# Cardiology Disorders

## 1. Atrial Septal Defect

### Clinical Presentation

**Presenting Symptoms:**
Most pts. present asymptomatic but w/ heart murmur
Symptoms may include dyspnea, fatigue, or recurrent lower respiratory tract infections in children and fatigue and palpitations (due to RE enlargement) in adults.

**Physical Exam:**
- **Mid-systolic ejection murmur**
  - (murmur from ↑ SV of RV → pulmonic turbulence)
- **Mid-diastolic filling murmur**
  - (↑ SV of RA → tricuspid turbulence)
- **Wide fixed split S₂**
- Prominent RV-heave (systolic impulse on lower sternal border)

### Lab Presentation

**Chest Film:**
- RA-dilation (may be some hypertrophy over time)
- RVD/H
- Pulmonary artery dilation

**ECG:**
- Incomplete RBBB (wide QRS, R’ in V₁)
- LAD in AVSD (endocardial cushion defect)
- RAD in other ASDs

**Echocardiography:**
- Reveals ASD

### Etiology and Pathogenesis

ASD is a persistent opening in the interatrial septum, occurring in 1 in 1,500 live births most commonly in the region of the foramen ovale and resulting from excessive resorption or inadequate development of the septum primum, inadequate formation of the septum secundum, or both, producing an ostium secundum ASD. Less commonly, an ASD appears in the inferior portion of the interatrial septum adjacent to the AV node resulting from failure of the septum primum to fuse with the endocardial cushions to produce a ostium primum defect (often associated with abnormal development of the mitral and tricuspid valves). A third type of ASD occurs near the entry of the superior vena cava and is termed sinus venosus ASD, resulting from incomplete absorption of the sinus venosus into the right atrium and often accompanied by the anomalous drainage of pulmonary veins from the right lung into the right atrium. The major consequence of ASD is RV&RA volume overload. The defect size, resistance, & downstream pressure are important in prognosis; in severe cases, ASD may progress to Eisenmenger Syndrome (right-to-left shunting), but ASD is less associated with pulmonary vascular disease than is VSD.

### Treatment

Elective surgical repair (age 4-5 or if symptomatic)
- In children and young adults, morphologic changes in the right heart often return to normal after repair

### Notes

A patent foramen ovale is present in 20% of people and is not a true ASD (the foramen ovale fails to close but is still functionally shut as long as left atrial pressure is higher than right atrial pressure), but in cases of ↑ RA pressure a right-to-left shunt can occur, leading to heart failure and possible paradoxical embolism

Because of the sensitivity and specificity of echocardiography, cardiac catheterization is rarely necessary for diagnosis, but may be used to assess pulmonary vascular resistance, CAD in older pts., &/or oxygen saturation in the RA (should be ↑ er in ASD)

**Differential (wide split S₂):**
1. RBBB
   - Split ↓ s on inspiration
2. Pulmonic stenosis
   - Split ↓ s on inspiration
# 2. Ventricular Septal Defect

## Clinical Presentation

**Presenting Symptoms:**
May present as **Heart Failure** (see #s 10 & 11)

**Physical Exam:**
- **Pansystolic murmur** (small VSD → loud murmur)
  - (medium VSD → filling murmur over MV)
  - (large VSD → ejection murmur + shunt murmur + filling murmur)
- **w/ ↑↑ pulm. vascular resistance before birth → no murmur**
- Possible mid-diastolic murmur (↑ flow over mitral valve)

## Lab Presentation

**ECG:**
- RVH: RAD → ↑ R in V1 & V2

## Etiology and Pathogenesis

VSD is an abnormal opening in the ventricular septum; they are most often located in the membranous (70%) and muscular (20%) portions of the septum with a minority of defects occurring just below the aortic valve or adjacent to the AV valve. In small VSDs, the defect itself offers more resistance to flow than the pulmonary or systemic vasculature, and so the shunt is “restrictive” to flow. In larger non-restrictive shunts, the volume of the shunt is determined by the relative pulmonary and systemic resistances – in the perinatal period, these resistances approximate each other and minimal shunting occurs; after birth, however, the pulmonary vascular resistance falls and a left-to-right shunt develops, leading to RV, pulmonary vasculature, and LV volume overload. Initially, the volume overload is compensated by the Frank-Starling mechanism, but over time the volume overload can result in chamber dilatation, systolic dysfunction, and heart failure. Augmented circulation through the pulmonary vasculature may cause pulmonary vascular disease as early as 2 years of age. VSD may progress to **Eisenmenger Syndrome**, where increased pulmonary vascular resistance exceeds systemic resistance causing the formerly left-to-right shunt becomes right-to-left and leading to severe hypoxemia – ES shows a prominent a-wave on the jugular venous pulse because of increased pulmonary resistance is transmitted to the right-heart, leading to increased atrial pressure on atrial contraction; P2 is loud because increased pulmonary resistance leads to more rapid closure of the pulmonic valve; the murmur of the inciting shunt is usually absent because the original left-to-right pressure gradient is negated by elevated right-heart pressures.

## Treatment

By age 2, 50% of small and moderate-sized VSDs undergo sufficient partial or complete spontaneous closure to make intervention unnecessary.

Surgical correction is recommended in the first few months of life for children with CHF or pulmonary vascular ds.

Moderate-sized defects without pulmonary vascular disease can be corrected later in childhood.

Medical management includes endocarditis prophylaxis for all VSDs.

## Notes

VSDs are relatively common, occurring in 1.5-3.5 per 1,000 live births.

**Eisenmenger Syndrome:**
- Physical Exam: prominent “a” wave on venous pulse
  - loud P2
  - murmur of inciting shunt is **absent**
  - lower extremity cyanosis & clubbing
- Chest film: proximal pulmonary arterial dilatation with peripheral tapering; may show calcifications
- ECG: RVH with RAE

Treatment: avoid strenuous activity, high-altitude, and peripheral vasodilator drugs; there is no good therapy to decrease elevated pulmonary resistance → the only effective long-term tx is lung or heart-lung transplant

Supportive measures: endocarditis prophylaxis, manage arrhythmias; phlebotomy for erythrocytosis

Epidemiology: rate of spontaneous abortion is 20-40%; maternal mortality is 45%

*So pregnancy is dangerous!*
## 3. Patent Ductus Arteriosus

**Clinical Presentation**

<table>
<thead>
<tr>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>May be asymptomatic (children with a small PDA)</td>
</tr>
<tr>
<td>Large PDA → develop symptoms of heart failure</td>
</tr>
<tr>
<td>- tachycardia, poor feeding, slow growth, recurrent RTIs</td>
</tr>
<tr>
<td>Moderate size PDA → fatigue, dyspnea, palpitations later in life</td>
</tr>
</tbody>
</table>

**Physical Exam:**
- Continuous, machine-like murmur (heard at left subclavicle)
- if pulmonary vascular disease develops, murmur may be shorter (aorta/pulm. artery pressure gradient is less)

**Lab Presentation**

<table>
<thead>
<tr>
<th>Chest Film: LAE &amp; LVE; prominent pulmonary vascular markings; calcification of the ductus may be seen</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG: LAE &amp; LVH (when large shunt is visible)</td>
</tr>
<tr>
<td>Echocardiography: reveals PDA and estimate right-side systolic pressures</td>
</tr>
</tbody>
</table>

**Etiology and Pathogenesis**

*Patent Ductus Arteriosus* results when the ductus fails to close after birth and there is a persistent shunt between the descending aorta and the left pulmonary artery. The pathogenesis similar to VSD, in that there is a left-to-right shunt and resulting volume overload of the LV, LA, and pulmonary circulation; Eisenmenger syndrome may develop. Atrial fibrillation may develop from atrial dilation, and turbulent flow across the defect may lead to endarteritis.

**Treatment**

- Surgical correction for even a small PDA. 
  - this eliminates risk of enarteritis 
- For neonates and premature infants with CHF, a trial of prostaglandin synthesis inhibitors (*indomethacin*) is used to promote ductus closure.

**Notes**

- Incidence: 1 in 2,500 – 5,000 live births.
- Risk Factors: first trimester maternal rubella; prematurity; birth at high altitudes

Cardiac catheterization is usually unnecessary, but it may show the ↑ oxygen saturation in the right heart.

Many spontaneously close within months after birth, but few close after that.
4. Congenital Aortic Stenosis

### Clinical Presentation

**Symptoms:**
- < 10% of infants experience heart failure before age 1
- Most older children are asymptomatic and develop normally
- Symptoms may include exertional dyspnea / angina / syncope

**Physical Exam:**
- Crescendo-decrescendo systolic murmur
  - loudest at base with radiation to the neck
  - often preceded by an ejection click
  - characteristically from birth
  - with advanced disease, ejection time becomes longer and peak occurs later in systole
  - in severe disease, may see reverse splitting of $S_2$

### Lab Presentation

- **Chest Film:** poststenoic aortic dilatation, normal pulmonary vasculature; enlarged LV
- **ECG:** LVH
- **Echocardiography:** sees valve structure, degree of LVH, and estimates the pressure gradient across the valve

### Etiology and Pathogenesis

CAS is caused by abnormal development of the aortic valve; commonly the valve develops with only two cusps (bicuspid). 2% of the population has a bicuspid aorta, and though this rarely results in congenital AS, it may produce AS in older adults as the leaflets fibrose and calcify over time. LV hypertrophy results from increased afterload due to resistance across the stenosed valve – dilatation of the proximal aortic wall may be caused by pressure from the high-velocity jet of blood that flows across the valve.

### Treatment

- Mild AS does not need to be corrected, but endocarditis prophylaxis should be followed.
- Severe obstruction during infancy may mandate immediate surgical or transcatheter balloon valvuloplasty.
  - valvuloplasty in infancy is only palliative and future surgical revision is generally needed.

### Notes

- 4 times as common in males as in females
- 20% of patients have an additional congenital abnormality, most commonly coarctation of the aorta.
4. Aortic Stenosis

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td>(same as CAS)</td>
</tr>
<tr>
<td>Angina</td>
<td></td>
</tr>
<tr>
<td>Syncope on exertion</td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Exam:</strong></td>
<td></td>
</tr>
<tr>
<td>Systolic ejection murmur (later peak → more severe stenosis)</td>
<td></td>
</tr>
<tr>
<td>Parvus-tardus carotid upstroke</td>
<td></td>
</tr>
<tr>
<td>Audible S₄</td>
<td></td>
</tr>
<tr>
<td>Possible reverse splitting of S₂ (or absence of A₂ component)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>In addition to congenital causes, AS is often caused by age-related degenerative calcific change of the valve. Most of the patients who present with AS after age 65 have the age-related form, whereas most younger patients have calcification of a congenitally bicuspid valve. Rheumatic AS may lead to progressive inflammatory fibrosis resulting in fusion of the commissures and calcification within the valve cusps. In severe AS, the pressure gradient across the stenotic valve may be greater than 100mmHg. Compensatory LVH occurs, which lowers ventricular wall stress but in doing so decreases compliance, resulting in resistance to diastolic filling and an abnormally large contribution of LA-contraction to the ventricular end-diastolic volume (as much as 25%); thus, LA-hypertrophy is beneficial but loss of effective atrial contraction (i.e., in AF) can be devastating. Angina results from increased myocardial oxygen demand caused by LVH and increased wall stress; syncope on exertion develops when the LV cannot generate sufficient pressure to increase CO across the stenotic valve in response to increased oxygen demand (also, in exertion SNS outflow dilates the peripheral vascular beds, thereby lowering SVR and decreasing perfusion pressure); CHF may develop progressively as LV contractile dysfunction results from insurmountably high afterload and CO falls precipitously while LA and pulmonary venous pressures increase.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>The only effective treatment is surgical valve replacement. 10y-survival rate exceeds 75%.</td>
<td>The normal aortic valve size is 3-4cm²; mild stenosis develops at &lt; 2cm², moderate stenosis at 1-1.5cm², and critical stenosis at &lt; 0.8cm².</td>
</tr>
<tr>
<td>Surgery is indicated when: 1. Patients with severe outflow obstruction develop symptoms. 2. There is evidence of progressive LV dysfunction without symptoms.</td>
<td>Median survival time in AS:</td>
</tr>
<tr>
<td>Valvuloplasty works less well in AS than it does in MS. ~ 50% of AS cases have recurrent stenosis within 6mos.</td>
<td>Symptom</td>
</tr>
<tr>
<td>Medical treatment includes: 1. Avoidance of drugs that could exacerbate hypotension. 2. Prophylaxis for endocarditis.</td>
<td>Angina</td>
</tr>
<tr>
<td></td>
<td>Syncope</td>
</tr>
<tr>
<td></td>
<td>CHF</td>
</tr>
<tr>
<td></td>
<td>AF</td>
</tr>
<tr>
<td>For pts. with severe, symptomatic AS who do not have surgery, 1yr-survival is only 57%.</td>
<td>For pts. with severe, symptomatic AS who do not have surgery, 1yr-survival is only 57%.</td>
</tr>
<tr>
<td>Mild, asymptomatic AS has a slow rate of progression over a 20yr period and so only 20% of pts. will progress to severe or symptomatic AS.</td>
<td>Mild, asymptomatic AS has a slow rate of progression over a 20yr period and so only 20% of pts. will progress to severe or symptomatic AS.</td>
</tr>
</tbody>
</table>
5. Congenital Pulmonic Stenosis

### Clinical Presentation

**Symptoms:**
- Children with mild or moderate PS are asymptomatic.
- Severe stenosis may manifest as exertional dyspnea and/or symptoms of right-sided heart failure (see # 13)

**Physical Exam:**
- Severe PS with RVH → Prominent “a” wave & RV-heave
  - Loud, late-peaking e/d systolic murmur
  - heard best at upper left sternal border
  - associated with palpable thrill
  - Wide split S₂ with soft P₂ component
- Moderate PS→ pulmonic ejection “click” after S₁ & before murmur
  - diminishes on inspiration

### Lab Presentation

- **Chest Film:** poststentotic dilatation of pulmonary artery
- clear lung fields; maybe RAE & RVH
- **ECG:** RVH & RAD
- **Venous Pressure Tracing:** prominent a-wave

### Etiology and Pathogenesis

Isolated PS may occur from an abnormally formed valve (90% of cases), within the body of the RV, or in the pulmonary artery itself – the result is obstruction to RV systolic ejection, leading to ↑ RV pressures and adaptive hypertrophy. The clinical course is determined by the severity of the obstruction: in the setting of normal CO, a peak systolic transvalvular pressure gradient < 55 mmHg is considered a mild stenosis, 50-80 mmHg a moderate stenosis, and > 80mmHg a severe stenosis.

### Treatment

- Mild pulmonic stenosis does not require tx.
- Moderate-to-severe PS is treated by valvuloplasty.
  - excellent results: RVH usually regresses
- Give antibiotic prophylaxis for endocarditis before & after valvuloplasty.

### Notes
### 6. Coarctation of the Aorta

#### Clinical Presentation

**Symptoms:**
May show symptoms of heart failure.

**Differential Cyanosis** (if ductus arteriosus remains open)

**Physical Exam:**
Femoral pulses are weak and delayed;

**Elevated BP in the upper body:**
- If coarctation occurs distal to the left subclavian artery, systolic BP in the arms is greater than that in the legs.
- If coarctation occurs proximal to the left subclavian artery, systolic BP in the right arm may be greater than left arm BP.

**Mid-systolic murmur** may be audible over chest & back.
- prominent tortuous collateral circulation may create continuous murmurs over the chest & back

#### Lab Presentation

- **Chest Film:** “notching” of inferior surface of the posterior ribs; aortic indentation may be seen.
- **ECG:** LVH
- **Echocardiography:** reveals coarctation and assesses the pressure gradient across the coarctation.
- **MRI:** reveals the length and severity of the coarctation

#### Etiology and Pathogenesis

Coarctation of the aorta is a discrete narrowing of the vessel lumen occurring pre-ductally (2%) or post-ductally (98%). Pre-ductal coarctation occurs when an intracardiac anomaly during fetal life decreases blood flow to the left side of the heart, resulting in hypoplastic development of the aorta; post-ductal coarctation is most likely the result of muscular ductal tissue extending into the aorta during fetal life – when ductal tissue constricts following birth the ectopic tissue within the aorta also constricts. Aortic coarctation causes an increased pressure load on the LV; if coarctation is not corrected, compensatory alterations include LVH and dilatation of compensatory collateral blood vessels from the intercostal arteries that bypass the coarctation: these collateral vessels enlarge and may erode the undersurface of the ribs. Post-ductal coarctation is generally less severe.

#### Treatment

In neonates with severe obstruction, *prostaglandin infusion* is given to keep the ductus arteriosus patent before surgery is undertaken.

In children, elective repair is usually performed to prevent systemic HTN.

For older children, adults, and patients with recurrent coarctation after previous repair, *transcatheter intervention* is usually successful.

For all, antibiotic therapy for endarteritis prophylaxis is necessary even after repair.

#### Notes

Incidence: 1/6,000 live births; often occurs in pts. with Turner’s syndrome

Catheterization and angiography and rarely necessary.
7. Tetrology of Fallot

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>Dyspnea on exertion / cyanosis / hyperventilation / irritability</td>
<td></td>
</tr>
<tr>
<td>‘Spells’ occur after exertion, feeding, or crying</td>
<td></td>
</tr>
<tr>
<td>- systemic vasodilation exacerbates symptoms</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Exam:</strong></td>
<td></td>
</tr>
<tr>
<td>Cyanosis &amp; hypoxemia (may present with clubbing of digits)</td>
<td>Chest Film: prominent RV and ↓ size of main pulmonary artery segment → &quot;boot-shaped&quot; heart; diminished pulmonary vascular markings</td>
</tr>
<tr>
<td>RVH palpable heave along left sternal border</td>
<td></td>
</tr>
<tr>
<td>Single S₂ with diminished pulmonary component</td>
<td></td>
</tr>
<tr>
<td>Systolic murmur heard best at left upper sternal border</td>
<td></td>
</tr>
<tr>
<td>- turbulent flow across stenotic RV outflow tract</td>
<td></td>
</tr>
<tr>
<td>- usually no murmur from large VSD</td>
<td></td>
</tr>
<tr>
<td>Echocardiography reveals defects</td>
<td></td>
</tr>
</tbody>
</table>

**Etiology and Pathogenesis**

Tetralogy of Fallot is characterized by: 1) ventricular septal defect, 2) obstruction of the pulmonic outflow tract, 3) overriding aorta that receives blood from both ventricles, 4) RVH. ToF results from a single developmental defect: an abnormal anterior and cephalad displacement of the infundibular portion of the septum – it is the most common form of cyanotic congenital heart disease seen after infancy and is often associated with other cardiac defects, such as right-sided aortic arch (25%), ASD (10%), and anomalous origin of the left coronary artery. Right-to-left shunting results from the obstruction to RV outflow and VSD – children learn to alleviate their symptoms by squatting down, which increases SVR by kinking the femoral arteries, thereby decreasing the right-to-left shunt and directing more blood in the RV into the lungs.

**Treatment**

Surgical correction involves closure of the VSD and enlargement of the subpulmonary infundibulum with the use of a pericardial patch.
- Elective repair is usually recommended by age 1

Antibiotic prophylaxis to prevent endocarditis.

**Notes**
### 8. Transposition of the Great Arteries

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong>&lt;br&gt;Progressive cyanosis (as duc tus arteriosus closes)&lt;br&gt;<em>Physical Exam:</em>&lt;br&gt;Right ventricular impulse felt on lower sternal border; Accentuated S₂ (closure of AV displaced anteriorly)&lt;br&gt;<strong>ECG:</strong> RVH&lt;br&gt;Diagnosis made definitively with <em>echocardiography.</em></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
</tr>
</thead>
</table>
TGA is characterized by the aorta and pulmonary artery originating from the RV and LV, respectively. This defect may result from failure of the aorticopulmonary septum to spiral in the normal fashion during development, or it may be caused by the abnormal growth and absorption of the subpulmonary and subaortic infundibuli during the division of the truncus arteriosus. TGA causes extreme hypoxia and cyanosis as the pulmonary and systemic circulations are separated – without intervention the patient will die soon after birth concurrent with closure of the foramen ovale and closure of the ductus arteriosus.

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
</table>
1. Maintain patency of the ductus arteriosus by *prostaglandin infusion* and creation of interatrial communication using a balloon catheter.<br>2. Following this, definitive surgical correction is done.

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
</table>
TGA accounts for 7% of congenital heart defects; it is the most common cause of cyanosis in the neonatal period.<br>- TOF is most common cause of cyanosis after infancy.<br>Prominent murmurs are uncommon.
9. Ischemic Heart Disease (Coronary Artery Disease)

Clinical Presentation

Angina pectoris
- sensation of pressure, tightness, heaviness, or constricting pain in the chest that may or may not be described as “pain”
- neither sharp or stabbing
- always lasts longer than a few seconds
- relieved within a few minutes &/or by sublingual nitroglycerin
- discomfort usually diffuse and may radiate, especially to the left shoulder and inner arm

Tachycardia / Diaphoresis / Nausea / Dyspnea / Fatigue

Impairments of activities of daily living

Physical findings during acute myocardial ischemia:
- Mitral regurgitation (papillary muscle dysfunction)
- Dyssynergic apical impulse
- Audible S4

Lab Presentation

ECG during acute myocardial ischemia:
- ST depression, horizontal or downsloping
- T wave inversion or flattening
- ST elevation
  - severe transmural ischemia
  - variant angina

ECG during periods free of ischemia
- Completely normal in 50% of patients.
- May see “non-diagnostic” ST and T wave abnormalities
- May see evidence of a prior MI (pathologic Q waves)

Etiology and Pathogenesis

Ischemia occurs when there is a mismatch between myocardial oxygen supply and demand; by far the most common cause of myocardial ischemia is coronary artery disease (atherosclerotic narrowing of the coronary arteries) presenting as angina.

In Chronic Stable Angina, fixed atheromatous plaques have developed in the coronary artery sub-endothelium – these plaques obstruct blood flow with angina upon exertion generally occurring when an arterial lumen is blocked more than 70%. Atheromatous plaques may also interfere with the normal endothelial vasodilatory response to increased metabolites, thereby potentiating exertional ischemia by promoting vasoconstriction. Patients in whom vasospasm &/or vascular tone plays a major role in angina show a variable degree of exercise tolerance and are said to have “variable-threshold” angina, whereas those in whom vasospasm plays a minimal role (and obstruction the major role) have a stable degree of exercise tolerance and are said to have “fixed-threshold” angina.

Unstable Angina is most often associated with breakage of the fibrous capsule of an atheromatous plaque, exposing the underlying tissue to clotting factors and precipitating a thrombus which further occludes the artery and exacerbates the symptoms of CSA. Unstable angina is often a precursor to MI, and presents as an acceleration of ischemic symptoms in one of three ways: 1) sudden increase in frequency, duration, and/or intensity of ischemic episodes, 2) angina at rest or without provocation, 3) new onset of severe angina in a pt. without previous symptoms of CAD.

Variant Angina is rare and is characterized by focal coronary artery spasm that results in vaso-occlusion in the absence of an atheromatous plaque. VA often occurs at rest with ischemia due to decreased oxygen supply rather than increased demand.

In coronary atherosclerosis (see #29), if the stenosis obstructs up to 60% of the lumen, maximal blood flow (i.e. blood flow in exertion) is not altered significantly; in stenosis of up to 70%, resting blood flow is normal but maximal flow is reduced even with maximal dilation of the resistance vessels, resulting in ischemia on exertion; in stenosis of 90% and greater, even with full dilation of the coronary resistance vessels ischemia may develop at rest as the basal oxygen demand of the myocardial tissue is not met, and although collateral channels may develop that prevent ischemia at rest, they are usually not sufficient to prevent ischemia in exertion. Further, the atherosclerotic endothelium shows an impaired release of endothelial vasodilators, such that with a sympathetic response the vasoconstricting effects of the α1-receptors in the coronary arteries go unopposed (normally they are outcompeted by release of local mediators such as NO and adenosine) and vasoconstriction, rather than vasodilation, results. In patients with risk factors for CAD this impaired endotheloid-dependent vasodilation is seen before visible atherosclerotic lesions develop.

The impaired release of NO in response to a developing thrombus also leads to thromboxane-mediated vasoconstriction following fibrous cap rupture and increased local platelet aggregation; these effects then exacerbate the arterial stenosis.

Consequences of myocardial ischemia include: 1) dyspnea, as reduced ATP generation leads to ↓ in ventricular systolic contraction and diastolic relaxation and subsequent ↑ in LA pressure which is transmitted to the pulmonary vasculature and induces congestion, 2) pain, as one or more accumulating local mediators (lactate, serotonin, adenosine) binds peripheral pain receptors in the C7-T4 distribution, and 3) arrhythmias, as accumulating local metabolites cause transient abnormalities of myocyte ion conduction. Depending on the severity and duration of the oxygen supply/demand imbalance, the myocardium may be: 1) able to undergo rapid and full recovery after an anginal episode, 2) hibernating myocardium, where the tissue manifests chronic contractile dysfunction in the presence of reduced blood supply that will immediately recover after blood supply is restored (e.g. by angioplasty or bypass surgery in multivessel CAD), 3) stunned myocardium, where the tissue will recover function gradually after blood flow is restored, and 4) irreversibly necrotic (i.e. MI).
Treatment

Medical Treatment of Acute Angina
1. Cease physical activity
2. Use sublingual nitroglycerine (vasodilation)
   - takes effect in 1-2 minutes

Medical Treatment to Prevent Recurrent Ischemic Episodes
1. Organic Nitrates (isosorbide dinitrate, nitroglycerine)
   - ↓ O₂ demand by ↓ preload (venodilation)
   - ↑ O₂ supply by ↑ perfusion and ↓ vasospasm
   - toxicity: HA, hypotension, reflex tachycardia
     (preventable by combining with β-blocker)
   - tolerance may develop; if so, provide nitrate-free
     interval each day (usually while pt. sleeps)
   - used for symptomatic relief; no evidence they
     prolong survival or prevent infarctions.
2. β-blockers
   - ↓ O₂ demand by ↓ CTY & ↓ HR
   - may ↑ O₂ supply by extending duration of diastole
   - considered first-line therapy because they have
     been shown to: 1) suppress angina, 2) ↓ rate of
     recurrent MI, 3) ↓ incidence of 1st MI in HTN
   - toxicity: bronchospasm, bradycardia, ↓ LV CTY,
     fatigue, exacerbation of diabetes
     - don’t use in pts. with obstructive airways ds
     - don’t use in pts. with decompensated LV ds
     - may mask hypoglycemic tachycardia in
       diabetics treated with insulin
       - β-block induced constriction of coronary arterioles
         is usually outcompeted by accumulation of
         vasodilatory local metabolites.
3. Calcium-channel blockers
   Dihydropyridines (nifedipine & amlodipine)
   - potent vasodilators: ↓ O₂ demand via ↓
     ventricular filling (venodilation) and ↓ TPR (arteriodilation),
   ↑ O₂ supply via coronary dilation
   Verapamil & Diltiazem
   - less potent vasodilators than dihydropyridines,
     but more potent HR and CTY depression:
     ↓ O₂ demand via ↓ HR and ↓ CTY.
   - take care to avoid heart failure when if combining
     with a β-blocker.

Anti-anginal drug treatment does not improve survival in
patients with chronic stable angina and preserved LV fxn.

Medical Treatment to Prevent MI and Death
1. Antiplatelet therapy (aspirin or clopidogrel)
2. Lipid-lowering therapy (statins)
   - reduce mortality for pts. w/ CAD
3. ACE inhibitor therapy

Surgical Revascularization
Indicated if anginal symptoms do not respond to drug tx, if
unacceptable side-effects of medication occur, or if the pt.
has a specific type of high-risk coronary ds for which
surgery is known to improve survival.
1. Percutaneous coronary interventions
   - angioplasty
   - coronary stent placement
   - directional coronary atherectomy
   - rotational atherectomy

PCI's have not been shown to reduce risk of MI or death

Risk factors: smoking, hypercholesterolemia, HTN, diabetes
family history of coronary disease
Precipitating factors: exertion, anger, emotional excitement,
large meal, cold weather

Silent (asymptomatic) ischemia occurs in 2-10% of middle-aged
men and is particularly common in diabetics; it can be detected
by ECG and other laboratory techniques.
Syndrome X refers to patients with typical signs & symptoms
of angina pectoris but without evidence of atherosclerotic
coronary stenoses on angiogram; this may be related to an
impairment of resistance vessels to dilate in response to
increased oxygen demand – these pts. have a better prognosis
than those with overt atherosclerosis.

Myocardial ischemia is the leading cause of death in
industrialized nations; still, age-adjusted death rate has fallen
more than 50% due to: 1) atherosclerosis risk reduction due to
lifestyle changes, 2) improve tx and longevity following acute
MI, and 3) advances in tx of CAD.

Candidates for PCIs:
1) uncontrolled recurrent angina with 1-2 coronary stenoses
2) some low-risk pts. with three-vessel disease

CABG shows improved survival in patients with:
1) > 50% left main stenosis
2) three-vessel CAD, esp. if LV contractile fn is impaired
3) two-vessel disease with > 75% LAD stenosis
4) diabetes and two- to three-vessel disease

Differential: (recurrent chest pain)
Cardiac Origin
1. Pericarditis
   • sharp pleuritic pain that varies with position
   • can last for hours or days; friction rub on auscultation
   • ECG: diffuse ST-elevations & PR-depression

GI Origin
2. GERD
   • precipitated by certain foods and worse when supine
   • relieved by antacids and not by nitroglycerin

3. Peptic Ulcer Disease
   • epigastric ache or burning occuring after meals
   • relieved by antacids and not by nitroglycerin

4. Esophageal Spasm
   • accompanied by dysphagia and not exertional
   • precipitated by meals; may be relieved by nitroglycerin

5. Biliary Colic
   • constant & long-lasting URQ pain
   • precipitated by fatty foods and not exertional

Musculoskeletal Origin
6. Costochondral Syndrome
   • tender costochondral junctions; worse with motion

7. Cervical Radiculitis
   • constant aches or shooting pains worsened by neck motion

Differential: (myocardial ischemia)
1. Decreased aortic perfusion pressure (AR, hypotension)
2. Severe anemia
3. Increased myocardial oxygen demand (severe AS)
Atherosclerosis is a chronic inflammatory vascular disease characterized by accumulation of lipid within the arterial intima, recruitment of leukocytes and smooth muscle cells to the vessel wall, and deposition of extracellular matrix. Non-desquamative injury to the endothelium from physical stress (HTN) or exposure to toxins (smoking, elevated LDL levels) probably represents the primary event in atherosclerosis. Loss of laminar flow at arterial branch points results in loss of normal shear, which leads to less local arterial elaboration of NO (endothelial vasodilator and anti-inflammatory molecule) & less production of the anti-oxidant enzyme superoxide dismutase; the pro-inflammatory state that then develops is susceptible to atherosclerosis (and it has been verified experimentally that atherosclerosis preferentially develops at arterial branch points) – Cigarette toxins and high circulating lipid levels induce endothelial production of reactive oxygen species (primarily superoxide anion) which also lead to damage and a pro-inflammatory state. In the early course of atherosclerosis, lesions may not be present but disease may be manifested by ↑ endothelial permeability, ↑ release of cytokines, ↑ transcription of adhesion molecules, ↓ release of NO and prostacyclin (local vasodilators and anti-inflammatories), and ↓ endothelial resistance to thrombosis.

Atherosclerotic plaques develop as follows: 1) Dysfunctional endothelium allows the passage of LDL particles into the arterial intima, where they accumulate and are fixed by binding proteoglycans (HTN may promote LDL retention by increasing proteoglycan synthesis in the intima), 2) Modification of LDL by oxidation (by local reactive oxygen species or pro-oxidant enzymes derived from activated endothelial cells, smooth muscle cells, or macrophages recruited from the circulation) or by glycation (in diabetics with severe hyperglycemia), 3) Modified LDL then acts as a chemoattractant for circulating monocytes, increases endothelial expression of pro-inflammatory proteins (M-CSF, MCP-1, LADs), and can be ingested by and accumulate in macrophages in large quantities because it is not regulated by negative feedback inhibition (scavenger receptors that take up mLDL are not downregulated as are LDL receptors) – macrophages then become engorged with cholesterol-rich lipid and become the “foam cells” that abound in early atherosclerosis as the major component of the “fatty streak” – T-lymphocytes and monocytes are recruited and migrate to the intima via chemoattractant properties of mLDL and mLDL- induced endothelial expression of cytokines and adhesion molecules, where they are activated by the pro-inflammatory environment (monocytes upregulate scavenger receptors and mature to macrophages), 4) Smooth muscle cells migrate from the media to the intima because of PDGF secreted from foam cells and dysfunctional endothelium, cytokines (TNF-α, IL-1, TGF-β) secreted by foam cells, and decreased heparan sulfate on the endothelial surface (increased heparinase resulting from thrombus and platelet activation by tissue factor secreted by foam cells and decreased NO and prostacyclin from the dysfunctional endothelium), 5) The smooth muscle cells secrete ECM and become embedded, forming a fibrous cap and sealing off the fibrotic plaque, a grey elevated lesion that may obstruct the lumen and contains a core of highly thrombogenic necrotic cell debris and cholesterol-secreting foam cells of smooth muscle (rather than monocyte) lineage.

Fibrous plaques develop first in the dorsal aspect of the abdominal aorta and proximal coronary arteries, followed by the popliteal arteries, descending thoracic, internal carotid, and renal arteries. Complications of fibrous plaques include: 1) calcification and subsequent increased fragility, 2) rupture or ulceration, which exposed the thrombogenic core to circulating clotting factors, precipitating a thrombus, which can then embolize or add to the volume of the plaque (and may completely obstruct the lumen), 3) hemorrhage into the plaque from rupture of tiny capillaries that vascularize the plaque, with the resulting hematoma further narrowing the vessel lumen, 4) embolization of pieces of the atheroma, 5) aneurysm formation as the plaque places increased stress on the neighboring media and weakens the vessel wall. Acute coronary events probably result from embolization, as degree of arterial obstruction has been found to correlate poorly with incidence of clinical events – Because of this, vulnerable plaques (those with thin, fragile fibrous caps) may be more dangerous than those with thickened caps or even the ones with cobblestone coverings even if the latter causes more pronounced arterial narrowing. Vulnerable plaques often have a rich lipid core and a high density of T-lymphocytes that secrete gamma-IFN, a chemokine that impairs the ability of smooth muscle cells to secrete collagen and thereby grow/repair the fibrous cap; macrophages may also localize to the plaque border and release matrix metalloproteinases, collagenases, and gelatinases that degrade the cap.

Smoking induces atherosclerosis via endothelial dysfunction due to toxins and local tissue hypoxia (replacement of Hb-oxygen with CO), increased oxidative stress (modification of LDL), platelet adhesion, and abnormal SNS stimulation of the vasculature. HTN induces atherosclerosis by direct physical endothelial damage, increasing the membrane permeability to lipids, the number of scavenger receptors on macrophages, and the production by smooth muscle cells of proteoglycans; also, angiotensin II is a pro-inflammatory cytokine as well as a vasoconstrictor. DM induces atherosclerosis via dyslipidemia, glycation of LDL, and the state of dysfunctional endothelium diabetes: pro-thrombic, ↑ leukocyte adhesion, ↓ NO synthesis; indeed, insulin resistance appears to promote atherosclerosis before the patient is found to be overtly diabetic. Estrogen may protect against atherosclerosis by lowering...
10. Atherosclerosis (continued)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Nomalize serum lipid levels:  
   1. Replace dietary saturated fats with polyunsaturated fats  
      - these activate transcription factor PPAR-α which induces the expression of HDL apoprotein A1 and inhibits endothelial expression of LADs.  
   2. Increase physical activity.  
      - ↑ insulin sensitivity and endothelial production of NO.  
   3. Give statins (HMG CoA reductase inhibitors)  
      - these lower LDL & increase HDL  
      - also they are correlated with increased NO synthesis, fibrinolytic activity, and activity of PPAR-α and decreased macrophage expression of proteases and cytokines.  

Treat HTN (see # 29)  
In diabetics, control serum glucose levels.  

| Major “non-modifiable” risk factors:  
   1) advanced age, 2) male gender, 3) family history of coronary disease prior to age 55 in males and 65 in females.  
   Major “modifiable” risk factors:  
   1) Dyslipidemia, 2) HTN, 3) smoking, 4) diabetes mellitus  
   5) obesity, 6) low level of physical activity.  
Low tar and low-nicotine cigarettes do not decrease MI risk.  
In diabetics, control of serum glucose reduces risk of microvascular complications (nephropathy, retinopathy) but maybe not macrovascular complications (MI, stroke); still, control of HTN and dyslipidemia does correlate with a reduced risk of cardiac and cerebrovascular events.  
Risk of coronary disease is twice as high for someone with a total cholesterol of 240mg/dL as it is for someone with 200.  
Individuals homozygous for inactive LDL receptors may suffer an MI within the first decade of life.  
High LDL levels (> 100mg/dL) increase the risk for atherosclerosis, and high HDL levels are protective (probably due to their ability to ferry lipids from the periphery to the liver).  
Glycation of LDL in diabetes can render it antigenic and additionally pro-inflammatory.  
The fatty streak is the first visible lesion of atherosclerosis, appearing as areas of yellow discoloration on the artery’s inner surface; they may be spots less than 1mm in diameter or streaks 1-2mm wide and up to 1cm long; they do not protrude into the lumen and do not obstruct blood flow; fatty streaks exist in the aorta and coronary arteries of most people by age 20, and though in some locations they do not cause symptoms and may regress, in the coronary arteries they may develop into fibrous plaques.  
In some plaques, the cells within the plaque appear to descend from one single smooth muscle cell. |
11. Acute Coronary Syndromes

Clinical Presentation

**Acute MI (both STEMI & NSTEMI):**
1. Ischemic pain in chest & C7-T4 distribution that does not wane with rest and shows little response to nitroglycerine. - up to 25% of pts are asymptomatic, esp. diabetics with peripheral neuropathy.
2. Systemic signs of increased SNS outflow.
3. Dyspnea
4. Fever / leukocytosis
5. Possible audible S1 & S4 (↓ LV function & ↓ LV compliance)
6. Possible new systolic murmur (damage to papillary muscle or rupture of IV-septum)
7. Dyskinetic bulge (in anterior wall MI)
8. Possible symptoms of left or right-heart failure

Lab Presentation

**ECG during acute attack:**
STEMI: ST-depression &/or T-wave inversion
STEMI: ST-elevation, pathologic Q-waves appear hours-days later.

**ECG weeks later:**
UA & NSTEMI: ST-dep. or T-wave inv.
STEMI: prolonged QRS duration, pathologic Q-waves

**Blood tests:**
STEMI & NSTEMI: elevated serum creatine kinase (-MB and cardiac-specific troponin
UA: normal serum levels of markers of necrosis

Etiology and Pathogenesis

The continuum of acute coronary syndromes ranges from unstable angina through Non-ST-elevation MI to ST-elevation MI, with each most often caused by coronary artery thrombosis. A small thrombus may be asymptomatically degraded by natural fibrinolysis or become incorporated into a progressively growing plaque; a larger thrombus that partially occludes a vessel (or transiently completely occludes it due to rapid recanalization of relief of vasospasm) will likely cause UA or NSTEMI – these are distinguished by the latter showing serum markers of necrosis in addition to ST-depression – and a thrombus that completely occludes a vessel will likely cause STEMI, although in cases where there is a substantial collateral circulation a complete occlusion may produce NSTEMI rather than STEMI.

Coronary thrombosis occurs as a result of atherosclerotic plaque rupture (see # 8) and/or endothelial dysfunction. The developing thrombus, intraplaque hemorrhage, and vasoconstriction (from activated platelet-derived mediators) contribute to arterial occlusion, as well as create turbulent blood flow that increases shear stress and further platelet activation/coagulation/occlusion. In the setting of dysfunctional endothelium (which is apparent even in mild atherosclerosis), reduced amounts of vasodilatory inhibitors of platelet aggregation (NO and prostacyclin) create a thrombogenic state: the endothelium is less able to prevent platelet aggregation as well as resist the vasoconstricting effect of activated-platelet released thromboxane & serotonin; vasoconstriction causes torsional stresses that can exacerbate plaque rupture and promotes coagulation by increases local concentrations of clotting factors.

**Transmural infarcts** (STEMIs) span the entire thickness of the myocardial wall and result from total, prolonged occlusion of an epicardial artery- transmural infarcts show ST-depression and pathologic Q-waves on ECG; subendocardial infarcts (NSTEMIs) involve only the innermost layers of the myocardium, an area especially susceptible to ischemia because it is subjected to the highest pressure from the ventricle, has fewer collateral vessels, and is perfused by vessels that must pass through contracted myocardium – subendocardial infarcts show ST-depression &/or T-wave inversion on ECG. Early pathologic changes during MI include histological evolution of the infarct and ischemic effects on myocytes that culminate in coagulative necrosis is 2-4 days. **Metabolic early changes:** hypoxia is associated with ↓ ATP, ↓ pH (↑ lactate), ↑ in intracellular Na and extracellular K (no ATP to drive Na/K pump), and the electrolyte imbalance alters transmembrane potential and predisposes the myocardium to arrhythmias; intracellular Ca accumulates and is thought to induce cell death by activation of apoptotic lipases & proteases. These metabolic changes decrease function as early as 2 minutes following occlusive thrombosis, and without intervention irreversible cell injury ensues in 20 minutes and is marked by development of membrane defects; enzymes leaking through damaged myocyte membranes serve as a clinical marker of acute infarction. Myocardial edema develops within 4 - 12 hours as interstitial oniocotic pressure increases; “wavy myofibers” caused by edematous separation of adjacent myocytes are the earliest histological changes (1-3 hours), and “contraction bands,” bright eosinophilic areas of consolidated sarcomeres bordering the infarct may also be seen. Infiltration of neutrophils occurs 4 hours after acute ischemia, and coagulative necrosis is evident in 18-24 hours and finished by 2-4 days. **Gross early changes:** occur 18 – 24 hours after coronary occlusion beginning in the subendocardium and extending outward to the epicardium; infarct expansion may occur corresponding to stretch of the necrotic myocytes – the increased ventricular size may be detrimental because it ↑s wall stress, ↓s CTY, and ↑s risk for aneurysm; compensatory dilation of the overworked non-infarcted tissue may occur as well predisposing the ventricle to arrhythmias and eventual heart failure. Late pathologic changes in acute MI include clearance of necrotic myocardium by macrophages (“yellow-softening” that may cause ventricular structural weakness) and deposition of collagen to form scar tissue in a process that is complete by 7 weeks. Functional changes after acute MI include: 1) **systolic dysfunction** as contractility decreases and synchronous contraction is lost, 2) **diastolic dysfunction** as diastolic relaxation (an energy dependent process) is impaired, further elevating ventricular filling pressure.

Acute MI causes dyspnea because ↓ LV-contractility and ↓ diastolic relaxation causes an increase in pressure in the left atrium which is transmitted to the pulmonary vasculature causing pulmonary congestion and activating juxtaglomerular receptors which effect a rapid & shallow breathing reflex. Fever and mild leukocytosis result from activated macrophages and endothelial cells secreting inflammatory cytokines (IL-1 and TNF) in response to tissue injury.
11. ACS (continued)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Treatments for all ACS Patients:</strong> (anti-ischemic tx)</td>
<td><strong>Biomarker:</strong> myoglobin CK-MB troponins LDH</td>
</tr>
<tr>
<td>1. Admit to ICU and put on bedrest (↓ O2 demand)</td>
<td>First appears in serum: 1-4h 3-8h 3-4h</td>
</tr>
<tr>
<td>2. Give supplemental O2 if any evidence of hypoxemia.</td>
<td>Peaks: 24h 18-36h 3-5d</td>
</tr>
<tr>
<td>3. Give morphine for pain control &amp; to ↓ O2 demand.</td>
<td>Gone by: 3d 14d</td>
</tr>
<tr>
<td>- aspirin ↓ mortality in all forms of ACS</td>
<td>- these likely because of association with ↑ SNS outflow and</td>
</tr>
<tr>
<td>- continued indefinitely in pts. without contraindications</td>
<td>subsequent ↓ in HR &amp; BP creating a greater chance an</td>
</tr>
<tr>
<td>5. Give nitrates to ↓ O2 demand &amp; ↑ O2 supply.</td>
<td>atherosclerotic plaque will rupture.</td>
</tr>
<tr>
<td>6. Give β-blocker IV to reach HR &lt; 70bpm then by</td>
<td>Causes of ACS</td>
</tr>
<tr>
<td>oral maintenance dose indefinitely; β-blockers reduce</td>
<td>1. atherosclerotic plaque rupture</td>
</tr>
<tr>
<td>- these do not reduce mortality</td>
<td>2. vasculitis</td>
</tr>
<tr>
<td>- do not use these in pts. with LV systolic dysfunction</td>
<td>3. coronary embolus</td>
</tr>
<tr>
<td>7. Give verapamil or diltiazem only for pts. in whom</td>
<td>4. congenital abnormalities of the coronary arteries</td>
</tr>
<tr>
<td>ischemia does not resolve w/ β-block &amp; nitrates.</td>
<td>5. coronary trauma or aneurysm</td>
</tr>
<tr>
<td><strong>UA/NSTEMI Specific Treatments:</strong> (anti-thrombotic tx)</td>
<td>6. increased blood viscosity (P.vera, thrombocytosis)</td>
</tr>
<tr>
<td>1. Consider thienopyridines to further inhibit platelets</td>
<td>7. ↑ ↑ myocardial O2 demand (severe AS)</td>
</tr>
<tr>
<td>- may reduce mortality when used with aspirin</td>
<td>8. cocaine abuse</td>
</tr>
<tr>
<td>- may substitute for aspirin in contraindicated pts.</td>
<td>&gt; 90% of ACS result from rupture of an atherosclerotic plaque</td>
</tr>
<tr>
<td>2. Give heparin as an anti-coagulant</td>
<td>Brief periods of ischemia may render a segment of myocardial</td>
</tr>
<tr>
<td>- unfractionated heparin is given IV as a weight-based</td>
<td>tissue resistant to subsequent episodes of ischemia (ischemic</td>
</tr>
<tr>
<td>bolus followed by continued infusion with dosage</td>
<td>preconditioning) and so patients who have an MI in the context</td>
</tr>
<tr>
<td>adjusted by monitoring aPTT.</td>
<td>of recent angina have less morbidity/mortality than those without</td>
</tr>
<tr>
<td>- low molecular weight heparin may be given sub-q,</td>
<td>preceding anginal episode.</td>
</tr>
<tr>
<td>has a more predictable pharmacokinetics, does not</td>
<td><strong>Locализing MI:</strong></td>
</tr>
<tr>
<td>require aPTT monitoring &amp; dosage adjustment, and</td>
<td>Inferior wall → II,III,aVF g(RCA)</td>
</tr>
<tr>
<td>selectively inhibits factor Xa.</td>
<td>Anteroapical → V1 – V4 (distal LAD)</td>
</tr>
<tr>
<td>3. Consider GP IIb/IIIa inhibitors for high-risk pts.</td>
<td>Anterolateral → V3 – V6, I, aVL (CFX)</td>
</tr>
<tr>
<td>4. Use “early invasive” approach (urgent catheterization</td>
<td>Posterior → V1 – V2 [tall R wave, not Q] (RCA)</td>
</tr>
<tr>
<td>and revascularization if needed) for pts. with high-</td>
<td><strong>Differential</strong></td>
</tr>
<tr>
<td>risk features (ST-abnormalities at presentation,</td>
<td><strong>Cardiac causes:</strong></td>
</tr>
<tr>
<td>↑ serum biomarkers, multiple cardiac risk factors).</td>
<td>1. Pericarditis</td>
</tr>
<tr>
<td>5. Use “early invasive” approach (urgent catheterization</td>
<td>- sharp pleuritic pain that worsens with inspiration</td>
</tr>
<tr>
<td>and revascularization if needed) for pts. with high-</td>
<td>- friction rub auscultated</td>
</tr>
<tr>
<td>risk features (ST-abnormalities at presentation,</td>
<td>- ECG: diffuse ST elevations</td>
</tr>
<tr>
<td>↑ serum biomarkers, multiple cardiac risk factors).</td>
<td><strong>Pulmonary causes:</strong></td>
</tr>
<tr>
<td><strong>STEMI Specific Treatments:</strong> (reperfusion tx)</td>
<td>3. Pulmonary Embolism</td>
</tr>
<tr>
<td>1. Give thrombolitics to degrade occlusive clot, followed</td>
<td>- localized pleuritic pain w/ dyspnea, friction rub</td>
</tr>
<tr>
<td>by anti-thrombic measures mentioned above.</td>
<td>4. Pneumonia</td>
</tr>
<tr>
<td>- bleeding is the major risk with these drugs</td>
<td>- cough &amp; sputum production;</td>
</tr>
<tr>
<td>- do not give to pts. w/ PUD, underlying bleeding</td>
<td>- infiltrate on chest radiograph; abnormal percussion</td>
</tr>
<tr>
<td>disorder, recent stroke, or recent surgery</td>
<td>5. Pneumothorax</td>
</tr>
<tr>
<td>- newer agents (tPA, rPA, TNK-tPA) bind</td>
<td>- pleuritic unilateral chest pain</td>
</tr>
<tr>
<td>preferentially to fibrin in a formed clot, i ing</td>
<td>- ↓ breath sounds on affected side</td>
</tr>
<tr>
<td>the chance of bleeding relative to streptokinase</td>
<td>- increased lucency on affected side</td>
</tr>
<tr>
<td>- rPA &amp; TNK-tPA have longer half-lives than tPA,</td>
<td><strong>GI causes:</strong></td>
</tr>
<tr>
<td>and so can be given as boluses</td>
<td>6. Esophageal spasm</td>
</tr>
<tr>
<td>- given w/in 2h of onset of symptoms → ½ the</td>
<td>- retrosternal pain worsened by swallowing</td>
</tr>
<tr>
<td>mortality of when given after 6h from onset</td>
<td>- history of dysphagia</td>
</tr>
<tr>
<td>- restores blood flow in 70-80% of occlusions</td>
<td>7. Acute cholecystitis</td>
</tr>
<tr>
<td>- successful reperfusion is marked by ST-segment</td>
<td>- RUQ tenderness w/ nausea</td>
</tr>
<tr>
<td>return to baseline, earlier-than-expected peaks of</td>
<td>- hx of fatty food intolerance</td>
</tr>
<tr>
<td>serum biomarker levels, and relief of angina.</td>
<td><strong>Adjunctive Therapies for both NSTEMI &amp; STEMI</strong></td>
</tr>
<tr>
<td>- anti-thrombotic treatment will not help and may</td>
<td>1. ACE inhibitors (most benefit for high-risk pts)</td>
</tr>
<tr>
<td>harm pts. with UA/NSTEMI – Be careful.</td>
<td>2. Statins (↓ mortality for pts. w/ CAD)</td>
</tr>
<tr>
<td>2. May use primary percutaneous coronary interventions</td>
<td></td>
</tr>
<tr>
<td>- esp. for pts. in whom thrombolitics are contraindicated</td>
<td></td>
</tr>
<tr>
<td>- achieves optimal blood flow in 95% of occlusions.</td>
<td></td>
</tr>
<tr>
<td>- limited to highly-equipped medical centers</td>
<td></td>
</tr>
</tbody>
</table>
Complications of ACS

Complications of UA include death (5-10%) and progression to MI (10-20%) over the ensuing days and weeks; immediate complications may result from myocardial necrosis, and those developing days to weeks later result from inflammation and healing of necrotic tissue.

Post infarction ischemia occurs in 20-30% of pts. following an MI and represents an increased risk for reinfarction. Patients often require urgent cardiac catheterization followed by revascularization. Incidence has not been reduced by thrombolytic therapy but is reduced in patients who have undergone percutaneous angioplasty or stent implantation.

Arrhythmias are common during and following MI and may result from multiple mechanisms: ↓ perfusion to normal conductive tissue, accumulation of toxic metabolites and abnormal transcellular ion gradients, SNS or PNS stimulation, administration of potentially arrhythmogenic drugs (e.g. dopamine). Ventricular fibrillation often occurs during the first 48 hours after MI and is the leading cause of MI-related death; VF during the first 48hrs may also be transient, however, and does not affect a pts. long-term prognosis – VF occurring later than 48hrs after acute MI is usually associated with severe LV dysfunction and high subsequent mortality rates. VF, ventricular tachycardia, and ventricular ectopic beats arise from re-entrant circuits or enhanced automaticity of ventricular myocytes – ectopy is common and usually not treated unless abnormal beats are frequent, multifocal, or consecutive; IV lidocaine (class IB anti-arrhythmic) is effective acutely for VF prevention but is not indicated in routine management of MI because of its potential side-effects and the ease of detecting emergent arrhythmias in the CCU.

Sinus bradycardia results from excessive vagal stimulation or SA-nodal ischemia, usually in an inferior wall MI. Sinus tachycardia is common and results from pain/anxiety, heart failure, vasodilator administration, or intravascular volume depletion – differentiating between heart failure and volume depletion may require a transvenous pulmonary artery catheter (pulmonary capillary wedge pressure is low in volume depletion but high in heart failure); because tachycardia → ↑ O₂ demand, it must be treated quickly. Atrial premature beats and/or atrial fibrillation may result from atrial ischemia or atrial enlargement following ventricular failure. Conduction blocks are also common in acute MI, resulting from ischemia/necrosis of the conduction tracts or, in the case of AV blocks, transient ↑ vagal stimulation caused by stimulation of vagal afferent fibers from the inflamed myocardium or generalized autonomic overdrive in association with the pain of an acute MI.

Congestive Heart Failure may develop as a result of MI-induced systolic and/or diastolic dysfunction, arrhythmias, or mechanical complications. Cardiogenic shock is a condition of severely decreased CO (systolic BP < 90mmHg) with inadequate perfusion of the peripheral tissues, occurring when more than 40% of LV mass has been infarcted or as a result of a severe mechanical dysfunction; cardiogenic shock is self-perpetuating because hypotension → ↓ perfusion → ↑ ischemic damage → ↓ SV and perfusion...ect – treatment is to give inotropic agents (e.g. dobutamine) to sustain CO and vasodilators to reduce periperal resistance, and tx may include placement of an intra-aortic balloon pump that expands during diastole (to ↑ perfusion pressure in the coronary arteries) and deflates during systole (to reduce afterload), but despite aggressive treatment, the mortality rate for cardiogenic shock is > 70% (early catheterization and CABG can decrease this).

Papillary Muscle Rupture may occur from ischemic damage and be fatal due to acute severe mitral regurgitation; partial rupture with more modest regurgitation is not immediately lethal but may result in pulmonary edema; the posteroemidal LV papillary muscle is more susceptible to infarction than the anterolateral one. Ventricular Free Wall Rupture may occur within the first 2 weeks following MI, more commonly in women and pts. with a history of HTN; hemorrhage into the pericardial space severely restricts blood flow and survival is rare; a pseudoaneurysm is when a tear in the ventricular wall is held together by a thrombus - if not caught (echocardiography) in time, complete rupture will happen. Ventricular Septal Rupture results in the formation of a new systolic murmur heard at the left sternal border. True ventricular aneurysm occurs weeks to months after acute MI as the ventricular wall is weakened but not perforated by phagocytic clearing of necrotic tissue; it results in dyskinesia when the residual viable muscle contracts, and its complications include: increased risk of thrombus/embolus, arrhythmias caused by stretched ventricle, heart failure due to reduced forward output – LV aneurysms show persistant ST elevation weeks after the acute MI and a bulge of the LV border in a radiograph.

Pericarditis may occur in the early (1-2 days) after MI as inflammatory necrosis and necrophilic infiltrate extends into the pericardium; it is associated with sharp pain, fever, and friction rub – anti-coagulants are contraindicated in pericarditis to avoid hemorrhage from the inflamed pericardial lining. Dressler Syndrome is an uncommon form of pericarditis that occurs in the first several weeks following MI – symptoms include fever, malaise, pleuritic chest pain, ↑ ESR and pleural effusion, and the cause is likely autoimmune; Dressler syndrome responds well to high-dose aspirin therapy.

Post MI Risk Stratification and Management

Most patients can be discharged in 5-6 days after an acute MI (sooner if aggressive reperfusion was done and there are no complications). The most important predictor of post-MI outcome is extent of LV dysfunction; bad prognostic markers include early recurrence of ischemia, a large volume of myocardium still at risk for ischemia, and high-grade ventricular...
12. Left-Sided Heart Failure

**Clinical Presentation**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea at rest or upon exertion</td>
<td>S3, S4, P2, audible S3, P2, diaphoresis, ↑ blood flow to brain</td>
</tr>
<tr>
<td>Chyne-Stokes respiration</td>
<td></td>
</tr>
<tr>
<td>Orthopnea</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea</td>
<td>(waking up breathless)</td>
</tr>
<tr>
<td>Nocturnal cough</td>
<td></td>
</tr>
<tr>
<td>Hemoptysis</td>
<td></td>
</tr>
<tr>
<td>Mental status changes</td>
<td>↓ in blood flow to brain</td>
</tr>
<tr>
<td>Daytime impaired urine output</td>
<td>(daytime ↓ renal perfusion)</td>
</tr>
<tr>
<td>Nocturia</td>
<td>(supine ↑ in renal perfusion)</td>
</tr>
<tr>
<td>Tachycardia/tachypnea/diaphoresis</td>
<td>Audible S3 (&amp; maybe audible S2 as well); Loud P2</td>
</tr>
<tr>
<td>Pulsus alternans</td>
<td></td>
</tr>
<tr>
<td>Pulmonary rales</td>
<td>possible pleural effusions</td>
</tr>
</tbody>
</table>

**Lab Presentation**

- Chest Film: cephalization of pulmonary vasculature, air bronchograms, pleural effusion, perivascular haziness.
- LA pressure > 15mmHg → vascular cephalization
- LA pressure > 20mmHg → Kerley B lines
- LA pressure > 25mmHg → opacification of air space
- ECG: LAD
- Serum: ↑ ADH, ↑ renin, ↑ angiotensin, ↑ ANP & BNP

**Etiology and Pathogenesis**

Heart failure results in decreased forward cardiac output and increased pressure in the pulmonary vasculature. Dyspnea results from an increased respiratory work necessary to move a volume of air – as pulmonary venous pressures exceed 20mmHg, the patient experiences pulmonary edema and resultant decreased pulmonary and alveolar compliance, increased diffusion path length, and stimulation of juxtaglomerular receptors which result in rapid, shallow breathing. Dyspnea may occur even in the absence of pulmonary congestion, as decreased CO leads to reduced blood flow to the respiratory muscles and the kidney.

**Systolic dysfunction** represents diminished capacity of the ventricle to eject blood because of ↓ ↓ CTY &/or ↑ ↑ AL. This may lead to elevated left-ventricular, left-atrial, and pulmonary venous pressures and subsequent pulmonary congestion. Diastolic dysfunction is caused by impaired early diastolic relaxation (an energy-dependent process) &/or increased stiffness of the ventricular wall.

Compensatory Mechanisms in heart failure include: Frank-Starling compensation, neurohormonal alterations, and development of myocardial hypertrophy & ventricular remodeling. In severe heart failure, Frank-Starling compensation (↑ preload leading to increased stroke volume) is inadequate and end-diastolic volume increases. Neurohormonal alterations encompass adrenergic stimulation, activation of the renin-angiotensin axis, and increased production of ADH – these all result in increased peripheral resistance that balances the loss in CO in keeping BP stable; in addition, these mechanisms result in salt & water conservation which increases intravascular volume and further increases BP and LV preload to maintain BP. The renin-angiotensin system is activated by decreased renal artery perfusion pressure, decreased salt delivery to the macula densa of the kidney, and direct stimulation of the juxtaglomerular & receptors by the SNS – angiotensin II then acts to increase intravascular volume by stimulating thirst (thirsty signal) and increasing aldosterone secretion (which increases salt/water reabsorption in the kidney). ADH secretion is increased in heart failure in response to ↓ BP and ↑ serum aldosterone. Compensatory mechanisms are initially beneficial but eventually harmful, as ↑ venous return may exacerbate pulmonary congestion, ↑ peripheral resistance may ↑ afterload and thereby ↓ SV, ↑ HR increases myocardial O2 demand, continued SNS activity results in desensitization at the adrenergic synapses and resulting ↓ in CTY, and chronically elevated levels of angiotensin II and aldosterone provoke an inflammatory response resulting in adverse fibrosis and remodeling of the heart.

Atrial natriuretic peptide and B-type natriuretic peptide are released in response to atrial distention (BNP is not detected in normal hearts but is produced when ventricular pressures increase) and act to increase Na and water secretion, vasodilation, inhibition of renin, aldosterone, and vasopressin secretion; while these effects are beneficial in HF, they are not sufficient to counteract the vasoconstriction and volume-retaining effects of the other hormones.
Main Goals of Treatment:
1. Identify and correct underlying cause of HF
2. Eliminate acute precipitating cause of symptoms in pts. with previously compensated HF.
3. Manage HF symptoms
   - diuretics and ↓ Na intake to reduce congestion
   - increase forward CO with positive inotropic drugs and vasodilators
4. Modulate neurohumoral response to help prevent adverse ventricular remodeling.
5. Interventions to improve long-term survival.

Standard Therapeutic Regimen:
1. ACE inhibitor
2. Diuretic if congestion or edema is present
3. β-blocker for pts. without recent clinical deterioration or volume overload
4. For persistent symptoms, add digoxin
5. For pts. in class IV HF, also add spironolactone

Diuretics:
- reduce intravascular volume and venous return
- use if there is evidence of pulmonary congestion or peripheral edema
- loop diuretics are most potent in HF
- overly vigorous diuresis may adversely ↓ CO by decreasing LVEDV (preload)

Vasodilators:
- venous vasodilators (e.g. nitrates)
  - increase venous capacitance & ↓ return;
  - pulmonary capillary pressure falls → ↓ congestion
- arteriolar vasodilators (e.g hydralazine)
  - reduced SVR → ↓ AL → ↑ systolic SV
  - increased CO prevents reflex ↑ in BP
- balanced vasodilators
- most important group is ACE inhibitors; these are the standard of care for chronic tx of HF
  - facilitate Na/water excretion
  - augment circulating bradykinin levels
  - limit inflammatory myocardial remodeling
- may use ARBs when ACE inhibitors are not tolerated
- may use hydralazine-isosorbide dinitrate when ACE inhibitors not tolerated (renal insufficiency or hyperkalemia)
- may use nesiritide (recombinant BNP) for pts. who do not respond to other vasodilators

Inotropic Drugs:
- β-agonists, phosphodiesterase inhibitors, digitalis
  - ↑ CTY → ↑ SV for a given PL&AL
  - not useful in pts. with pure diastolic failure
  - β-agonists & phosphodiesterase inhibitors are used IV for temporary hemodynamic support
  - tolerance rapidly develops
  - no demonstrated improvement in survival
- Digitalis increases sensitivity to baroreceptors, reduces cardiac enlargement, ↑ s CO, and ↓ s rate of AV conduction (good for pts. in atrial fibrillation).
  - not useful in diastolic dysfunction because it does not help the ventricles relax

Additional Therapies:
1. β-blockers (paradoxically, may help in HF)
2. Spironolactone (K-sparing diuretic)
   - ↓ mortality in pts. taking ACE inhibitors and

Notes

New York Heart Association Classification of Heart Failure:
Class I: No limitation of physical activity.
Class II: Slight limitation of activity. Dyspnea & fatigue with moderate physical activity.
Class III: Marked limitation of activity. Dyspnea with minimal activity.
Class IV: Severe limitation of activity. Symptoms present even at rest.

ACC/AHA Staging of Heart Failure:
Stage A: Patients without present structural cardiac dysfunction who are at risk of developing HF
Stage B: Patients with structural dysfunction but no symptoms
Stage C: Patients with current or prior symptoms of HF associated with structural dysfunction.
Stage D: Patients with structural dysfunction and marked HF symptoms despite maximal medical therapy and who require advanced interventions (transplant).

Precipitating factors in compensated HF:
1. Increased O2 demand: fever/infection, anemia, tachycardia hyperthyroidism, pregnancy.
2. Increased circulating volume (↑ preload): ↑ Na intake, excess fluid, renal failure
3. ↑ afterload: HTN, pulmonary embolism
4. ↓ CTY: negative inotropic medications, MI, EtOH
5. Excessive bradycardia (↑ O2 supply)

Prognosis:
- 50% mortality in absence of correctable underlying cause
- class III or IV pts. have 1y survival of only 40%
  - greatest mortality is due to refractory HF, but arrhythmias are also a major cause of death
- bad prognostic markers: high serum NE level, reduced serum Na level, ↑ serum endothelin, ↑ serum TNF-α, ↑ serum BNP
13. Right-Sided Heart Failure

Clinical Presentation

**Symptoms**
- Dyspnea
- RUQ pain (hepatic enlargement)
- Anorexia & Nausea (edema within GI tract)
- Possible weight gain (increased fluid retention)
- Profound hypotension

**Physical Exam**
- Peripheral edema
- JVD
- Hepatomegaly
- Possible right-sided audible S₃ or S₄
- Possible right-ventricular heave; possible pleural effusion

Lab Presentation

ECG: RAD

Etiology and Pathogenesis

Right HF results in elevated systemic venous pressures which can cause painful *hepatomegaly* (as liver is engorged with blood), *lower-extremity edema* that worsens upon standing and improves upon lying down, and GI edema that may cause nausea and anorexia – weight-gain due to interstitial fluid retention may actually be found in patients before signs of peripheral edema are present. JVD is the prominent symptom is caused by elevated pressures in the RV (because of decreased RV stroke volume) being transmitted to the RA and from there to the jugular vein. Hypotension may develop from reduced left ventricular filling.

Approximately 1/3 of patients with infarction of the LV wall will also develop necrosis of portions of the RV (same coronary artery perfuses sections of both ventricles), leading to right heart failure.

Compared to the LV, the RV is a highly compliant chamber that ejects against a much lower resistance; as a result, the RV can accept a large increase in filling volume without a corresponding increase in filling pressure – the RV is vulnerable then to failure in situations of high afterload (such as acute increase in pulmonary vascular resistance). The most common cause of right-sided heart failure is left-sided heart failure; isolated right-heart failure is less common and is usually due to increased pulmonary vascular resistance (e.g. disease of the lung parenchyma), and right-sided heart failure that results from a primary pulmonary process is called *cor pulmonale*. Isolated right-heart failure may reduce LV stroke volume as less blood is delivered to the left heart.

Notes

New York Heart Association Classification of Heart Failure:
- **Class I**: No limitation of physical activity.
- **Class II**: Slight limitation of activity. Dyspnea & fatigue with moderate physical activity.
- **Class III**: Marked limitation of activity. Dyspnea with minimal activity.
- **Class IV**: Severe limitation of activity. Symptoms present even at rest.

ACC/AHA Staging of Heart Failure:
- **Stage A**: Patients without present structural cardiac dysfunction who are at risk of developing HF
- **Stage B**: Patients with structural dysfunction but no symptoms
- **Stage C**: Patients with current or prior symptoms of HF associated with structural dysfunction.
- **Stage D**: Patients with structural dysfunction and marked HF symptoms despite maximal medical therapy and who require advanced interventions (transplant).
14. Atrial Premature Beats

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>ECG: one or more abnormally-shaped P-waves occurring earlier than expected from the underlying rhythm.</td>
</tr>
<tr>
<td>Palpitations</td>
<td></td>
</tr>
<tr>
<td>(most instances of APBs are asymptomatic, however)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial premature beats originate from automaticity or re-entry in an atrial focus that is not the SA node – they are common in both healthy and diseased hearts and may be precipitated by caffeine, alcohol, emotional &amp;/or physical stress (adrenergic stimulation). Since the impulse driving the APB does not arise from the SA node, the P-wave will be abnormally-shaped and occur earlier than expected from the underlying rhythm. The impulse may arise when the AV node is refractory to stimulation (a “blocked” APB) and not induce a subsequent QRS, or it may reach a conductive AV node but encounter portions of the His-Purkinje system that are refractory, producing an abnormaly wide QRS (as the impulse spreads via junctions of the ventricular myocytes), or it may reach an AV node susceptible to stimulation and produce a normal QRS.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-blockers for symptomatic patients.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>
15. Atrial Flutter

**Clinical Presentation**

**Symptoms**
- palpitations
- dyspnea
- weakness

**Physical Exam**
- hypotension (when ventricular rate is very high)

**Lab Presentation**
- ECG: rapid, regular “sawtooth” P waves, with many not followed by a QRS

**Etiology and Pathogenesis**

Atrial flutter is characterized by a rapid, regular atrial activity at a rate of 180-350 bpm. Since many of these impulses reach the AV node while it is refractory, the ventricular rate is slower than the atrial rate (and often an even fraction of the atrial rate). Since vagal maneuvers (e.g. carotid sinus massage) decrease AV nodal conduction, these maneuvers increase the degree of AV block and slow ventricular conduction. AFI is generally caused by reentry over a large & anatomically fixed circuit, and in the most common form of AFI, this circuit runs through the interatrial septum and the roof and free wall of the right atrium, though other parts of the right &/or left atrium may be involved. AFI generally occurs in patients with preexisting heart disease, may be paroxysmal/transient, persistent (lasting days-weeks), or permanent, and frequently degenerates into atrial fibrillation. Clinical symptoms of AFI depend on the corresponding ventricular rate: < 100 bpm the patient may be asymptomatic; faster rates may cause symptoms. Paradoxically, AFI may be made worse if the atrial rate slows such that the ventricular rate is able to match it, resulting in a ventricular rate that is higher than if some atrial impulses were blocked at the AV node.

**Treatment**

1. **Electrical cardioversion** for symptomatic patients with recent onset AF and for chronic AF that does not respond to other therapy.

2. **Burst pacing** (rapid atrial stimulation) via a temporary or permanent pacemaker.

3. **Pharmacologic therapy** for patients without need for immediate cardioversion.
   - step 1: slow ventricular rate with drugs that increase AV block (β-blockers, CCBs, digoxin)
   - step 2: restore sinus rhythm with antiarrhythmics that slow conduction or prolong refractory period of atrial myocardium (IA, IC, III)
     - if this fails, use electrical cardioversion
   - step 3: once sinus rhythm is restored, use IA, IC, or III antiarrhythmics chronically to prevent recurrence

4. **Radiofrequency catheter ablation** of the reentry circuit may eliminate the need for chronic drug therapy.

**Notes**
16. Atrial Fibrillation

### Clinical Presentation

Presenting symptoms may be those of:
- Heart Failure
- Atrial Flutter
- Acute Pulmonary Edema

### Lab Presentation

ECG: no discernable P-waves; baseline shows continuous low-amplitude undulations.

### Etiology and Pathogenesis

AF is a chaotic rhythm with an atrial rate of 350-600bpm, with an average ventricular rate of 160bpm. AF appears to result from multiple “wandering” reentrant circuits in the atria, and in some patients, AF shifts into and out of atrial flutter. AF is often associated with right or left atrial enlargement (increasing the likelihood of multiple reentry circuits) but may also develop from a rapidly firing atrial ectopic focus. AF is common in patients with hypertension, CAD, alcohol intoxication, pulmonary ds, thyrotoxicosis, and following cardiothoracic surgery. It is dangerous because: 1) ventricular tachycardia may → ↓ CO, especially in pts. with a hypertrophied LV (where atrial contraction is important to ventricular filling) → ↓ CO → systemic hypotension and pulmonary congestion, and 2) disorganized atrial contractions promote blood stasis in the atria, which increases the risk for thrombus (especially in the left atrial appendage) and subsequent embolization and stroke.

### Treatment (similar to tx for atrial flutter)

1. **β-blockers** or **CCBs** to increase the AV nodal block and decrease the ventricular rate.

2. **Cardioversion** via class IA, IC, or III antiarythmics or electrical cardioversion to restore sinus rhythm.

3. **Anticoagulation** if AF has been present for more than 48 hours to reduce risk of thromboembolism.
   - In urgent situations, transesophageal echocardiography is used to evaluate for atrial thrombus, and if no thrombus is present, cardioversion can be attempted; otherwise, anticoagulation should be done (at least a 3 week course) before cardioversion to reduce the risk of thromboembolism.

4. **Chronic antiarythmic therapy** to prevent or reduce AF episodes in symptomatic patients; because these drugs cause significant side effects, in asymptomatic patients should continue anticoagulation plus drugs to decrease the ventricular rate.

5. **Non-pharmacological options**: more permanent but less widely available:
   - **Maze procedure**: multiple surgical incisions in atria to interrupt & prevent reentry circuits.
   - **Catheter ablation** of atrial ectopic foci, usually near the insertion of the pulmonary veins.
   - **Catheter ablation** of the AV junction, when sinus rhythm and HR cannot be maintained with medications; this procedure requires the simultaneous placement of a permanent pacemaker to ensure an adequate ventricular
17. Paroxysmal Supraventricular Tachycardias (AVNRT & AVRT)

### Clinical Presentation

**Symptoms:**
- AVNRT (often presents in teenagers and young adults)
  - usually well-tolerated
  - may present as felt palpitations, lightheadedness, or SOB
  - in elderly pts. with more severe ds, may → syncope, angina, or pulmonary edema

**Physical Exam:**
- AVNRT: vagal maneuvers may terminate the tachycardia

### Lab Presentation

**ECG:**
- Atrial rates of 140-250bpm;
- AVNRT → regular tachycardia with normal-width QRS complexes and P-waves “hidden” in QRS; if P waves are seen they are inverted in II, III & aVF and superimposed on the terminal QRS

(See #14 for info on AVRTs)

### Etiology and Pathogenesis

PSVTs are most often the result of reentry involving the AV node, SA node, atrium, or accessory pathways between an atrium and ventricle, but they may also be caused by enhanced automaticity. Clinically, they show a sudden onset and termination. **AV Nodal Reentrant Tachycardia** is the most common PSVT in adults – resulting from the impulse of an atrial premature beat reaching an AV node that has two pathways of conduction: a fast pathway with a long refractory period, and a slow pathway with a short refractory period; normally when the slow-pathway impulse reaches the Bundle of His, the BoH is refractory to stimulation because the fast-pathway impulse has just passed, but in an APB, the premature impulse can reach the AV node when the fast pathway is refractory but the slow pathway is not, resulting in a depolarization of the ventricles via the slow pathway and if the distal fast pathway has become repolarized by the time the slow-pathway-traveling impulse reached the BoH, the impulse can travel retrograde along the fast pathway to the atria, setting up a reentry circuit. Because ventricular and atrial depolarization occur simultaneously, P-waves are masked by the QRS complexes in the ECG.

**Atrioventricular Reentrant Tachycardia** is similar to AVNRT except that one limb of the reentrant circuit is an “accessory pathway” (an abnormal band of myocytes that connects atrial to ventricular muscle) rather than a pathway in the AV node. The accessory pathway may allow conduction from ventricle to atria, atria to ventricle, or in both directions. Depending on the direction of conduction, a Ventricular Preexcitation Syndrome or a Concealed Bypass Tract is the result – These are discussed in #14 below.

### Treatment

**AVNRT:** (prevent reentry by ↓ AV node conduction)
- IV adenosine to stop the reentrant rhythm
  - this is the most effective pharmacotherapy
- CCBs or β-blockers
  - digitalis is less effective in an acute situation
  - because of its slow onset of action, but may be used in chronic treatment
- most patients will have infrequent episodes that will terminate with vagal maneuvers (ex. carotid massage) and will not need drug therapy
- radiofrequency catheter ablation of the slow pathway is effective for symptomatic pts. who do not respond to drug therapy.

### Notes

**Conditions necessary for AVNRT:**
1. unidirectional block in fast pathway of AV node
   - (often from APB reaching it in its refractory period)
2. relatively slow conduction in another AV node pathway

There is a rare variant of AVNRT where the reentrant loop involves retrograde conduction down the slow pathway; this is called “uncommon AVNRT” and yields visible retrograde (inverted in II, III, aVF) P-waves following the QRS complexes.

Approximately 1 in 1,500 people have an accessory pathway.

PVSTs fall into two subtypes:
1. AVNRTs
2. AVRTs
   - AVRTs themselves fall into two subtypes:
     1. Ventricular preexcitation syndrome
     2. Concealed bypass tracts
18. Atrioventricular Reentrant Tachycardias (a subtype of Paroxysmal Supraventricular Tachycardias)

**Clinical Presentation**

**Lab Presentation**

**ECG:**
- WPW Syndrome: shortened PR interval; slurred QRS upstroke (“delta wave”); wide QRS
- orthodromic AVRT: retrograde P-waves seen; QRS becomes normal; delta waves disappear
- antidromic AVRT: retrograde P-waves seen; QRS becomes very widened

**CBT:** normal P and QRS during sinus rhythm; orthodromic AVRT findings during tachycardia

---

**Etiology and Pathogenesis**

The two subtypes of AVRTs are: 1) Ventricular Preexcitation Syndromes, and 2) Concealed Bypass Tracts.

In patients with a VPS, atrial impulses can pass through both the AV node and the accessory tract; since the accessory tract conduction velocity is usually faster, the ventricles are stimulated earlier than they would be by the normal impulse. Wolff-Parkinson-White Syndrome is an example of a VPS. The characteristic ECG findings (see above) result from ventricular preexcitation and excitation via the AV nodal and accessory pathways – In patients with WPWS, an atrial premature beat may cause an orthodromic AVRT, where the impulse travels anterograde via the AV node then retrograde via the accessory pathway leading to ECG findings of retrograde P-waves and disappearance of the delta wave (ventricles are no longer depolarized by the accessory pathway – now the atria are). An APB may also induce an antidromic AVRT, where the impulse passes retrograde via the AV node and anterograde via the accessory pathway, showing ECG findings of an exaggerated widened QRS and appearance of retrograde P-waves. Atrial flutter or fibrillation is very dangerous in patients with WPWS, because the tachycardic atrial beats may be transmitted 1:1 via the accessory pathway and induce ventricular fibrillation and cardiac arrest.

A Concealed Bypass Tract is an accessory pathway that does not normally cause ventricular pre-excitation (and the corresponding ECG findings) because it is capable only of mediating retrograde conduction. CBTs can form a limb of an orthodromic AVRT circuit, however.

---

**Notes**

**Lown-Ganong-Levine Syndrome** is a rare condition characterized by shortened PR interval but normal QRS complex in sinus rhythm; can be due enhanced AV node conduction or a short accessory pathway connecting the atria to the Bundle of HIs.

**PVSTs** fall into two subtypes:
1. AVNRTs
2. AVRTs
- AVRTs themselves fall into two subtypes:
  1. Ventricular preexcitation syndrome
  2. Concealed bypass tracts
19. Atrial Tachycardias (EAT & MAT)

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Exam:</strong></td>
<td>ECG findings:</td>
</tr>
<tr>
<td>Vagal maneuvers will not slow the tachycardia (since it is not dependent on impulse transmission through the AV node).</td>
<td>EAT: sinus tachycardia with abnormal P-wave morphology</td>
</tr>
<tr>
<td></td>
<td>MAT: irregular rhythm with multiple (at least three) P-wave morphologies; atrial rate &gt; 100bpm; regular baseline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ectopic Atrial Tachycardia</em> most commonly results from automaticity in an atrial focus and less often from a reentry circuit – EAT can be caused by digitalis toxicity and elevated sympathetic turn; it may be paroxysmal or persistent, but short bursts of EAT are common even in healthy people.</td>
</tr>
<tr>
<td><em>Multifocal Atrial Tachycardia</em> is characterized by multiple foci of automaticity within the atria and most often occurs in severe pulmonary ds and hypoxemia. Patients with MAT are usually critically ill from their underlying disorder and so treatment most often involves treating the causative condition.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAT: β-blockers, CCBs, Class IA, IC, III antiarrhythmics</td>
<td></td>
</tr>
<tr>
<td><em>Catheter ablation</em> when symptoms do not respond to drugs.</td>
<td></td>
</tr>
<tr>
<td>MAT: Treat underlying disease. <em>Verapamil</em> (CCB) to slow the ventricular rate as a temporary measure.</td>
<td></td>
</tr>
</tbody>
</table>
# 20. Ventricular Premature Beats

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most often asymptomatic &amp; benign</td>
<td>ECG: widened QRS; ectopic beat not preceded by P wave</td>
</tr>
</tbody>
</table>

## Etiology and Pathogenesis

A VPB results from the activity of an ectopic ventricular focus. The ECG shows a wide QRS because the impulse traverses the ventricle via cell-to-cell conduction (slower than conduction via the Purkinje fibers). VPBs are not dangerous in patients without heart disease, but may confer an increased risk of ventricular fibrillation; when VPBs occur frequently in couplets or triplets they are markers of increased mortality. “Bigeminy” refers to every other beat being a VPB; “trigeminy” refers to every third beat being a VPB.

## Treatment

Most patients do not need treatment.
Symptomatic control with β-blockers.

## Notes
# 21. Ventricular Tachycardia & Fibrillation

## Clinical Presentation
Range from asymptomatic to severe hypotension and loss of consciousness due to low cardiac output.

## Lab Presentation
**ECG**: VT: wide QRS; 100-200bpm; no relationship between P waves and QRS complexes; concordance of QRS in precordial leads.

Torsade de pointes: widened QRS complexes demonstrate a waxing and waning pattern.

VF: chaotic irregular waveform with complexes of varying amplitude and morphology.

## Etiology and Pathogenesis
*Ventricular Tachycardia* is the a series of three or more VPBs in a row -- it is called “sustained VT” if it occurs for more than 30 seconds or requires termination because of severe symptoms, otherwise it is called “nonsustained VT”. Both forms are found most commonly in patients with structural heart disease. In *monomorphic VT* (regularly appearing QRS) there is usually a structural abnormality such as a region of old infarction. In *polymorphic VT* (QRS complexes vary in shape), the cause is usually multiple ectopic foci or a changing reentry circuit resulting from acute MT or Torsades de pointes (produced by early afterdepolarizations, esp. in patients who have a prolonged QT interval).

*Ventricular Fibrillation* is the most dangerous arrhythmia and is a major cause of mortality in acute MI; VT usually precedes VF.

## Treatment
Sustained VT: electrical cardioversion followed by anti-arrhythmic drugs for chronic suppression

Patients at high risk receive an *implantable cardioverter defibrillator* that will automatically stop further episodes.

Use β-blockers for asymptomatic nonsustained VT.

Use β-agonists for Torsade de pointes to shorten the QT interval, but in the rare case when Tdp is due to a congenital long QT interval use β-blockers.

VF: prompt electrical defibrillation followed by correction of underlying cause of the arrhythmia &/or implantation of an ICD.

## Notes
### 22. Atrioventricular Blocks

#### Clinical Presentation

<table>
<thead>
<tr>
<th>First-degree AV block: usually benign &amp; asymptomatic</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I second-degree AV block: usually benign &amp; asymptomatic</td>
<td>ECG: 1st degree → regularly lengthened PR interval</td>
</tr>
<tr>
<td>Type II second-degree block &amp; Third-degree block: lightheadedness / syncope</td>
<td>Type I 2nd degree → PR interval that progressively lengthens until a QRS occurs that is not preceded by a P-wave</td>
</tr>
<tr>
<td></td>
<td>Type II 2nd degree → occasional QRS complex that is not preceded by a P-wave, may show wide QRS and pattern of RBBB or LBBB</td>
</tr>
<tr>
<td></td>
<td>3rd degree → P wave and QRS complex completely independent of one another – depending on the site of escape rhythm QRS may be normal width &amp; 40-60bpm (escape in AV node) or wide and slower</td>
</tr>
</tbody>
</table>

#### Etiology and Pathogenesis

First degree AV block indicates prolongation of the normal delay between atrial & ventricular contraction – the PR interval is greater than normal (> 0.2s), with all QRS complexes still preceded by P-waves. The conduction abnormality is normally within the AV node itself, and may result from reversible (↑ vagal tone, transient AV-node ischemia, drugs than slow AV conduction velocity) and structural (MI, chronic degenerative ds of conduction system) causes. First-degree block may increase susceptibility to higher degree blocks in patients recieving drugs that slow AV-node conduction velocity.

Second degree AV block indicates intermittent failure of AV conduction. Type I block (Wenckebach block) is characterized by a gradually increasing delay in conduction (gradually ↑ing PR interval) followed by an eventual QRS not preceded by a P-wave – it is most always due to a defect in the AV node itself and is usually benign and may be seen in kids, athletes, & pts. with ↑ vagal tone (esp. during sleep) but may occur during an acute inferior wall MI (↑ vagal stimulation or ischemic damage to AV node. Type II 2nd-degree block indicates a sudden and unpredictable loss of AV conduction (QRS not preceded by P) – it is usually due to conduction block in the Bundle of His or in the Purkinje system.

Third degree AV block indicates complete failure of conduction between the atria and ventricles, after which the atria and ventricles beat independently.

#### Treatment

<table>
<thead>
<tr>
<th>First degree: generally does not require tx</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I 2nd degree: generally benign,</td>
<td>Type II 2nd-degree block is “high-grade” if it lasts for two or more sequential beats.</td>
</tr>
<tr>
<td>• in symptomatic patients, use IV isoproterenol or atropine to reset rhythm.</td>
<td>Third-degree block is also known as “complete” block.</td>
</tr>
<tr>
<td>• pacemaker for symptomatic block that does not respond to drugs.</td>
<td>Third-degree block is an example of an “atrioventricular dissociation”, any situation where the atria and ventricles beat independently.</td>
</tr>
<tr>
<td>Type II 2nd degree:</td>
<td></td>
</tr>
<tr>
<td>• pacemaker even in asymptomatic pts. because the block may progress suddenly to third-degree</td>
<td></td>
</tr>
<tr>
<td>Third degree:</td>
<td></td>
</tr>
<tr>
<td>• pacemaker is almost always necessary</td>
<td></td>
</tr>
</tbody>
</table>
23. Other Conduction Blocks (Bundle Branch Blocks and Fascicular Blocks)

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
</table>

**Etiology and Pathogenesis**

(this section is omitted because of a lack of study time, the fact that it wasn’t mentioned in class, and the fact that Dr. Willis implied we didn’t have to know it.)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
</table>
24. Mitral Regurgitation

Clinical Presentation

### Symptoms
- Acute MR: symptoms of **acute pulmonary edema** (see # 28)
- Chronic MR: symptoms of **left-heart failure** (see # 12)
  - in severe MR symptoms of right-heart failure may develop

### Physical Exam:
- **Holosystolic murmur** that offers radiates to the axilla
  - late systolic murmur in mild MR due to prolapse
  - early systolic murmur in severe acute MR
- Enlarged & lateralized apical impulse – LV-enlargement
- Wide-split S₂
- Audible S₃, ↑ blood flow over MV in diastole from LA overload

### Lab Presentation
- **ECG:**
  - LAE: prolonged P-wave, exaggerated P-wave downward deflection in V₁
  - LVE: LAD with exaggerated upright T-waves
- **Chest Film:** LA & LV enlargement, in severe MR RVE; signs of pulmonary congestion &/or mitral annulus calcification may be seen.
- **Venous Pressure Tracing:** large systolic v wave

### Etiology and Pathogenesis

MR is characterized by systolic ejection or a portion of the LV stroke volume backwards into the LA, resulting in ↑ LA-volume & pressure, ↓ LV-volume, and ↓ CO. MR may result from abnormalities of or damage to any aspect of the mitral apparatus: chordae tendinea, papillary muscle, LV, leaflets, or annulus. Functional MR may result when too much volume is pumped across a normal valve. Ischemic heart disease may cause papillary dysfunction and subsequent MR with probable prolapse; the resulting acute MR is a medical emergency and presents as acute pulmonary edema (see # 28) as there is no time for compensatory volume change in the LV (systolic backflow into the pulmonary veins may also be seen). Infective endocarditis may cause perforation of valve leaflets or rupture of infected chordae; MR with thickened valve leaflets is almost always associated with rheumatic fever and MS. Hypertrophic cardiomyopathy (see # 36) causes MR in 50% of pts., as there is abnormal movement of the anterior mitral leaflet during systole. Marked LV enlargement of any cause may result in MR if the mitral annulus is stretched or if the spatial separation between the papillary muscles is increased. MR may also be caused by calcification of the mitral annulus (occurs in normal aging but most common in pts. with HTN or AS), which immobilizes the basal portion of the valve leaflets & interferes with their excursion and systolic coaptation.

The **regurgitant fraction** in MR is the ratio of reguritant volume to total LV stroke volume, and this ratio rises whenever SVR is increased; the extent to which LA-pressure rises in response to increased volume is determined by left atrial compliance.

Acute MR is characterized by normal LV stroke volume and normal LA size and compliance → high LA pressure → high pulmonary venous pressure → pulmonary congestion; this is because compensatory LA-dilation (increased size & compliance) has not yet developed. In chronic MR, LA dilation decreases the LA pressure and resulting backpressure into the pulmonary circulation, but the decreased LA pressure leads to decreased CO because the regurgitant fraction increases as LA resistance decreases in ln SVR

### Treatment

#### Acute MR:
- Medical Therapy:
  1. **Diuretics** to relieve pulmonary congestion.
  2. **Vasodilators** (e.g. nitroprusside) to reduce SVR and favor forward CO.
- Emergency valve repair/replacement surgery may be necessary.

#### Chronic MR:
- Perform corrective surgery before decompensated volume overload results in heart failure.
  - but operative mortality and other risks demand we delay surgery as long as possible.
  - this is because survival after MV-replacement is not better than in the natural course of the disease, though symptoms may improve.
- **Mitrval valve repair** has a better morbidity/mortality risk than does valve replacement; repair is indicated in younger patients with myxomatous valve leaflets.

**Operative Mortality Rate:** repair 2-4%, replacement 8-10%
**10yr Survival:** repair 80%, replacement 50%

#### Notes
- Most common valvular defect.
- Chronic atrial dilation predisposes the patient to AF.
- Regarding the **holosystolic murmur:** if MR is due to papillary muscle dysfunction and the regurgitant jet is directed towards the right left atrial wall immediately posterior to the aorta, the murmur may be best heard in the aortic area and confused with AS. To distinguish this kind of MR from AS, ask patient to clench his/her fists (thereby ↑ ing SVR) – after this maneuver, the murmur from MR will intensify whereas the murmur of AS will not. In contrast, in pts. with AF or rapid premature beats (where the amount of LV diastolic filling is determined by the length of time since the last beat), longer times between beats will make the AS murmur more severe (more flow across valve) whereas the MR murmur will remain unchanged.
- Echocardiography and cardiac catheterization can reveal defect and grade severity; and cahn. is especially useful for identifying MR due to papillary muscle ischemia.
25. Mitral Valve Prolapse

### Clinical Presentation

**Symptoms:**
- Often asymptomatic
- May show chest pain &/or palpitations (associated arrhythmias)

**Physical Exam:**
- **Mid-systolic click & late systolic murmur** best heard at apex.
  - squat → murmur softer/shorter & click later
  - stand → murmur louder/longer & click earlier

### Lab Presentation

**ECG:** normal or LAE & LVE (chronic MR)

**Echocardiography:** demonstrates displacement of valve leaflets in systole.

### Etiology and Pathogenesis

MVP is a chronic and mostly asymptomatic billowing of mitral valve leaflets into the LA during systole; it may be inherited as a primary disorder or secondary to another connective tissue disorder. Pathologically, the valve leaflets are enlarged and composed of less dense (“myxomatous”) connective tissue. More severe MVP can be associated with annular enlargement and thickened leaflets, and it may be caused by damage to the papillary muscle. MVP is often associated with MR, and the most severe complication of MVP is sudden rupture of the myxomatous chordae causing acute MR. On auscultation, the mid-systolic click corresponds to the sudden tensing of the chordae as the mitral leaflets are forced into the LA, and the subsequent murmur corresponds to regurgitant flow through the incompetent valve – these sounds are delayed and muffled by maneuvers that increase LV volume and accentuated/lengthened by maneuvers that decrease LV volume.

### Treatment

Treatment includes reassurance about good prognosis.

Use antibiotic prophylaxis for endocarditis only if substantial valve thickening or MR is present.

### Notes

MVP occurs in 2.4% of the general population, especially among women with lean body types.

Rare complications of MVP include: infective endocarditis, peripheral microthrombic emboli, and atrial or ventricular arrhythmias.
26. Acute Rheumatic Fever & Rheumatic Heart Disease

### Clinical Presentation

**ARF:** chills, fever, migratory arthralgias, fatigue, history of streptococcal pharyngitis, tachycardia, pericardial friction rub, transient murmur of mitral or aortic regurgitation, mid-diastolic murmur at the cardiac apex

**RHD:** left-sided heart failure

### Lab Presentation

**Aschoff bodies** seen in perivascular position of myocardial interstitium

Anitschkow cell

Aschoff myocyte

- these defining cells are MPs not monocytes

Pericarditis: fibrinous exudate

Acute Rheumatic Fever → globular LV (myocarditis), valvular vegetations

Fish-mouth deformity seen in MV pathology

### Etiology and Pathogenesis

Acute rheumatic fever is an inflammatory condition involving the heart, skin, and connective tissue that is a complication of URT infection by group A streptococcus. During epidemics, 3% of patients with streptococcal pharyngitis develop ARF 2-3 weeks after the initial throat infection – rheumatic carditis may affect all three layers of the heart, though the cardiac pathogenesis of acute rheumatic fever is unknown it does not involve direct bacterial infection of the heart. Histopathologic examination often demonstrates the “Aschoff body,” an area of focal fibrinoid necrosis surrounded by inflammatory cells that later resolves to scar tissue – the most devastating sequela result from involvement of the valvular endocardium, which leads to chronic rheumatic heart disease. RHD is characterized by valve scarring & calcification and arises 10-30 years after rheumatic fever. The pathogenesis is likely an autoimmune reaction to valvular glycoproteins and myocardial sarcolemma induced by the group-A streptococcus infection – transient murmurs reflect turbulent flow across inflamed valve leaflets.

### Treatment

**Acute ARF**

1. High-dose aspirin to reduce inflammation
2. Penicillin to eliminate residual streptococcal infection
3. Treat complications such as CHF or pericarditis

### Notes

**Incidence:**

- Mitral: 50%
- Aortic&Mitral: 45%

ARF recurs in 10% of patients, and these recurrences can incite further damage, so ARF pts. should receive low-dose penicillin prophylaxis until young adulthood.

**Jones’ Criteria for Diagnosis of Rheumatic Fever:**

(diagnosis requires infection plus 2 major or 1 major & 2 minor)

- Major criteria: carditis, polyarthritis, chorea, subcutaneous nodules, erythema marginatum
- Minor criteria: migratory arthralgias, fever, ↑ ESR or leukocytosis, prolonged PR interval

Evidence of Streptococcal Infection: antistreptolysin O Abs positive throat culture
27. Mitral Stenosis

## Clinical Presentation
### Symptoms
- **Mild MS:** exertional dyspnea
- **Severe MS:** dyspnea at rest; orthopnea, PND; right-heart failure (JVD, ascites, peripheral edema, hepatomegaly)
- Hemoptyis (bursting of engorged pulmonary vessels)
- Hoarseness (compression by LA of recurrent laryngeal nerve)

### Physical Exam:
- **Opening Snap** in early diastole (earlier snap → worse MS);
- ↑ loudness of S1 (valve closes from large range of excursion);
- **Mid-diastolic murmur**, decresendo from OS with pre-systolic accentuation (↑ LA pressure in atrial contraction);
- May have RV “tap” on precordial palpation

## Lab Presentation
### ECG:
- LAE; possible RVH

### Chest Film:
- LA & RV enlargement with normal LV, small aorta (if chronic low CO), may show pulmonary venous congestion (as in CHF).

### Echocardiography:
- Reveals thickened valve leaflets &/or abnormal fusion of valve commissures, measures mitral valve area, and looks for intra-atrial thrombus.

## Etiology and Pathogenesis
Mitral stenosis is almost always associated with rheumatic heart disease; other rare causes include congenital mitral stenosis, prominent calcification extending from the mitral annulus, or endocarditis with very large vegetations. Acute and recurrent inflammation produce the typical pathologic symptoms: fibrous thickening and calcification of valve leaflets, fusion of the commissures, and thickening & shortening of the chordae tendineae. Restricted flow into the LV causes an increase in LA pressure and subsequent increase in LA volume (dilation) as well as increase in pulmonary vascular pressure – LV pressures are usually normal in MS, but impaired filling of the chamber across the narrowed mitral valve may reduce SV & CO. The elevation in LV pressure may cause passive or reactive pulmonary hypertension; reactive hypertension is seen in 40% of MS pts. and is characterized by medial hypertrophy and intimal fibrosis, which protects the pulmonary vasculature from further increases in pressure but transmits the increased LA-pressure to the right-heart and causing (in chronic MS) RVH and right-heart failure.

Left atrial enlargement may promote atrial arrhythmias; if atrial fibrillation develops, CO is further compromised (as ↑ HR → ↓ diastolic filling time) and risk of thromboembolism greatly increases. Clinical severity of MS is directly proportional to the reduction in valve area. In mild MS, dyspnea develops on exertion as ↑ HR → ↓ diastolic filling time → ↑ LA-pressure. In severe MS, † † LA pressure may be transmitted to the pulmonary vasculature and right-heart, causing dyspnea at rest and symptoms of right-heart failure. Regarding the physical exam, the opening snap and loud S1 do not depend on pressure gradients and are early signs – further, changes in diastolic filling time change the patients response to mitral stenosis...in exercise, ↑ HR → ↓ filling time → ↑ symptoms. Atrial fibrillation will also exacerbate symptoms (via ↑ LA pressure), and the pre-systolic accentuation of the diastolic murmur does not occur (because there is no atrial contraction).

## Treatment
1. Prophylaxis against recurrent ARF (see # 26) in young pts. and against endocarditis in all pts.
2. Diuretics to lower LA-pressure & treat pulmonary congestion.
3. β-blockers or CCBs to slow HR
   - use digoxin only if pt. has concurrent AF or systolic dysfunction
4. Anticoagulant tx if pt. has concurrent AF or CHF, or if a prior thromboembolic event has occured.
5. If symptoms do not resolve with diuretics and control of rapid HR, consider percutaneous balloon mitral valvuloplasty or open mitral commissurotomy.
   - severe cases may necessitate MV replacement
   - peri-operative mortality: 1-2%
   - 10y-survival rate: 80%

## Notes
- The normal mitral valve cross-sectional area is 4-6 cm²; hemodynamically significant MS occurs when the valve area is reduced to < 2 cm², and critical MS occurs at < 1 cm².
- Risk of developing thromboembolism is directly proportional to the pts. age and size of the left atrial appendage and inversely proportional to the pts. cardiac output.
- Infective endocarditis occurs less frequently with MS than with other valvular diseases.
- Without intervention, median survival is 7y; even pts. with mild symptoms are likely to die within 10y.
- MS is often found in conjunction with MR, may induce TR, and may be associated with AR in RHD.
### 28. Acute Pulmonary Edema

#### Clinical Presentation

<table>
<thead>
<tr>
<th>Symptoms:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea &amp; Anxiety</td>
<td></td>
</tr>
<tr>
<td>Wheezing</td>
<td>(fluid in conduction airways)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical Exam:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia</td>
</tr>
<tr>
<td>Cold, clammy skin</td>
</tr>
<tr>
<td>“Frothy” sputum</td>
</tr>
<tr>
<td>Rales</td>
</tr>
</tbody>
</table>

#### Lab Presentation

- Chest film: pleural effusions, **interstitial edema**

#### Etiology and Pathogenesis

Elevated capillary hydrostatic pressure causes rapid accumulation of fluid in the pulmonary interstitium, leading to compression of the alveoli and creation of local regions of hypoventilation. Acute pulmonary edema may occur in an asymptomatic patient after an MI or in a patient with controlled CHF after some precipitating event. SNS activation in attempt to increase CO causes peripheral vasoconstriction and **cold & clammy skin** on physical examination – **Rales** are initially present at the lung base but eventually spread throughout the lung fields. **Wheezing** results from fluid in the conducting airways.

Pulmonary edema develops when the pulmonary capillary wedge pressure is greater than 25mmHg.

#### Treatment

Pulmonary edema is life-threatening and needs to be treated immediately:

1. *Sit patient upright* to minimize venous return to heart.
2. *Give supplemental O₂*.
3. *Give morphine IV* to reduce anxiety and as a vasodilator to facilitate blood pooling in the lower extremities (further ing venous return to heart)
4. *Give furosemide* (Lasix), a rapidly acting diuretic IV to further reduce LV preload and pulmonary capillary hydrostatic pressure.
5. *Administer nitrates* also to reduce preload.

Remember LMNOP → lasix, morphine, nitrates, supplemental O₂, position

Inotropic drugs (e.g. dopamine) may be used to increase forward cardiac output, and, in extreme cases, venous phlebotomy is an option as well.

#### Notes
## 29. Aortic Regurgitation

### Clinical Presentation

**Symptoms:**
- Usually asymptomatic for many years.
- Angina
- Dyspnea on exertion
- CHF

**Physical Exam:**
- **Wide pulse pressure** (may present as “bounding” pulses)
- **Hyperdynamic LV-impulse**
- **Early diastolic decrescendo murmur** heard along left sternal border & best heard with pt. leaning forward after expiration
- May show **Austin Flint murmur** (turbulence across MV from displacement of leaflet by regurgitant jet, heard at apex)

### Lab Presentation

**Chest Film:**
- acute AR → pulmonary congestion
- chronic AR → LVE

**Echocardiography:** reveals regurgitant jet

### Etiology and Pathogenesis

AR is characterized by backleak of blood from the aorta into the LV during diastole caused by dysfunction of the aortic-valve leaflets or distention of the aortic root. AR results in volume overload to the LV, leading eventually to compensatory LV-dilation.

In acute AR, the LV is of normal size and is relatively non-compliant so the ↑ volume load causes LV pressure to rise drastically and may be transmitted to the LA and pulmonary circulation resulting in pulmonary edema.

In chronic AR, the LV undergoes compensatory dilation in response to the chronic volume overload; this allows the LV to accommodate an increased volume without a corresponding increase in pressure (and thus ↓ing the risk of acute pulmonary edema), but this also causes the aortic and diastolic pressure to drop, producing a **wide pulse pressure** (difference between arterial systolic and diastolic pressure) and associated decrease in coronary perfusion pressure, which along with LVE can produce angina. Eventually CHF develops when the LV-dilation is no longer able to compensate for volume overload.

### Treatment

Acute severe AR is usually a surgical emergency, requiring an immediate valve replacement.

Asymptomatic chronic AR → periodic assessment of LV function (usually by echocardiography) and endocarditis prophylaxis.

Symptomatic pts. with preserved LV function may respond to therapy with diuretics and afterload-reducing vasodilators (ACEIs, nifedipine)
- nifedipine has been shown to reduce reduce LVE, increase LV EF, and delay need for surgery

Surgical valve replacement in chronic AR if:
1. Patients become symptomatic
2. Patients begin to develop impaired systolic function.

### Notes

60% of pts. with asymptomatic chronic AR will remain asymptomatic at a 10yr follow-up.
30. Hypertension

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN is most often asymptomatic until an acute cardiovascular event strikes – preventive screening is important.</td>
<td>EH: normal serum [K], normal UA</td>
</tr>
<tr>
<td><strong>Diagnosis of HTN:</strong> systolic BP diastolic BP</td>
<td>SH:</td>
</tr>
<tr>
<td>Stage 1 140-159 or 90-99</td>
<td><strong>Chronic renal ds:</strong> ↑ serum creatinine, abnormal UA</td>
</tr>
<tr>
<td>Stage 2 160-179 or 100-109</td>
<td><strong>Renovascular ds:</strong> ↓ serum [K]</td>
</tr>
<tr>
<td>Stage 3 &gt;179 or &gt;109</td>
<td><strong>Pheochromocytoma:</strong> ↓ serum catecholamines or HVA &amp; VMA in urine.</td>
</tr>
<tr>
<td><strong>Possible general signs &amp; symptoms:</strong> arterial bruits, flushing, sweating, blurred vision, HA, LVH, retinopathy.</td>
<td>Aortic Coarctation: see # 6</td>
</tr>
<tr>
<td><strong>Some signs associated with specific disease processes:</strong></td>
<td><strong>Primary aldosteronism:</strong> ↓ serum [K]</td>
</tr>
<tr>
<td>Renal ds: hx of repeated UTIs.</td>
<td>ECG: LVH</td>
</tr>
<tr>
<td>Renovascular ds: abdominal bruit (40-60% of pts.)</td>
<td><strong>Cardiology - 36</strong></td>
</tr>
<tr>
<td>Pheochromocytoma: paroxysmal palpitations, diaphoresis, anxiety; weight loss.</td>
<td></td>
</tr>
<tr>
<td>Aortic Coarctation: see # 6</td>
<td></td>
</tr>
<tr>
<td>Cushing’s syndrome: “Cushingoid” appearance (hirsutism, central obesity, rounded face), weight gain, proximal muscle weakness.</td>
<td></td>
</tr>
</tbody>
</table>

HTN may be due to cardiac, vascular, or renal causes, yet renal involvement is especially important since no matter how high the cardiac output and vascular constriction, renal excretion can normalize BP by reducing intravascular volume (thus chronic HTN requires renal involvement) – and while the baroreceptor reflex is important in reducing momentary BP variations, it resets itself continuously such that after 1-2 days of exposure to a higher-than-baseline BP, the baroreceptor firing rate slows to normal at the new baseline (thus baroreceptors can be normal in chronic HTN).

**Essential hypertension** (HTN of unknown etiology) is most likely familial and involves multiple possible genetic predispositions, such as defects in renal excretion, Na-transport across membranes, and high autonomic responses to stress. Environmental etiologies are also possible, as suggested by concordance between spouses and amongst populations of low socio-economic status. Experimental findings in patients with EH and their first-degree relatives include: 1) excessive stress-mediated SNS stimulation of the heart, 2) abnormal SNS stimulation, local regulation, or ion channels in vascular smooth muscle, 3) abnormal regulation of blood flow, ion-channels, and hormonal responses in the kidney (ex. renin levels are abnormally high in 40% of pts. with EH), and 4) catecholamine leak or malregulation in the adrenal gland. EH may also be associated with insulin resistance (esp. in the obese and in diabetics) that leads to hyperinsulinaemia, which can theoretically raise arterial pressure by ↑ing renal Na-absorption, ↑ing SNS outflow & circulating catecholamines, stimulation of vascular smooth muscle hypertrophy, ↑ing intracellular Ca in smooth muscle by altering cell-membrane ion transport. Obese patients may be more prone to HTN because leptin (protein released from adipose tissue) increases SNS outflow in addition to promoting appetite suppression, though this remains to be verified experimentally.

In EH pts. younger than 40, HTN tends to be driven by increased CO with normal TPR (the “hyperkinetic phase”); eventually, the contribution from CO declines and TPR increases as vessels adapt to the prolonged stress (ex. the development of LVH in chronic HTN compromises diastolic filling, thereby ↓ing CO while arterial medial hypertrophy reduces lumen diameter and ↑es TPR), and this shifting from high CO / normal TPR to low CO / high TPR happens regardless of whether MAP has changed over time.

**Secondary hypertension** (HTN of definite etiology) arises from multiple discrete causes including: 1) Medications: estrogens increase hepatic synthesis of angiotensinogen, EPO increases blood viscosity and reverses local hypoxic vasodilation, sympathomimetics increase vasoconstriction & heart rate; glucocorticoids, cyclosporine A, and chronic ethanol consumption can also cause HTN, 2) Renal parenchymal disease (diverse etiologies) via ↓ filtration/Na-excretion and ↑ intravascular volume or via ↑ renin secretion, 3) Renovascular hypertension (renal artery stenosis) via atherosclerosis or fibromuscular dysplasia (fibrous &/or muscular proliferation in the arterial media) resulting in reduced blood flow to the kindey which responds by increased secretion of renin, 4) Coarctation of the Aorta via decreased renal perfusion causing increased renin secretion and via blunting of the baroreceptor response resulting from medial hyperplasia and accelerated atherosclerosis in the proximal aorta – desensitization of the baroreceptors may continue after surgical correction and keep the BP from completely normalizing, 5) Pheochromocytoma via increased secretion of catecholamines, 6) Primary aldosteronism (generally from an adrenal adenoma but may also be from adrenal hyperplasia) via increased production of aldosterone, 7) Secondary aldosteronism, a renin-secreting tumor, 8) Chronic liver disease via decreased angiotensin II degredation, 9) Cushing’s syndrome (ACTH excess) via blood volume expansion, increased renin synthesis, and inhibition of cholinergic vasodilation resulting from increased serum glucocorticoids, 10) Hypothyroidism via increased blood volume and myocardial hyperactivity, and 11) Hypothyroidism via local loss of vasodilating metabolites as basal metabolic rate falls.

Chronic hypertensive trauma to the vasculature promotes weakening of the arterial media and atherosclerosis by disrupting local regulation and inducing smooth muscle hypertrophy – Atherosclerosis further potentiates HTN and increases the risk for MI, aortic aneurysm, aortic dissection (tearing of intima), and hemorrhagic and atherosclerotic stroke. Effects on the heart include concentric LVH, CAD, and eventual systolic dysfunction (made worse by worsening CAD). In the brain, “watershed infarct” of the distal ends of arterial branches may result from hypertensive cerebral arterial narrowing and micro-infarct lacunae may develop. In the kidney, hyaline arteriolar sclerosis, smooth muscle hypertrophy, and fibrinoid necrosis lead to further elevation of BP as the kidney can no longer regulate intravascular volume. Acute onset HTN may cause retinal hemorrhage (in which case it is termed “accelerated-malignant hypertension”), lipid exudation, and areas of local infarction; blurred vision may result from optic nerve ischemia and patchy vision loss from retinal ischemia; papilledema may result from hypertensive loss of cerebrovascular autoregulation – Chronic
### 30. Hypertension (cont.)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **General HTN:** Immediate drug therapy is not recommended in stage 1 HTN, because risk elevation is small – try lifestyle changes first: weight reduction, exercise, low-fat & high-fruit/vegetables diet, moderation of daily Na intake (<6g NaCl), ↓ EtOH consumption, ↓ smoking, relaxation therapy | **Epidemiology of EH:**
- 95% of cases of HTN are essential hypertension.
- EH characteristically arises after young adulthood and incidence increases with age.
- more than 60% of Americans >60y have a diastolic BP of >90mmHg
- Around age 60, the average systolic pressure of women exceeds that of men.
- Both systolic and diastolic BP rise with age, and incidence of cardiovascular complications rises progressively with increases in BP, with systolic pressure equal to or more important than diastolic in predicting clinical events.
- EH is likely genetic because of: 1) a high concordance between identical twins, and 2) normotensive relatives of pts. with HTN often show abnormalities that would predispose them to HTN if other defects were also present, and 3) across distributions, HTN incidence is higher in African-Americans than in any other ethnic group.
- Most often associated with stage 1 & 2 HTN, but also associated with most deaths because of the large number of pts. with EH relative to SH.
- Na-sensitivity is more common in African-American and elderly patients. |
| If lifestyle changes don’t work there are many pharmacological options: 1. **Diuretics** to lower intravascular volume; these are most effective in pts. with mild-to-moderate HTN with normal renal function and especially in pts. who are Na-sensitive (often AAs & the elderly); loop diuretics only for patients with renal insufficiency who do not respond to other diuretics. 2. **Sympatholytics** (β-blockers, α₂-agonists, α₁-blockers) to reduce heart rate and reduce renin secretion; these are less effective than diuretics in pts. who are Na sensitive. β-blockers without sympathomimetic activity may cause dyslipidemia (↑ HDL & ↓ LDL) 3. **Ca-channel blockers** to reduce cardiac CTY and vascular smooth muscle tone; use the long-acting (once a day) formulations, as they are associated with less adverse cardiovascular outcomes. 4. **Hydrazine or Minoxidil** to directly relax vascular smooth muscle of precapillary resistance vessels; use with β-blocker to prevent reflex increase in heart rate. 5. **ACE-inhibitors** to ↓ vasopressor activity of AII, to ↓ AII-mediated aldosterone secretion, and to ↓ degradation of the vasodilator bradykinin. ACE inhibitors reduce post-MI mortality, chronic systolic heart failure, and in pts. with high risk of cardiovascular disease; they also slow the deterioration of renal function in diabetic nephropathy. 6. **Angiotensin II receptor blockers** to promote vasodilation and decreased aldosterone secretion. | **Epidemiology of SH:**
- Developed before age 20 or after age 50
- Often causes Stage 3 HTN
- Onset is often rapid rather than gradually progressive.
- Often associated with lack of family hx of HTN.
- % of hypertensive patients: Chronic renal ds: 2-4% Renovascular ds: 1% Pheochromocytoma: 0.2% Aortic Coarctation: 0.1% Primary aldosteronism: 0.1% Cushing’s syndrome: 0.1% |
| First-line therapy is diuretics and β-blockers because of proven effectiveness and low cost. If this is not sufficient, an ACE inhibitor, ARB, CCB, or α₁-blocker is added; consider ACE inhibitors especially in pts. with concurrent heart failure, diabetes, or systolic dysfunction from MI. Use combination-therapy to prevent physiologic response to one drug blunting that drugs effect – for example, give diuretic with a direct vasodilator to prevent kidney from activating renin-angiotensin system to cause vasoconstriction in response to the vasodilator-induced drop in renal perfusion pressure. Disease-specific therapies for SH: Renovascular HTN: ACE inhibitors, surgical correction. Pheochromocytoma: β-blocker plus α-blocker; surgical correction or α-methyltyrosine (a drug that inhibits catecholamine synthesis) Primary aldosteronism: surgical removal of tumor or spironolactone. | Renal artery stenosis is most often caused by atherosclerosis (2/3 cases of renovascular hypertension, most common in old men) and fibromuscular dysplasia (1/3 of cases and occurs in young women).
- In pheochromocytoma, some pts. are normotensive between attacks but most show chronic HTN; 10% of these tumors are malignant.

Typical screening studies for the patient who presents with acute HTN include: 1) UA and serum creatine to evaluate renal function, 2) serum potassium, 3) blood glucose level, 4) serum cholesterol, 5) chest radiograph looking for coarctation of aorta. If no abnormalities are found the pts. is assumed to have EH. Without treatment, 50% of hypertensive pts. dia of CAD or CHF, 33% from stroke, and 10-15% from renal failure. HTN is major modifiable risk factor for stroke, with systolic pressure most important in predicting risk. |
31. Acute Pericarditis

### Clinical Presentation

**Symptoms:**
- Non-exertional dyspnea
- Sharp, pleuritic, and positional chest pain (may be relieved by sitting and leaning forward)
- Fever

**Physical Exam:**
- Friction rub on auscultation

### Lab Presentation

- ECG: Diffuse ST-elevation (except in V1 & aVL); PR-depression (in some cases)

### Etiology and Pathogenesis

Acute pericarditis is most often of idiopathic origin but can be caused by:
1. *viral infections* (echovirus, cocksackie group B, flu, hepB, varicella, mumps, EBV),
2. *tuberculosis* – spread of inflammation from the lung to the pericardium,
3. *pyogenic bacteria* – following chest trauma, contamination during surgery, extension of infective endocarditis or pulmonary infection, or hematogenous spread from a remote infection,
4. *MI* - early pericarditis within days 1-2 following MI likely results from inflammation extending from the epicardial surface to the pericardium, and so is most common in transmural infarcts (this form appears in fewer than 5% of pts. with acute MI who are treated with thrombolitics); *Dressler’s syndrome* is post-MI pericarditis that occurs 2 weeks after acute MI and is likely of autoimmune origin,
5. *uremia associated with chronic renal failure*,
6. *pericardial neoplasm*,
7. *radiation* to the thorax,
8. *autoimmune disease* such as SLE, rheumatoid arthritis, and progressive systemic sclerosis,
8. *procainamide* or *hydralazine* drug therapy.

The pathogenesis of acute pericarditis is similar to other inflammatory processes: local vasodilation and increased vascular permeability allows transudation into the pericardial space, after which leukocytes adhere and invade the area, releasing damaging inflammatory mediators. *Serous pericarditis* is the common early inflammatory response and is characterized by thin exudative fluid of few cells; *serofibrinous pericarditis* (“bread & butter” pericarditis) is the most commonly observed morphologic pattern, with the pericardial exudate containing plasma proteins – portions of the visceral and parietal pericardium may become thickened and fused, occasionally leading to a dense scar that restricts movement and diastolic filling; *suppurative pericarditis* is an intense inflammatory response associated with bacterial infections with a erythematous and purulent serosal surfaces; *hemorrhagic pericarditis* refers to grossly bloody inflammation and occurs most often with tuberculosis or malignancy.

### Treatment

**For Idiopathic & Viral pericarditis:**
- usually resolves within 1-3 weeks

1. **Rest** to reduce interaction of the inflamed pericardial layers.
2. **Pain relief** with aspirin or other NSAIDs.
   - oral corticosteroids are often effective for severe or recurrent pericardial pain but should not be used in uncomplicated cases because gradual withdrawal often leads to recurrent symptoms.
   - use aspirin in post-MI pericarditis because other NSAIDs have been shown to delay healing.

**For Purulent pericarditis:**
- Catheter drainage of the pericardium
- Aggressive antibiotic therapy
- mortality is high even with treatment

**For Uremic pericarditis:**
- usually resolves after intensive dialysis

### Notes

Most common disease of the pericardium.
32. Pericardial Effusion

### Clinical Presentation

**Symptoms:**
- May be asymptomatic
- Dull constant ache in the left-chest
- Symptoms of cardiac tamponade
  - Dysphagia (compression of esophagus)
  - Dyspnea (compression of lungs)
  - Hoarseness (compression of recurrent laryngeal nerve)
  - Hiccups (phrenic nerve stimulation)

**Physical Exam:**
- Muffled heart sounds
- Friction rub from pericarditis may disappear
- Ewart’s sign (dullness to percussion of left lung posteriorly)

### Lab Presentation

**Chest film:**
- May be normal (small effusion < 250mL)
- Cardiac silhouette enlarges in globular & symmetric way

**ECG:**
- Reduced voltage of all complexes (large effusions)
- **Electrical alternans** (very large effusions)
  - height of QRS varies from beat to beat as electrical axis is constantly changing due to heart swinging within large pericardial volume

**Echocardiography:**
- Can directly ID effusions as small as 20mL

### Etiology and Pathogenesis

*Pericardial effusion* is the accumulation within the pericardial space of more than the normal 15-50ml of fluid, possibly resulting in compression of the heart chambers and adjacent structures; effusion may result from inflammatory conditions (e.g. acute pericarditis), increased capillary permeability (hypothyroidism), increased capillary hydrostatic pressure (CHF), decreased plasma oncotic pressure (cirrhosis or nephropathy), or obstruction to lymphatic drainage (TB or CA). At low volumes of pericardial fluid (< 200ml), increases in pericardial volume do not result in significant increases in pericardial pressure; at higher volumes, however, a critical volume is reached beyond which further increases in volume drastically increase pericardial pressure. Three factors determine the clinical significance of pericardial effusion: 1) the volume of pericardial fluid, 2) the rate at which that fluid accumulates, and 3) the compliance of the pericardium. A sudden increase in pericardial volume (e.g. trauma with pericardial hemorrhage) or an effusion into a non-compliant pericardium (e.g. fibrosis or CA) is likely to greatly increase pressure, whereas if volume accumulates slowly (over weeks to months) the pericardium will gradually stretch to accommodate more fluid (up to 1-2 liters) without marked elevation of pericardial pressure and subsequent compression of the heart. Differences in these factors account for the wide range of clinical presentations associated with pericardial effusion.

### Treatment

1. If underlying cause is known, treat it.
2. An asymptomatic effusion, even of large volume, can be followed for months-to-years without treatment.
3. Pericardiocentesis (removal of pericardial fluid) if:
   - i. there is a precipitous rise in pericardial volume
   - ii. hemodynamic compression of the heart is present

### Notes
### Clinical Presentation

**Symptoms:**
- Dyspnea & Tachypnea
- Confusion/agitation (severe hypotension in acute C.T.)
- Fatigue with peripheral edema (slowly developing C.T.)

**Physical Exam:**
- JVD with Systemic Hypotension and Muffled Heart Sounds
- Pulsus paradoxus (decrease in BP >10mmHg on inspiration)
- Pulmonary Rales
- Sinus Tachycardia
- Quiet precordium on palpation

### Lab Presentation

**Echocardiography:**
- reveals RV & RA compression in diastole
- differentiates C.T. from other causes of ↓↓ CO, (such as ventricular systolic dysfunction)

Definitive diagnostic procedure is cardiac catheterization
- can measure intracardiac and intrapericardial pressure
- usually combined with therapeutic pericardiocentesis

**Jugular Venous Pressure Recording:**
- Blunted y-descent (impaired RV filling)

### Etiology and Pathogenesis

Cardiac Tamponade is a kind of pericardial effusion characterized by accumulation of fluid under high pressure and rapid compression of the cardiac chambers. Stroke volume and CO decline precipitously and potentially cause hypotensive shock and death. Any etiology of acute pericarditis can cause cardiac tamponade, as can chest trauma, post-MI rupture of the left ventricular wall, complication of a dissecting aortic aneurysm. Compression of the heart results in the diastolic pressure within the chambers becomes elevated and equal to the pericardial pressure – As a result of this, venous return is compromised and systemic and pulmonary venous pressures rise (causing peripheral edema & pulmonary congestion), and reduced ventricular filling during diastole leads to reduced stroke volume and subsequent severe hypotension. Reflex SNS activation acts to maintain tissue perfusion, but is ultimately insufficient unless the effusion is removed by pericardiocentesis.

### Treatment

**Pericardiocentesis** to remove excess pericardial fluid.
- after removal or pericardial fluid, catheter may be left in place for 1-2 days to allow more complete drainage
- stain and culture pericardial fluid for bacteria, fungi, and TB, do cytology to look for malignancies, do CBC to look for inflammatory conditions, and measure the adenosine deaminase levels to look specifically for TB
  - if fluid has ratio of pericardial protein to serum protein > 0.5 or pericardial LDH to serum LDH of >0.6, fluid is an exudate.
  - otherwise fluid is likely a transudate.

Remember to not use diuretics, as they may kill the patient.
34. Constrictive Pericarditis

### Clinical Presentation

**Symptoms:**
- Fatigue
- Hypotension

**Physical Exam:**
- **JVD with Kussmaul’s sign** (↑ JVD during inspiration)
- Diastolic “knock” following S₂ (in calcific constriction)
- Hepatomegaly
- Peripheral edema (systemic congestion is more common than pulmonary congestion in this syndrome).
- Reflex tachycardia

### Lab Presentation

**Chest Film:** normal or mildly enlarged cardiac silhouette; pericardial calcification seen in 50% of cases

**ECG:** atrial arrhythmias are common; may show non-specific ST & T-wave changes

**Echocardiography:** thickened pericardium; small and vigorously contracting ventricular cavities; early termination of ventricular filling.

- CT or MRI visualization of normal pericardial thickness (< 2 mm) generally rules out C.P.

**Cardiac catheterization:**
1. elevation and equalization of diastolic pressures in each of the chambers.
2. right and left ventricular tracings show **dip and plateau configuration**
3. RA-pressure tracing shows accentuated y descent

### Etiology and Pathogenesis

*Constrictive Pericarditis* is fibrosis of the pericardium following an episode of acute pericarditis, after which the excess fluid is not reabsorbed (as is normal) but rather undergoes progressive organisation with fusion of the pericardial layers, fibrosis, and possible calcification. The result is a decreased compliance of the pericardium which causes inhibition of ventricular filling in diastole and subsequent increase in systemic venous pressure and decrease in forward cardiac output. Clinical symptoms resulting from this develop over months to years and may mimic those of hepatic cirrhosis or abdominal cancer. Careful inspection of the JVD is necessary to distinguish C.P. from other disorders. The diastolic knock found in severe calcific C.P. represents the sudden cessation of ventricular filling imposed by the rigid pericardium. Kussmaul’s sign appears because negative intrathoracic pressure on inspiration draws blood to the thorax, but it cannot be accomodated by the constricted right-heart chambers, so the blood backs up into the intra-thoracic systemic veins – (normally, inspiration results in a ↓ JVP as blood is drawn into the heart from the systemic veins). The **dip and plateau** configuration of the ventricular pressure waves results as ventricular filling abruptly stops early in diastole, resulting in a plateau on the pressure waves; because of the constriction, RV and LV pressures are approximately equal in diastole. Y-decent is accentuated because ↑ atrial pressure causes rapid atrial emptying early in diastole before it is rapidly arrested by constriction.

### Treatment

Only effective treatment is **surgical removal of the pericardium**.
- signs and symptoms may not resolve immediately because of associated stiffness of the outer heart walls
- eventual symptomatic improvement is effective in most who undergo this procedure

### Notes

An endocardial biopsy may be needed to distinguish C.P. from restrictive cardiomyopathy; biopsy is normal in C.P.
35. Dilated Cardiomyopathy

### Clinical Presentation

**Signs and Symptoms of Heart Failure & AV-valve Regurgitation**
- fatigue, dyspnea, orthopnea, PND
- pulmonary rales, audible S3, maybe JVD/hepatomegaly/edema

May present with **Atrial Fibrillation, Ventricular Tachycardia, or Thromboembolism**

### Lab Presentation

- **Chest Film**: enlarged cardiac silhouette; vascular changes as seen in heart failure
- **ECG**: evidence of atrial and ventricular enlargement; patchy fibrosis may → many arrhythmias &/or conduction blocks
- **Diffuse ST & T-wave abnormalities**
- **Echocardiography**: reveals the underlying cardiac dilation
- **Cardiac catheterization**: ↑ diastolic pressures & ↓ CO

### Etiology and Pathogenesis

* Dilated cardiomyopathy is characterized by ventricular chamber enlargement with little hypertrophy and impaired systolic function. Though most cases are idiopathic, DCM may be congenital or caused by chronic alcohol ingestion, doxorubicin, hypothyroidism, viral infection, chronic hypocalcemia or hypophosphatemia, connective tissue disease, or sarcoidosis. Acute viral myocarditis usually affects young & healthy people and most often involves echovirus or coxsackie B virus; it is usually self-limiting but progresses in some pts. to DCM – it is thought that myocardial destruction & fibrosis involves viral-induced immune-mediated injury, but immunosuppressive drugs have not been shown to improve prognosis in this condition. Alcohol may cause cardiomyopathy by inhibiting mitochondrial oxidative phosphorylation and fatty-acid oxidation. Marked enlargement of all four heart chambers is characteristic of DCM, although the ds may be limited to the left or right side; wall thickness may be increased slightly, but is out of proportion with the width of the chamber – microscopically, there is evidence of myocyte degeneration with irregular hypertrophy and myofiber atrophy; interstitial and perivascular fibrosis is often extensive. Myocyte degeneration leads to ↓ CTY (and subsequent ↓ CO) which may be compensated for some time by ↑ preload (Frank-Starling mechanism), ↑ SNS activation, and ↑ renin secretion, but eventually progressive myocyte loss and ↓ afterload (from vasoconstriction effects of angiotensin II and SNS) results in volume overload and heart failure; additionally, chronically ↑ levels of angII and aldosterone promote myocardial and vascular fibrosis.

As the ventricles enlarge over time, the mitral and tricuspid valves may become incompetant, and the resulting regurgitation exacerbates ventricular volume overload, further ↓ SV and CO, and may cause atrial fibrillation (due to atrial enlargement from atrial volume overload) – fibrosis &/or enlargement causes conduction blocks in most cases, and local regions of dense fibrosis may lead to pathologic Q waves seen on the ECG (like those seen after an MI).

### Treatment

- **For alcoholic cardiomyopathy**: stop drinking alcohol
- this is one of the few reversible cardiomyopathies

**Tx to relieve vascular congestion & increase CO are the same as in HF** (see #s 10 & 11)
  1. ACE inhibitor
     - can even benefit asymptomatic pts. by slowing progression from mild systolic dysfunction to HF
  2. β-blocker
     - must begin at low dosage and slowly increase so as to not worsen HF by its negative inotropic effect
  3. Diuretic
     - use spironolactone w/other diuretic & ACEI in class IV HF

**Tx and prevent arrhythmias**:

1. Maintain serum electrolytes within normal range.
2. No evidence that drug therapy helps in DCM, though amiodorone is the safest choice.
3. ICD does reduce mortality, so use this if possible.
   - use pacemaker for conduction abnormalities

**Tx hypercoagulable state**: use warfarin when →

1. Patient is in atrial fibrillation
2. Patient has had at least one thromboembolic event
3. An LV thrombus is visualized by echocardiography

**Consider heart transplant.**

### Notes

- Cardiac catheterization is often done to see whether CAD is contributing to the systolic dysfunction, esp. in pts. with angina pectoris or who have ECG evidence of a prior MI.
- 40% of deaths from DCM due to arrhythmias.
- May also use warfarin in pts. with EF of < 30%.
- **Prognosis**: 5y-survival < 50%
- Heart Transplant offers the best prognosis of any therapy, with 5y-survival at 74% and 10y-survival at 55%, but there is a scarcity of donor hearts (2,500 per year for 20,000 pts.)
36. Hypertrophic Cardiomyopathy

### Clinical Presentation

- Dyspnea (especially during exertion)
- Angina pectoris (especially but not only in obstructive HCM)
- Syncope (due to arrhythmias caused by structural abnormalities)
- Orthostatic hypotension (obstructive HCM)
- Sudden cardiac death.

**Physical Exam:**
- Audible S4
  - If outflow obstruction present:
    - LV outflow murmur that ↑ upon standing or Valsalva
    - and ↓ upon squatting (opposite the changes in AS)
  - Palpable pre-systolic apical impulse → “double” apical impulse

### Lab Presentation

- **Histology:** characteristically abnormal myofibers (see E&P)
- **ECG:** LVH & LAE; may show diffuse T-wave inversions &/or prominent Q waves in inferior leads; atrial and ventricular arrhythmias are frequent
- **Echocardiography:** identifies structural abnormalities and outflow pressure gradient as well seeing MR.

### Etiology and Pathogenesis

**Hypertrophic cardiomyopathy** is characterized by septal or LV hypertrophy that is not due to chronic pressure overload; it is a familial disease with multiple genetic forms each inherited in an autosomal dominant fashion with variable penetrance, and in each case the gene involved encodes a protein of the sarcomere complex (β-MHC, troponin T, or MBP-C). Incorporation of one or more mutant proteins into sarcomeres damages their structural integrity and impairs contractile function; reflex hypertrophy results to maintain CO. Asymmetric hypertrophy of the ventricular septum is the most common (90% of cases), but hypertrophy can involve any portion of the ventricles; histologically, the myocardial fibers appear short, wide, hypertrophied, chaotic in orientation, and surrounded by numerous fibroblasts and much ECM – this organisation likely results in the arrhythmias that are common in HCM.

HCM causes diastolic dysfunction, as ventricular hypertrophy impairs myocardial relaxation and ↑ diastolic pressure (thereby impairing ventricular filling). HCM may also be cause an outflow obstruction during systole, as a hypertrophic portion of the ventricle (esp. the septum) blocks the aortic outflow tract; the increased systolic pressure caused by the obstruction increases myocardial oxygen demand and may induce angina, and the rapid blood flow (and possible contraction of the abnormally hypertrophic tissue) draws the anterior mitral leaflet away from its closed position and may cause mitral regurgitation (50% of pts). This could worsen symptoms of dyspnea and contribute to the development of atrial arrhythmias (esp AF). The systolic pressure gradient observed in obstructive HCM is dynamic – its magnitude varies during contraction depending on the distance between the anterior mitral leaflet and the hypertrophied septum: conditions that decrease LV chamber size (↓ venous return) promote obstruction and ↑ pressure, whereas conditions that increase LV chamber size (↑ venous return) partially relieve the obstruction.

Most of the symptoms of obstructive HCM, however, are simply due to the ↓ LV compliance and diastolic dysfunction that are also

### Treatment

1. **β-blockers** are the standard tx because they reduce myocardial oxygen demand, lessen the outflow pressure gradient (by ↓ CTY), ↑ diastolic filling time (↓ HR), and ↓ frequency of ventricular ectopic beats.
   - but these have not been shown to prevent arrhythmias
2. CCBs can be used in pts. who don’t respond to β-blocker
3. ICD for those who have survived cardiac arrest or who show high-risk ventricular arrhythmias
5. **Myomectomy** for pts. who do not respond to drugs.
6. Genetic counseling & screening of 1° degree relatives.

Be careful when using:
- Diuretics: ↓ venous return may worsen obstruction
- Vasodilators: ↓ return may worsen obstruction
  - do not use these at all
- Digitalis: ↑ CTY worsens obstruction

### Notes

- Most common cardiac abnormality in young athletes who die suddenly during vigorous exertion.
  - risk factors for sudden cardiac death: hx of syncope, family hx sudden death, high-risk mutations, LV > 30mm thick.
  - Incidence: 1/500
  - Average age of presentation is mid-20s.

As they grow, children and adolescents with HCM should have serial echocardiograms done to look for progressive ds.

**Prognosis:**
- Incidence of sudden death is 2-4% per year in adults and 4-6% in children & adolescents; different underlying mutations have vastly different phenotypes: from mild ds and normal life-span to early, severe presentation and death.
37. **Restrictive Cardiomyopathies**

**Clinical Presentation**

<table>
<thead>
<tr>
<th>Signs and Symptoms of Heart Failure.</th>
</tr>
</thead>
<tbody>
<tr>
<td>- dyspnea, fatigue</td>
</tr>
</tbody>
</table>

**Physical Exam:**

Findings associated with systemic and pulmonary HTN.
- rales, dyspnea, JVD/hepatomegaly/perioheral edema

_**Kussmaul’s sign**_ may be present.

**Lab Presentation**

<table>
<thead>
<tr>
<th>Chest Film: normal cardiac shadow with pulmonary congestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG: non-specific ST &amp; T-wave abnormalities; many conduction blocks and arrhythmias are possible</td>
</tr>
</tbody>
</table>

**Etiology and Pathogenesis**

RCMs are characterized by abnormally rigid (but not necessarily thickened) ventricles with impaired diastolic filling but near-normal systolic function – this results from fibrosis of the endomyocardium or infiltration of the myocardium by an abnormal substance such as amyloid. Rigidity of the ventricles leads to diastolic dysfunction as atrial pressures increase and ventricular filling is impaired, leading to elevated systemic and pulmonary pressures. Infiltrative etiologies may also cause various types of conduction blocks.

RCMs are nearly identical in clinical features to constrictive pericarditis, but it is important to distinguish them because the C.P. can be treated whereas RCMs are most often untreatable – to distinguish them, CT or MRI will show the presence or absence of thickened pericardium, and _transvenous endomyocardial biopsy_ may indicate the presence in the myocardium of infiltrative matter (amyloid, iron deposits, metastatic tumors).

**Treatment**

Only treatment is to treat the underlying cause, which is usually not possible.

*For hemochromatosis (↑↑ iron), phlebotomy and iron-chelation therapy may help.*

Symptomatic therapy includes salt-restriction and cautious use of diuretics to improve symptoms of congestion and chronic oral anticoagulation for the types of RCMs that are prone to thrombus formation.

**Notes**

Less common than DCM & HCM
38. Aortic Aneurysm

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>Often asymptomatic</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>(erosion of vertebrae by AA)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>(compression of the esophagus)</td>
</tr>
<tr>
<td>Dyspnea/wheezing</td>
<td>(compression of the trachea)</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>(compression of recurrent laryngeal nerve)</td>
</tr>
<tr>
<td>HF</td>
<td>(distortion of the aortic ring by AA in ascending aorta → regurgitation &amp; HF)</td>
</tr>
<tr>
<td><strong>Physical Exam:</strong></td>
<td></td>
</tr>
<tr>
<td>May feel a pulsatile mass (esp. in abdominal AA)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
</tr>
</thead>
</table>

*Aortic aneurysm* is an abnormal, localized dilatation of the aorta where the diameter of a portion of the aorta is increased by 50% or more or a portion of the abdominal aorta has enlarged to greater than 3.5-4cm in diameter. A *true aneurysm* represents a dilatation of all three layers of the aorta, creating a large bulge in the vessel wall; true aneurysms are either *fusiform* (dilation of entire aortic circumference, more common) or *saccular* (localized outpouching) depending on the circuferential extent of the aneurysm. In contrast, a *pseudoaneurysm* is a hematoma that extends beyond the intima and media but is contained by the adventitia &/or a perivascular thrombus – these are very unstable and prone to rupture. Atherosclerosis is implicated in 90% of abdominal AAs, but most AAs of the ascending aorta are due to degenerative changes (cystic medial degeneration) with subsequent accumulation of collagenous and mucoid material within the media – it most often presents in the ascending aorta because this area is subject to the greatest pulsatile shear stress; medial degeneration may also occur in association with connective tissue disorders or as a result of HTN or aging. The most severe consequence of AA is rupture – an aneurysm may rupture slowly, extravasating blood into the vessel wall and causing local pain and tenderness, or it may rupture acutely and dangerously: thoracic AAs may rupture into the pleural space, mediastinum, or bronchi; abdominal AAs may rupture into the retroperitoneal space or abdominal cavity or erode into the intestines (causing massive GI bleeding).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Transabdominal surgical repair</em> with placement of a prosthetic graft for AAs exceeding 4.5-5cm or those expanding in a diameter faster than 1cm/year.</td>
<td>Most common area for AA is the abdominal aorta.</td>
</tr>
<tr>
<td>- percutaneous deployment of an endovascular graft may rival morbidity/mortality rate of open repair.</td>
<td>5-10% of pts. have a first-degree relative who has been diagnosed with AA.</td>
</tr>
<tr>
<td>- surgical repair is recommended for thoracic aneurysms &gt;6cm or that compress adjacent structures.</td>
<td>5y-risk of rupture for abdominal aortic aneurysm &lt;5cm: 1-2%</td>
</tr>
<tr>
<td>- for pts. with Marfan syndrome, do surgical repair at thoracic aneurysm &gt; 5cm</td>
<td>5y-risk of rupture for abdominal aortic aneurysm &lt;5cm: 20-40%</td>
</tr>
</tbody>
</table>

Atherosclerotic AAs rarely develop before age 50, are more common in men, and have several risk factors: smoking, HTN, dyslipidemia.
### 39. Aortic Dissection

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>Sudden, severe “ripping” pain in the anterior chest (type A) or between the scapulae (type B).</td>
<td></td>
</tr>
<tr>
<td>Symptoms associated with complications: pericardial effusion, occlusion of aortic branches, or aortic regurgitation.</td>
<td></td>
</tr>
<tr>
<td>Usually associated with HTN.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aortic Dissection</strong> is characterized by a fluid-filled channel splitting the medial layer of the aorta from the adventitial layer; it is thought to arise from a tear in the endothelial wall that allows blood from the aortic lumen under high pressure to tear through the media and propagate along the medial/adventitial plane; AD may also result from rupture of the vasa vasorum, forming a hematoma in the arterial wall that cleaves the intima. Any condition that interferes with the normal integrity of the elastic or muscular layer may predispose someone to AD; trauma to the aorta can also incite dissection. Type A dissections (proximal dissections) are those where the ascending aorta is involved; type B (distal dissections) are confined to the descending aorta – type A is more common (67% of cases) and more dangerous (because it may extend into the coronary and arch vessels, support structures of the aortic valve, or the pericardial space). If AD occludes flow to a subclavian artery, a difference in systolic BP between the two arms is noted; neurologic deficits may accompany dissection into carotid vessels, and a dissection into the pericardial sac may produce cardiac tamponade; involvement of the aortic valve area may cause aortic regurgitation.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. β-blockers to reduce force of contraction and HR and to reduce BP.</td>
<td>Most common from age 50-70 and in men; more than 2/3 of patients with AD have a hx of HTN.</td>
</tr>
<tr>
<td>2. Vasodilators (nitroprusside) to rapidly ↓ BP.</td>
<td>Most commonly involves the ascending aorta (65%), descending aorta (20%), whereas the aortic arch (10%) and abdominal aorta (5%)</td>
</tr>
<tr>
<td>In acute Type A situations, surgical repair has been shown to improve the outcome compared with medical tx alone.</td>
<td><em>Acute AD</em> is AD of less than 2 weeks duration.</td>
</tr>
<tr>
<td>Type B dissections do not need surgery until there is clinical evidence of propagation of the dissection, compromise of major aortic branches, impending rupture, or continued pain.</td>
<td></td>
</tr>
</tbody>
</table>

---

**Acute AD** is AD of less than 2 weeks duration.
# 40. Peripheral Artery Disease

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td>Ultrasonography: will reveal a stenotic reduction in blood flow.</td>
</tr>
<tr>
<td>Claudication (exertional limb fatigue and pain relieved by rest)</td>
<td></td>
</tr>
<tr>
<td>Pain even at rest (severe PAD)</td>
<td></td>
</tr>
<tr>
<td>Skin ulceration, infection, skin necrosis</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Exam:</strong></td>
<td></td>
</tr>
<tr>
<td>May show ABI &lt; 1.0 (ABI &lt; 0.5 seen in pts. with rest pain)</td>
<td></td>
</tr>
<tr>
<td><strong>Signs &amp; Symptoms of Acute Arterial Obstruction:</strong></td>
<td></td>
</tr>
<tr>
<td>Pain / pallor / pulselessness / paraesthesia / paralysis / coolness</td>
<td></td>
</tr>
</tbody>
</table>

## Etiology and Pathogenesis

PAD is the peripheral equivalent of CAD and can affect any artery, though it is often limited to arteries of the pelvis and lower limbs (iliac, femoral, popliteal, tibioperoneal) – its pathology and pathophysiology are the same as CAD and its complications arise from ischemia distal to the peripheral atherosclerotic stenosis. Ischemia develops in areas distal to the obstruction because: 1) physical obstruction limits blood flow, and 2) normal regulatory mechanisms that increase blood flow in response to increased oxygen demand (vasodilator release by endothelial cells and subsequent relaxation of smooth muscle cells) fail in atherosclerotic dysfunctional endothelium – smooth muscle adaptation to ischemia by loss of fibers, changes in mitochondrial metabolism (seen even in viable fibers) and denervation potentiate the reduction in exertional capacity. Severe peripheral atherosclerosis can cause ischemia so pronounced the basal metabolic oxygen demand of distal tissue cannot be met – this results in critical limb ischemia with pain at rest which may progress to tissue necrosis, gangrene (and may threaten viability of the limb).

Acute Arterial Occlusion is caused by thromboembolism or thrombus formation in situ resulting in obstruction of arterial blood flow and possible distal ischemia.

## Treatment

1. Give anti-platelet therapy (though it hasn’t been proven reduce thrombotic events)
2. Risk-factor modification: quit smoking, less fat intake, control lipid levels, diabetes, & HTN.
3. Exercise (esp. walking) improves endurance by ↑ oxygen extraction and metabolic efficiency of the legs.
4. Cilostazol, a selective phosphodiesterase inhibitor, is used to induce vasodilatation and inhibit platelet aggregation; it works for intermittent claudication, but most other vasodilators do not.
5. Pentoxifylline, a drug which improves the deformability of RBCs and WBCs helps symptoms in some pts.
6. Mechanical revascularization is indicated when medical therapy has failed for disabling claudication or as first-line therapy in severe limb ischemia; in severe cases of limb ischemia, amputation is sometimes necessary.

New direction: pharmacological revascularization with VEGF and bFGF.

**Treatment of Acute Arterial Occlusion:**
1. Heparin to prevent propagation of the thrombus and further clotting.
2. Thrombolytic therapy or catheter-based thrombectomy are used in some cases to eliminate acute thrombi.
3. Surgical thrombectomy or bypass surgery may be

## Notes

Most prevalent vascular disorder; symptomatic incidence of 0.3% of the entire population and 5.2% of pts. over 70.

45% of pts. with symptomatic PAD have concurrent clinically significant CAD.

High-risk: Diabetes mellitus, Cigarette smoking.

The femoral and popliteal arteries are the most common sites; the upper limb is less often affected but brachiocephalic or subclavian arteries can cause arm claudication.
41. Vasculitic Syndromes

Clinical Presentation

**PAN:**
- Generalized inflammatory symptoms (fever, malaise, MS pains)
- Symptoms of ischemic end-organ damage or loss of blood flow
- HTN due to ↓ RBF and resulting ↑ renin-angiotensin activation

**TA:**
- Generalized inflammatory symptoms or symptoms of end-organ ischemia; may show HTN if the renal artery is involved;
- **diminished carotid & limb pulses** (85% of cases)

**GCA:**
- visual impairment/blindness (ophthalmic artery ds);

**TO:**
- Distal arterial occlusion / Reynolds phenomenon / migrating superficial vein thrombophlebitis
- Arm & foot claudication with digital ischemia

Lab Presentation

**PAN:**
- PMN infiltration; acute fibrinoid necrosis;
- aneurysmal dilatation; ANCA in the circulation

**TA:**
- granulomatous arteritis with fibrosis; lumenal stenosis

**GCA:**
- lymphocyte infiltration, intimal fibrosis, necrosis;
- granulomas seen; ↑ CRP & ↑ ESR; hypoechoic halo around lumen in ultrasonography

**TO:**
- highly cellular inflammatory thrombus without necrosis and with preservation of the internal elastic lamina; arteriography reveals local areas of stenosis with more severe ds distally and "corkscrew" collateral

Etiology and Pathogenesis

_Vasculitis_ results from immune-complex deposition or cell-mediated immune reactions directed against the vessel wall; the inflammatory response causes immune-mediated injury to the endothelium as well as decreased endothelial structural integrity (i.e. ↑ permeability), which may lead to end-organ ischemia because of vascular necrosis or thrombosis. There are multiple types of vasculitic syndromes: 1) _Polyarteritis nodosa_ is a necrotizing systemic vasculitis of small and medium-sized arteries, especially those of the kidney, heart, liver, and skeletal muscle; it takes its name from the many nodules found along the course of these vessels, 2) _Takayasu’s arteritis_ is a granulomatous & fibrotic disease of unknown cause that targets the aorta and its major branches, 3) _Giant cell arteritis_ (temporal arteritis) is a disease of medium-sized to large arteries that most commonly involves the cranial vessels, aortic arch, and its branches – renal, hepatic, and coronary vessels are usually spared, 4) _Thromboangitis obliterans (Buerger’s disease)_ is an inflammatory ds of the small and medium-sized arteries, veins, and nerves of the distal upper extremities; traditional laboratory markers of inflammation are not detected.

Treatment

**PAN:**
- Prednisone & other anti-inflammatory agents.

**TA:**
- Steroids & cytotoxic drugs to alleviate symptoms;
- Surgical bypass in severe cases.

**GCA:**
- High-dose systemic steroids

**TO:**
- Stop smoking (usually prevents complications and progression of the disease)

Notes

**PAN:**
- Prevalence: 6/100,000; 1.6:1 male-to-female ratio
- Prognosis: 5y-survival if untreated is 15%
- 5y-survival with therapy is 80%
- Diagnosis is established by biopsy.

**TA:**
- Prevalence: most often occurs in women younger than 40 in Asia and Africa (but distribution is worldwide)

**GCA:**
- Incidence: 24/100,000
- Occurs most commonly in pts. older than 55 and in female pts.
- Usually runs a self-limited course in 1-5 years.

**TO:**
- Most common in men younger than 40 ; < 2% pts. are female
- Strong association with cigarette smoking
- Associated with HLA-A9 and HLA-B5
42. Reynaud’s Disease

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>Triphasic color response: white → cyanotic → ruddy</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>Paresthesia</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Reynaud’s Disease</em> is a vasospastic condition of the digital arteries (most often in the fingers) that occurs when patients are exposed to cold temperature or to emotional stress – vasospasm is an extreme vasoconstrictor response that causes occlusion of the vessel lumen and obstruction of blood flow. Involved tissue shows a triphasic color response to vasospasm: firstly, the tissue turns white (as blood flow is interrupted), secondly it becomes cyanotic (accumulation of desaturated hemoglobin), and finally it turns ruddy pink as blood flow resumes. Primary RD is an isolated condition and is mostly benign, with only 16% of pts. reporting that their symptoms worsen over time; secondary RD may appear as a component of connective tissue disease (SLE, scleroderma), arterial occlusive disease, carpal tunnel syndrome, blood dyscrasias, drug reactions, or thermal/vibrational injury. The mechanism of RD may be ↑ SNS outflow, ↑ vascular susceptibility to adrenergic stimulation, or ↑ release of local vasoconstrictive mediators (thromboxane, serotonin, endothelin).</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid the cold &amp; dress warmly.</td>
<td>Primary Reynaud’s disease most commonly affects female patients between ages 20 – 40; genetics does not seem to be involved.</td>
</tr>
<tr>
<td>May use Ca-channel blockers or α-antagonists.</td>
<td>40% of pts. with fingers involvement also have ds in toes.</td>
</tr>
</tbody>
</table>
### 43. Varicose Veins

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>May be asymptomatic</td>
<td></td>
</tr>
<tr>
<td>Dull ache in legs after prolonged standing</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Exam:</strong></td>
<td></td>
</tr>
<tr>
<td>Dilated, tortuous superficial vessels</td>
<td></td>
</tr>
<tr>
<td>May show ankle swelling and/or skin ulceration</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
</tr>
</thead>
</table>

Varicose Veins are dilated, tortuous superficial vessels that often develop in the lower extremities, most commonly in the saphenous veins of the leg and their tributaries; they may also develop in the anorectal area (hemorrhoids), the lower esophageal veins (varices), and in the spermatic cord (varicocele). VVs likely result from intrinsic weakness of the vessel wall, from increased intraluminal pressure, or from defects in the venous valves. Primary VVs are those that originate in the superficial system, and factors that contribute to their development are pregnancy, prolonged standing, and obesity – Secondary VVs develop because abnormalities in the deep venous system cause superficial varicosities, as when deep venous valves are insufficient or perforating veins are occluded. In secondary VVs, superficial venous insufficiency may cause ankle edema and increase the risk for thrombosis and hematoma (after rupture of weakened vein).

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
</table>

VVs are usually treated conservatively:
- elevate legs when sitting
- wear compression stockings
- avoid prolonged standing

Small symptomatic VVs may be treated by injecting a sclerosing solution into the vein.

Surgical therapy includes vein ligation and removal and is reserved for pts. who are very symptomatic, suffer recurrent venous thrombosis, or develop skin ulceration.

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
</table>

VVs occur in 10-20% of the general population, affecting women 2-3 times more often than men, with ½ of pts. having a family history of VVs.
44. **Deep Venous Thrombosis**

### Clinical Presentation

<table>
<thead>
<tr>
<th>DVT:</th>
</tr>
</thead>
<tbody>
<tr>
<td>May be asymptomatic</td>
</tr>
<tr>
<td>Thigh or leg discomfort on standing or walking</td>
</tr>
<tr>
<td>Unilateral edema</td>
</tr>
<tr>
<td>Tenderness over the course of a phlebitic vein</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Pulmonary Embolism:</td>
</tr>
<tr>
<td>Dyspnea / Pleuritic chest pain / Cough / Tachypnea</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Post-phlebitic Syndrome:</td>
</tr>
<tr>
<td>Chronic leg swelling, Stasis pigmentation Skin ulcerations</td>
</tr>
</tbody>
</table>

### Lab Presentation

<table>
<thead>
<tr>
<th>Imaging:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonography: reveals venous obstruction</td>
</tr>
<tr>
<td>- more sensitive and specific for proximal vein DVT</td>
</tr>
<tr>
<td>MR venography: reveals pelvic vein obstruction</td>
</tr>
<tr>
<td>Contrast venography is invasive but provides definite dx</td>
</tr>
<tr>
<td>Blood Tests:</td>
</tr>
<tr>
<td>Elevated serum D-dimer levels</td>
</tr>
</tbody>
</table>

### Etiology and Pathogenesis

DVT is the formation of a thrombus in a deep vein of the leg, most commonly occurring in the veins of the calves but also found in the popliteal, femoral, and iliac vessels; initially, the thrombus is composed of platelets & fibrin, but eventually RBCs become interspersed within the fibrin net – these thrombi may cause minimal changes in the vessel wall or may lead to granulocyte invasion, loss of endothelium, edema, &/or vascular obstruction; most dangerously, they may also dislodge and form a thromboembolism. This may lead result in acute pulmonary embolism – DVT may also cause post-phlebitic syndrome, a condition characterized by chronic leg swelling, stasis pigmentation, and skin ulcerations that result from chronic deep venous insufficiency.

During late pregnancy and the early post-partum period, women have a greatly increased risk of DVT because fetal compression of the IVC causes stasis and high levels of estrogens induce a hypercoagulable state (oral contraceptives may also induce a hypercoagulable state for the same reason).

### Treatment

1. **LMW-heparin** initially to prevent thrombus progression and embolism; may use IV UFH as well.
2. **Warfarin** orally for long-term management (> 6mos.)
3. Insertion of an intravascular filter in the IVC in pts. who cannot be given anti-coagulants.
4. **Catheter-based thrombolysis** is useful for some pts. with iliofemoral DVT.

Treatment of calf-vein thrombosis is controversial because thromboemboli rarely emerge from that site:
- Some MDs use serial non-invasive monitoring
- Some MDs treat with IV heparin followed by 3-6mo of warfarin

**Treatment of superficial thrombophlebitis:**
1. Local application of heat & rest of involved extremity.
2. Aspirin to relieve discomfort.

### Notes

If untreated, 20-30% of DVTs in distal veins will migrate to the iliac, femoral, or popliteal veins.

Pulmonary embolism is common (incidence 600,000 per year in US), and 30-40% of untreated cases are fatal.

Remember Virchow’s Triad from coagulation lectures:
1. stasis, 2) hypercoagulable state, 3) vascular damage

DVT prophylaxis with LMWH, low-dose warfarin, compression stockings &/or intermittent external compression of the legs is done in clinical situations where the risk of DVT is high, such as during bed rest following surgery.
## 45. Tricuspid Stenosis & Tricuspid Regurgitation

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong></td>
<td><strong>Venous Pressure Tracing:</strong></td>
</tr>
<tr>
<td>TS: similar to MS, with hepatomegaly and abdominal distention</td>
<td>TS: <em>large a wave</em></td>
</tr>
<tr>
<td>TR: <em>pulsatile liver</em>; systolic murmur heard at left lower sternal border</td>
<td>TR: <em>prominent v wave</em></td>
</tr>
<tr>
<td><strong>Physical Exam:</strong></td>
<td></td>
</tr>
<tr>
<td>TS: similar to MS, except snap &amp; murmur are heard closer to the sternum and intensify during inspiration;</td>
<td></td>
</tr>
<tr>
<td>TR: <em>pulsatile liver</em>; systolic murmur heard at left lower sternal border</td>
<td></td>
</tr>
</tbody>
</table>

### Etiology and Pathogenesis

TS is rare and usually a consequence of rheumatic heart disease coexisting with MS.

TR is usually “functional” rather than structural, developing from RVE rather than primary valve disease. In patients with rheumatic MS, 20% have TR. Pulsatile liver develops because of regurgitation of RV blood into the systemic circulation.

### Treatment

TS: Surgical therapy is usually required.

TR: Treat underlying cause of RVE; diuretics, surgical repair for severe cases.

### Notes
### 46. Pulmonic Stenosis & Pulmonic Regurgitation

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Lab Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR: decrescendo murmur along the left sternal border that is often indistinguishable of from the murmur of AR.</td>
<td><em>Echocardiography</em>: differentiates PR from AR.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology and Pathogenesis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PS is rare and almost always caused by a congenital deformity of the valve; severe cases are associated with a pressure gradient of &gt; 80mmHg, moderate cases 40-80 mmHg, and mild cases &lt; 40mmHg. Only those with moderate or severe cases are symptomatic.</td>
<td>PR most commonly develops in the setting of severe pulmonary hypertension and results from dilation of the valve ring by an enlarged pulmonary artery.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS: Transcatheter balloon angioplasty</td>
<td></td>
</tr>
</tbody>
</table>
47. Infective Endocarditis

**Clinical Presentation**

- **Symptoms:**
  - ABE: fulminant illness with high fever and shaking chills
  - SBE: fatigue, anorexia, weakness, night sweats, myalgia
  - Symptoms associated with CHF or embolic end-organ infarction
  - Skin findings from septic embolism or immune-complex vasculitis
    - petechiae, “splinter hemorrhage” in nail-beds
  - Systemic inflammation → fever / splenomegaly / leukocytosis

- **Physical Exam:**
  - Auscultation may reveal new murmur or progressing murmur.

**Lab Presentation**

- **Echocardiography:**
  - TTE → detects large vegetations & those involving right-heart with high specificity but low sensitivity
  - TEE → more sensitive for detection of small vegetations

- **Blood culture** reveals the microorganism in 95% of cases.

**Etiology and Pathogenesis**

Acute bacterial endocarditis presents as a fulminant infection and a highly virulent organism such as *Staph. aureus* is implicated; subacute bacterial endocarditis takes a more insidious course and a less virulent organism such as *Strep. viridians* (70% of cases) is likely involved. SBE most frequently occurs in pts. with underlying valvular damage. The pathogenesis of IE requires four conditions: 1) endothelial injury, 2) thrombus formation at the site of injury, 3) bacterial entry into the circulation, and 4) bacterial adherence to the injured endocardial surface. The most common cause of endothelial injury is turbulent blood flow, and about 70% of patients with endocarditis have an underlying structural or hemodynamic abnormality. Gram-(+) organisms account for 90% of cases of endocarditis, in large part because of their resistance to complement-mediated destruction in the circulation; further, the production by certain strains of streptococcus of dextran allows them to bind thrombi and correlates with their capacity to cause endocarditis – there is an increasing dominance of staphylococcal endocarditis seen in tertiary-care centers, however. Bacteremia may lead to mechanical cardiac injury, thrombotic or septic emboli, or immune-mediated injury – each of these is potentially fatal.

**Treatment**

- Prolonged (4-6 weeks) high-dose IV antibiotics.
- Surgery for pts. with persistant bacteremia even on maximal antibiotics, with CHF, myocardial abcesses, or recurrent thromboembolic events.
- Most important is to prevent IE in the first place with proper prophylaxis for pts. with structural or hemodynamic abnormalities.

**Notes**

- 10-30% mortality rate even with therapy and near 100% if untreated or treated incorrectly.