- **Left-to-right** shunts increase pulmonary blood flow, but are not initially associated with cyanosis.
  - These shunts chronically elevate both volume and pressure in the pulmonary circulation.
  - The muscular pulmonary arteries respond by undergoing medial hypertrophy and vasoconstriction.
  - Prolonged vasoconstriction stimulates the development of irreversible obstructive intimal lesions.
  - Right ventricle may also undergo hypertrophy.
  - Eventually, pulmonary vascular resistance approaches systemic levels, and the original right-to-left becomes left-to-right introducing poorly oxygenated blood to the circulation, known as Eisenmenger Syndrome.
  - Once irreversible pulmonary hypertension develops, the structural defects are considered irreversible.
- **Obstructive** congenital heart diseases occur when there is narrowing of cardiac chambers, valves, or blood vessels.
  - This includes coarctation of the aorta, aortic and pulmonary stenosis.
  - Complete obstruction is called an atresia.
  - In Tetralogy of Fallot, both obstruction and shunt is present.

**Left-to-Right Shunts**

**ATRIAL SEPTAL DEFECT (ASD)**
- ASDs are abnormal, fixed openings in the atrial septum caused by incomplete tissue formation that allows communication of blood between the left and right atrium.
- Usually asymptomatic until adulthood.
- ASD should not be confused with PFO (Patent Foramen Ovale) which represents the failure to close of a foramen.
- Developmental Stages:
  - **Septum Primum** is a crescent-shaped membranous ingrowth that sits posteriorly between the right and left atria, and partially separates them; the remaining opening called **Ostium Primum** allows movement of blood during fetal development.
  - Before it completely obliterates, it develops a secondary posterior opening called **Ostium Secundum**.
  - The **Septum Secundum** is a subsequent membrane ingrowth located right and anterior of the septum primum.
  - As septum secundum grows, it leaves a small opening called the **Foramen Ovale**. The septum secundum continuously grows until it forms a flap of tissue that covers the ovale on its left side.
  - In fetal life, the pulmonary circulation has higher pressure gradient than the systemic, thus the flap of tissue from septum secundum permits right-to-left shunting during development.
  - At birth, with lung expansion, pulmonary vascular pressure drops, right atrial pressure fall below those in the left atrium, the foramen ovale closes permanently.

**Morphology**
- ASDs are classified according to their location:

<table>
<thead>
<tr>
<th>ASD TYPE</th>
<th>LOCATION</th>
<th>ASSOCIATED ANOMALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.) Secundum (90%)</td>
<td>Oval Fossa</td>
<td>Tetralogy of Fallot</td>
</tr>
<tr>
<td>2.) Primum</td>
<td>Adjacent to AV valves</td>
<td>Cleft Anterior Mitral Leaflet</td>
</tr>
<tr>
<td>3.) Sinus Venosus</td>
<td>Near entrance of SVC</td>
<td>Anomalous connection of right pulmonary veins to SVC or right atrium</td>
</tr>
</tbody>
</table>

**Clinical Features**
- ASD result in a left-to-right shunt, largely because pulmonary resistance is less than systemic resistance and because the compliance of the right ventricle is greater than the left.
- Asymptomatic before age 30, generally well tolerated.
- Murmur is often present through the pulmonary valve and/or through the ASD.
- Surgery or diameter-based closure of ASD reverses hemodynamic abnormalities and prevents complications.
- Mortality is low and long-term survival.

**PATENT FORAMEN OVALE**
- Closes permanently in 80% of the population by 2 years of age.
- In the remaining 20%, the unsealed flap can open if right-sided pressures become elevated.
- Thus, sustained pulmonary hypertension, or transient increase in right-sided pressure during bowel movement, coughing, or sneezing, can produce brief periods of right-to-left shunting.

**VENTRICULAR SEPTAL DEFECT (VSD)**
- Incomplete closure of the ventricular septum.
- **Most common** form of congenital heart disease.

**Morphology**
- Classified according to their size and location:
  - Most common are about the size of the aortic valve orifice and about 90% of the region of the membranous ventricular septum hence called Membranous VSD.
  - The remainder occur below the pulmonary valve (Infundibular VSD) or within the muscular septum (Swiss-cheese septum).
  - Most VSD’s are single, but those in the muscular septum may be multiple.
Hypertensive Heart Disease (HHD)

- A consequence of increased demands placed on the heart by hypertension causing pressure overload and ventricular hypertrophy.

- 2 types:
  1. Systemic HHD (Left-Sided)
  2. Pulmonary HHD (Right-Sided) / Cor pulmonale

SYSTEMIC HHD (LEFT-SIDED)

- Minimal pathologic criteria for the diagnosis of systemic HHD are the following:
  1. Left ventricular Hypertrophy (usually concentric) in the absence of other cardiovascular pathology.
  2. A clinical history or pathologic evidence of hypertension in other organs (e.g. kidney)

- Hypertension induces left ventricular pressure overload hypertrophy, initially without ventricular dilation resulting to its thickening and increase in the total weight of the heart.

  → Thickness may exceed 2 cm and the weight may exceed 500g

- Compensated systemic HHD may be asymptomatic, producing only ECG evidence of left ventricular enlargement.

- Systemic HHD comes to attention due to new atrial fibrillation induced by left atrial enlargement or by progressive CHF.

PULMONARY HHD (RIGHT-SIDED) / COR PULMONALE

- Isolated pulmonary HHD or cor pulmonale, stems from right ventricular overload.

- Chronic cor pulmonale is characterized by right ventricular hypertrophy, dilation, and potentially right-sided heart failure.

- Chronic cor pulmonale

  → Typical causes are diseases of the lungs, especially chronic parenchymal diseases such as emphysema or primary pulmonary hypertension.

  → Right ventricular hypertrophy secondary to prolonged pressure overload.

  → Sometimes, the hypertrophied right ventricle compresses the left ventricular chamber, or leads to regurgitation and fibrous thickening of the tricuspid valve.

- Acute cor pulmonale

  → Follow massive pulmonary embolism (saddle embolus).

  → Dilated right ventricle without hypertrophy (sudden)

- Diseases predisposing to cor pulmonale:

<table>
<thead>
<tr>
<th>Diseases of Pulmonary Parenchyma</th>
<th>Diseases of Pulmonary Vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>Recurrent Pulmonary Embolism</td>
</tr>
<tr>
<td>Diffuse Interstitial Fibrosis</td>
<td>Primary Pulmonary HTN</td>
</tr>
<tr>
<td>Pneumoconiosis</td>
<td>Extensive Pulmonary Arteritis</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>Vascular Obstruction (Drug/Toxin)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Pulmonary Tumor Embolism</td>
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<tr>
<td>Disorders affecting chest movement</td>
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<tr>
<td>Kyphoscoliosis</td>
<td></td>
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<tr>
<td>Obesity</td>
<td></td>
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<tr>
<td>Neuromuscular Diseases</td>
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</tbody>
</table>

Valvular Heart Disease

- Stenosis is the failure of a valve to open completely, which impedes forward flow.

- Insufficiency (regurgitation or incompetence) results from failure of a valve to close completely, thereby allowing backflow of the blood.

<table>
<thead>
<tr>
<th>Table 12-8 Major Etiologies of Acquired Heart Valve Disease</th>
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<tbody>
<tr>
<td>Mitral Valve Disease</td>
</tr>
<tr>
<td>Aortic Valve Disease</td>
</tr>
<tr>
<td>Mitral Stenosis</td>
</tr>
<tr>
<td>Aortic Stenosis</td>
</tr>
<tr>
<td>Postinflammatory scarring (rheumatic heart disease)</td>
</tr>
<tr>
<td>Postinflammatory scarring (rheumatic heart disease)</td>
</tr>
<tr>
<td>Mitral Regurgitation</td>
</tr>
<tr>
<td>Aortic Regurgitation</td>
</tr>
<tr>
<td>Abnormalities of Leaflets and Commissures</td>
</tr>
<tr>
<td>Postinflammatory scarring (rheumatic heart disease)</td>
</tr>
<tr>
<td>Infective endocarditis</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
</tr>
<tr>
<td>Drugs (e.g., fen-phen)</td>
</tr>
<tr>
<td>Degenerative aortic dilatation</td>
</tr>
<tr>
<td>Syphilitic aortic stenosis</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Merman syndrome</td>
</tr>
</tbody>
</table>

- Function in regurgitation is used to describe the incompetence of a valve due to an abnormality in one of its support structures.

- Clinical consequences of valve dysfunction vary depending on the valve involved, the degree of impairment, the tempo of disease onset, and the rate and quality of compensatory mechanism.

- Valvular abnormalities can be congenital or acquired.

  → Acquired Valvular Stenosis has relatively few causes, almost always as a consequence of a remote or chronic injury.

  → Acquire Valvular Incompetence can result from intrinsic disease of the cusps or damage to or distortion to supporting structures.

  → Most frequent causes of valvular lesions are:

    → Aortic Stenosis – calcification and sclerosis, or congenitally bicuspid valve.

    → Aortic Insufficiency – Dilation of ascending aorta often secondary to HTN or aging.

    → Mitral Stenosis – Rheumatic Heart Disease

    → Mitral Insufficiency – Myxomatous Degeneration (Mitral Valve Prolapse)

Calcific Valvular Degeneration

- The valves are subjected to high levels of repetitive mechanical stress particularly at the hinge points of the cusps and leaflets.

- This is a consequence of the frequency of contractions (30-40 million / year), substantial tissue deformation, and transvalvular pressure gradients.
Morphology

During acute RF, distinctive lesions occur in the heart called Aschoff bodies consist of foci of T lymphocytes, occasionally plasma cells and plump activated macrophages called Anitschkow Cells or caterpillar cells (pathognomonic for RF).

→ These anitschkow cells have abundant cytoplasm and central round to ovoid nuclei.

→ Diffuse inflammation and aschoff bodies may be found in all 3 layers of the heart (pancarditis).

→ "Bread and Butter" pericarditis.

→ Typically results in fibrinoid necrosis within the cusps or tendinous cords, overlying these necrotic foci are small vegetation called verrucae.

→ Subendocardial lesions exacerbated by regurgitant jets can induce irregular thickenings called MacCallum Plaques, usually in the left atrium.

→ Cardinal anatomic change of the mitral valve is leaflet thickening, commissural fusion and shortening, and thickening and fusion of tendinous cords.

→ In mitral stenosis, calcification and thickening of the mitral leaflets can produce a fish mouth or buttonhole stenosis.

Clinical Features

→ Diagnosis is based on Jones Criteria, evidence of a preceding group A streptococcal infection with the presence of 2 or more major manifestation, or 1 major and 2 minor manifestations.

Jones Criteria:

<table>
<thead>
<tr>
<th>MAJOR CRITERIA</th>
<th>MINOR CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migratory Polyarthritis of large joints</td>
<td>Fever</td>
</tr>
<tr>
<td>Carditis</td>
<td>Arthralgia</td>
</tr>
<tr>
<td>Subcutaneous Nodules</td>
<td>Elevated acute phase reactants</td>
</tr>
<tr>
<td>Erythema Marginatum</td>
<td></td>
</tr>
<tr>
<td>Sydenham Chorea</td>
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</tbody>
</table>

→ Acute RF appears 10 days to 6 weeks after a group A strep infection.

→ After an initial attack, there is increased vulnerability to reactivation of the disease with subsequent pharyngeal infections and the same manifestations are likely to appear.

→ Chronic RHD may suffer from arrhythmias (particularly atrial fibrillation in the setting of mitral stenosis), thromboembolic complications and infective endocarditis.

Infective Endocarditis

→ IE is a microbial infection of the heart valves or the mural endocardium that leads to the formation of vegetation composed of thrombotic debris and organisms, often associated with the destruction of underlying cardiac tissue.

→ Most infections are bacterial.

→ Can be classified into acute and subacute.

ACUTE INFECTIVE ENDOCARDITIS

→ Typically caused by infection of previously normal heart by a highly virulent organism (e.g. S. aureus).

→ Rapidly produces necrotizing and destructive lesions.

→ Difficult to cure with antibiotics alone and may require surgery.

→ Death can ensue within days to weeks (50%).

SUBACUTE INFECTIVE ENDOCARDITIS

→ Characterized by organisms with lower virulence (S. viridans).

→ Causes insidious infections of deformed valves with overall less destruction.

→ Disease may pursue a protracted course of weeks to months.

→ Cures can be achieved with antibiotics.

Pathogenesis

→ Endocarditis of native or previously damaged or abnormal valves is caused most commonly by Streptococcus viridans.

→ Another prevalent S. aureus can infect either healthy or deformed valves. It is the major offender in IE among intravenous drug abusers.

→ Other bacterial causes include Enterococci and a group called HACEK (Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, and Kingella), all are commensals of the oral cavity.

→ Prosthetic valve endocarditis is caused commonly by coagulase negative staphylococci (S. epidermidis).

→ Other agents include gram negative bacilli and fungi.

Morphology

→ Vegetation on heart valves is the classic hallmark of IE, these are friable, bulky, potentially destructive lesions containing fibrin, inflammatory cells, and bacteria.

→ Aortic and mitral valves are the most common site.

→ Vegetation can be single or multiple and may involve more than one valve, can erode into the myocardium & produce abscess

→ Microscopically exhibit granulation tissue.

Clinical Features

→ Stormy onset with rapidly developing fever, chills, weakness, and lassitude. Fever being the most consistent sign.

→ Flu-like syndrome.

→ Murmurs are present in 90% of patients with left sided IE.

→ So called Modified Duke Criteria is used to evaluate suspected IE, either uses a Pathologic Criteria or a Clinical Criteria.

→ If a clinical criterion is used, 2 major, 1 major + 3 minor, or 5 minor criteria are required for diagnosis.