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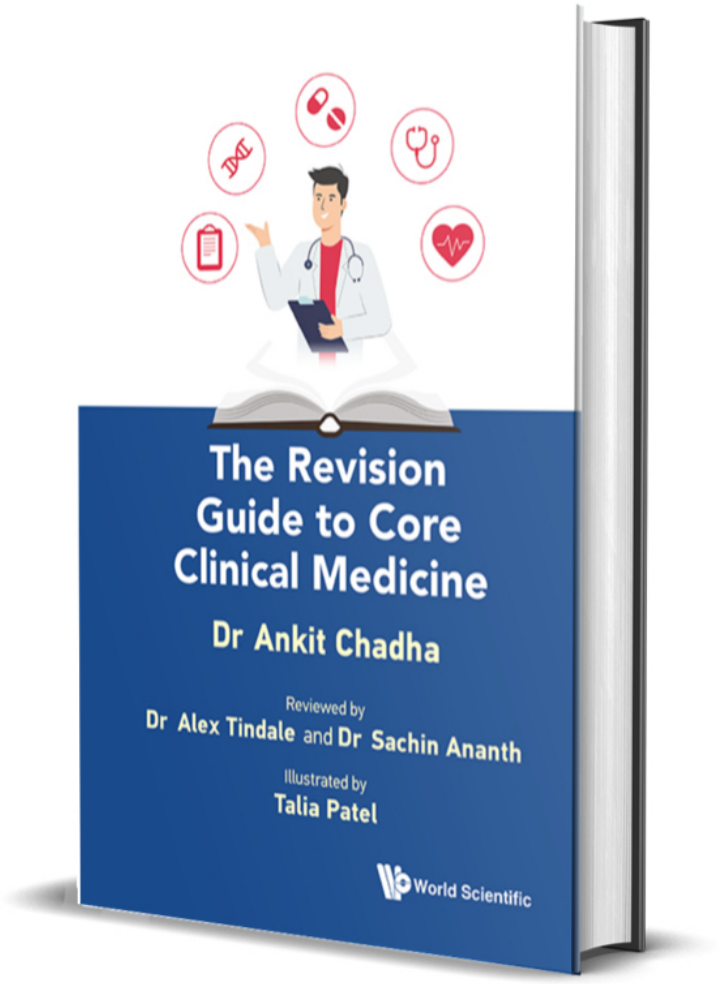

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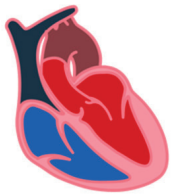
The Revision Guide to Core Clinical Medicine

Contents

Cardiovascular



BACKGROUND

PHARMACOLOGY

MEDICAL CONDITIONS

Tests and Investigations

- **Echocardiography**

This uses ultrasound waves to provide live imaging of the heart.
- The ultrasound is taken using either a transthoracic (TTE) or transoesophageal (TOE) probe. TTE is more convenient, but TOE gives higher resolution pictures and is more sensitive.
- It is used to help quantify global LV function by measuring the end-diastolic volume and the ejection fraction of the left ventricle, which is key in diagnosing heart failure.
- It can also measure right heart haemodynamics and assess for valve disease.

- **Cardiac CT**

This is used to provide information about cardiac structure and function.
- In CT angiography, the patient receives an IV injection of contrast whilst in a CT scanner it is used to diagnose stenosis in coronary disease with high sensitivity.

- **Cardiac MRI**

This is a radiation free method of looking at cardiac structure and function, which uses radio waves in a magnetic field.
- It is the first-choice imaging method to look at diseases affecting the myocardium including cardiomyopathies and quantification of scarring post MI.
- Modern pacemakers are usually safe for MRI scanning.

- **Myocardial perfusion scan**

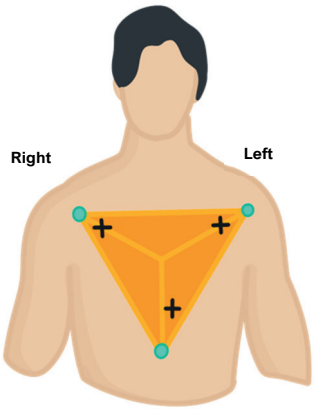
This works by the infusion of a radioactive marker which flows to the heart.
- This emits radioactive particles which can be detected by a scanner.
- It can be used to assess perfusion of an area under conditions of rest and stress.
- This is useful when assessing quantitatively how much myocardium becomes ischaemic with stress, and whether the myocardium distal to stenosis is viable.
- This indicates whether PCI or CABG will be of any clinical benefit to the patient.

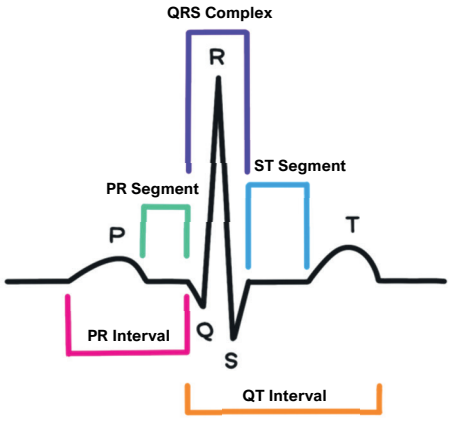
- **Cardiac catheterisation**

This involves the insertion of a catheter via the femoral/radial artery or veins. It is used to inject contrast into vessels to image the coronary vessels and perform angioplasty.
- It can sample the pressure of the right and left atrium and calculate cardiac output.
- It is also used to perform intravascular ultrasound and measure oxygen saturations.

- **ECG**

The ECG uses electrodes placed on the skin to measure the electrical activity of the heart. The standard ECG consists of 10 electrodes, which provide a 12-lead output.
- There are 6 electrodes placed on the chest and 1 on each limb.
- One of these is a ground electrode to prevent electrical interference.





Interpreting an ECG

The ECG graph displays voltage over time:
- Y-axis represents voltage, measured in mV
- X-axis represents time.
- The standard length is 25 mm/s and it captures a recording over 10 seconds.
- Each small box is 0.04 s, and large box = 0.2 s

An interval is the time taken from the start of one wave to the end of another.
A segment is the time taken from the end of one wave to the start of another.

You should interpret an ECG systematically.

1) Check patient details

- Name
- Age
- Hospital number
- ECG date

2) Calculate heart rate

The strip at the bottom records electrical activity for 10 seconds.
- Therefore, count the QRS complexes along the rhythm strip and multiply by 6.

3) Assess the rhythm

The regularity can be checked using the paper-and-pen method on the rhythm strip.

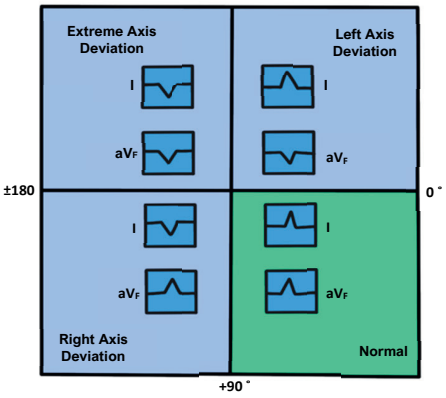
- Place a paper over the ECG trace.
- Mark the position of two consecutive QRS complexes, marking the R/R interval.
- Move the paper along the strip and check whether the R/R interval is the same.
- If the rhythm is abnormal, it can be regularly irregular or irregularly irregular.

4) Calculate the cardiac axis

As leads I–III and the augmented leads provide a frontal view of the heart, the net positive deflection of the current indicates the axis the heart is aligned on.

To quickly calculate the axis, you can use the quadrant method.

- Look at leads I and aV_F.
- Under normal circumstances, due to the way that these leads follow the current, the QRS deflections in both these leads should be positive.



However, if the heart undergoes hypertrophy on either side, this can alter the axis.

- It can be used to give a crude (qualitative) measure of the overall axis of the heart.

Lead I QRS deflection	aV_F QRS deflection	Axis
Positive	Positive	Normal
Negative	Positive	Right axis deviation
Positive	Negative	Left axis deviation
Negative	Negative	Extreme axis deviation

Left axis deviation

- Left anterior hemiblock
- Left ventricular hypertrophy
- Inferior heart attack
- Wolff-Parkinson-White syndrome

Right axis deviation

- Left posterior hemiblock
- Right ventricular hypertrophy (e.g., after pulmonary embolism)
- Anterolateral myocardial infarction
- Wolff-Parkinson-White syndrome

5) Examine distinct parts of the ECG waveform

P wave

This wave signals the electrical activity flowing through the atria and should precede each QRS complex.

- It is usually a positive deflection in leads II and III but is inverted in aV_R.
- Absent P waves are seen in atrial fibrillation and atrial flutter (although atrial activity is seen as regular "pseudo" P waves at a rate of around 300/min).

PR interval

This interval is the electrical activity passing from the atria to the ventricles.

- The normal range 0.12–0.20 seconds.

Prolongation of the PR interval suggests that there is a delay in conduction between atria and ventricles, e.g., 1st/2nd degree heart block, digoxin and hypokalaemia.

- A short PR interval suggests very fast AV conduction down an accessory pathway, e.g., Wolff-Parkinson-White syndrome.
- If the PR segment is depressed, this is associated with pericarditis.

QRS complex

This signals electrical activity through the ventricles. The normal duration is < 0.12 s.

- Any positive deflection is an R wave.
- After an R wave, any subsequent negative line is an S wave.
- A negative deflection before an initial R wave is called a Q wave.

A broad QRS (> 0.12 s) means the ventricular rate is determined by a focus in the ventricles, e.g., bundle branch block, ventricular ectopic, hyperkalaemia.

A narrow QRS (< 0.12 s) means the ventricular rate is determined by a focus before the ventricles, e.g., SVT.

QT interval

This measures the time from the start of contraction to the end of relaxation and should be 0.38–0.42 seconds.

- The corrected QT interval is QT interval divided by the square root of the R/R interval.

Prolongation of the QT interval can lead to ventricular fibrillation and sudden death.

- A long QT interval is found in long QT syndrome, as well as secondary to hypocalcaemia, hypokalaemia and many drugs (e.g., SSRI, TCA).

ST segment

This is usually isoelectric. However, elevation or depression of the ST segment can be a sign of ischaemia to the heart.

- The territories in which the ST elevation occurs can determine which part of the heart has an infarct.

T wave

This wave represents repolarisation of the ventricles. It can normally be inverted in aVR, V1 and sometimes V2. T wave inversion can be a sign of ischaemia in patients.

- Peaked (tall) T waves are associated with hyperkalaemia.
- Flattened T waves are associated with hypokalaemia.

Sometimes some additional waves can be present on the ECG trace.

U wave

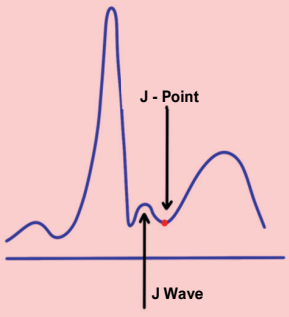
This wave represents the recovery of the Purkinje fibres and occurs after the T wave.

- It is a positive rounded deflection, but it is usually not seen in a normal ECG trace.
- Prominent U waves are seen in hypercalcaemia, hypokalaemia and digoxin toxicity.

J wave

This is a notch in the point where the S wave finishes and the ST segment starts.

- Again, it is not usually seen in a normal ECG trace.
- Prominent J waves are seen in hypothermia and hypercalcaemia.



Drugs Affecting the Heart

- **Beta-blockers – Propranolol** (non-specific), **atenolol, bisoprolol** (B_1-specific)

These drugs are antagonists of beta receptors. They inhibit sympathetic stimulation of the heart to reduce both the heart rate and the force of contraction, reducing cardiac demand for oxygen.

- They also have secondary effects of causing a sustained reduction in peripheral vascular resistance and inhibiting renin release.

Side effects

- Bronchoconstriction
- Fatigue
- Sleep disturbance/nightmares
- Coldness of extremities
- Impotence
- Less hypoglycaemic awareness

Contraindications

- Uncontrolled heart failure
- Asthma
- Sick sinus syndrome
- Co-prescribing beta-blockers with verapamil due bradycardia

- **Ivabradine**

This medicine blocks the I_f funny current, a mixed Na-K inward current in the SAN.

- It lowers pacemaker activity in the SAN, which slows the heart rate down.
- It is primarily used in angina but can also be used in heart failure.

Side effects

- Luminous phenomenon (as retinal I_h channels are similar to cardiac I_f channels)

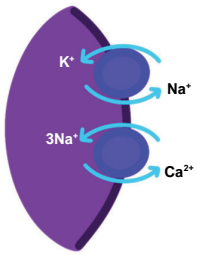
- **Phosphodiesterase inhibitors – Milrinone, inamrinone**

These are phosphodiesterase inhibitors which inhibit the enzyme PDE type 3 in the heart as well as in smooth muscle.

- In the heart, they mimic sympathetic stimulation which leads to an increase in the heart rate and the force of contraction.
- In smooth muscle, they lead to a rise in cAMP which activates protein kinase A.
- This leads to inhibition of myosin light chain kinase which leads to vasodilation.
- Their use is limited to heart failure unresponsive to other therapies, as they can cause dysrhythmias.

- **Cardiac glycosides – Digitoxin, digoxin**

These inhibit the Na^+/K^+ – ATPase, which increases the intracellular Na^+ concentration.
- It reduces the concentration gradient for the NCX exchanger which removes Ca^{2+} ions from the cell.
- This leads to a build-up of Ca^{2+} in the cell, increasing the force of muscle contraction next time.



Digoxin also increases vagal activity, which helps to slow the heart down.
- It is mainly used clinically to slow down the heart rate in atrial fibrillation.
- It is also an old heart failure treatment that has been shown to reduce hospitalisations in the pre-ACE-inhibitor era, although not mortality.

Side effects
- Arrhythmias
- GI upset (nausea, diarrhoea)
- Dizziness
- Blurred or yellow vision
- Gynaecomastia (with long-term use)

Digoxin toxicity

This is where raised levels of the drug can lead to systemic symptoms.
- On the ECG, digoxin toxicity can cause arrythmias and a "reverse" tick sign.
- To reverse, give digoxin-specific antibody fragments and correct K^+ abnormalities.

There are several factors which increase the risk of digoxin toxicity:
- Hypokalaemia – digoxin binds to the K^+ site of the sodium pump. In hypokalaemia, glycosides have a greater effect due to reduced competition for the binding site.

- Decreased renal clearance – this is because digoxin is excreted by the kidneys. Therefore, there is a higher risk in patients with renal failure and who take drugs which compete for secretion in the DCT (e.g., ciclosporin, amiodarone, verapamil)

- **B_1 agonists – Dobutamine, dopamine**

These are agonists of the B_1 receptor which mimic sympathetic stimulation.
- They cause an increase in contractility as well as heart rate.
- They are known as inotropes and given to ill patients in settings like intensive care units for those who have acute cardiac failure and hypotension.

Side effects
- May precipitate hypertension and dysrhythmias (tachycardia)

- **Ca^{2+} channel blockers – Verapamil, diltiazem**

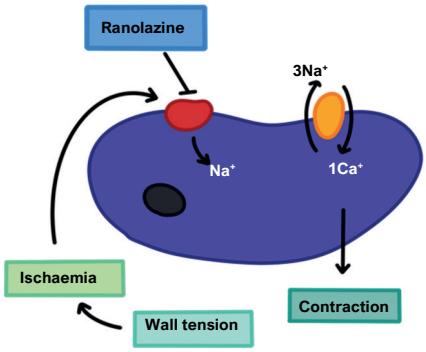
These are inhibitors of voltage gated calcium channels, which are found in the heart and the smooth muscle of artieroles.
- These drugs have high use dependence which gives them more selectivity for cardiac channels than in smooth muscle.
- This is because the channels in the heart are constantly opening and closing with each heartbeat, whereas in smooth muscle they remain open or closed for longer.
- They inhibit calcium entry at the SAN and AVN, which slows the heart rate down.
- They also lead to smooth muscle dilation, and so can be used to decrease blood pressure and dilate coronary blood vessels in angina.
- Verapamil can also be used for prophylaxis of cluster headaches.

Side effects
- Increases mortality in patients with heart failure
- Bradycardia (do not use with beta-blockers as can cause heart block)
- Hypotension
- Ankle swelling
- Verapamil also causes constipation

- **Ranolazine**

Towards the end of the action potential, there is a late inward sodium current.
- Increased intracellular $[Na^+]_i$ reduces the driving force for the NCX exchanger.
- This leads to increased intracellular calcium which impairs ventricular relaxation.
- Less relaxation increases wall tension, which compromises myocardial blood flow.

This drug blocks the late inward Na^+ current allowing the cell to get rid of more Ca^{2+}, reducing Ca^{2+} overload.
- It improves left ventricular relaxation in diastole increasing coronary blood flow.
- It is used in angina, which is refractory to other treatments.



Heart Failure

- **Heart failure**

This is a clinical syndrome consisting of symptoms (e.g., breathlessness, oedema, fatigue) that occurs due to abnormalities in cardiac structure or function, causing inadequate cardiac output or raised intracardiac pressures.

- Usually, it is due to myocardial dysfunction, but can be due to other causes like valvular disease, pericardial disease or arrhythmias.

o **Systolic failure**

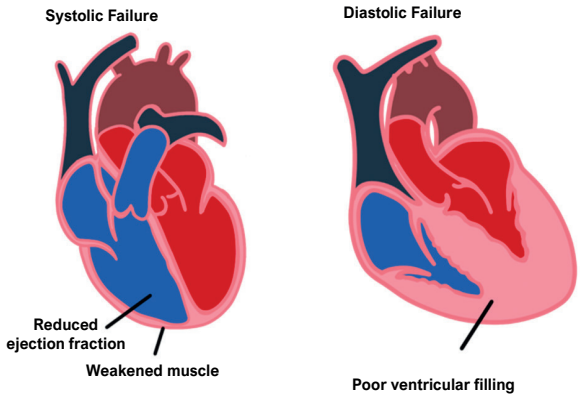
This is an inability for the ventricle to contract properly, decreasing cardiac output.

- In this case, the ejection fraction (EF) is < 40%.
- It occurs due to conditions which weaken the heart muscle reducing contractility, e.g., ischaemic cardiomyopathy, dilated cardiomyopathy and myocarditis.

o **Diastolic failure**

Refers to an inability of the ventricles to fill normally causing increased filling pressure.

- The ejection fraction here is usually > 50%, but because the ventricles cannot fill, the cardiac output is low and filling pressures are raised.
- Causes include disorders of heart muscle such as hypertrophy, extrinsic compression from pericardial disease and tamponade from pericardial fluid.



Traditionally, heart failure has been divided into left and right sided heart failure depending on the main ventricle affected. These can occur separately, but if both are present it is known as congestive cardiac failure (CCF).

o **Right ventricular failure**

This usually occurs after left-sided failure and pulmonary hypertension.
- It is also due to left-to-right shunts, which increases the pulmonary blood flow.
- It results in congestion of the peripheral venous circulation.

Symptoms
- Raised JVP, pitting ankle oedema and ascites
- Hepatosplenomegaly with a smooth "nutmeg" liver which is pulsatile

o **Left ventricular failure**

This is often caused by ischaemic and non-ischaemic cardiomyopathies.
- The raised filling pressures and reduced contractility can reduce cardiac output and increase congestion of the pulmonary circulation.

Symptoms
- Dyspnoea, paroxysmal nocturnal dyspnoea and orthopnoea (SOB lying down)
- Polyphonic expiratory wheeze with bibasal crackles due to pulmonary oedema
- Gives a 3rd heart sound
- Weight loss (however, the patient will also have weight gain due to the oedema)
- Pulsus alternans (alternation of force of arterial pulse: hard then soft)

Grading
- Heart failure is graded using the New York classification of heart failure:
- Grade 1 – asymptomatic with no dyspnoea from ordinary activity
- Grade 2 – mild symptoms, dyspnoea from ordinary activities but comfortable at rest
- Grade 3 – moderate symptoms present, dyspnoea from less than ordinary activity but comfortable at rest
- Grade 4 – severe symptoms present with dyspnoea at rest

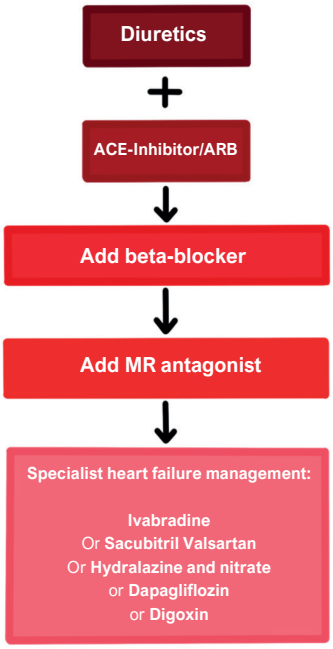
Key tests
- Blood tests show raised natriuretic peptides (BNP and NT-proBNP). These are secreted when heart chambers become overloaded
- Echocardiogram – used to assess the ventricular ejection fraction
- ECG – this shows signs such as axis deviation and may show ischaemia
- Chest X-ray – left ventricular failure shows signs of fluid overload such as pulmonary oedema, pleural effusions, Kerley B lines

Acute management

- The aim is to drive the fluid out of the lungs reducing breathlessness
- This is achieved through diuretics and then nitrates to reduce pre/afterload
- Give oxygen to keep saturations > 94%
- IV furosemide
- If BNP is still raised, start IV nitrates
- CPAP can be used to drive out fluid from lungs
- You should avoid beta-blockers in acute heart failure as they are negatively ionotropic and can severely reduce (already-struggling) cardiac output

Chronic management

- The aim of treatment is to oppose the body's natural compensatory mechanisms which try to increase cardiac output, as this just makes the situation worse.
- Patients with heart failure should also be offered the annual Influenza vaccine and a single pneumococcal vaccine.



- **Diuretic e.g., furosemide**

Used for symptomatic (fluid overload) relief but has no proven mortality benefit.

- **ACE inhibitor e.g., ramipril**

1st line treatment which is given to patients with EF < 40%.

- **Beta-blocker e.g., bisoprolol**

This is given in addition to ACE-i in patients with EF < 40% or those with LV systolic dysfunction after myocardial infarction.

- **Mineralocorticoid receptor antagonist e.g., spironolactone**

This is recommended as a 3rd drug added on for patients persisting with symptoms or when LVEF < 35%.

- **Angiotensin receptor blocker (ARB) e.g., candesartan**

This can be used when the ACE-i is not tolerated (due to dry cough) or as the 3rd drug when the MRA not tolerated with ACE-i and the B-blocker.

If the patient is still symptomatic after ACE-i, beta-blockers and mineralocorticoid receptor antagonists, then options for further treatment include:

o **Combination of sacubitril and valsartan (Entresto)**

You can switch the ACE-inhibitor for an angiotensin receptor-neprilysin inhibitor (ARNI). Entresto is the licensed ARNI, a combination of sacubitril and valsartan.

- Sacubitril is a neprilysin inhibitor and valsartan is an angiotensin receptor blocker.
- Neprilysin degrades signaling molecules including ANP, which results in increased sodium excretion and vasodilation.
- They show a mortality benefit in clinical trials in place of ACE-inhibitors, but in the UK, it is currently limited to patients with refractory heart failure on ACE-i, aeta-blocker and MRA with an EF < 35% and > NYHA II symptoms.

o **Dapgliflozin**

Dapagliflozin is an SGLT-2 inhibitor which inhibits the reabsorption of glucose in the proximal convoluted tubule. It is typically used to treat type 2 diabetes.

- It can also be used to treat chronic heart failure with reduced ejection fraction in adults, as an add-on to standard care with an ACE inhibitor, beta-blocker and MRA.

o **Ivabradine**

This can be used as a 4th drug in patients with EF < 35%, sinus rhythm and HR > 75 bpm with persisting symptoms, who are in sinus rhythm and have maximal beta-blockade. It reduces the risk of hospitalisation but not mortality.

o **Digoxin**

This can be used as a 4th drug with ACE-i, beta-blocker and MRA in patients with persisting symptoms.

o **Vasodilators e.g., hydralazine, nitrates**

These are used as an alternative to an ACE-i/ARB when neither are tolerated.

- They are especially useful in patients of Afro-Caribbean descent.

o **Implantable cardioverter defibrillator**

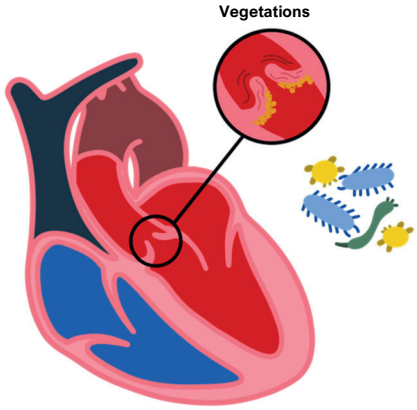
This is considered after medical therapy is the LVEF is still < 35% and QRS < 120 ms.

For heart failure, the following medications do not have a mortality benefit:

- Furosemide
- Statin
- Digoxin
- Ivabradine

Infective Endocarditis

This refers to inflammation of the endocardium that lines the surface of heart valves.
- It can lead to vegetations on the valve surface that can destroy the valve.
- In addition, it can lead to septic emboli formation leading to other complications.



Causes

1) Staphylococcus aureus

This is the most common cause of IE which is usually seen in IV drug abusers.
- It is a high virulence organism that destroys valves (commonly tricuspid).
- Risk factors for this bacterium include skin breaches (dermatitis, IV lines), kidney failure and diabetes.

2) Viridans streptococci

This is a group of low-virulence bacteria that affects previously damaged valves.
- It is associated with poor dentition and sequelae of dental procedures.
- It causes small vegetations that do not completely destroy the valve and so causes a subacute endocarditis. The damaged endocardium develops small thrombotic vegetations of platelets and bacteria.

3) Staphylococcus epidermidis

This is associated with endocarditis of prosthetic valves.

4) Streptococcus bovis

This is associated with endocarditis in patients with colorectal carcinoma.

5) HACEK organisms

These are Gram negative bacteria which give negative blood cultures

Haemophilus	**A**ctinobacillus	**C**ardiobacterium
Eikenella	**K**ingella	

6) Fungi, e.g., candida and aspergillus

These are seen in IV drug users and immunocompromised patients.

7) Non-infectious causes

Non-bacterial thrombotic endocarditis is due to sterile vegetations that arise in association with a hypercoagulable state or an underlying adenocarcinoma.

- Libman Sacks endocarditis is sterile vegetations associated with SLE. Vegetations occur on both sides of the mitral valve and lead to mitral regurgitation.

Symptoms

- Septic symptoms – fever, anaemia, clubbing, weight loss
- Cardiac symptoms – heart murmur (due to valve disease), heart failure, chest pain
- Immune complex deposition – Roth spots (retinal haemorrhage with pale centers), splinter haemorrhages and Osler nodes (tender lesions on fingers and toes)
- Septic emboli – these can cause abscesses in organs, e.g., in skin they are called Janeway lesions (on palms), ischaemic strokes

Diagnosis

- The is done using the modified Duke criteria, which use major and minor criteria:

Major Criteria:

- 2 Positive blood cultures – 3 cultures are taken from different sites when the patient is febrile, looking for typical microorganisms which cause infective endocarditis
- Involvement of the endocardium, which is shown by an echocardiogram. A transthoracic echocardiogram cannot rule out IE – perform TOE if high suspicion

Minor Criteria:

- Predisposition (e.g., valve prolapse)
- IV drug use
- Fever > 38°C
- Microbiologic evidence (e.g., blood cultures not meeting major criterion)
- Immunologic phenomena, e.g., Osler nodes/Roth spots
- Vascular signs e.g., splinter haemorrhages, Janeway lesions

Management

- Antibiotic therapy according to cultures and sensitivity
- Initial empirical therapy may involve amoxicillin and low dose gentamicin
- Some severe cases may require valve replacement surgery, e.g., if there is acute heart failure, severe valve incompetence or recurrent embolic events

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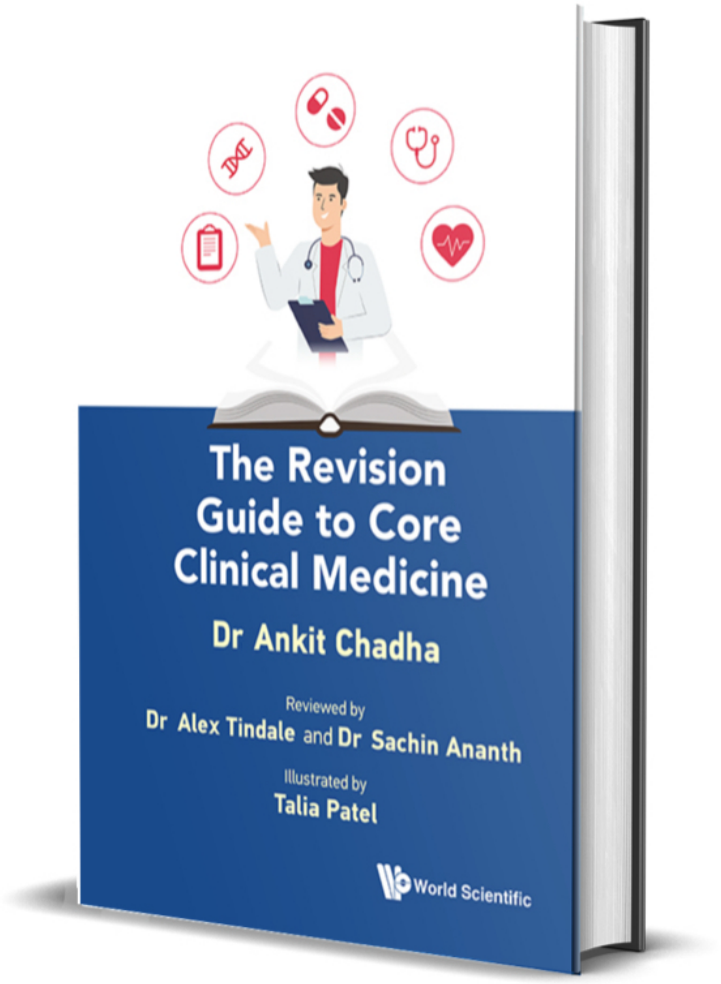

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