Valvular heart diseases
Acute rheumatic fever
Infective endocarditis

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Objectives

• The students should be able to
  – Describe the pathogenesis, morphology and clinical features of valvular heart disease.
  – Describe the pathogenesis, morphology and clinical features of acute rheumatic fever and rheumatic heart diseases.
  – Describe the pathogenesis, morphology and clinical features of infective endocarditis.
  – Apply the basic medical knowledges to clinical problems.
Valvular heart diseases

- Divided to
  - Stenosis
  - Insufficiency (regurgitation)
  - Both

- Stenosis $\rightarrow$ failure of a valve to open completely, which impedes **forward flow**
- Insufficiency $\rightarrow$ failure of a valve to close completely, thereby allowing **reversed flow**
Valvular heart diseases

• Alone or coexist
• A single valve (isolated disease) or more than one valve (combined disease)
• Functional regurgitation
  – Incompetence of a valve stemming from an abnormality in one of its support structures
Valvular heart diseases

- Clinical consequences depending on
  - The valve involved
  - The degree of impairment
  - How fast it develops
  - The rate and quality of compensatory mechanisms

- Certain conditions can complicate valvular heart disease by increasing the demands on the heart
Valvular heart diseases

- Valvular stenosis or insufficiency often produces secondary changes
  - Valvular stenosis $\rightarrow$ pressure overload of the heart
  - Valvular insufficiency $\rightarrow$ volume overload of the heart.
- The ejection of blood through narrowed stenotic valves can produce high speed "jets" of blood that injure the endocardium where they impact.
Pressure overload

Pressure overload → Angiotensin II → AT1 → TGF-β → myocyte hypertrophy, cardiac hypertrophy, matrix deposition.
Volume overload

Angiotensin II  Inflammatory mediators

TGF-β

fibrosis  dilative remodeling

normal  dilated
Valvular heart diseases

- Congenital or acquired
- 2/3 of valvular heart diseases: acquired stenoses of the aortic and mitral valves
- Valvular stenosis is almost always due to a chronic abnormality of the valve cusp that becomes clinically evident after many years.
Valvular heart diseases

- **Aortic stenosis**
  - Calcification of anatomically normal and congenitally bicuspid aortic valves

- **Aortic insufficiency**
  - Dilation of the ascending aorta, usually related to hypertension and aging

- **Mitral stenosis**
  - Rheumatic heart disease

- **Mitral insufficiency**
  - Myxomatous degeneration (mitral valve prolapse)
Calcific aortic stenosis

- Most common of all valvular abnormalities
- Consequence of age-associated
- “Wear and tear"
- Normal valves or congenitally bicuspid valves
- 2% and is increasing with the rising average age of the population
Calcific aortic stenosis

• Stenoses of normal valve comes to clinical attention in the seventh to ninth decades of life,
• Stenotic bicuspid valves tend to present in patients 50 to 70 years of age.
Calcific aortic stenosis

- Prior work attributed aortic valve calcification
- Dystrophic and passive accumulation of hydroxyapatite
- Hyperlipidemia, hypertension, inflammation, and other factors implicated in atherosclerosis
Calcific aortic stenosis

- The abnormal valves contain cells resembling osteoblasts
  - Synthesize bone matrix proteins and promote the deposition of calcium salts
- Bicuspid valves incur greater mechanical stress than normal tricuspid valves
Calcific aortic stenosis

• Morphology
  – Heaped-up calcified masses within the aortic cusps
    • The calcific process begins in the valvular fibrosa
  – Ultimately protrude through the outflow surfaces into the sinuses of Valsalva
    • Preventing the opening of the cusps
  – No involving of free edges of the cusps
Calcific aortic stenosis

- The functional valve area is decreased sufficiently by large nodular calcific deposits
- Pressure overload to left ventricle
- In contrast to rheumatic (and congenital) aortic stenosis commissural fusion is not usually seen.
Calcific degenerative AS
Bicuspid AV
Calcific aortic stenosis

- Clinical features
  - Concentric left ventricular (pressure overload) hypertrophy
  - The hypertrophied myocardium tends to be ischemic
  - Angina pectoris
  - Cardiac decompensation and heart failure
  - Systolic ejection murmur
Calcific aortic stenosis

- 50% with angina will die within 5 years
- 50% with CHF will die within 2 years
- Medical therapy is ineffective in severe symptomatic aortic stenosis
- Asymptomatic patients with aortic stenosis generally have an excellent prognosis.
Aortic regurgitation

• Etiology
  – Isolated aortic valve root dilation
  – Infective endocarditis
    • Most common cause of acute aortic regurgitation
  – Long-standing essential hypertension
  – Chronic rheumatic fever, aortic dissection, coarctation
Aortic regurgitation

- **Pathophysiology**
  - Retrograde blood flow into the left ventricle
    - Due to an incompetent valve or dilated valve ring
    - Decreases diastolic pressure
      - Due to drop in arterial volume as blood flows back into the left ventricle
    - Volume overload of the left ventricle
      - Increases stroke volume (Frank-Starling mechanism)
  - Increased pulse pressure (difference between systolic and diastolic pressure)
    - Produces hyperdynamic circulation (e.g., bounding pulses)
Normal valve operation

Aortic valve

Valve closes after left ventricle pumps blood into aorta

Leakage of valve

Valve does not close completely, leaking blood into heart
Aortic regurgitation

• Clinical findings
  – Early diastolic murmur
  – Bounding pulses (water hammer pulse), head nodding, pulsating uvula
  – Austin Flint murmur
    • Regurgitant stream from incompetent aortic valve hits the anterior mitral valve leaflet producing a diastolic murmur
    • Presence of this murmur indicates the need for replacement of the valve.
Mitral valve stenosis

• Etiology
  – Most often caused by recurrent attacks of rheumatic fever

• Pathophysiology
  – Narrowing of the mitral valve orifice
  – Left atrium becomes dilated and hypertrophied
    • Due to increased work in filling the ventricle in diastole
Mitral valve stenosis

• Morphology
  – Irregular, stony hard, occasionally ulcerated nodules (2-5 mm in thickness)
  – Behind the leaflets
Rheumatic mitral valvular disease
Mitral stenosis

- Rheumatic heart disease (99%)
- Congenital
- Massive calcification of mitral annulus
Mitral valve stenosis

- Clinical findings
  - Opening snap followed by mid-diastolic rumble
  - Dyspnea and hemoptysis with rust-colored sputum (heart failure cells)
    - Due to pulmonary capillary congestion and hemorrhage into the alveoli
  - Atrial fibrillation
    - Due to left atrial dilation and hypertrophy
    - Intra-atrial thrombus develops due to stasis.
      - Danger of systemic embolization
Mitral valve stenosis

– Pulmonary venous hypertension
  • Due to chronic backup of atrial blood into the pulmonary vein
  • RVH eventually develops

– Dysphagia for solids
  • Left atrium is the most posteriorly located chamber in the heart.
  • Dilation of the left atrium compresses the esophagus.
Mitral regurgitation

• Etiology
  – Mitral valve prolapse (most common cause)
  – Left-sided heart failure
  – Infective endocarditis, rupture or dysfunction of the papillary muscle
Mitral regurgitation

- **Pathophysiology**
  - Retrograde blood flow into the left atrium during systole
    - Due to an incompetent mitral valve or dilated mitral valve ring
  - Volume overload in the left ventricle and left atrium leads to LHF.

- **Clinical findings**
  - Pansystolic murmur with radiation to the axilla
  - Dyspnea and cough from LHF
Mitral regurgitation

• Sequelae
  – LV hypertrophy & dilatation
  – Lt. atrial dilatation
  – Pulmonary congestion
  – LV failure → RV failure
Acute rheumatic fever

- Rheumatic fever (RF) is an acute, immunologically mediated, multisystem inflammatory disease
- Occurs a few weeks after an episode of group A streptococcal pharyngitis
- Acute rheumatic carditis is a frequent manifestation during the active phase of RF and may progress over time to chronic rheumatic heart disease (RHD)
Acute rheumatic fever

- RHD is characterized principally by deforming fibrotic valvular disease, particularly mitral stenosis.
- The incidence and mortality rate of RF and RHD have declined.
- Rheumatic fever only rarely follows infections by streptococci at other sites, such as the skin.
Acute rheumatic fever

- **Pathogenesis**
  - Immune responses to group A streptococci, which happen to cross-react with host tissues.
  - Antibodies directed against the M proteins of streptococci
  - CD4+ T cells specific for streptococcal peptides also react with self proteins in the heart, and produce cytokines that activate macrophages.
Acute rheumatic fever

- About 3% of infected patients
- 10 days to 6 weeks after an episode of pharyngitis caused by group A streptococci.
- Children between ages 5 and 15, but first attacks can occur in middle to later life.
- Pharyngeal cultures for streptococci are negative by the time the illness begins.
- Antibodies such as streptolysin O and DNase B can be detected.
Acute rheumatic fever

• Arthritis
  – Common in adults than in children.
  – Migratory polyarthritis
  – Subsides spontaneously

• Acute carditis
  – Pericardial friction rubs
  – Weak heart sounds
  – Tachycardia
  – Arrhythmias
Acute rheumatic fever

- After an initial attack, there is increased vulnerability to reactivation of the disease.
- Carditis is likely to worsen with each recurrence, and damage is cumulative.
- Other hazards include embolization from mural thrombi and infective endocarditis.
Acute rheumatic fever

• Clinical features
  – RF is characterized by a constellation of findings that includes as major manifestations: Jones criteria
    • Presence of two of the major manifestations or one major and two minor manifestations
    • Evidence of a preceding group A streptococcal infection
# Diagnosis of Rheumatic Fever

**JONES' CRITERIA**

<table>
<thead>
<tr>
<th>Major Manifestations</th>
<th>Minor Manifestations</th>
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<tbody>
<tr>
<td>• Carditis</td>
<td>• Clinical</td>
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<tr>
<td>• Polyarthritis</td>
<td>– Previous rheumatic fever or rheumatic heart disease</td>
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<tr>
<td>• Chorea</td>
<td>– Arthralgia</td>
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<tr>
<td>• Erythema marginatum</td>
<td>– Fever</td>
</tr>
<tr>
<td>• Subcutaneous nodules</td>
<td>• Laboratory</td>
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<tr>
<td>2 major manifestations or 1 major and 2 minor manifestations</td>
<td>– Acute phase reactions (ESR, C-reactive protein)</td>
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<td>– Prolonged PR interval</td>
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Acute rheumatic fever

• Morphology
  – Focal inflammatory lesions
  – Distinctive lesions occur in the heart, called Aschoff bodies
    • Consist of foci of lymphocytes (primarily T cells), occasional plasma cells, and plump activated macrophages called Anitschkow cells (pathognomonic for RF).
Acute rheumatic fever

- These macrophages have abundant cytoplasm and central round-to-ovoid nuclei in which the chromatin is disposed in a central, slender, wavy ribbon (hence the designation "caterpillar cells"), and may become multinucleated.

- Diffuse inflammation and Aschoff bodies may be found in any of the three layers of the heart, causing pericarditis, myocarditis, or endocarditis (pancarditis).
Acute rheumatic fever

– Inflammation of the endocardium and the left-sided valves typically results in fibrinoid necrosis within the cusps or along the tendinous cords.
– Overlying these necrotic foci are small (1- to 2-mm) vegetations, called verrucae, along the lines of closure.
Acute rheumatic fever

– Subendocardial lesions, perhaps exacerbated by regurgitant jets
  • May induce irregular thickenings called MacCallum plaques
    – Usually in the left atrium.
Rheumatic heart disease

• Acute rheumatic carditis during the active phase of RF → chronic rheumatic heart disease (RHD).

• Possibly due to cross reactivity of anti-M capsular Abs
Rheumatic heart disease

- Chronic rheumatic carditis usually does not cause clinical manifestations for years or even decades after the initial episode of RF.
- The signs and symptoms of valvular disease depend on which cardiac valve(s) are involved.
Rheumatic heart disease

- Slight familial predisposition
- 3% of infections progress to RF
- RHD $\rightarrow$ most frequent cause of mitral stenosis (99% of cases)
- The mitral valve alone is involved in 65% to 70% of cases
Rheumatic heart disease

- Mitral and aortic in about 25%
- Mitral valve involvement $\rightarrow$ women
- Aortic valve involvement $\rightarrow$ men
- Stenosis > regurgitation
- Incidence on decline- Antibiotic Rx, socioeconomics
Rheumatic heart disease

• Morphology
  – Chronic RHD
  • The cardinal anatomic changes of the mitral (or tricuspid) valve are leaflet thickening, commissural fusion and shortening, and thickening and fusion of the tendinous cords
  • Fibrous bridging across the valvular commissures and calcification create fish mouth or buttonhole stenoses
Rheumatic heart disease

• Microscopically
  – Diffuse fibrosis, neovascularization, Aschoff bodies are replaced by fibrous scar
Complications of Chronic Rheumatic Heart Disease

- **Bacterial endocarditis**: follows episodes of bacteremia
- **Mural thrombi**: form in atrial or ventricular chambers in 40% of patients with rheumatic valvular disease.
Complications of Chronic Rheumatic Heart Disease

• Congestive heart failure: associated with rheumatic disease of both mitral and aortic valves.

• Adhesive pericarditis: commonly follows the fibrinous pericarditis of the acute attack, but almost never results in constrictive pericarditis.
Infective endocarditis (IE)

- A serious infection characterized by colonization or invasion of the heart valves or the mural endocardium by a microbe.
- Formation of vegetations composed of thrombotic debris and organisms
- Associated with destruction of the underlying cardiac tissues.
Infective endocarditis (IE)

- The aorta, aneurysmal sacs, other blood vessels, and prosthetic devices
- Most cases are caused by bacterial infections (bacterial endocarditis).
- Fungi and other classes of microorganisms can be responsible
- Prompt diagnosis and effective treatment of IE is important.
Infective endocarditis (IE)

• Classified on clinical grounds into acute and subacute forms
  – Acute infective endocarditis
    • Infection of a previously normal heart valve
    • Highly virulent organism
    • Necrotizing, ulcerative, destructive lesions
    • Difficult to cure with antibiotics and usually require surgery
    • Death within days to weeks ensues in many patients with acute IE, despite treatment
Infective endocarditis (IE)

- Subacute IE
  - Lower virulence
  - Insidious infections of deformed valves that are less destructive
  - In such cases the disease may pursue a protracted course of weeks to months
  - Cures are often produced with antibiotics.
Infective endocarditis (IE)

- **Etiology and pathogenesis**
  - IE can develop on previously normal valves
    - Especially with highly virulent organisms
  - A variety of cardiac and vascular abnormalities predispose to this form of infection
    - Rheumatic heart disease
    - Mitral valve prolapse
    - Degenerative calcific valvular stenosis
    - Bicuspid aortic valve
    - Artificial (prosthetic) valves
    - Unrepaired and repaired congenital defects
Infective endocarditis (IE)

- Endocarditis of native but previously damaged or otherwise abnormal valves is caused most commonly (50% to 60% of cases) by Viridans *Streptococcus*
- *S. aureus* (the major offender in intravenous drug abusers) can infect either healthy or deformed valves and are responsible for 10% to 20% of cases overall
Infective endocarditis (IE)

- The roster of the remaining bacteria includes enterococci and the so-called HACEK group (*Haemophilus, Actinobacillus, Cardiobacterium, Eikenella*, and *Kingella*).
- Prosthetic valve endocarditis is caused most commonly by coagulase-negative staphylococci (e.g., *S. epidermidis*).
- Other agents causing endocarditis include gram-negative bacilli and fungi.
Infective endocarditis (IE)

- In about 10% to 15% of all cases of endocarditis, no organism can be isolated from the blood ("culture-negative" endocarditis).
Infective endocarditis (IE)

- The most factor is bacteremia.
- The source of the organism
  - Obvious infection elsewhere
  - A dental or surgical procedure
  - A contaminated needle shared by intravenous drug users
  - Trivial breaks in the epithelial barriers of the gut, oral cavity, or skin.
- The risk can be lowered by prophylaxis with antibiotics.
Infective endocarditis (IE)

• Morphology
  – Friable, bulky, potentially destructive vegetations
  – Fibrin, inflammatory cells, and bacteria or other organisms
  – The aortic and mitral valves
  – The valves of the right heart may also be involved
  • Particularly in intravenous drug abusers.
Infective endocarditis (IE)

- The vegetations may be single or multiple and may involve more than one valve.
- Vegetations sometimes erode into the underlying myocardium and produce an abscess (ring abscess).
- Emboli may be shed from the vegetations at any time
Infective endocarditis (IE)

- The embolic fragments may contain large numbers of virulent organisms
  - Abscesses often develop at the sites where the emboli lodge
  - Septic infarcts or mycotic aneurysms
Infective endocarditis (IE)

- The vegetations of subacute endocarditis are associated with less valvular destruction
  - Microscopically
    - Granulation tissue indicative of healing at their bases.
    - With time, fibrosis, calcification, and a chronic inflammatory infiltrate can develop.
Infective endocarditis (IE)

**Clinical Features**
- Fever
- Fatigue
- Loss of weight
- A flulike syndrome
- Acute endocarditis
  - Rapidly developing fever, chills, weakness

**Complications**
- Glomerulonephritis
- Embolic phenomenon
  - Splinter or subungual hemorrhages
  - Subconjunctival petechiae
  - Osler nodes
  - Janeway lesions
  - Roth spots
Nonbacterial thrombotic endocarditis (NBTE)

- Marantic endocarditis
- Deposition of small masses of fibrin, platelets, and other blood components on the leaflets of the cardiac valves.
- The valvular lesions of NBTE are sterile and do not contain microorganisms.
Nonbacterial thrombotic endocarditis (NBTE)

- **Pathogenesis**
  - A common origin in a hypercoagulable state
  - This may be related to some underlying disease, such as a cancer (paraneoplastic syndrome).
Nonbacterial thrombotic endocarditis (NBTE)

- **Morphology**
  - The vegetations are sterile, nondestructive, and small (1 to 5 mm)
  - Vegetations occur singly or multiply along the line of closure of the leaflets or cusps
  - Composed of bland thrombus without accompanying inflammatory reaction or induced valve damage
Endocarditis of systemic lupus erythematosus

- Libman-Sacks endocarditis
- Mitral and tricuspid valvulitis with small, sterile vegetations
- Morphology
  - Small single or multiple, sterile, granular pink vegetations ranging from 1 to 4 mm
  - On the undersurfaces of the atrioventricular valves, on the valvular endocardium, on the cords, or on the mural endocardium
Endocarditis of systemic lupus erythematosus

– Histologically consist of a finely granular, fibrinous eosinophilic material that may contain hematoxylin bodies
Complications of artificial valves

• Two types of artificial valves
  – Mechanical prostheses
    • Different kinds of rigid mechanical valves, such as caged balls, tilting disks, or hinged semicircular flaps
    • Nonphysiologic material
  – Tissue valves, usually bioprostheses
    • Chemically treated animal tissue
    • Porcine aortic valve tissue
Complications of artificial valves

• Approximately 60% of substitute valve recipients develop a serious prosthesis-related problem within 10 years postoperatively.

• The nature of these complications differs among types
Complications of artificial valves

- Complications
  - Thrombosis/thromboembolism
  - Anticoagulant-related hemorrhage
  - Prosthetic valve endocarditis
  - Structural deterioration (intrinsic)
    - Wear, fracture, poppet failure in ball valves, cuspal tear, calcification
  - Other forms of dysfunction
    - Inadequate healing (paravalvular leak), exuberant healing (obstruction), disproportion, hemolysis, noise
End of the lecture
Any questions ???