Valve abnormalities: general

- **Congenital**
  - Bicuspid aortic valve
    - Affects approx. 1% of population, males > females
    - 2 cusps of equal size, or one larger, one smaller cusp, the larger cusp having a midline raphe
    - Usually function normally
    - A small proportion are incompetent early on
    - Susceptible to ‘wear and tear’ related dystrophic calcification and stenosis, infective endocarditis
    - Patients also have increased risk of aortic dissection
  - Congenital aortic stenosis - rare
  - ‘Floppy’ mitral valve/mitral valve prolapse/myxomatous mitral valve
    - Affects approx. 2% of population, females > males
    - Enlarged hooded cusps containing excessive glycosaminoglycan (‘myxoid’ or ‘myxomatous’) material
    - ? pathogenesis, ?congenital, some cases acquired, some cases inherited including in Marfan Syndrome
    - Valve prolapses back into left atrium in systole but generally cause at most only very mild incompetence and are asymptomatic
    - Complications
      - Clinically significant mitral incompetence
      - Rupture of chordae tendineae
      - Infective endocarditis
      - Arrhythmias and palpitations
      - Rarely: sudden death, thromboemboli
  - Degenerative
    - ‘Wear and tear’ dystrophic calcification of the aortic valve, either age related or in a bicuspid valve
    - Annular calcification of mitral valve. Usually asymptomatic but can cause stenosis or incompetence or complete heart block (if calcification extends into conduction system)
  - Inflammatory
    - Acute rheumatic fever and chronic rheumatic valve disease
  - Infective
    - Infective endocarditis
  - Prosthetic valves
  - Other

These abnormalities

- Are not necessarily symptomatic (with the exception of infective endocarditis)
- May cause a murmur that can be heard on examination, even if the patient is asymptomatic
- Predispose to infective endocarditis, even if asymptomatic
- May cause incompetence and/or stenosis of the valve, depending on the disease, leading to various symptoms, commonly related to heart failure. Chronic aortic and mitral stenosis and incompetence can progress gradually and be asymptomatic for many years due to compensatory mechanisms. Symptoms develop when compensatory mechanisms fail.
- Mitral incompetence and stenosis predispose to atrial fibrillation

Valve abnormalities, when severe, are generally treated by some form of surgery, frequently by replacement of the valve by mechanical or bioprothestic valves made from synthetic and/or biological material. Mechanical valves require anticoagulation. All types are susceptible to infective endocarditis and have limited life spans.

### Stenosis and incompetence

**Stenosis and incompetence** (insufficiency, regurgitation): may be pure or mixed

**Aortic stenosis (AS)**

**Causes**

- Valvular stenosis:
  - Senile degenerative calcification (most common)
  - Degenerative calcification developing in congenitally bicuspid valve (develops earlier than in normal tricuspid valves)
Post inflammatory (usually chronic rheumatic valve disease)
- Subvalvular: congenital (rare), asymmetric left ventricular hypertrophy e.g. hypertrophic cardiomyopathy
- Supravalvular: congenital or genetic (rare)

Effects: compensatory concentric left ventricular hypertrophy (LVH) -> exertional syncope, angina, subendocardial infarction, LVF and CCF and slightly increased risk of sudden cardiac death (from ischaemia induced fatal arrhythmia). Increased risk of infective endocarditis.

Aortic incompetence or regurgitation (AR)

Causes
- Cusp disease: congenitally malformed valve (usually bicuspid), post inflammatory (usually chronic rheumatic valve disease), infective endocarditis
- Aortic ring dilation: non-inflammatory medial changes (e.g. Marfan syndrome), inflammatory medial changes (aortitis e.g. syphilitic, autoimmune connective tissue disease)
- Lack of cusp support: aortic dissection

Effects:
- Acute AR: diastolic pressure in LV rises rapidly (can’t dilate acutely) and is transmitted backwards -> acute pulmonary oedema
- Chronic AR: compensatory eccentric LVH, asymptomatic for many years but eventually -> decreased forward output and increased LA and pulmonary pressures -> pulmonary congestion and RHF. High LV stroke volume and low diastolic pressure -> increased pulse pressure. Increased risk of infective endocarditis

Mitral stenosis (MS)

Causes: post inflammatory (vast majority related to chronic rheumatic valve disease). Other causes include mitral annular calcification

Effects:
- Increased left atrial pressures and enlarged left atrium -> increased pulmonary venous and capillary pressures -> pulmonary congestion followed by RHF, increased risk of atrial fibrillation.
- Increased risk of infective endocarditis

Mitral incompetence or regurgitation (MR)

Causes:
- Cusp disease: infective endocarditis, post inflammatory (usually chronic rheumatic valve disease), mitral valve prolapse (‘floppy’ mitral valve)
- Papillary muscle or chordae dysfunction: rupture (papillary muscle) following myocardial infarction, rupture (chordae) in infective endocarditis, rupture (chordae) with floppy mitral valve, scarring (papillary muscle) post myocardial infarction
- Mitral ring dilation: from LV dilation

Effects:
- Acute MR: high LA pressure (can’t dilate acutely) transmitted backwards -> acute pulmonary oedema, LV output often maintained
- Chronic MR: eccentric hypertrophy with volume load, significant LA dilatation lessens effect on pulmonary circulation, low forward output predominates initially. Ultimately pulmonary congestion and RHF will develop. Risk of atrial fibrillation. Increased risk of infective endocarditis

Acute rheumatic fever

- Immunologically mediated multi-system inflammatory disease.
- Occurs 10 days – 6 weeks following a Group A, beta haemolytic Streptococcal pharyngitis in approx. 1-3% of untreated patients.
- Usually affects children.
- Now uncommon in developed countries. More common in indigenous Australians. Still common in developing countries.
- Predisposing factors: lower standard of living with overcrowding predisposes to Strep infection, genetic factors influence immune response
- Pathogenesis uncertain: ? antibodies to streptococcal M proteins and CD4 T cells specific for streptococcal peptides may cross react with self proteins (‘antigenic mimicry’)
- Acute or insidious onset, or may be subclinical
- Most symptoms subside within 6 weeks
- Diagnosis established by the modified Jones’ criteria which utilise major and minor criteria (either two or more major criteria, or one major criterion and two or more minor criteria AND evidence of recent Gp A Strep. infection)
  - Major criteria: migratory polyarthritis, carditis, subcutaneous nodules, erythema marginatum, Sydenham’s chorea
  - Minor criteria: fever, arthralgia, prolonged PR interval on ECG, elevated acute phase reactants

Major criteria
- Migratory polyarthritis of large joints
  - Most often affecting the ankles, wrists, knees, and elbows over a period of days
  - Occurs early in course
  - Most common manifestation in initial attack
  - Painful
- Sydenham's chorea
  - Latent period between throat infection and onset may be several months
• Erythema marginatum
  • Often on trunk
  • Rounded borders
• Subcutaneous nodules
  • Over extensor surfaces of joints
  • Appear later in course of disease
• Carditis
  • In 40-60%, becomes more common with recurrences
  • Pancarditis: involving pericardium (-> fibrous or serofibrinous pericarditis), myocardium, endocardium (-> oedema and erythema of cusps, tiny thrombi along lines of closure of cusps). N.B. No organisms present in heart.
  • Focal characteristic microscopic inflammatory lesions (Aschoff bodies or nodules) which may persist for many years and which contain Anitschkow cells (characteristic modified macrophages), multinucleate macrophages, lymphocytes, degenerate connective tissue
  • Mitral incompetence may develop in the acute phase and is reported to be associated with dilatation of the mitral annulus, elongation of the chordae tendineae and often prolapse of the anterior leaflet. It frequently disappears with adequate treatment and antibiotic prophylaxis.
  • Carditis worsens with each recurrence, promoting valve fibrosis and increasing the risk of chronic valve problems
• Clinically
  • Often asymptomatic, but can cause arrhythmias from inflammation in conducting system, heart failure from mitral incompetence and possibly myocarditis
  • May hear a pericardial friction rub from pericarditis
  • Other: sinus tachycardia, diastolic mitral flow murmur (Carey-Coombs), S3 gallop
• Outcome
  • Mild mitral regurgitation frequently disappears with effective treatment and prophylaxis
  • Progressive disease
    • Usually mitral valve (90%), occasionally also aortic valve (25%)
    • The typical outcome in developed countries in the past was the development of mitral stenosis (+/- incompetence and aortic valve involvement) over the longer term (10-30+ years), as patients were less likely to suffer recurrent Strep. infection and repeat attacks of rheumatic fever. Slowly progressive fibrosis leads to cusp fusion and cusp and chordal thickening, taking many years to develop into a haemodynamically significant valve lesion. Incompetence from cusp and chordal fibrosis and shortening may also develop over the longer term.
    • Progression over the shorter term (months-years) may also occur, particularly in countries/communities with a low standard of living where recurrent Strep. infection and repeat attacks of rheumatic fever are more likely and management and prophylaxis more likely to be inadequate, allowing uncontrolled persistent and recurrent disease with the development of clinically severe valve problems. Progressive mitral incompetence is relatively more common, associated with dilatation of the mitral annulus, elongation of the chordae tendineae and leaflet prolapse.

**Chronic rheumatic valve disease**
• Usually mitral valve (90%), occasionally also aortic valve (25%)
• Frequently takes 10 - 30 or even more years following acute rheumatic fever to develop clinically significant stenosis or incompetence related to ongoing organization -> fibrosis, commissural fusion +/- calcification of valve, fibrosis and shortening of chordae. Some of these patients may have had subclinical or mild disease/carditis. Sometimes disease may progress more rapidly in underdeveloped countries/communities, as above
• Increased likelihood with recurrence of Streptococcal pharyngitis/acute rheumatic fever.
• Effects: mitral stenosis/incompetence, aortic stenosis/incompetence, increased risk of infective endocarditis.

**Infective endocarditis**
• Usually affects aortic or mitral valves, sometimes both valves involved. Right sided valves in IV drug users.
• Large range of potential infective agents including bacteria, fungi, rickettsia
• Pathogenesis:
  • Source of circulating micro-organisms e.g. dental procedures, skin wounds, IV drug use, indwelling catheters, occult source in oral cavity or trivial injury
  • Cardiac abnormalities cause localised turbulence of blood flow, endocardial injury and formation of tiny platelet-fibrin thrombi, providing sites on endocardium in which organisms can settle and adhere
    • Congenital heart disease e.g. bicuspid aortic valve, VSD, patent ductus, aortic coarctation
    • Prosthetic material e.g. valves
    • Chronic rheumatic valve disease
    • Floppy mitral valve/mitral valve prolapse
    • Senile calcific aortic stenosis
    • et al
• Sometimes normal hearts are affected
Immunocompromise, diabetes etc are additional predisposing factors especially to infection with opportunistic organisms

Vegetations
- Organisms in the blood colonize the tiny thrombi and proliferate leading to further endocardial damage and the formation of larger thrombotic masses containing organisms on valves, chordae or sites of impaction of regurgitant jets
- These vegetations are irregular masses, soft and friable or firm, varying in size and colour, may be single or multiple
- Vegetations provide relative protection of organisms from the immune system and antibiotics
- Neutrophils present in acute vegetations
- Inflammation +/- necrosis is present in underlying tissue
- Heal by organization

Spectrum of severity and time course of disease depends on virulence of organism
- Acute infective endocarditis: virulent organisms (e.g. *Staphylococcus aureus*) often on normal valve; necrotising destructive vegetations; patients severely ill, acute course
- Subacute infective endocarditis: organisms of lower virulence (e.g. different types of streptococci) on deformed valves, more chronic/insidious course (weeks-months), generally smaller, less destructive valve lesions, may get gradual valve fibrosis
- Can also be classified based on underlying risk factors: native valve, prosthetic valve, IV drug use. Different organisms and clinical courses are associated with each.

Causative organisms include
- *Strep. viridans*
- *Staph. aureus*
- Enterococci
- *Staph. epidermidis*
- Others including fungi

Clinical effects and potential complications:
- Fever, malaise, night sweats
- Anaemia of chronic disease, splenomegaly (from ongoing immune response), clubbing in more long standing cases
- Cardiac:
  - Physical bulk of vegetation may cause incompetence or stenosis
  - Cusp perforation or chordal rupture -> valve incompetence and cardiac failure
  - Paravalvular abscesses (usually aortic and more commonly with prosthetic valves) ->
    - Conduction defects
    - Dehiscence of prosthetic valve
    - Fistulae (with aorta, heart chambers, pericardial cavity -> pericarditis)
  - Myocardial infarction from embolism (uncommon)
  - Healing over weeks/months may -> valve stenosis/incompetence -> heart failure
  - Congestive heart failure develops in 30 to 40% of patients; usually a consequence of valvular dysfunction
  - Murmurs
    - May be pre-existing, may be caused by turbulent flow across vegetations, may arise following development of valve incompetence or stenosis
    - Changing murmurs more likely in acute infective endocarditis
  - Embolism: -> infarction, abscess formation, mycotic aneurysm formation at distant sites, splinter haemorrhages
  - Bacteraemia may lead to infection at distant sites
  - Septic shock
  - Immunological: excessive immune response due to constant bacteraemia with formation of antigen-antibody complexes
    - Glomerulonephritis
    - Petechiae on skin and mucous membranes

- Prevention: prophylactic antibiotic therapy in those at risk undergoing at risk procedures
- Investigation: blood cultures, echocardiogram, ESR, CBE etc
- Treatment: antibiotics (prolonged course, intravenous route, high dose, bacteriocidal agents and synergistic combinations when possible as antibiotics penetrate vegetations poorly) +/- valve replacement
- Morbidity and mortality is high, particularly with prosthetic valve endocarditis

**Nonbacterial thrombotic endocarditis**
- Usually normal valve
- Small vegetations, but usually larger than in acute rheumatic fever, predominantly along line of closure. No underlying inflammation.
- Mitral valve most often affected but multiple valves may be involved
- Tend to occur in those with a hypercoagulable state e.g. terminal malignancy, debilitated
- May be firmly attached or friable and embolise
- Rarely cause valvular dysfunction

**Libman-Sacks endocarditis in SLE**