CARDIOMYOPATHY/MYOCARDITIS/
PERICARDIAL HEART DISEASE

I. Cardiomyopathy
Heart disease resulting from a primary abnormality in the myocardium
(note: ischemic heart disease, valvular heart diseases, hypertensive heart disease can result in dilated, systolic myocardial dysfunction but are not “cardiomyopathies” by the strict definition because the primary abnormalities are of the vasculature and valves, not the myocardium)

A. There are three clinical, functional, and pathologic patterns (refer to Robbins Table 11.5)
   i. Dilated Cardiomyopathy (most common)
   ii. Hypertrophic Cardiomyopathy
   iii. Restrictive Cardiomyopathy (least common)

II. Dilated Cardiomyopathy
A. Most common pattern of “cardiomyopathy”
B. Pathology
   i. Enlarged heart with 4 chamber dilatation
      -left ventricle wall will display hypertrophy (eccentric hypertrophy)*
   ii. Progressive systolic (contractile) dysfunction
C. Etiologies (important to be able recite this list of etiologies)
   i. Post myocarditis
      -Coxsackie B and other enterovirus infections most commonly associated with resultant dilated cardiomyopathy
   ii. Alcohol (alcoholic cardiomyopathy)
      -Result of long term, heavy consumption
      -Precise mechanism for myocyte dysfunction not known, no specific morphologic findings
      -Hypotheses: direct toxic effect of alcohol vs secondary nutritional deficiency
   iii. Toxins other than alcohol
      -Doxorubicin and Daunarubicin (chemotherapeutic agents)
      -Cardiotoxicity is dose-dependent
   iv. Peripartum cardiomyopathy
      -Develops late in pregnancy or in the 5 months after delivery
      -Precise etiology unknown; recent studies suggest prolactin driven defect in angiogenesis leading to ischemia
      -Other causes of dilated cardiomyopathy should be ruled out
   v. Genetic (refer to Robbins Figure 11.24)
      -Familial occurrence of dilated cardiomyopathy thought to occur in 25-50% of patients
      -Genetic abnormalities most commonly affect the cytoskeleton
vi. Iron overload (hereditary hemochromatosis or multiple blood transfusion hemosiderosis)
   - iron accumulates within myocytes and interferes with metal-dependent enzyme systems
vii. Stress associated - Takasubo cardiomyopathy ("broken heart syndrome"); likely due to increased sympathetic stimulation.
   Echocardiogram pattern - ballooning of LV apex
viii. Idiopathic

D. Treatment
i. Medical management of systolic heart failure and its complications
   - Complications include fluid overload, arrhythmias, systemic emboli from mural thrombi
ii. Heart transplantation may be the option for patients whose symptoms are recalcitrant to optimal medical therapy and who are appropriate candidates

*Eccentric vs Concentric Hypertrophy*
In dilated cardiomyopathy the heart responds to the increased diastolic pressure by fiber elongation and replication of sarcomeres in series, which leads to increased ventricular volumes. Because systolic pressure remains relatively unchanged, increased wall stress—by Laplace law—can be compensated for by an additional increase in wall thickness. This response, “eccentric hypertrophy” - named because the ventricular cavity enlarges laterally in the chest and becomes eccentric to its normal position.
In response to the pressure overload, such as with aortic stenosis, left ventricular wall thickness markedly increases—while the cavitary radius remains relatively unchanged—by parallel replication of sarcomeres. These compensatory changes are termed “concentric hypertrophy,”

Summary: Concentric hypertrophy is associated with increased left ventricular wall thickness whereas eccentric hypertrophy is characterized by dilatation of the left ventricular chamber; however, there occurs a general increase in the overall size of cardiomyocytes (hypertrophy) under both conditions.

III. Hypertrophic cardiomyopathy (HCM)
“Hypertrophic obstructive cardiomyopathy” (HOCM)
A. Caused by missense mutation in 1 of at least 12 genes encoding cardiac sarcomere proteins
   - Mutations in the B-myosin heavy chain are most common
B. Most cases are familial
   i. Autosomal dominant with variable expression
C. Pathology
   i. Marked myocardial hypertrophy (septum > free wall)
   ii. Bulging of septum into the left ventricle lumen (results in a “banana shaped” left ventricle)
   iii. During systole the anterior mitral valve leaflet contacts the ventricular septum
iv. Abnormal diastolic filling as a result the ventricular hypertrophy
v. Left ventricle outflow tract obstruction
   -most common cause is the systolic anterior motion of the mitral valve and mitral-septal contact
vi. Histology – Disorganized, haphazardly arranged myocytes; myocytes are extensively hypertrophied

D. Clinical features
i. Cardiac insufficiency develops due to impaired diastolic filling of the massively hypertrophied left ventricle, reduced myocardial compliance and reduced stroke volume (diastolic CHF)
ii. Systolic ejection murmur that increases in loudness during maneuvers that decrease preload (ie squatting to standing position)
   Why? Maneuvers that affect the degree of LV outflow obstruction cause a change in murmur intensity: An increase in intensity of the murmur, due to enhancement of obstruction, is seen with maneuvers that decrease preload, left ventricular volume and therefore LV chamber size. These include the assumption of an upright posture from a squatting, sitting, or supine position, the Valsalva maneuver, and following the administration of vasodilators. A decrease in murmur intensity, due to attenuation of obstruction, is heard after going from a standing to a sitting or squatting position, with handgrip, and following passive elevation of the legs.
iii. Anginal pain, dyspnea, syncope may develop
iv. Intractable heart failure may develop
v. Arrhythmias, including atrial fibrillation
vi. Mural thrombi with embolic complications
vii. Sudden death (most common cause of sudden death in young athletes)

Resource: LUMEN online video- HOCM which further discusses hemodynamics and pathophysiology

E. Treatment
i. Medical therapy aimed at enhancing ventricular relaxation so that diastolic filling is enhanced (ie beta blockers, non-dihydropyridine calcium channel blockers)
ii. Surgical septal excision (myectomy)

IV. Restrictive Cardiomyopathy
A. Primary decrease in ventricular compliance, resulting in impaired ventricular filling during diastole. Systolic function is unaffected
B. Pathology
i. Ventricle and left ventricle cavity are generally normal in size and caliber
ii. The myocardium is firm and stiff impeding expansion of the left ventricle cavity
iii. Histologic findings vary depending on the etiology
C. Etiologies:
   i. Radiation fibrosis
   ii. Amyloidosis
      - Results from pathologic proteinaceous substance deposited in the myocardial interstitium

   **Amyloidosis in general**
   - There are at least 15 biochemically distinct forms of amyloid protein
   - The proteins have common morphologic properties
     -- Ultrastructurally all forms of amyloid have interlacing bundles of parallel arrays of fibrils; the protein in the amyloid fibrils contains a large proportion of cross $\beta$–pleated sheet structure
     -- They have affinity for congo-red stain with an apple-green birefringence under polarized light
   - The symptomatology of amyloidosis is governed by the type and organ locations of the protein deposits (ie brain, kidney, heart)

   iii. Sarcoidosis – Systemic disease characterized by noncaseating granulomas in multiple organs. Precise etiology is not known – likely due to CD4 helper T-cell response to an antigen which has not yet been identified (Sarcoidosis will be covered formally in the pulmonary block lectures)
   iv. Metastatic tumor
   v. Inborn errors of metabolism
   vi. Endomyocardial fibrosis – disease of children in Africa and tropics. Dense, diffuse fibrosis of endocardium reduces volume and compliance of chambers leading to restrictive physiology.
   vii. Loeffler endomyocarditis – endomyocardial fibrosis with an eosinophilic infiltrate and peripheral blood eosinophilia; no geographic predilection.
   viii. Idiopathic

D. Clinical signs and symptoms result from reduced myocardial compliance and stroke volume (**diastolic CHF**)

E. Treatment – determine the underlying etiology. Medical management of diastolic heart failure

V. Myocarditis
   A. Inflammatory process resulting in myocardial injury
   B. Etiologies - many
      i. Infections
Viruses – most common etiology in US
- Enterovirus (Coxsakie A and B and others) – viral genome may be detected by PCR in myocardial biopsy samples
- Influenza Virus
- HIV

Bacteria
- Borrelia (Lyme disease)
- Corynebacterium diphtheriae

Parasites
- Trypanosoma cruzi – Chagas disease (endemic in parts of South America)
- Trichinosis
- Toxoplasmosis

II. Immune Mediated
- Hypersensitivity reactions (ie to drugs)
- Rheumatic fever
- Systemic lupus erythematosus

III. Unknown mechanisms
- Sarcoidosis
- Giant cell myocarditis

C. Pathologic findings – vary depending on the etiology, extent of myocardium involved
i. Gross – Normal or flabby heart with mottled myocardium
ii. Microscopic – Interstitial inflammatory infiltrate (often lymphocytic), focal myocyte necrosis
   - The type of inflammatory response depends on the etiologic agent (refer to Robbins Figure 11.28)
iii. As the acute phase of the inflammatory process resolves there may be no residual changes vs progressive fibrosis

D. Clinical manifestations
i. There is a range
   - No symptoms
   - Nonspecific symptoms (ie fever, fatigue)
   - Acute congestive heart failure
   - Arrhythmias, sudden death
   - Progressive cardiac dysfunction resulting in dilated cardiomyopathy

ii. Treatment - supportive

VI. Pericardial Disease
A. Pericardial effusions
i. Normally there is 30-50cc of pericardial fluid in pericardial sac
ii. Fluid may accumulate in the pericardial sac for a large variety of reasons. Fluid may be serous, purulent, or bloody. Effusions may be acute or chronic
Etiologies of moderate to large pericardial effusions include: neoplasms, uremia (seen in renal failure), iatrogenic, post-acute myocardial infarction, viral, collagen vascular diseases, tuberculosis, idiopathic

iii. If there is a slow accumulation of less than 500cc fluid - the effusion may be clinically asymptomatic (one may see a globular heart shadow on chest x-ray)

iii. If rapidly accumulating or chronically larger than 500cc, symptoms develop
   “Cardiac tamponade” may develop
   In cardiac tamponade, fluid in the pericardial sac compresses atria and vena cavae, compresses the ventricles, and restricts cardiac filling leading to decreased cardiac output.
   Clinical findings – hypotension, increased venous pressure (increased JVD), distant heart sounds, pulsus paradoxus

   Resource: LUMEN online Video – Cardiac Tamponade which further discusses pathophysiology and hemodynamics

B. Pericarditis
i. Inflammation of the pericardium
ii. Often the inflammation is a response to a cardiac, thoracic or systemic process
iii. Many etiologies
   - Infection
     - Viruses (one of most common causes of pericarditis, coxsackievirus A and B, echovirus, adenovirus, HIV)
     - Bacteria, TB, fungi, parasites
   - Immune mediated reactions
     Rheumatic fever, SLE, Dressler syndrome*, drug hypersensitivity
     *what is “Dressler syndrome”? – an autoimmune phenomenon resulting in pericarditis several weeks post myocardial infarction.
     (Note that this is a different pathogenesis than the pericarditis that is seen several days post transmural MI)
   - Acute MI
   - Uremia
   - Neoplasm (especially lung and breast cancer, Hodgkin’s disease, mesothelioma)
   - Trauma
   - Mediastinal Radiation
   - Idiopathic
iv. **Pathology**

Depending on the etiology, the pericardial surface/exudate may be

- **Fibrinous/Serofibrinous**
  - Pericardial surface is dry/rough (fibrinous) or may have thick, yellow fluid on pericardial surface with inflammatory cells, blood, fibrin (serofibrinous)
  - Etiologies – acute MI, Dressler syndrome, uremia, chest radiation, rheumatic fever, lupus, trauma
  - Friction rub is heard on physical exam with fibrinous pericarditis

- **Suppurative**
  - Frank pus with reddened granular pericardial surface
  - Etiology – Acute bacterial infection from invasion of the pericardial space by microorganisms

- **Hemorrhagic**
  - Etiology most commonly malignancy, TB

- **Caseous**
  - TB

v. **Clinical signs and symptoms of pericarditis** – depend on the etiology

- Spectrum - clinically silent to chest pain to systemic complaints (fever, chills)
- Pericardial friction rub (particularly with fibrinous pericarditis)
- EKG changes (classic finding diffuse ST-segment elevation, often with depression of the PR segment)

vi. **Healing process** may result in no sequela, focal plaque-like thickening of pericardium or mild adhesions

vii. **Constrictive pericarditis**

- Pericardial space is obliterated by dense scar tissue through the healing process
- Diastolic expansion is limited, cardiac output is reduced
- Seen particularly with TB, suppurative pericarditis
- Treatment = pericardiectomy, surgical removal of constricting pericardium

VII. **Cardiac Transplantation**

A. **Most common indications** – dilated cardiomyopathy, chronic ischemic heart disease

B. **90% 1 year survival**

C. **>70% 5 year survival**

D. **Complications**

  i. Acute rejection
  ii. Graft Arteriopathy
  iii. Infections
iv. Post-transplant lymphoproliferative disorder (Epstein Barr virus related)