Pathology C 601
Cardiac Disease

Reading:

Robbins: Chapter 12

Clinical lab Source:
- ASO
- AST
- CPK and its fractions
- LDH
- Troponin, I and T (which is best?)
- Myoglobin
- Serum lipids, take a good look at LDL and HDL
- Activated clotting time (ACT)
- CRP (C Reactive Protein)

Wheater:

- Atherosclerosis
- Cardiovascular system

Laboratory assignment: C601/C602 Histopathology Manual: Cardiovascular unit

- Take a look at the movies showing various cardiac abnormalities.

On-line assignment: Cases 3, Mr. Raymond. You must take the on-line quiz at the end. As you will see, there are two for each case. One is for you to practice with and the other is for grade. To do the graded quiz, you must connect to the Quizsite Server through the Internet.
I. Normal state of affairs and regions referred to when describing diseases processes.

A. Size and weight
   1. Adult is 300 to 350 gm
   2. Left ventricle is 1.3 to 1.5 cm thickness at the papillary muscle (but not including the papillary muscle) on the lateral wall.
   3. Right ventricle is 0.3 to 0.5 at lateral wall

B. Two coronary arteries
   1. Big area of pathology
   2. Collateral connections
   3. Which is “dominant”

C. Endocardium and valves
   1. Valves are an extension of the endocardium

D. Myocardium
   1. Good old Starling
   2. Syncytium of myocardial muscle cells
   3. Fibroconnective tissue
   4. Conduction elements
E. Epicardium, pericardial sac and adjacent mediastinal structures

F. Aorta

II. All the major causes of disease can result in cardiac malfunction, and we will look at examples of all of them. However, in the otherwise health adult, clinical symptoms manifest themselves for reasons of mechanical dysfunction. Here are the clinically relevant categories of presentation.

A. Leaks in the circulatory system that allows blood to escape (blood loss), leading to reduced filling and diminished effective blood volume.
   1. Bullet holes

B. Conduction system abnormalities leading to irregular heart rhythm and lousy pumping coordination and efficiency
   1. Disrrhythmias associated with coronary vascular narrowing

C. Obstructions to blood flow.
   1. Vascular narrowing

   2. Restrictions of valve action
   3. Asymmetry of heart muscle leading to restricted outflow of the ventricles

D. Incompetent valves leading to regurgitation of blood flow back into the pumping
chambers of the heart and thereby wasting a part of each pumping stroke.

1. Scarred aortic valve that does not allow it to close

2. Mitral valve following rheumatic heart disease
   - Strep antibody cross reaction

E. Failure of the pump itself

1. Contractile failure - systolic failure
   - poor vascular flow to myocardium
   - loss of muscle as happens following myocardial infarction

2. Ventricular filling problem - diastolic failure
   - restriction to relaxation of the heart
     - external
       - trapped by scarred pericardium
       - post surgical
       - post inflammatory
       - myocardial
         - something in the heart muscle itself
III. Congenital Heart disease

- Grouped by the development of cyanosis

  - late of tardive cyanotic heart disease
  
  - cyanotic (early) cyanotic heart disease
  
  - non-cyanotic heart disease
A. Present at the time of birth

1. Genetic
   - “familial tendency” - greatly increased incidence among siblings

<table>
<thead>
<tr>
<th>TABLE 12-3 Selected Examples of Genetic Causes of Congenital Heart Disease</th>
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<tbody>
<tr>
<td><strong>Affected Gene(s)</strong></td>
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<tr>
<td><em>Non-syndromic</em></td>
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<tr>
<td>NKX2-5</td>
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<td>GATA-4*</td>
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<td>TBX20*</td>
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<tr>
<td><em>Syndromic</em></td>
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<td>TBX5</td>
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<td>TBX1, JAG1, NOTCH2</td>
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2. Environmental factors
   - maternal infections - name one
   - toxic - fetal alcohol syndrome
3. Incidence really unknown, figure is 6-8 per 1000 live births

4. Must know embryology to understand what can go wrong

B. Tardive or late cyanotic heart disease: Becomes “blue” or cyanotic some years after birth.

1. Left to right shunt at first, but later becomes right to left
   - large flow through pulmonary vasculature
   - in time increased pulmonary vascular pressures and reaction of pulmonary vessels.
     - **Eisenmenger’s reaction**
   - eventually pressure in pulmonary vasculature rises so shunt becomes right to left.
   - will see right ventricular hypertrophy as a result of years increased workload
     - may even see right ventricular failure with hemodynamic changes back stream. What are some of these?
   - Now with mixing of right-sided blood in systemic circulation, the child exhibits cyanosis.
2. Atrial septal defect (ASD)
   - Primum type: low in atrial septum
     - may be associated with cleft anterior mitral leaflet
     - this type of ASD is not really common
   
   - Secundum - vast majority of ASD’s
     - central opening
     - if large, results in single atrium configuration
   
   - Sinus venosus defects - high in septum, uncommon

3. Ventral septal defect (VSD)
   - again left to right initially, then right to left
   - same pulmonary process as above, only happens earlier than with ASD
   - increased incidence of bacterial endocarditis on low pressure side.
4. Patent ductus arteriosis (PDA)
   - same problem with increased pulmonary flow because of initial left to right, followed by increased pulmonary vascular resistance leading to reversal of the shunt.

5. Be absolutely sure you understand this shunt reversal business. What was the eponym? Try explaining it to someone else.

C. Conditions leading to early cyanosis - right to left shunts right from the get go.

1. Tetralogy of Fallot (really a trilogy with one feature being reactive)
   - VSD
   - narrowing of pulmonary outflow tract (subpulmonary stenosis)
   - overriding aorta (position is shifted so that it overrides the VSD)
   - right ventricular hypertrophy (the compensatory one)
   
   They have mixing of right blood with systemic blood right off
2. Transposition of great vessels

- That’s right, the pulmonary artery and aorta are reversed
  - two independent circulatory systems
  - What keeps the kid from dying immediately?
  - Can you think of a fix? No you can’t whack off the vessels and switch them. Why not?

3. Truncus arteriosus

   - Common ventricular outflow tract for both right and left ventricles.
   - Obvious mixing of right sided blood with systemic circulation

4. Major anomalous pulmonary venous return

D. Non-cyanotic and/or obstructive conditions

1. Aortic coarctation (narrowing of aorta)
   - infantile
     - proximal to ductus arteriosus
- hypoplasia of the aortic arch
- symptoms manifest early, may die right there
- adult
- symptoms late
- constriction occurs after the ductus arteriosus

- for some reason, this condition is seen more commonly in males and girls with Turner’s syndrome.

Ref: Robbins, Pathologic Basis of Disease

2. asymmetric ventricular hypertrophy
3. Bicuspid aortic valves
4. Conduction system abnormalities
5. Anomalous coronary vessels
IV. Congestive heart failure (CHF) - mechanical pump failure.

A. Most cases are due to coronary heart disease or hypertension and subsequent chronic ischemic injury
   1. Could also develop suddenly after acute myocardial infarction. How?
   2. Infectious process like viral myocarditis
   3. Toxic such as ETOH
   4. Actually many possibilities here. Come up several on your own after we have finished the heart unit.

B. Systolic vs diastolic dysfunction
   1. Systolic failure = loss of contractile function
   2. Disatolic = chambers cannot expand during diastole
      - constriction or restriction of heart

C. For systolic failure, remember **STARLING’S CURVE !!**
   1. The muscle gets stretched to the point where the ventricles can’t empty
   2. Downward spiral

D. Right vs left sided failure and combined
   1. Pure right failure is very, very uncommon.
   2. Left sided failure because of bad vasular flow or some intrinsic myocardial problem.
- pressure backs up in pulmonary circulatory system
  - acute can lead to **acute pulmonary edema**
    - simply squeezes fluid through the alveolar/capillary membrane.
  - Symptoms
    - **dyspnea**
    - **orthopnea**
    - **paroxysmal nocturnal dyspnea**
  - chronic leads to “heart failure cells” = hemosiderin containing alveolar macrophages. How does this come about?
  - leads to over distension of right ventricle and eventual failure of pumping strength of right ventricle.
  - By what mechanism do the right and left ventricles accommodate to increase blood volume?
  - pressure in venous system continues to back up into liver and spleen.
    - hepatomegaly and splenomegaly
    - can even lead to fibrosis around the central veins of liver lobules if sufficiently prolonged.
- peripheral edema
  - “dependent” = gravity pulls it down
    - legs and ankles
    - if bedfast = sacral edema

E. Pathology

1. Lungs
   - edema
   - heart failure cells
   - vascular response

2. Heart
   - pathological hypertrophy of muscle
   - left leads to right failure

3. Liver and spleen

4. Peripheral edema

5. Renal = lousy perfusion = poor urine output = fluid retention
   - renin angiotensin

6. Brain = hypoxic encephalopathy

7. “Hollow spaces” or “potential spaces” fill up with fluid
   - pleural effusion
   - peritoneal effusion
   - pericardial effusion
V. Ischemic heart disease (IHD)

A. Restriction of blood flow to myocardium
   1. Acute vs chronic
      - important with respect to what will happen

B. Insufficient oxygen transport
   1. Anemia, chronic or sudden loss from massive hemorrhage
   2. Some forms of congenital heart disease

C. Clinical picture four basic scenarios, all depend on rate and severity of narrowing
   1. Angina pectoris
   2. Myocardial infarction
   3. Chronic ischemic heart disease with CHF
   4. Sudden death

D. Pathology
   1. Atherosclerosis by far the most common
      - progressive narrowing
- fixed obstruction
- material from the plaque may embolize and cause obstruction
- sudden complete occlusion from thrombosis on surface of plaque or hemorrhage into the plaque matrix.

2. Importance of collateral circulation

Ref: Robbins, Pathologic Basis of Disease

E. Acute myocardial infarction may result of blood flow is not restored quickly following complete occlusion.
1. Oddly enough atherosclerosis is not present in all cases
   - spasm (?)

1. Transmural vs subendocardial

2. Coagulative necrosis of myocardium takes time to develop
   - up to ½ hour, reversible. No visible changes in myocardium

   - 1-2 hrs, irreversible injury
     - Not much to see, maybe a little change in the myofibrils

   - 4-12 hrs, early change of coagulative necrosis

Ref: Robbins, Pathologic Basis of Disease
- pallor grossly
- micro: edema, hemorrhage, neutrophils start to appear

- 18-24 hrs; nuclear changes of dead myocardial cells
  - pyknosis
  - more neutrophils

- 1-3 days
  - hyperemia grossly
  - micro: fully developed coagulative necrosis, glassy pink cytoplasm, many neutrophils.

- 3-7 days
  - yellow-brown color to area of dead muscle with central softening
  - micro: disintegration and removal of dead muscle with early revascularization at margins, infiltrate showing more macrophages and fewer neutrophils.
  - critical time because wall is weakest, could rupture through the area of infarction.

- 10 days
  - yellow-grey grossly
  - micro: mostly macrophages with extensive removal of dead muscle; much granulation tissue.
- 6-7 weeks = healing largely complete
- white area of mature scar tissue
- micro: mature fibroblast with much collagen, few hemosiderin containing macrophages.

| Table 13-4. EVOLUTION OF MORPHOLOGIC CHANGES IN MYOCARDIAL INFARCTION |
|-----------------|-----------------|-----------------|
| Time            | Gross Features  | Light Microscope | Electron Microscope |
| Reversible injury | None            | None            | Relocation of myofibers, pycnotic nuclei, mitochondrial swelling |
| 0-4 hr          | None            | Usually none; variable wall thickness of fibrous cap | |
| 4-12 hr         | Occasional darkening | Beginning coagulation necrosis, adventitia, hemorrhage | |
| 12-24 hr        | Darkening       | Ongoing coagulation necrosis, granulation of nuclei, syncytial hyperplasia, marginal connective tissue necrosis, beginning mononuclear abscesses | |
| 1-3 days        | Matting with yellow-tan necrosis | Coagulation necrosis, wall loss of nuclei and strands, intervillous fibrin | |
| 3-7 days        | Hypereosin, central yellow-tan softening | Beginning dissociation of dead nuclei, with dying stromal cells, phagocytes of dead cells by macrophages at infarct margin | |
| 7-10 days       | Maximally yellow-tan soft, soft depressed red-tan margin | Well-developed phagocytes of dead cells, early formation of capillary granulation tissue at margin | |
| 10-14 days      | Red-gray depressed infarct borders | Well-established granulation tissue with new blood vessels and collagen deposition | |
| 2-8 wk          | Gray-white scar, progressive from border toward center of infarct | Focalized collagen deposition, with decreased vascularity | |
| >2 mo           | Scarring complete | Dense collagenous scar | |

Ref: Robbins, Pathologic Basis of Disease

E. What else can go wrong now?!

1. Cardiogenic “Failure” (CHF) because of loss of muscle power
2. Arrhythmias
3. Valvular dysfunction if involves papillary muscle
4. Rupture with death from tamponade (sac fills with blood, therefore the heart cannot fill during diastole)
5. Later on the development of an aneurysm
6. Pericarditis with effusion and possibly scarring
7. “Extension” of the MI

F. Lab help

1. Troponin
2. AST, CK, LDH
3. CRP (unstable angina)

VI. Hypertensive heart disease

A. Long term pressure overload.

1. Left compensates with hypertrophy
   - generally concentric thickening of the left ventricle
   - about 140/90 mm Hg systemic
2. Right sided failure and hypertrophy from increased pulmonary pressure

- Also known as Cor pulmonale

- fibrosing conditions of lungs leading to increased pulmonary vascular pressure

- primary problems of pulmonary vessels
  - embolism
  - inflammatory arteritis (one variety is Wegener’s granulomatosis)
  - drug and toxins causing increased vascular pressure

- things effecting chest wall movement
  - kyphosis
  - obesity (Pickwickian syndrome)

- things causing pulmonary artery constriction
  - altitude sickness
- others I can’t think of right now

VII. Valvular heart disease and conditions of the endocardium.

- valves are an extension of endocardium
- calcific and atherosclerosis
- immune
- infectious
- function changes with diameter of valve and valve ring

A. Clinical manifestation

1. Stenosis
2. Incompetence
3. Embolization from junk on heart valves

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<th>Table 13-6. MAJOR CAUSES OF ACQUIRED HEART VALVE DISEASE</th>
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<td>Postinflammatory scarring (rheumatic heart disease)</td>
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<td>Mitral Regurgitation</td>
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<tr>
<td>Abnormalities of leaflets and commissures</td>
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<tr>
<td>Postinflammatory scarring</td>
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<tr>
<td>Infective endocarditis</td>
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<tr>
<td>Mitral valve prolap</td>
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<tr>
<td>Abnormalities of ventricle apparatus</td>
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<tr>
<td>Rupture of papillary muscle</td>
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<td>Papillary muscle dysfunction (fibrosis)</td>
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<td>Rupture of chordae tendine</td>
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<td>Abnormalities of left ventricular cavity and/or annulus</td>
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<td>Left ventricular enlargement (myocarditis, dilated cardiomyopathy)</td>
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<td>Calcification of mitral annulus</td>
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<td><strong>Aortic Valve Disease</strong></td>
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<td>Aortic Stenosis</td>
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<td>Postinflammatory scarring (rheumatic heart disease)</td>
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<td>Sessile calcific aortic stenosis</td>
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<td>Calcification of congenitally deformed valve</td>
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<td>Aortic Regurgitation</td>
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<tr>
<td>Intrinsic valvular disease</td>
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<td>Postinflammatory scarring (rheumatic heart disease)</td>
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<td>Infective endocarditis</td>
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<td>Aortic disease</td>
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<td>Degenerative aortic dilation</td>
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<td>Ankylosing spondylitis</td>
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<tr>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Marfan syndrome</td>
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B. Rheumatic heart disease, not just valves

1. Actually a **Pancarditis**
   - endocardium
   - myocardium
   - epicardium and pericardium

2. Post strep infection

3. Cross reaction of antibody with matrix protein all over the body. There are many problems and complaints, makes up the basis of the **Jones criteria**

   - Major
     - migratory polyarthritis
     - evidence of carditis
     - subcutaneous nodules
     - erythema marginatum
     - Sydenham’s chorea (St. Vita’s dance)

   - minor
     - fever
     - history of strep throat
- arthralgia

- diagnosis takes two majors or one major and two minors
  - St. Vita can stand alone according to some

4. Laboratory

- **ASO titer**
  - throat culture not often helpful
  - specific antobie titers
  - cardiac enzymes

5. Cardiac pathology

- **ASCHOFF NODULES**, know these guys
  - pancarditis
  - possible fibrinous pericarditis
  - sterile vegetations on valve margins
  - valular edema
  - eventually valvular scarring with shortening of cordae tendonae
    - “fish mouth” mitral valve
      - both stenotic and incompetent
      - mitral and aortic most often involved
C. Congenital

1. Marfan’s syndrome

2. Bicuspid aortic valve
   - arrhythmia
   - possibly altered coronary flow

3. Mitral valve prolapse (Myxomatous degeneration)
   - parachute deformity
4. Calcific aortic valvular stenosis

- ? Really congenital or acquired?

D. Infective endocarditis

1. Often superimposed on pre-existing valvular disease of high pressure shunt.

- old rheumatic

- congenital defect - VSD
2. Bugs range the gambit from terribly aggressive to chronic and indolent.

- staff and pneumococcus can eat the valve away in a day or so

- “Group D strep and staph epi. may stew for months

3. Vegetations of bugs and fibrin on valve margins

- may embolize - septic emboli
  - brain
  - kidney
  - spleen

4. Consequences

- valve scarring and stenosis

- no valve left = incompetence of a grand scale

- many small septic emboli and abscesses
E. Non-infective endocarditis (sterile)

1. Marantic endocarditis - thrombotic
   - hypercoagulation state
   - associated with various types of glandular (adeno) carcinomas
   - sterile vegetations on valves and endocardium

2. Libman-Sachs
   - SLE
   - sterile vegetations
   - marked inflammation of valve in some cases
   - fibrosis and deformity may follow

Ref: Robbins, Pathologic Basis of Disease
F. Artificial heart valves

1. Reasons for replacement

2. Types

3. Problems

Ref: Robbins, Pathologic Basis of Disease

VIII. Myocardial disease

A. Two basic categories

1. “primary” or idiopathic

2. that which has a specific cause

B. Clinical presentation is often starting point, says something about pathological pattern. Describes appearance of heart, not necessarily mechanism
1. Dilated (90% of cases)

2. Hypertrophic

3. Restrictive

4. Biopsy is often the best way to diagnose.

C. Dilated cardiomyopathy (DCM) - idiopathic

1. Most common by far

2. Gradually developing heart failure (months)

3. Dilatation and hypertrophy of all four chambers

4. No well understood cause but several conditions are associated
   - ETOH
   - previous myocarditis
   - pregnancy

5. Pathology
   - heavy, large, dilated heart - “flabby”
- mitral regurgitation because of dilatation of valve ring

- micro: bland and non-diagnostic: some inflammation and fibrosis

D. Hypertrophic cardiomyopathy (idiopathic)

1. Either symmetric or asymmetric hypertrophy

- asymmetric often involves only septum

2. Pathology

- myocyte hypertrophy

- Myofiber disarray
E. Restrictive cardiomyopathy (idiopathic type)

1. Diastolic filling is impeded because cannot dilate

   - something in muscle or endocardium that prevents relaxation

   - not pericardial sac, this is something different, here we are dealing with things of the heart proper.

2. Endomyocardial fibrosis

3. Endocardial fibroelastosis

4. Carcinoid related scarring

F. Myocarditis

1. Inflammation from any cause

   - infectious

       - virus

       - bacterial

       - protozoal
- Rickettsia

- immune mediated
  - Rheumatic fever
  - other immune reactions

- Who know’s
  - Sarcoid
  - Giant cell myocarditis

- Outcome
  - CHF

  - fibrosis

  - rhythm disturbances

2. Toxic and/or metabolic

- ETOH
  
  - Medications like adriamycin
  
  - excessive catacholamines
- amyloid
- hemosiderosis

IX. Pericardium

A. Most problems are related to restriction of cardiac action or the source of pain

B. Effusions

1. CHF
2. Metastatic tumor
   - much more common than metastatic to heart itself

C. Blood - tamponade

D. Inflammatory fluid
   - bacterial or viral pericarditis
   - rheumatic fever

Table 13-11. CAUSES OF PERICARDITIS

- Infections
- Presumably Immune-Mediated Reactions
- Miscellaneous

Ref: Robbins, Pathologic Basis of Disease

E. Other system failure
   - renal failure with pericardial effusion (you have one in your slide set)

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F. Scarring conditions that lead to
- adhesive pericarditis
- complete fibrous obliteration of pericardial space even with calcification
- post surgical fibrosis

Ref: Robbins, Pathologic Basis of Disease

X. Neoplastic disease
- primary
- metastatic

A. Very rare

B. Primary
1. Myxoma
   - atrial myxoma
   - “ball valve” type of obstruction
   - embolus
2. Lipomas

3. Rhabdomyosarcoma in infants
   - malignancy of cardiac muscle origin

4. Angiosarcoma

C. Metastatic

1. Very uncommon
2. About anything from cancers to lymphomas

XI. Age related changes seen in the heart
   - Not every change is truly “pathological”

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<td>Increased left atrial cavity size</td>
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<td>Decreased left ventricular cavity size</td>
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<tr>
<td>Sigmoid-shaped ventricular septum</td>
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<td><strong>Valves</strong></td>
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<tr>
<td>Aortic valve calcific deposits</td>
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<td>Mitral valve annular calcific deposits</td>
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<tr>
<td>Fibrous thickening of leaflets</td>
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<td>Hooding of mitral leaflets toward the left atrium</td>
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<td>Lambl excrescences</td>
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<td><strong>Epicardial Coronary Arteries</strong></td>
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<tr>
<td>Tortuosity</td>
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<td>Increased cross-sectional laminal area</td>
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<td>Calcific deposits</td>
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<td>Atherosclerotic plaque</td>
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<td><strong>Myocardium (Walls)</strong></td>
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<tr>
<td>Increased mass</td>
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<td>Increased subepicardial fat</td>
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<td>Brown atrophy</td>
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<td>Lipofuscin deposition</td>
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<td>Lipidic degeneration</td>
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<td>Amyloid deposits</td>
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<tr>
<td><strong>Aorta</strong></td>
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<tr>
<td>Dilated ascending aorta with rightward shift</td>
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<td>Elongated (tortuous) thoracic aorta</td>
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<tr>
<td>Sinotubular junction calcific deposits</td>
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<tr>
<td>Elastic tissue fragmentation and collagen accumulation</td>
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<td>Atherosclerotic plaque</td>
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XII. Transplant
Cardiac Diseases Case Studies

Case 1.

HISTORY: This 50-year-old man was admitted for severe congestive heart failure associated with signs of mitral insufficiency. He had rheumatic fever at age 9.

PHYSICAL FINDINGS: Dyspneic man with peripheral edema and bubbling rales over both lung fields.

LABORATORY RESULTS:
- EKG: atrial fibrillation
- Chest x-ray: cardiac enlargement; pulmonary edema

CLINICAL COURSE: He was treated for heart failure. Three days later he developed persistent mild hemoptysis associated with increasing dyspnea. He failed to respond to treatment, produced increasing amounts of frothy pink fluid and died 10 days later. At autopsy, the mitral valve was found to be thickened by scar tissue and laminated blood clot was noted in the right atrial appendage. A red, wedge-shaped lesion was present in the left lower lobe of the lungs.

What is the most likely explanation for the lesion in the lower lobe of the left lung?

From the information presented above, what are the important factors in the pathogenesis of the lung lesion?

Gross and microscopic examination of the heart would likely reveal what other changes?

Case 2.

HISTORY: This 74-year-old woman was admitted because of pain in the right hip following a fall. She had a prior history of non-insulin dependent diabetes mellitus, and had smoked one pack of cigarettes daily since 16 years of age.

PHYSICAL FINDINGS: Pain over the right hip joint and inability to bear weight on the right leg. There was external rotation of the right leg.

LABORATORY RESULTS:
- X-ray: subcapital fracture of the right femoral neck

CLINICAL COURSE: A metal screw was inserted to stabilize the fracture. One day before she was to be discharged, she suddenly developed severe chest pain and hypotension and her skin was cold and clammy. The next day the following laboratory values were
obtained:

CK: 250 IU/l (nl: 25-125)
LDH: 80 mU/ml (nl: 45-90)
SGOT: (AST) 80 mU/ml (nl: 8-40)

CBC revealed a WBC count of 18,000 with a left shifted differential
Chest x-ray showed pulmonary edema. She was treated for heart failure but died 3 days after the onset of chest pain.

What is the most likely cause of the chest pain?

What additional laboratory tests would be of most value?

What do you think is the most likely cause of her fractured femur?

Case 3.

HISTORY: A 58-year-old male physician with a history of a previous myocardial infarction (5 years before), came to the emergency room acutely short of breath. He had no chest pain. He admitted to smoking two packs of cigarettes per day since the age of 19. He has moderate hypertension, for which he treats himself with diuretics and salt restriction. He is equivocal when asked about his blood pressure control and salt intake.

PHYSICAL FINDINGS: Rales in both lung fields; heart noted to be enlarged by percussion. The subject is afebrile, pulse = 92/min; BP = 164/94 mmHg; respirations 34/min and visibly labored.

LABORATORY RESULTS:

EKG: left ventricular hypertrophy
GOT: (AST) 28 mU/ml (normal 8-40)
LDH: 237 mU/ml (normal 100-225)
CK: 49 IU/l (normal 35-200) No MB fraction detected
Troponin within normal range

CLINICAL COURSE: Because of severe acute pulmonary congestion he was started on digitalis and diuretics. Tourniquets were placed on his extremities to decrease the venous return. These were kept on for approximately 15 minutes and alternated from one extremity to another. Rotating tourniquets were maintained for the first 24 hours of admission. Enzyme studies were repeated 12, 24, and 48 hours after admission with the following results:

12 hours after admission:
GOT: (AST) 68 mU/ml
LDH: 311 mU/ml
CK: 146 IU/l No MB fraction detected
Troponin normal

24 hours after admission:
GOT: (AST) 111 mU/ml
LDH: 319 mU/ml
CK: 818 IU/l  No MB fraction detected
Troponin normal
48 hours after admission:
  GOT (AST): 57 mU/ml
  LDH: 278 mU/ml
  CK: 586 IU/l  No MB fraction detected
  Troponin normal
Treatement by rotating tourniquets, diuretics and oxygen brought about rapid clinical improvement. No complications developed, and the subject was discharged on the 4th hospital day.

The most likely diagnosis in this case is?

What laboratory or EKG data supports your diagnosis?

Since the MB fraction of the CK is not elevated, and no elevation of troponin was found, what can account for the other elevated enzymes?

**Vascular Diseases Case Studies**

**Case 1.**

**HISTORY:** This 56-year-old man with a long history of hypertension presented with episodes of light-headedness. He had had 3 previous heart attacks.

**PHYSICAL FINDINGS:** Bruit over both internal carotid arteries.

**LABORATORY RESULTS:**
  - aortic arch angiogram: total occlusion of left internal carotid artery 1 cm above the bifurcation; irregularity and mild stenosis of right internal carotid at the bifurcation.

**CLINICAL COURSE:** A left carotid endarterectomy was performed. Postoperatively, he was flaccid and unresponsive. A tracheostomy was performed and he was placed on mechanical ventilatory assistance. His temperature rose to 38 C on the second postoperative day and fluctuated between 38-39 C until his death on the sixth postoperative day.

The vascular disease process most likely present in this person would have what histological appearance?

Important factors in the pathogenesis of this lesion?

What does the “bruit” over both internal carotid arteries tell you?

How can there be total occlusion of the internal carotid arteries and this patient not have been dead at the time initial evaluation?
Case 2.

HISTORY: This 32-year-old woman was admitted for treatment of hypertension. Her symptoms included headache, dizziness, and poor vision. She gave a vague history of hematuria and urinary tract infection.

PHYSICAL FINDINGS: Blood pressure 240/150 mm Hg; mild ankle edema was present. Retinal vessels showed severe arterial narrowing with blurring of the optic discs.

LABORATORY RESULTS:
- Hemoglobin: 11.5 g/dl
- Urea nitrogen: 45 mg/dl
- Creatinine: 4.7 mg/dl
- Urinalysis: RBC: 10-15/hpf; WBC: 0-1/hpf; no casts; epithelial cells: 0-1/lpf; ketones: neg; glucose: neg; protein: 3 plus

CLINICAL COURSE: She became anuric and required peritoneal dialysis. She died of Staphylococcus aureus sepsis while awaiting renal transplantation.

What vascular changes in the kidney would reflect the hypertension present in this woman?

How do you think vascular disease of the kidney could contribute to the high blood pressure in this patient?

What other medical conditions might be made worse, or accelerated, by hypertension?

Case 3.

HISTORY: This 47-year-old man was admitted with a painful right leg. He had a long history of hypertension with multiple episodes of congestive heart failure. Coarctation of the aorta had been diagnosed 6 months earlier but no surgical repair was attempted because of his longstanding cardiomegaly and heart failure.

PHYSICAL FINDINGS: Pain, swelling and erythema of the right leg with marked calf tenderness.

CLINICAL COURSE: He was placed at bed rest. Later that evening he developed sudden chest pain, cyanosis, hemoptyisis and shortness of breath. The next morning symptoms were somewhat relieved. He developed intractable congestive heart failure and died a day later.

What do you consider to be the initiating cause of the sequence of events leading to the fatal outcome was? What do you think is the cause of the patient’s sudden development of chest pain, cyanosis, hemoptyisis and shortness of breath?
A 59-year-old woman with a history of rheumatic heart disease presented with an eight-month history of increasing ascites. Her condition was complicated by mitral stenosis, which had required a Bjork–Shiley mitral-valve replacement 20 years earlier. Chest radiography showed massive cardiomegaly (Panels A and B). A computed tomographic scan of the chest (Panel C) revealed severe enlargement of the left atrium (LA), which measured 15.0 by 15.8 cm and filled the entire lower right hemithorax; the scan also revealed anterior displacement of the Bjork–Shiley valve (arrow) and compression of the left ventricle (LV), right ventricle (RV), and right atrium (RA) against the anterior chest wall. Echocardiography showed abrupt cessation of diastolic expansion of the interventricular septum, with a rapid Y descent on hemodynamic tracings — findings consistent with a constrictive physiological process. The patient was treated with serial large-volume paracentesis, and an aggressive diuretic regimen was started. However, she died shortly after admission as a result of newly diagnosed acute myelogenous leukemia. A giant left atrium has been described almost exclusively in rheumatic heart disease due to pancarditis with eccentric dilatation.

Tung and DeSanctis 351 (14): 1437, Figure 1  September 30, 2004

The NEW ENGLAND JOURNAL of MEDICINE