Pathology of Ischemic and Hypertensive Heart Disease

I. Congestive Heart Failure
Physiologic state resulting from impaired cardiac function that renders the heart unable to maintain output sufficient to meet the metabolic requirement of tissues and organs

A. Systolic Heart Failure (heart failure with reduced ejection fraction*)
   i. Result of progressive deterioration of myocardial contraction
   ii. Damaged myocardium contracts weakly or inadequately
   iii. Chambers do not empty properly
   iv. Etiologies include ischemic injury; pressure or volume overload

B. Diastolic Heart Failure (heart failure with preserved ejection fraction*)
   i. Heart chambers do not sufficiently relax, expand, and fill during diastole
   ii. Etiologies include left ventricular hypertrophy, myocardial infiltrative disease, constrictive pericarditis

C. Left sided heart failure
   i. Results in damming of blood in pulmonary circulation
      -Pulmonary congestion and edema, pleural effusions
   ii. Results in decreased peripheral blood flow
      -Renal hypoperfusion
      -Muscle fatigue
      -Cerebral hypoperfusion

D. Right sided heart failure
   i. Engorgement of systemic and portal venous circulation leading to
      -Dependent peripheral edema
      -Ascites
      -Hepatic congestion
      -Congestive splenomegaly
      -Renal congestion

E. Biventricular failure

*Review: Definition of Ejection Fraction:
The ratio of the volume of blood ejected from the left ventricle per beat (stroke volume) to the volume of blood in the left ventricle at the end of diastole (end-diastolic volume); used clinically as an index of contractility.

II. Ischemic Heart Disease
Imbalance between the supply and demand of the heart for oxygenated blood either through a) reduced coronary blood flow (in >90% of cases) or b)increased
myocardial demand exceeding vascular supply.

A. Stable Angina Pectoris
   i. Transient myocardial ischemia (without myocardial necrosis or infarction)
   ii. Pathogenesis- Fixed coronary artery stenoses (usually >75% stenosis)
   iii. Classic manifestation – substernal chest pressure
        -Onset with activity, stress (increased cardiac demand and workload needs unmet)
        -Relieved with rest
        -Relieved with vasodilator (ie nitroglycerin)

B. Unstable Angina Pectoris (preinfarction angina, crescendo angina)
   i. Pathogenesis – Atherosclerotic plaque disruption (fissure, ulceration)
   ii. Results in superimposed partially occluding platelet aggregation or mural thrombus (thromboemboli, vasospasm may play roles as well)
   iii. Plaques most vulnerable are moderately stenotic (ie < 50-75%), lipid rich, inflammation
   iv. Symptoms (ie chest pressure) more frequent, with less effort, at rest, longer duration as compared to stable angina

C. Prinzmetal Angina
   i. Pathogenesis – coronary artery vasospasm
   ii. Chest pain occurs at rest
   iii. Treatment – vasodilators (ie nitroglycerin, calcium channel blockers)

D. Myocardial Infarction
   Leading cause of death in the US and industrialized nations
   i. Transmural infarct– Ischemic necrosis involves full (or nearly full) thickness of ventricle
      a. Pathogenesis – Occlusive coronary thrombus overlying a disrupted atherosclerotic plaque
         -Plaque erosion, fissure, ulceration, rupture or hemorrhage
         -Platelet adhesion, aggregation, activation, release of aggregators
         -Vasospasm
         -Extrinsic coagulation pathway activation
         -Lumenal occlusion by thrombus
      b. In 10% of cases, no evidence of atherosclerotic plaque disruption and thrombosis
         -Mechanisms - vasospasm, emboli, other?
      c. Characteristically ST segment elevation on EKG corresponding to distribution of occluded coronary artery
   ii. Subendocardial (nontransmural) Infarct – Ischemic necrosis limited to inner one third, or at most one half of ventricular wall
a. Pathogenesis - In majority of cases there is diffuse stenosing coronary atherosclerosis and reduction of coronary flow. 
   *Rarely* evidence of plaque disruption or superimposed thrombus (was thrombus lysed prior to myocardial necrosis extending across entire wall thickness?)

b. May result from prolonged and severe reduction in systemic blood pressure (ie shock, hemorrhage)
   -With global hypotension subendocardial infarct usually circumferential

iii Myocardial morphology post infarct (refer to Robbins Table 11-2; Robbins Figure 11-11)
   - 30 minutes to 4 hours
     - No gross or microscopic changes
   - 4-12 hours
     i. Beginning coagulation necrosis
   - 12-24 hours
     - Gross – dark myocardial mottling
     - Microscopic – Ongoing coagulation necrosis, pyknosis of nuclei
   - 1-3 days
     - Loss of myocardial nuclei and myocytes
     - Neutrophilic infiltrate
   - 3-7 days
     - Gross- yellow-tan softening
     - Microscopic-Myocyte disintegration, degenerating neutrophils, phagocytosis of dead cells
   - 7-10 days
     - Well-developed phagocytosis and early granulation tissue
   - 10-14 days
     - Granulation tissue
   - 2-8 weeks
     - Scar formation

iv. Clinicopathologic correlation
   a. Symptoms/signs – crushing substernal chest pain, dyspnea, diaphoresis, tachycardia, pulmonary congestion, edema
   b. 10-15% of patients have “silent” MI (no classic symptoms)
      Elderly, patient with diabetes mellitus
   c. Laboratory – Myoglobin, elevations
   d. EKG
   e. Treatment
      - Antiplatelet agents
      - Heparin
      - Thrombolytic therapy (drug vs interventional)
      - Beta blockers
f. Reperfusion injury
Restoration of blood flow (via thrombolytic therapy, angioplasty/stent placement, bypass surgery) to ischemic tissue leads to further local damage as a result of
- production of oxygen derived free radicals
- myocyte hypercontracture – after reperfusion contraction of myofibrils is augmented (intracellular levels of calcium are increased as a result of ischemia) leading to cytoskeletal damage, death
- leukocyte aggregation which may occlude vasculature; leukocyte proteases and elastases may cause cell death
- mitochondrial injury leads to apoptosis

v. Complications
a. Cardiogenic shock. Occurs most often in the setting of large infarcts (ie involving >40% of the ventricle)
b. Arrhythmias (tachy and brady)
   - Ventricular fibrillation - greatest risk first several hours
c. Myocardial rupture (days 3-7)
   - May involve free wall (resultant hemopericardium, cardiac tamponade), ventricular septum, papillary muscle
d. Pericarditis
   - Acute pericarditis
     - Occurs with transmural infarcts with 2-3 days after the infarct
     - Dressler Syndrome is a form of autoimmune pericarditis which occurs several weeks to months after a myocardial infarction. It is also referred to as post-myocardial infarction syndrome.
e. Ventricular aneurysm (late complication)
f. Mural Thrombus

vi. Chronic ischemic heart disease
a. “Ischemic Cardiomyopathy”
b. Progressive heart failure as a consequence of ischemic myocardial damage
   - Decompensation of noninfarcted myocardium
c. Hearts are enlarged, heavy with left ventricular hypertrophy and dilatation
d. Coronary arteries have stenosing atherosclerosis

vii. Sudden Cardiac Death
a. Severe chronic coronary atherosclerosis with an associated lethal arrhythmia is the etiology in 80-90% of cases
At autopsy findings of acute plaque disruption are not found in most cases.

Irritability of myocardium triggers arrhythmia.

b. Other, non-atherosclerotic, causes of sudden cardiac death:
   - Hereditary or acquired abnormalities of cardiac conduction system
   - Congenital coronary artery abnormalities
   - Myocarditis
   - Mitral valve prolapse
   - Dilated or hypertrophic cardiomyopathy
   - Pulmonary hypertension
   - Myocardial hypertrophy (increased cardiac mass)

III. Left Sided Hypertensive Heart Disease
a. Left ventricular hypertrophy (LVH) is the adaptive response to pressure overload:
   i. Increased rate of myocyte protein synthesis
   ii. Increased size of myocytes
   iii. Increased number of sarcomeres and mitochondria
   iv. Increased mass and size of heart
      - Concentric LV wall thickness may exceed 2cm, weight may exceed 500gm
   v. For the hypertrophied myocardium, there are increased metabolic requirements, abnormal protein structure, inadequate vasculature, and fibrosis which may lead to cardiac dysfunction:
     - Systolic or diastolic heart failure
     - Arrhythmias (ie atrial fibrillation), result of left atrial enlargement
     - Neurohormonal stimulation
   vi. Blood pressure control can prevent LVH
     - Regression with some agents (ie ACE inhibitors)

IV. Pulmonary (Right Sided) Hypertensive Heart Disease (Cor Pulmonale)
a. Pulmonary hypertension caused by disorders of the lungs and pulmonary vasculature - i.e. COPD, pulmonary fibrosis, recurrent pulmonary thromboembolism, primary pulmonary hypertension, sleep apnea, marked obesity (Refer to Robbins Table 11-3)
b. Above disorders may lead to:
   i. Right ventricular hypertrophy
   ii. Right ventricular dilatation
   iii. Right sided heart failure