Quantitative Alterations of Leukocytes

- Leukocytosis
  - Leukocytosis is a normal protective physiologic response to physiologic stressors
- Leukopenia
  - Leukopenia is not normal and not beneficial
  - A low white count predisposes a patient to infections

Granulocytosis (Neutrophilia)

- Neutrophilia is evident in the first stages of an infection or inflammation
- If the need for neutrophils increases beyond the supply, immature neutrophils (banded neutrophils) are released into the blood

Granulocytosis (Neutrophilia)

- This premature release is detected in the manual WBC differential and is termed a shift to the left
- When the population returns to normal, it is termed a shift to the right

Monocytes

- Monocytosis
  - Poor correlation with disease
  - Usually occurs with neutropenia in later stages of infections
  - Monocytes are needed to phagocytize organisms and debris
- Monocytopenia
  - Very little known about this condition

Lymphocytes

- Lymphocytosis
  - Acute viral infections
    - Epstein-Barr virus
- Lymphocytopenia
  - Immune deficiencies, drug destruction, viral destruction

Infectious Mononucleosis

- Acute, self-limiting infection of B-lymphocytes transmitted by saliva through personal contact
- Commonly caused by the Epstein-Barr virus (EBV)—85%
  - B cells have an EBV receptor site
  - Others viral agents resembling IM
    - Cytomegalovirus (CMV), hepatitis, influenza, HIV

Infectious Mononucleosis

- Symptoms: fever, sore throat, swollen cervical lymph nodes, increased lymphocyte count, and atypical (activated) lymphocytes
- Serious complications are infrequent (<5%)
  - Splenic rupture is the most common cause of death

Infectious Mononucleosis

- >50% lymphocytes and at least 10% atypical lymphocytes
- Diagnostic test
  - Monospot qualitative test for heterophilic antibodies
- Treatment: symptomatic

Leukemias

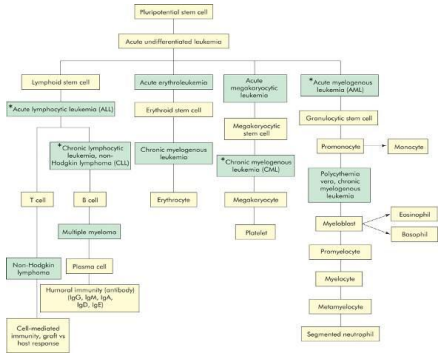
- Malignant disorder of the blood and blood-forming organs
- Excessive accumulation of leukemic cells
- Acute leukemia
  - Presence of undifferentiated or immature cells, usually blast cells
- Chronic leukemia
  - Predominant cell is mature but does not function normally
- Lymphocytic leukemia
- Myeloid leukemia

Leukemias

- ❑ Acute lymphocytic leukemia (ALL)
  - 80% of all childhood leukemias (~81% remission)
- ❑ Acute myelogenous leukemia (AML)
  - One of most common leukemias in adults
  - 1 yr. survival after diagnosis w/ aggressive treatment
- ❑ Chronic myelogenous leukemia (CML)
  - Myeloproliferation in bone marrow, middle aged mostly
- ❑ Chronic lymphocytic leukemia (CLL)
  - Most benign and slow growing; affects elderly

- ❑ Pathophysiology
  - Immature hematopoietic cells→ leukemic cells
  - Leukemic cells multiply → crowding other cell
  - → abnormal RBCs, WBCs, platelets and decreased numbers

Leukemias



Leukemias

- Signs and symptoms of leukemia
  - Anemia, bleeding purpura, petechiae, ecchymosis, thrombosis, hemorrhage, DIC, infection, weight loss, bone pain, elevated uric acid, and liver, spleen, and lymph node enlargement

Disorders of Platelets

- Thrombocytopenia
  - Platelet count <150,000/mm^3
    - <50,000/mm^3—hemorrhage from minor trauma
    - <15,000/mm^3—spontaneous bleeding
    - <10,000/mm^3—severe bleeding

Disorders of Platelets

- Thrombocytopenia
  - Causes
    - Hypersplenism, autoimmune disease, hypothermia, and viral or bacterial infections that cause disseminated intravascular coagulation (DIC), HIT
- ITP (Idiopathic thrombocytopenia)
  - I- immune system makes antibodies against platelets
  - T- trapped platelets appear in spleen and liver
  - P- phagocytosis causes thrombocytopenia

  - Symptoms:
    - Nosebleed, oral bleeding
    - Purpura
    - Petechiae

Disorders of Platelets

- Immune thrombocytopenic purpura (ITP)
  - IgG antibody that targets platelet glycoproteins
  - Antibody-coated platelets are sequestered and removed from the circulation
  - The acute form of ITP that often develops after a viral infection is one of the most common childhood bleeding disorders

Disorders of Platelets

- Immune thrombocytopenic purpura (ITP)
  - Manifestations
    - Petechiae and purpura, progressing to major hemorrhage

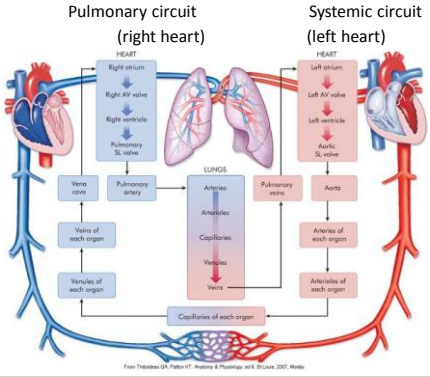
Disseminated Intravascular Coagulation (DIC)

- Complex, acquired disorder in which clotting and hemorrhage simultaneously occur
- DIC is the result of increased protease activity in the blood caused by unregulated release of thrombin w/ subsequent fibrin formation and accelerated fibrinolysis
- Endothelial damage is the primary initiator of DIC

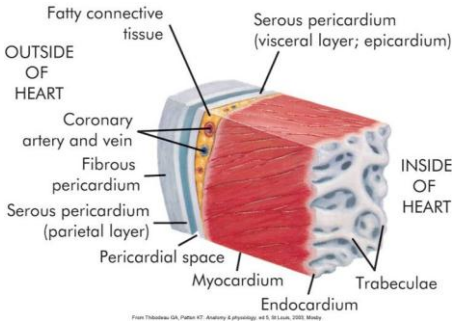
Structure and Function of the Cardiovascular and Lymphatic Systems

Chapter 22

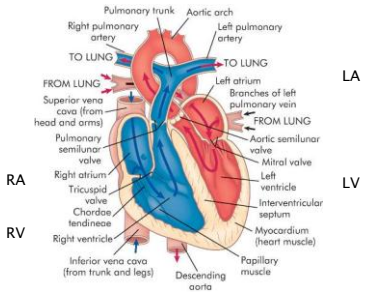
Circulatory System



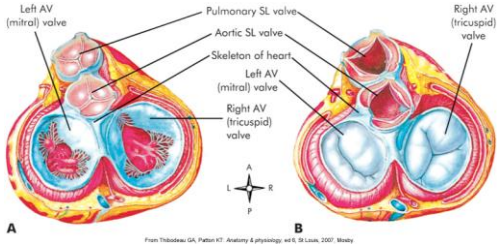
The Heart Wall



The Chambers of the Heart



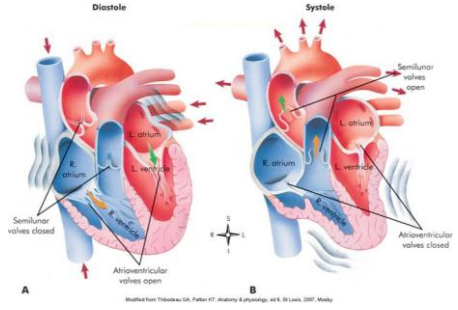
The Valves of the Heart



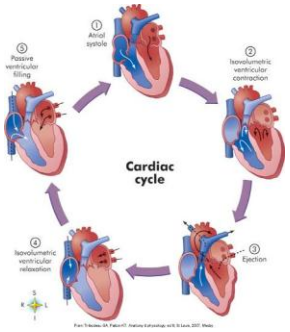
Blood Flow

- Cardiac cycle
- Diastole
- Systole
- Phases of the cardiac cycle

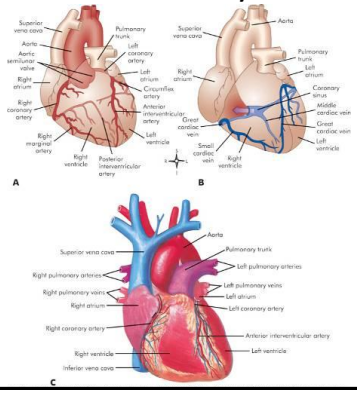
Blood Flow and Cardiac Cycle



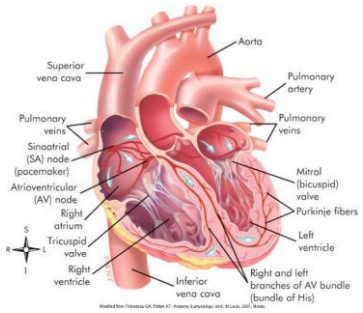
Blood Flow and Cardiac Cycle



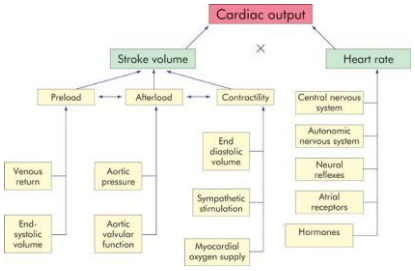
The Coronary Vessels



Conduction System of the Heart



Cardiac Output



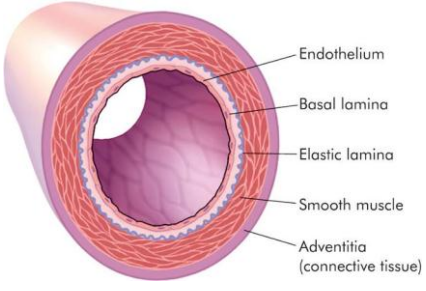
Systemic Circulation

- Arteries
- Arterioles
- Capillaries
- Venules
- Veins

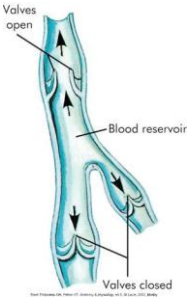
Structure of Blood Vessels

- Lumen
- Tunica intima
- Tunica media
- Tunica externa (adventitia)

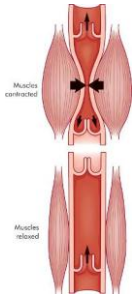
Endothelium



Structure of Blood Vessels



Structure of Blood Vessels



Concept Check

- 1. Oxygenated blood flows through:
  - A. SVC
  - B. Pulmonary veins
  - C. Pulmonary arteries
  - D. Coronary veins
- 2. In the normal cardiac cycle which of the following occurs? (more than one is correct)
  - A. RA and RV contract together
  - B. The 2 atria contract together, while the 2 ventricles relax
  - C. The 2 ventricle contract together , while the 2 atria relax.
  - D. Both the ventricles and the atria contract simultaneously to increase cardiac output.

- 3. The normal heartbeat is initiated by:
  - A. Coronary sinus C. SA node
  - B. AV bundle D. AV node
- 4. Which does not significantly affect HR:
  - A. SNS nerves C. AV valves
  - B. PSN nerves D. ACh

5. Which is the correct sequence of the pulmonary circuit?

a. Pulm. Veins
b. Pulm. Arteries
c. Lungs
d. RV
e. LA

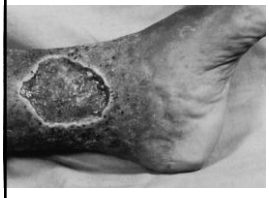
Alterations of CV Function

- Chapter 23

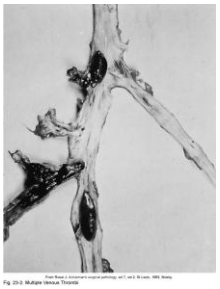
Diseases of the Veins

- **Deep venous thrombosis (DVT)**
  - Obstruction of venous flow leading to increased venous pressure
  - Factors
    - Poor circulation → Venous stasis (immobile, age, CHF)
    - Venous endothelial damage (drugs, trauma)
    - Hypercoagulable states (inherited states, BCP)
    - Venous thrombi are more common than arterial due to low pressure in veins

Diseases of Veins



Venous stasis ulcer

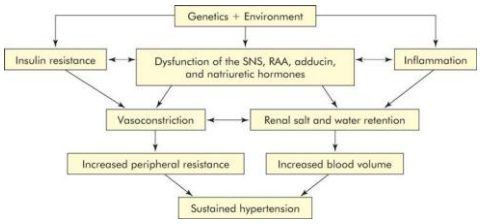


Venous thrombi

Diseases of the Arteries and Veins

- **Hypertension (HT)**
  - – consistent elevation of BP
  - Systolic > 140 mmHg; Diastolic > 90 mmHg
  - **Primary HT**
    - aka essential or idiopathic HT
    - Genetic and environmental factors
    - Affects 92% to 95% of individuals with hypertension
  - **Secondary HT**
    - Caused by a systemic disease that raises PR or CO

Primary Hypertension



Understanding HT

- 1. Kidneys → renin into blood
- 2. Renin converts angiotensin to angiotensin I
  - (in liver)
- 3. Angiotensin I → Angiotensin II (in lungs)
  - Angiotensin II - potent VC
- 4. Angiotensin II → constriction in arterioles and secretion of aldosterone
- 5. Aldosterone → Na+ and H_20 retention
- 6. Retained Na+ and H_2O → incr. blood vol.
- 7. VC → increased PR
- 8. Incr. blood vol. and PR → HT

HT

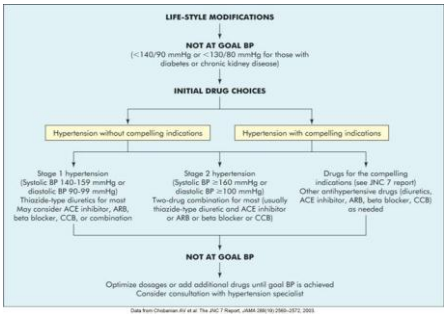
- Complications
  - - can occur late in the disease
  - - can attack any organ
  - - CAD, angina, MI, arrhythmias, sudden death

Location, location, location

Symptoms depend on location of vessel damage

- brain – stroke, TIAs
- retina – blindness
- heart – MI
- kidneys – proteinuria, edema → renal failure

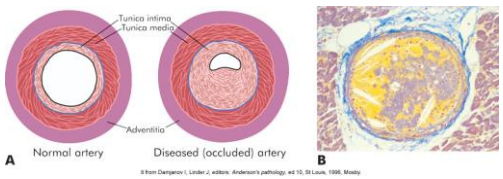
Treatment for Hypertension



Diseases of the Arteries and Veins

- **Arteriosclerosis**
  - – Chronic disease of the arterial system
    - Abnormal thickening and hardening of vessel walls
    - Smooth muscle cells and collagen fibers migrate to the tunica intima
    - Results in narrowing of lumen

Arteriosclerosis



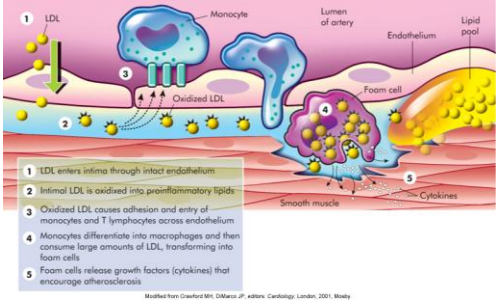
Diseases of the Arteries and Veins

- **Atherosclerosis**
  - Most common form of arteriosclerosis
  - Thickening and hardening is caused by accumulation of lipid-laden macrophages in the arterial wall
  - Plaque development

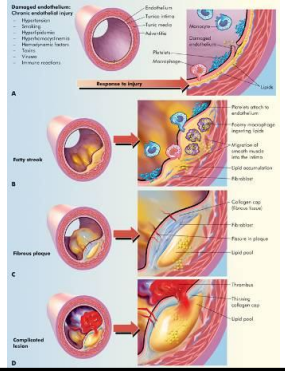
Diseases of the Arteries and Veins

- Atherosclerosis
  - Progression
    - Damaged endothelium
    - Cellular proliferation & macrophage migration
    - Macrophages → foam cells that accumulate fat
    - Fatty streak (lesion)
    - Fibrous plaque due to SMC proliferation

Atherosclerosis



Atherosclerosis



Peripheral Arterial Disease

- Atherosclerotic disease of arteries that perfuse limbs
- Intermittent claudication

Coronary Artery Disease

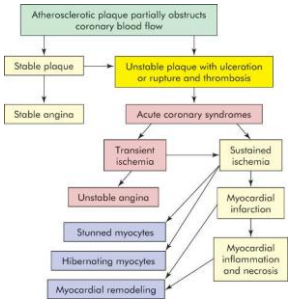
- Any vascular disorder that narrows or occludes the coronary arteries
- Atherosclerosis is the most common cause

➢Risk factors
Dyslipidemia (abnormal blood levels of lipids)
Hypertension
Cigarette smoking
Diabetes mellitus
Obesity/sedentary lifestyle

Coronary Artery Disease

- Nontraditional risk factors
  - Markers of inflammation and thrombosis
    - C-reactive protein (C-rp), fibrinogen, protein C, and plasminogen activator inhibitor
  - Hyperhomocysteinemia (lack of enz. to breakdown homocysteine)
  - Infection *(Clamydia pneumonae, H. pylori)*

Myocardial Infarction



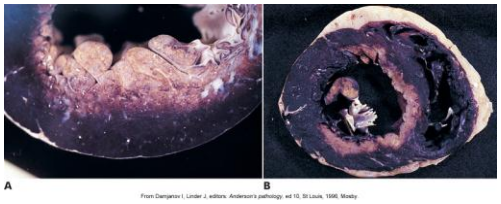
Coronary Artery Disease

- **Myocardial infarction (MI)**
  - Sudden and extended obstruction of the myocardial blood supply
  - Subendocardial MI- if thombus breaks up before necrosis, only will involve myocardium under endocardium
  - Transmural MI – if thrombus permanently lodged in vessel , infarct will extent throughout heart wall

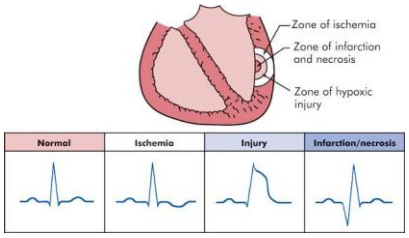
Myocardial Infarction

- Pathophysiology
  - Cellular injury – cardiac cells can w/stand 20 min. of ischemia prior to cell death
  - - Ischemic cells loose contractile ability (pH and electrolyte changes)
  - Cellular death – 20 min. of ischemia → irreversible damage and cells death
  - - release of CPK from damaged cardiac cells
- Symptoms:
  - - crushing chest pain (unrelenting indigestion)
  - -decr. BP
  - SNS stimulation (rel. of catecholamines) → diaphoresis and peripheral VC

Myocardial Infarction



Myocardial Infarction



EKG changes evident within 30-60 sec.
Gross changes take hours

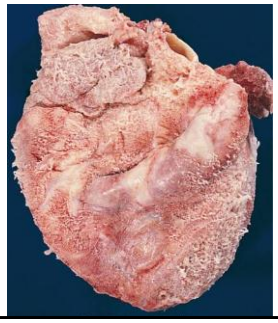
Disorders of Heart wall

- Acute Pericarditis
  - Causes:
    - Viruses or idiopathic (90%)
    - MI, cardiac surgery, autoimmune
  - Symptoms
    - Severe retrosternal pain
    - Phrenic nerve irritation

  Treatment: anti-inflammatory drugs, colchicine

Acute Pericarditis

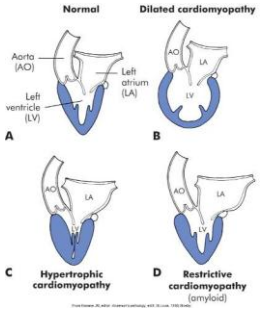
- pericardial membranes inflammed, exudate/ shaggy fibers may form



Disorders of the Myocardium

- Cardiomyopathies – disorders that affect myocardium
  - Dilated cardiomyopathy (congestive cardiomyopathy)
    - Due to extensive damage of ventricular myocardial cells
    - Gives heart globular shape
    - Dilation of all 4 chambers (increased P and V)
    - Thrombosis
    - Left-sided heart failure → right-sided heart failure
    - → low CO → valve insufficiency → heart failure → A-fib → decreased CO

Cardiomyopathy



Valvular Disorders

- **Mitral Valve Prolapse (MVP)**
  - One or more cusps of mitral valve billow up (prolapse)
  - Degeneration of valve leaflet → thickening → regurgitation into LA
  - Most common valve disorder in US (1-3% adults)
  - Asymptomatic typically; good prognosis
  - Only small no. of high-risk individuals → complications (endocarditis, stroke, sudden death)

Arrhythmias

- Disturbance of the heart rhythm
- Range from occasional "missed" or rapid beats to severe disturbances that affect pumping ability of heart
- Caused by an abnormal firing of SA node (pacemaker) or conduction system

Dysrhythmias

- Examples:
  - Tachycardia (HR > 100-120 bpm)
  - Flutter (HR =250- 300)
  - Fibrillation (HR > 300)
  - Bradycardia (HR < 60 bpm)
  - Premature ventricular contractions (PVCs)
  - Premature atrial contractions (PACs)

Congestive Heart Failure

- Myocardium cannot pump effectively
- **Left – sided heart failure** usually occurs first
- Due to infarction, mitral stenosis (blood vol. low), V or P overload, arrhymthmias
- LV function decreases → blood backs up in pulmonary veins → pulmonary edema
- Dysfunction of myocardium → activate RAA and SNS → remodel of ventricle
- Treatment: ACE inhibitors, beta blockers, Angiotensin II blockers slow progression

Concept Check

- 1. Factors in the dev. of atherosclerotic plaque include all of the following except:
  - A. accumulation of LDL
  - B. SMC proliferation
  - C. calcification
  - D. decreased elasticity
  - E. complement activation
- 2. Complications of uncontrolled HT include all of the following except:
  - A. CVAs
  - B. Anemia
  - C. Renal injury
  - D. Cardiac hypertrophy
  - E. All of the above

- 3. Most common cause of CAD is:
  - A. Myocarditis
  - B. Hypoglycemia
  - C. Atherosclerosis
  - D. Vasospasm

Matching:

___4. aortic stenosis
___ 5. cardiomyopathy
___ 6. infarction
___ 7. mitral stenosis
___ 8. fibrous plaque
___ 9. thromboembolism

A. Clot detached from vessesl wall
B. Lesion of atherosclerosis
C. Assoc. with RHD
D. Death of myocardial tissue
E. Disease of myocardium
F. Dec. blood flow from LV due to narrowed aortic semilunar valve