10 Cardiovascular disease

COMMON PRESENTING SYMPTOMS OF HEART DISEASE

The common symptoms of heart disease are chest pain, breathlessness, palpitations, syncope, fatigue and peripheral oedema, but none are specific for cardiovascular disease. The severity of anginal pain, dyspnoea, palpitations or fatigue may be classified according to the New York Heart Association (NYHA) grading of 'cardiac status' (Table 10.1).

Chest pain

Chest pain or discomfort is a common presenting symptom of cardiovascular disease and must be differentiated from non-cardiac causes. The site of pain, its character, radiation and associated symptoms will often point to the cause (Table 10.2).

Dyspnoea

Causes are discussed on page 507. Left heart failure is the most common cardiac cause of exertional dyspnoea and may also cause orthopnoea and paroxysmal nocturnal dyspnoea.

Palpitations

Palpitations are an awareness of the heartbeat. The normal heartbeat is sensed when the patient is anxious, excited, exercising or lying on the left side. In other circumstances it usually indicates a cardiac arrhythmia, commonly ectopic beats or a paroxysmal tachycardia (p. 421).

Syncope

This is a temporary impairment of consciousness due to inadequate cerebral blood flow. There are many causes and the most common is a simple faint or vasovagal attack (Table 17.3; page 720). The cardiac causes of syncope are the result of either very fast (e.g. ventricular tachycardia) or very slow heart rates (e.g. complete heart block) which are unable to maintain an adequate cardiac output. Attacks occur suddenly and without warning. They last only 1 or 2 minutes, with complete recovery in seconds (compare with epilepsy, where complete recovery may be delayed for some hours). Obstruction to

Table 10.1 The New York Heart Association grading of 'cardiac status' (modified)

Grade 1	Uncompromised (no breathlessness)
Grade 2	Slightly compromised (on severe exertion)
Grade 3	Moderately compromised (on mild exertion)
Grade 4	Severely compromised (breathless at rest)

Table 10.2 Common causes of chest pain

Central	
Angina pectoris	Crushing pain on exercise, relieved by rest. May radiate to jaw or arms
ACS	Similar in character to angina but more severe, occurs at rest, lasts longer
Pericarditis	Sharp pain aggravated by movement, respiration and changes in posture
Aortic dissection	Severe tearing chest pain radiating through to the back
Massive PE	With dyspnoea, tachycardia and hypotension
Musculoskeletal	Tender to palpate over affected area
GORD	May be exacerbated by bending or lying down (at night). Pain may radiate into the neck
Lateral/peripheral	
Pulmonary infarct Pneumonia Pneumothorax	Pleuritic pain, i.e. sharp, well-localized, aggravated by inspiration, coughing and movement
Musculoskeletal	Sharp, well-localized pain with a tender area on palpation
Lung carcinoma	Constant dull pain
Herpes zoster	Burning unilateral pain corresponding to a dermatome that appears 2 to 3 days before the typical rash

ACS, acute coronary syndrome; GORD, gastro-oesophageal reflux disease; PE, pulmonary embolus.

ventricular outflow also causes syncope (e.g. aortic stenosis, hypertrophic cardiomyopathy), which typically occurs on exercise when the requirements for increased cardiac output cannot be met. Postural hypotension is a drop in systolic blood pressure (BP) of 20 mmHg or more on standing from a sitting or lying position.

Other symptoms

Tiredness and lethargy occur with heart failure and result from poor perfusion of brain and skeletal muscle, poor sleep, side effects of medication, particularly β-blockers, and electrolyte imbalance due to diuretic therapy. Heart failure also causes salt and water retention, leading to oedema, which in ambulant patients is most prominent over the ankles. In severe cases it may involve the genitalia and thighs.

INVESTIGATIONS IN CARDIAC DISEASE

The chest X-ray

A chest X-ray is usually taken in the postero-anterior (PA) direction at maximum inspiration (p. 509). A PA chest film can aid the identification of cardiomegaly, pericardial effusions, dissection or dilatation of the aorta, and calcification of the pericardium or heart valves. A cardiothoracic ratio (p. 510) of greater than 50% on a PA film is abnormal and normally indicates cardiac dilatation or pericardial effusion. Examination of the lung fields may show signs of left ventricular failure (Fig. 10.1), valvular heart disease (e.g. markedly enlarged left atrium in mitral valve disease) or pulmonary oligaemia (reduction of vascular markings) associated with pulmonary embolic disease.

THE ELECTROCARDIOGRAM

The electrocardiogram (ECG) is a recording from the body surface of the electrical activity of the heart. Each cardiac cell generates an action potential as it becomes depolarized and then repolarized during a normal cycle. Normally, depolarization of cardiac cells proceeds in an orderly fashion beginning in the sinus node (lying in the junction between superior vena cava and right atrium) and spreading sequentially through the atria, atrioventricular (AV) node (lying beneath the right atrial endocardium within the lower inter-atrial septum), and the His bundle in the interventricular septum, which divides into right and left bundle branches (Fig. 10.2). The right and left bundle branches continue down the right and left side of the interventricular septum and supply the Purkinje network which spreads through the subendocardial surface of the right ventricle and left ventricle, respectively. The main left bundle divides into an anterior superior division (the anterior hemi-bundle) and a posterior inferior division (the posterior hemi-bundle).

The standard ECG has 12 leads:

- Chest leads, V_1–V_6, look at the heart in a *horizontal plane* (Fig. 10.3).
- Limb leads look at the heart in a *vertical plane* (Fig. 10.4). Limb leads are unipolar (AVR, AVL and AVF) or bipolar (I, II, III).

The ECG machine is arranged so that when a depolarization wave spreads towards a lead the needle moves upwards on the trace (i.e. a positive deflection), and when it spreads away from the lead the needle moves downwards.

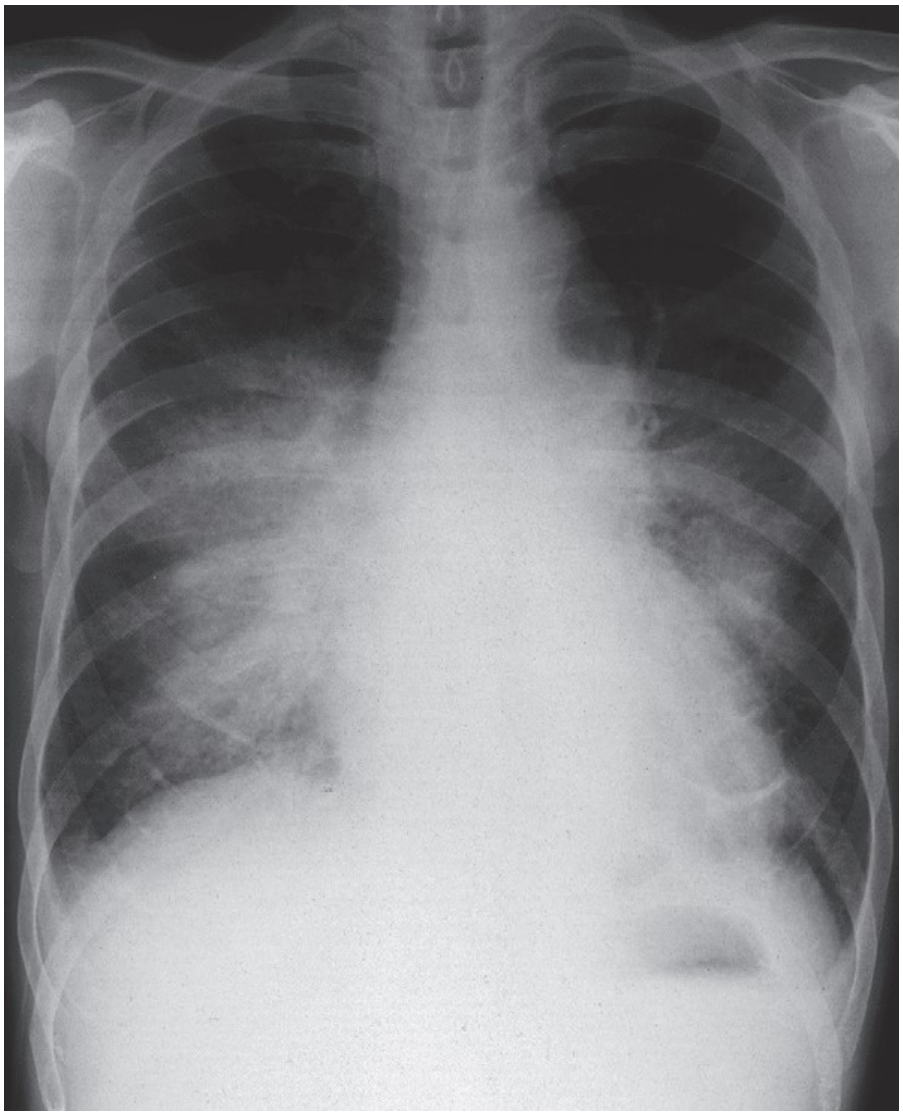


Fig. 10.1 Chest X-ray in acute left ventricular failure. This chest X-ray demonstrates cardiomegaly, hilar haziness, Kerley B lines, upper lobe venous blood engorgement and fluid in the right horizontal fissure. Hilar haziness and Kerley B lines (thin linear horizontal pulmonary opacities at the base of the lung periphery) indicate interstitial pulmonary oedema.

ECG waveform and definitions (Fig. 10.5)

Heart rate At normal paper speed (usually 25 mm/s) each 'big square' measures 5 mm wide and is equivalent to 0.2 s. The heart rate (if the rhythm is regular) is calculated by counting the number of big squares between two consecutive R waves and dividing into 300.

The P wave is the first deflection and is caused by atrial depolarization. When abnormal, it may be:

- Broad and notched (>0.12 s, i.e. three small squares) in left atrial enlargement ('P mitrale', e.g. mitral stenosis)
- Tall and peaked (>2.5 mm) in right atrial enlargement ('P pulmonale', e.g. pulmonary hypertension)

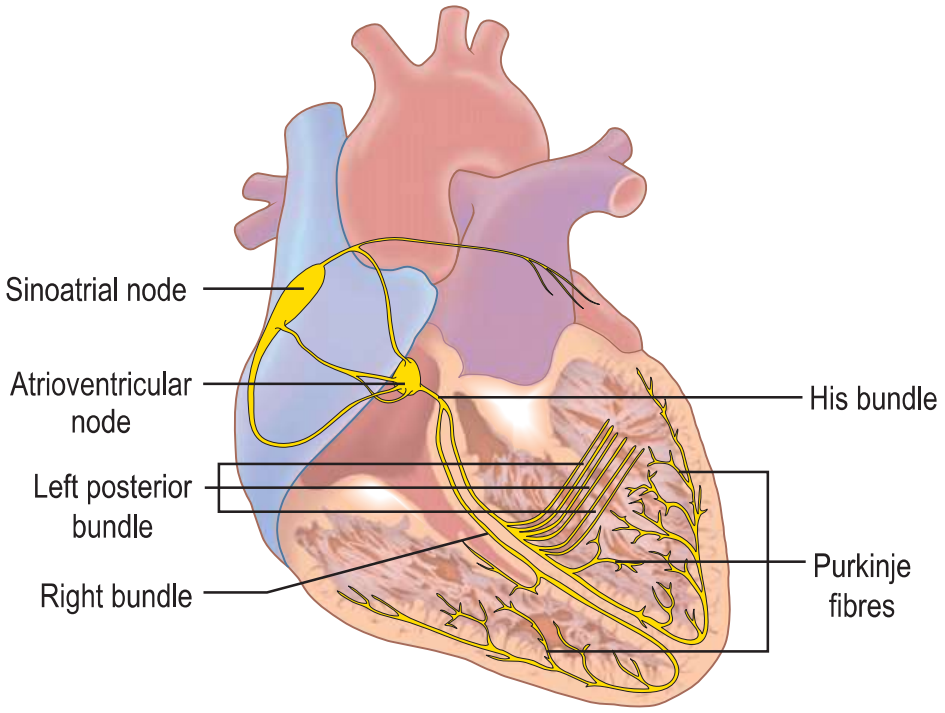


Fig. 10.2 The conducting system of the heart. In normal circumstances only the specialized conducting tissues of the heart undergo spontaneous depolarization (automaticity), which initiates an action potential. The sinus (SA) node discharges more rapidly than the other cells and is the normal pacemaker of the heart. The impulse generated by the SA node spreads first through the atria, producing atrial systole, and then through the atrioventricular (AV) node to the His-Purkinje system, producing ventricular systole.

- Replaced by flutter or fibrillation waves (p. 430)
- Absent in sinoatrial block (p. 423).

The *QRS complex* represents ventricular activation or depolarization:

- A negative (downward) deflection preceding an R wave is called a Q wave. Normal Q waves are small and narrow; deep (>2 mm), wide (>1 mm) Q waves (except in AVR and V_1) indicate myocardial infarction (MI) (p. 453).
- A deflection upwards is called an R wave whether or not it is preceded by a Q wave.
- A negative deflection following an R wave is termed an S wave.

Ventricular depolarization starts in the septum and spreads from left to right (Fig. 10.2). Subsequently, the main free walls of the ventricles are depolarized. Thus in the right ventricular leads (V_1 and V_2) the first deflection is upwards (R wave) as the septal depolarization wave spreads towards those leads. The second deflection is downwards (S wave) as the bigger left ventricle (in which depolarization is spreading away) outweighs the effect of the right ventricle (Fig. 10.3). The opposite pattern is seen in the left ventricular leads (V_5 and V_6), with an initial downwards deflection (small Q wave reflecting septal depolarization) followed by a large R wave caused by left ventricular depolarization.

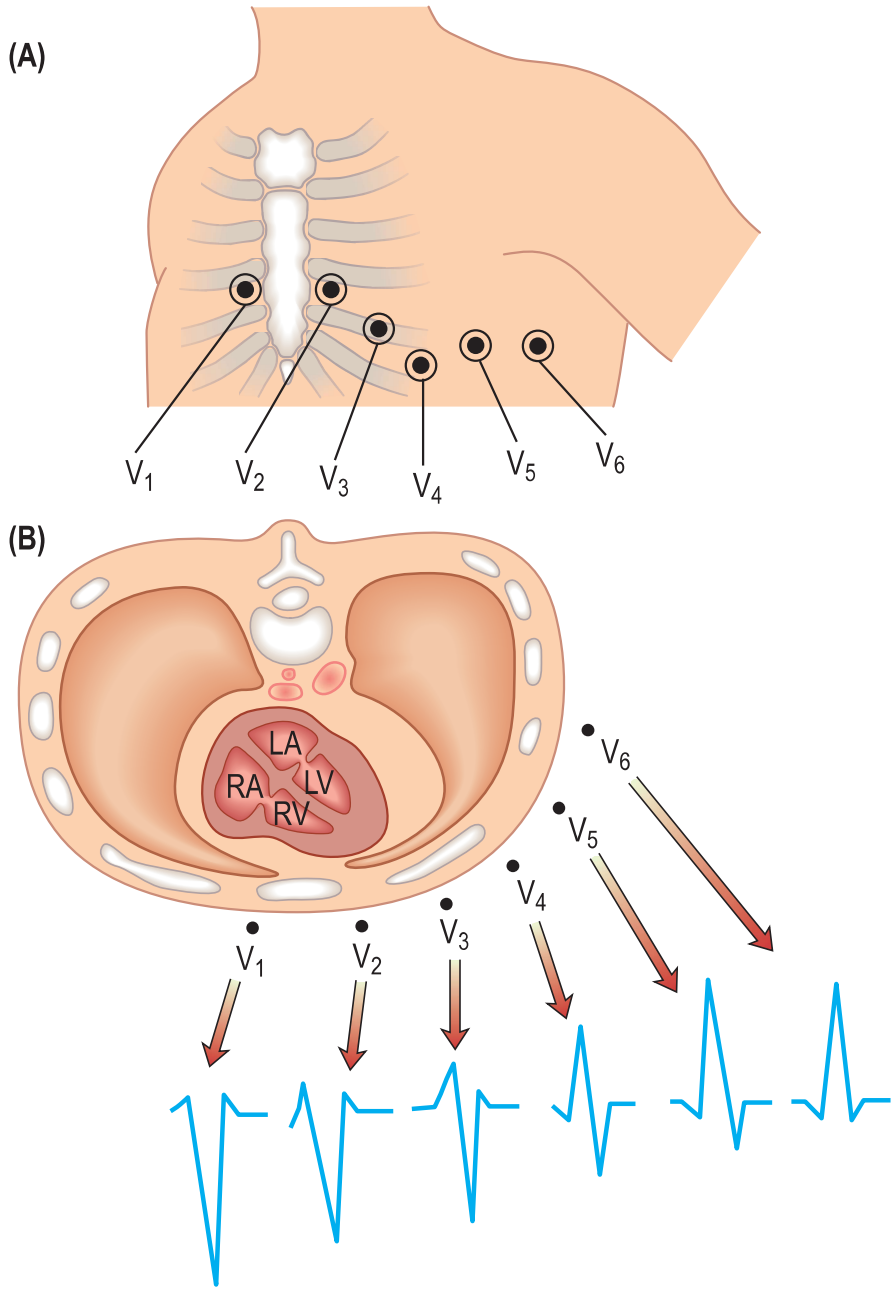


Fig. 10.3 ECG chest leads. (A) The V leads are attached to the chest wall overlying the intercostal spaces as shown: V_4 in the mid-clavicular line, V_5 in the anterior axillary line, V_6 in the mid-axillary line. (B) Leads V_1 and V_2 look at the right ventricle, V_3 and V_4 at the interventricular septum, and V_5 and V_6 at the left ventricle. The normal QRS complex in each lead is shown. The R wave in the chest (precordial) leads steadily increases in amplitude from lead V_1 to V_6 with a corresponding decrease in S wave depth, culminating in a predominantly positive complex in V_6. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Left ventricular hypertrophy with increased bulk of the left ventricular myocardium (e.g. with systemic hypertension) increases the voltage-induced depolarization of the free wall of the left ventricle. This gives rise to tall R waves (>25 mm) in the left ventricular leads (V_5, V_6) and/or deep S waves (>30 mm) in the right ventricular leads (V_1, V_2). The sum of the R wave in the left

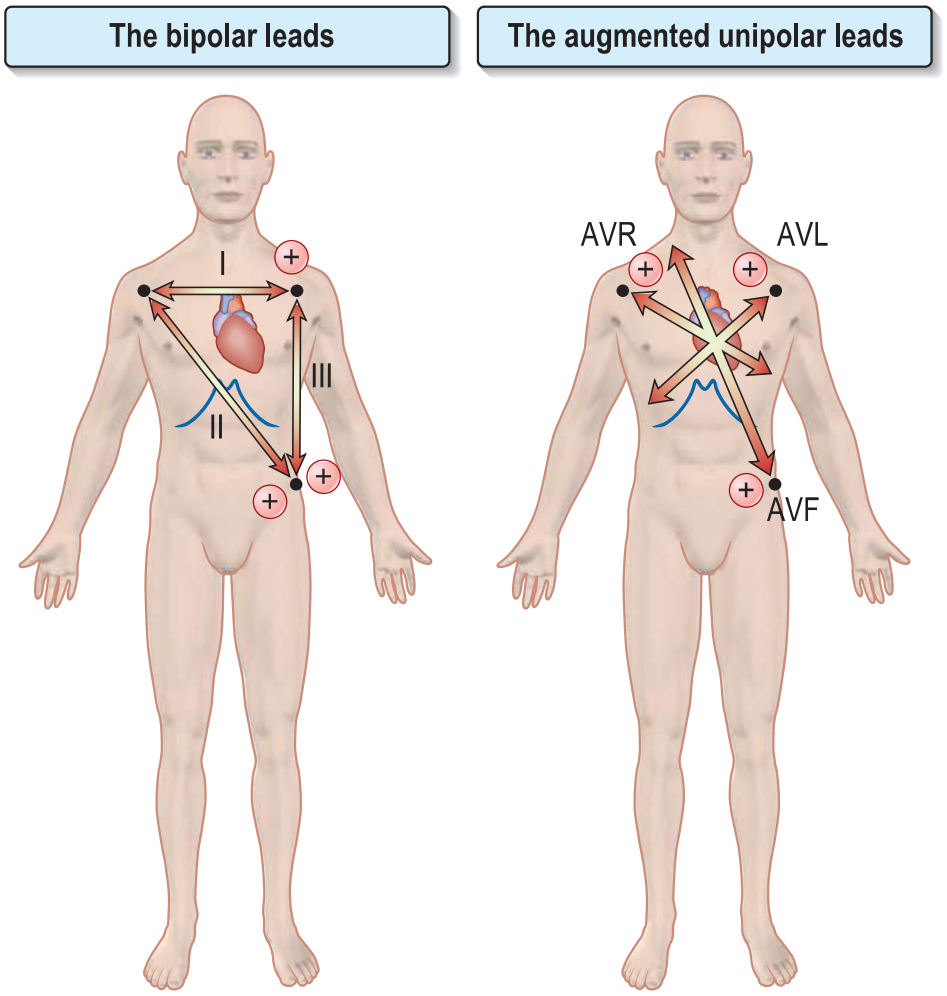


Fig. 10.4 ECG limb leads. Lead I is derived from electrodes on the right arm (negative pole) and left arm (positive pole), lead II is derived from electrodes on the right arm (negative pole) and left leg (positive pole) and lead III from electrodes on the left arm (negative pole) and the left leg (positive pole).

ventricular leads and the S wave in the right ventricular leads exceeds 40 mm. In addition to these changes, there may also be ST-segment depression and T-wave flattening or inversion in the left ventricular leads.

Right ventricular hypertrophy (e.g. in pulmonary hypertension) causes tall R waves in the right ventricular leads.

The QRS duration reflects the time that excitation takes to spread through the ventricle. A wide QRS complex (>0.10 s, 2.5 small squares) occurs if conduction is delayed, e.g. with right or left bundle branch block, or if conduction is through a pathway other than the right and left bundle branches, e.g. an impulse generated by an abnormal focus of activity in the ventricle (ventricular ectopic).

T waves result from ventricular repolarization. In general the direction of the T wave is the same as that of the QRS complex. Inverted T waves occur in many conditions and, although usually abnormal, they are a non-specific finding.

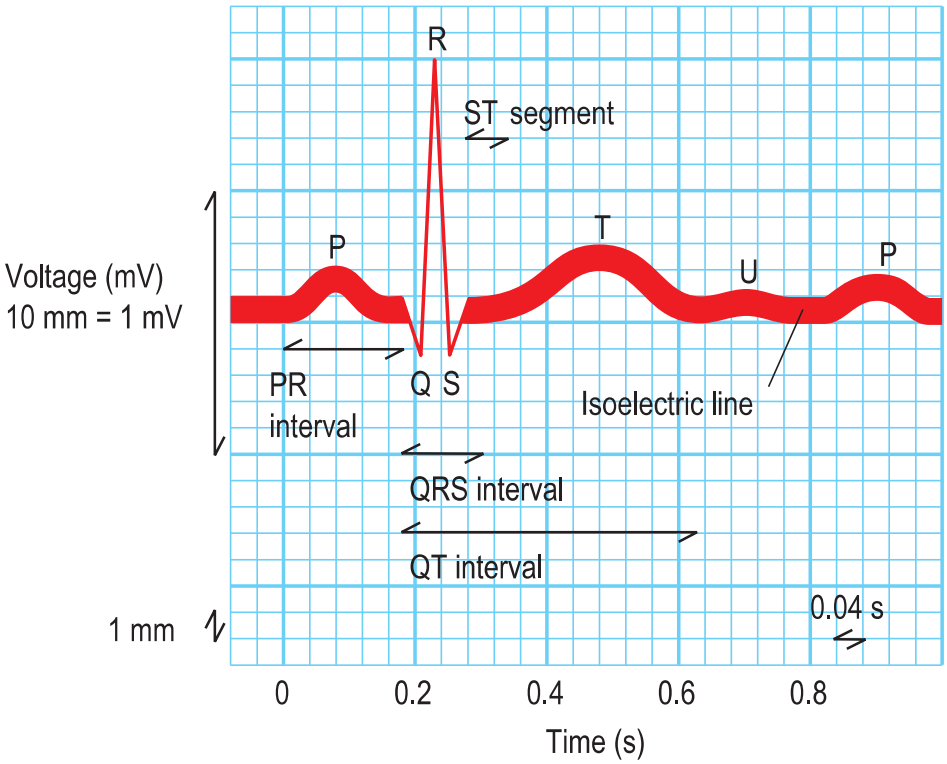


Fig. 10.5 The waves and elaboration of the normal ECG.

The *PR interval* is measured from the start of the P wave to the start of the QRS complex whether this is a Q wave or an R wave. It is the time taken for excitation to pass from the sinus node, through the atrium, atrioventricular node and His-Purkinje system to the ventricle. A prolonged PR interval (>0.2 s) indicates heart block (p. 423).

The *ST segment* is the period between the end of the QRS complex and the start of the T wave. ST elevation (>1 mm above the isoelectric line) occurs in the early stages of MI (p. 453) and with acute pericarditis (p. 458). ST segment depression (>0.5 mm below the isoelectric line) indicates myocardial ischaemia.

The *QT interval* extends from the start of the QRS complex to the end of the T wave. It is primarily a measure of the time taken for repolarization of the ventricular myocardium, which is dependent on heart rate (shorter at faster heart rates). The QT interval, corrected for heart rate ($QTc = QT/\sqrt{^2}(R-R)$), is normally ≤ 0.44 s in males and ≤ 0.46 s in females. Long QT syndrome (p. 433) is associated with an increased risk of torsades de pointes ventricular tachycardia and sudden death.

The *cardiac axis* refers to the overall direction of the wave of ventricular depolarization in the vertical plane measured from a zero reference point (Fig. 10.6). The normal range for the cardiac axis is between −30° and +90. An axis more negative than −30° is termed left axis deviation and an axis more positive than +90° is termed right axis deviation. A simple method to calculate the axis is by inspection of the QRS complex in leads I, II and III. The axis

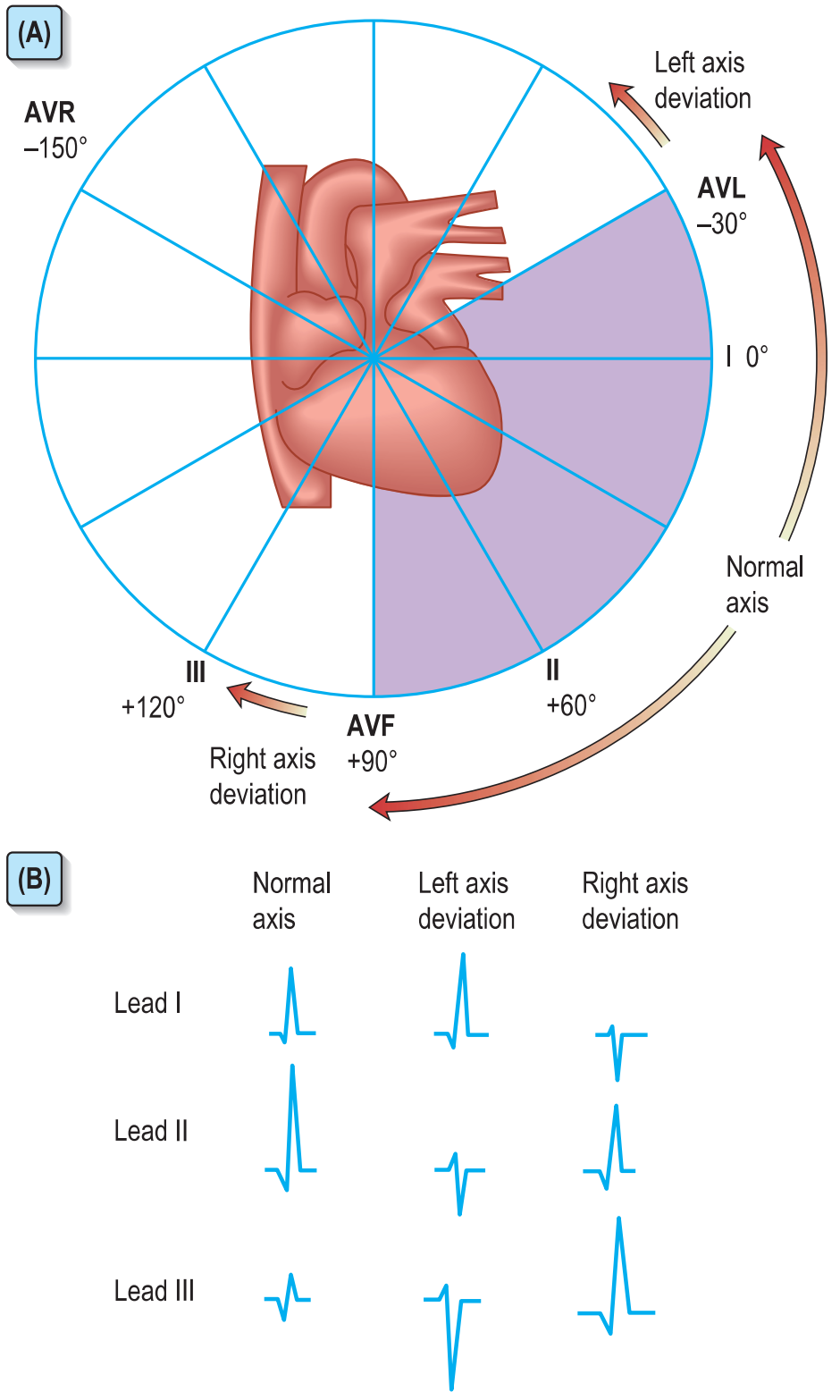


Fig. 10.6 Cardiac vectors. (A) The hexaxial reference system, illustrating the six leads in the frontal plane, e.g. lead I is 0°, lead II is +60°, lead III is 120°. (B) ECG leads showing the predominant positive and negative deflection with axis deviation.

is normal if leads I and II are positive; there is right axis deviation if lead I is negative and lead III positive, and left axis deviation if lead I is positive and leads II and III negative. Left axis deviation occurs due to a block of the anterior bundle of the main left bundle conducting system (Fig. 10.2), inferior MI and the Wolff–Parkinson–White syndrome. Right axis deviation may be normal and occurs in conditions in which there is right ventricular overload, dextrocardia, Wolff–Parkinson–White syndrome and left posterior hemiblock.

Exercise electrocardiography

Exercise electrocardiography assesses the cardiac response to exercise, but is used less often than previously because of its low sensitivity. The 12-lead ECG and BP are recorded whilst the patient walks or runs on a motorized treadmill using a standardized method (e.g. the Bruce protocol). Myocardial ischaemia provoked by exertion results in ST segment depression (>1 mm) in leads facing the affected area of ischaemic cardiac muscle. Exercise normally causes an increase in heart rate and BP. A sustained fall in BP usually indicates severe coronary artery disease. A slow recovery of the heart rate to basal levels has also been reported to be a predictor of mortality. Contraindications include unstable angina, severe hypertrophic cardiomyopathy, severe aortic stenosis and malignant hypertension. A positive test and indications for stopping the test are:

- Chest pain
- ST segment depression or elevation >1 mm
- Fall in systolic BP >20 mmHg
- Fall in heart rate despite an increase in workload
- BP $>240/110$
- Significant arrhythmias or increased frequency of ventricular ectopics.

24-hour ambulatory taped electrocardiography

A 12-lead ECG is recorded continuously over a 24-hour period and is used to record transient changes such as a brief paroxysm of tachycardia, an occasional pause in rhythm or intermittent ST segment shifts. It is also called 'Holter' electrocardiography after its inventor. Event recording is used to record less frequent arrhythmias in which the patient triggers an ECG recording at the time of symptoms. They are both outpatient investigations.

Tilt testing

Tilt testing is performed to investigate suspected neurocardiogenic (vasovagal) syncope in which patients give a history of repeated episodes of syncope which occur without warning and are followed by a rapid recovery. The patient lies on a swivel motorized table in a flat position with safety straps applied across the chest and legs to hold them in position. BP, heart rate, symptoms and ECG are recorded after the table is tilted $+60^\circ$ to the vertical for 10–60 minutes, thus

simulating going from a flat to an upright position. Reproduction of symptoms, bradycardia or hypotension indicates a positive test. The overall sensitivity, specificity and reproducibility are low.

Echocardiography

Echocardiography is an ultrasound examination of the heart (Fig. 10.7). Different modalities (e.g. M mode, two- and three-dimensional) are used to provide information about cardiac structure and function. The examination is performed in two ways:

- *Transthoracic echo* is the most common method and involves the placement of a handheld transducer on the chest wall. Ultrasound pulses are emitted through various body tissues, and reflected waves are detected by the transducer as an echo. The most common reasons for undertaking an echocardiogram are to assess ventricular function in patients with symptoms suggestive of heart failure, or to assess valvular disease. Left ventricular function is assessed by the ejection fraction (percentage of blood ejected from the left ventricle with each heartbeat) – normally $>55\%$.
- *Transoesophageal echo* uses miniaturized transducers incorporated into special endoscopes. It allows better visualization of some structures and pathology, e.g. aortic dissection, endocarditis.

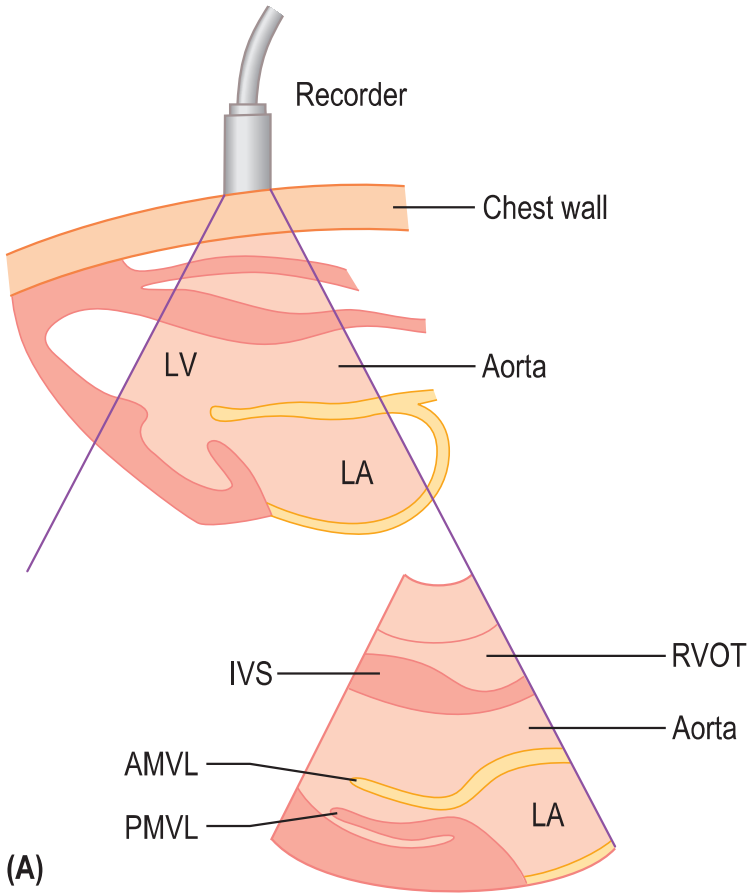
Further refinements of the echocardiogram are Doppler and stress echocardiography. Doppler echocardiography uses the Doppler principle (in this case, the frequency of ultrasonic waves reflected from blood cells is related to their velocity and direction of flow) to identify and assess the severity of valve lesions, estimate cardiac output and assess coronary blood flow. Stress (exercise or pharmacological) echocardiography is used to assess myocardial wall motion as a surrogate for coronary artery perfusion. It is used in the detection of coronary artery disease, assessment of risk post-MI and perioperatively, and in patients in whom routine exercise ECG testing is non-diagnostic. For those who cannot exercise, pharmacological intervention with dobutamine is used to increase myocardial oxygen demand.

Cardiac nuclear imaging

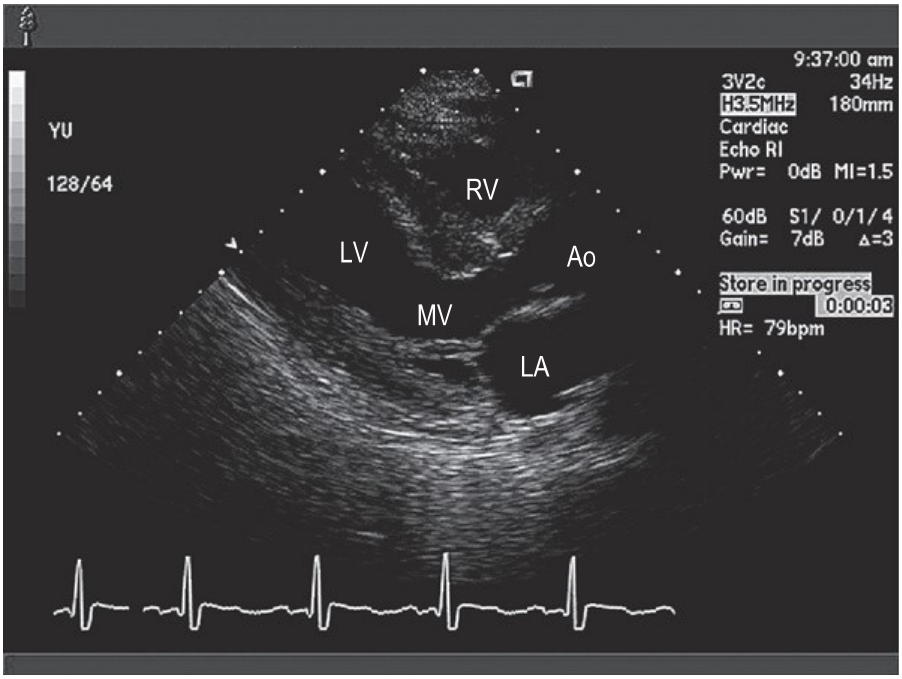
Cardiac nuclear imaging is used to detect MI or to measure myocardial function, perfusion or viability, depending on the radiopharmaceutical used and the technique of imaging. A variety of radiotracers can be injected intravenously and these diffuse freely into myocardial tissue or attach to red blood cells.

Thallium-201 is taken up by cardiac myocytes. Ischaemic areas (produced by exercising the patient) with reduced tracer uptake are seen as 'cold spots' when imaged with a γ camera.

Technetium-99 m is used to label red blood cells and produce images of the left ventricle during systole and diastole.



(A)



(B)

Fig. 10.7 **Echocardiogram: an example of a two-dimensional long-axis view.** (A) Diagram showing the anatomy of the area scanned and a diagrammatic representation of the echocardiogram. (B) Two-dimensional long-axis view. AMVL, anterior mitral valve leaflet; Ao, aorta; IVS, Inter-ventricular septum; LA, left atrium; LV, left ventricle; MV, mitral valve; PMVL, posterior mitral valve leaflet; RV, right ventricle; RVOT, right ventricular outflow tract.

Cardiac computed tomography

Computed tomography (CT) is useful for the assessment of the thoracic aorta and mediastinum, and multidetector thin slice scanners can assess calcium content of coronary arteries as an indicator of the presence and severity of coronary artery stenoses. CT coronary angiography has high sensitivity for the detection of coronary artery diseases. The current National Institute for Health and Care Excellence (NICE) chest pain guidelines recommend the use of CT calcium scoring in patients with chest pain and a 10–29% likelihood of coronary artery disease.

Cardiovascular magnetic resonance

Cardiovascular magnetic resonance (CMR) is a non-invasive imaging technique that does not involve harmful radiation. It is increasingly utilized in the investigation of cardiovascular disease to provide both anatomical and functional information. Contraindications are permanent pacemaker or defibrillator, intracerebral clips and significant claustrophobia. Coronary stents and prosthetic valves are not a contraindication.

Cardiac catheterization

A small catheter is passed through a peripheral vein (for study of right-sided heart structures) or artery (for study of left-sided heart structures) into the heart, permitting the securing of blood samples, measurement of intracardiac pressures and determination of cardiac anomalies. Specially designed catheters are then used to selectively engage the left and right coronary arteries, and contrast cine-angiograms are taken in order to define the coronary circulation and identify the presence and severity of any coronary artery disease. Coronary artery stenoses can be dilated (angioplasty) and metal stents can be placed to reduce the rate of restenosis – this is referred to as percutaneous coronary intervention (PCI). A further development is the introduction of stents coated with drugs (sirolimus or paclitaxel) to reduce cellular proliferation and restenosis rates still further. However, there is a risk of late-stent thrombosis.

CARDIAC ARRHYTHMIAS

An abnormality of cardiac rhythm is called a cardiac arrhythmia. Arrhythmia may cause sudden death, syncope, dizziness, palpitations or no symptoms at all. Twenty-four-hour ambulatory ECG monitoring and event recorders (p. 418) are often used to detect paroxysmal arrhythmias.

There are two main types of arrhythmia:

- *Bradycardia:* the heart rate is slow (<60 beats/min). Slower heart rates are more likely to cause symptomatic arrhythmias.
- *Tachycardia:* the heart rate is fast (>100 beats/min). Tachycardias are more likely to be symptomatic when the arrhythmia is fast and sustained. They are subdivided into *supraventricular tachycardias* (SVTs), which arise

from the atrium or the atrioventricular junction, and *ventricular tachycardias*, which arise from the ventricles.

Arrhythmias and conduction disturbances complicating acute MI are discussed on page 457.

General principles of management of arrhythmias

Patients with adverse symptoms and signs (low cardiac output, chest pain, hypotension, impaired consciousness or severe pulmonary oedema) require urgent treatment of their arrhythmia. Oxygen is given to all patients, intravenous access established and serum electrolyte abnormalities (potassium, magnesium, calcium) are corrected.

Sinus rhythms

The normal cardiac pacemaker is the sinus node (p. 411) with the rate of sinus node discharge under control of the autonomic nervous system with parasympathetic predominating (resulting in slowing of the spontaneous discharge rate).

Sinus arrhythmia

Fluctuations of autonomic tone result in phasic changes in the sinus discharge rate. During inspiration, parasympathetic tone falls and the heart rate quickens, and on expiration the heart rate falls. This variation is normal, particularly in children and young adults, and typically results in predictable irregularities of the pulse.

Bradycardia

Sinus bradycardia

Sinus bradycardia is normal during sleep and in well-trained athletes. Causes are:

- *Extrinsic to the heart:* drug therapy (β-blockers, digitalis and other antiarrhythmic drugs), hypothyroidism, hypothermia, cholestatic jaundice, raised intracranial pressure. Treatment of symptomatic bradycardia is that of the underlying cause.
- *Intrinsic to the heart:* acute ischaemia and infarction of the sinus node (as a complication of MI) and chronic degenerative changes such as fibrosis of the atrium and sinus node (sick sinus syndrome) occurring in elderly people. Patients with persistent symptomatic bradycardia are treated with a permanent cardiac pacemaker. First-line treatment in the acute situation with adverse signs is atropine (500 μg intravenously repeated to a maximum of 3 mg, but contraindicated in myasthenia gravis and paralytic ileus). Temporary pacing (transcutaneous, or transvenous if expertise available) is an alternative.

- *Sick sinus syndrome.* Bradycardia is caused by intermittent failure of sinus node depolarization (sinus arrest) or failure of the sinus impulse to propagate through the perinodal tissue to the atria (sinoatrial block). The slow heart rate predisposes to ectopic pacemaker activity and tachyarrhythmias are common (tachy–brady syndrome). The ECG shows severe sinus bradycardia or intermittent long pauses between consecutive P waves (>2 s, dropped P waves). Permanent pacemaker insertion is indicated in symptomatic patients. Antiarrhythmic drugs are used to treat tachycardias. Thromboembolism is common in sinus node dysfunction and patients are anticoagulated unless there is a contraindication.
- Neurally mediated, e.g. carotid sinus syndrome and vasovagal attacks, resulting in bradycardia and syncope.

Heart block

The common causes of heart block are coronary artery disease, cardiomyopathy and, particularly in elderly people, fibrosis of the conducting tissue. Block in either the AV node or the His bundle results in AV block, whereas block lower in the conduction system (Fig. 10.2) produces right or left bundle branch block.

Atrioventricular block

There are three forms:

First-degree AV block This is the result of delayed atrioventricular conduction and is reflected by a prolonged PR interval (>0.22 s) on the ECG. No change in heart rate occurs and treatment is unnecessary.

Second-degree AV block This occurs when some atrial impulses fail to reach the ventricles.

There are several forms (Fig. 10.8):

- *Mobitz type I* (Wenckebach) *block* is generally caused by AV node block and results in progressive PR interval prolongation until a P wave fails to conduct, i.e. absent QRS after the P wave. The PR interval then returns to normal and the cycle repeats itself.
- *Mobitz type II block* is due to a block at an infra-nodal level so the QRS is widened and QRS complexes are dropped without PR prolongation. The ratio of non-conducted P waves to QRS complexes is usually specified. For example, a 2:1 Mobitz type II block refers to two P waves for every QRS complex.

Progression from second-degree AV block to complete heart block occurs more frequently following acute anterior MI and in Mobitz type II block, and treatment is with a cardiac pacemaker. Patients with Wenckebach AV block or those with second-degree block following acute inferior infarction are usually monitored.

Third-degree AV block Complete heart block occurs when there is complete dissociation between atrial and ventricular activity; P waves and QRS complexes occur independently of one another and ventricular contractions

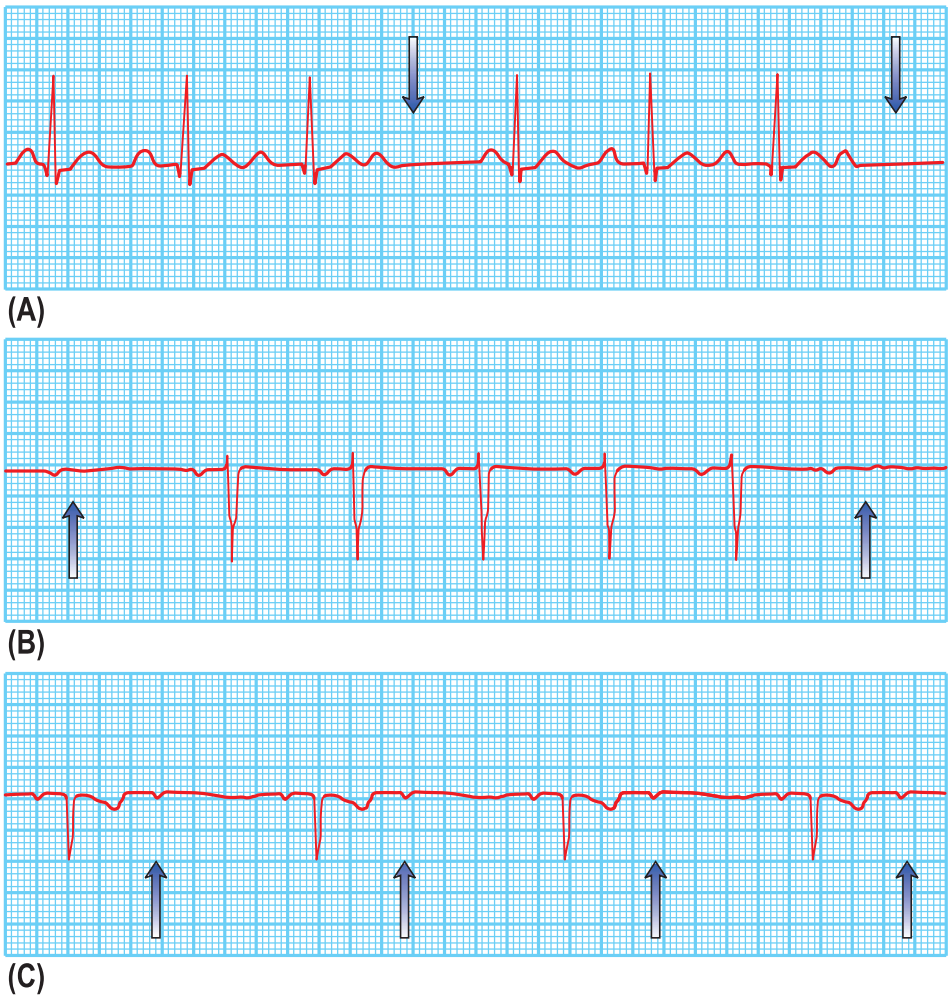


Fig. 10.8 **Three varieties of second-degree atrioventricular (AV) block.** (A) Wenckebach (Mobitz type I) AV block. The PR interval gradually prolongs until the P wave does not conduct to the ventricles (arrows). (B) Mobitz type II AV block. The P waves that do not conduct to the ventricles (arrows) are not preceded by gradual PR interval prolongation. (C) Two P waves to each QRS complex. The PR interval prior to the dropped P wave is always the same. It is not possible to define this type of AV block as type I or type II Mobitz block and it is, therefore, a third variety of second-degree AV block (arrows show P waves), not conducted to the ventricles.

are maintained by a spontaneous escape rhythm originating below the site of the block in the:

- *His bundle* (Fig. 10.2) – which gives rise to a narrow complex QRS (<0.12 s) at a rate of 50–60 beats/min and is relatively reliable. Recent onset block due to transient causes, e.g. ischaemia, may respond to intravenous atropine (p. 422) without the need for pacing. Chronic narrow-complex AV block usually requires permanent pacing.
- *His-Purkinje system* (i.e. distally) – gives rise to a broad QRS complex (>0.12 s), is slow (<40 beats/min), unreliable and often associated with dizziness and blackouts (Stokes–Adams attacks). Permanent pacemaker insertion is indicated.

Bundle branch block

Complete block of a bundle branch (see Fig. 10.2) is associated with a wide QRS complex ($\geq$0.12 s) with an abnormal pattern and is usually asymptomatic. The shape of the QRS depends on whether the right or the left bundle is blocked (Fig. 10.9):

- Right bundle branch block (RBBB) – there is sequential spread of an impulse (i.e. first the left ventricle and then the right) resulting in a secondary R wave (RSR′) in V_1 and a slurred S wave in V_5 and V_6. RBBB occurs in normal healthy individuals, pulmonary embolus, right ventricular hypertrophy, ischaemic heart disease and congenital heart disease, e.g. atrial and ventricular septal defect and Fallot's tetralogy.
- Left bundle branch block (LBBB – the opposite occurs with an RSR′ pattern in the left ventricular leads (I, AVL, V_4–V_6) and deep slurred S waves in V_1 and V_2. LBBB indicates underlying cardiac pathology and occurs in aortic stenosis, hypertension, severe coronary artery disease and following cardiac surgery.

Supraventricular tachycardias

SVTs arise from the atrium or the atrioventricular junction. Conduction is via the His-Purkinje system and the QRS shape during tachycardia is usually similar to that seen in the same patient during baseline rhythm.

Sinus tachycardia

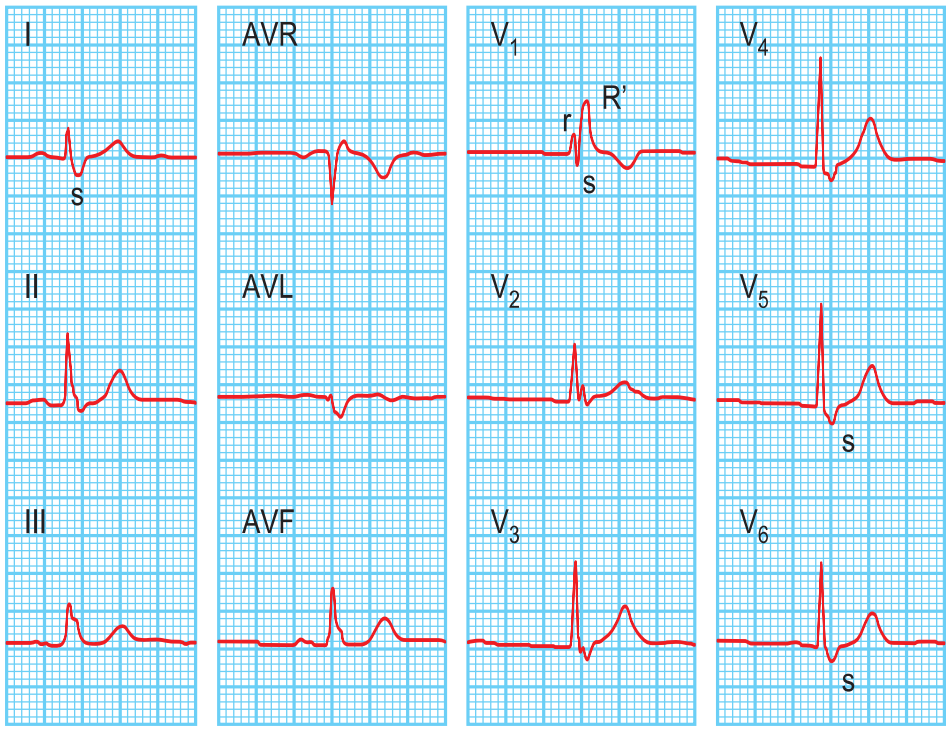
Sinus tachycardia is a physiological response during exercise and excitement. It also occurs with fever, pain, anaemia, heart failure, thyrotoxicosis, acute pulmonary embolism, hypovolaemia and drugs (e.g. catecholamines and atropine). Treatment is aimed at correction of the underlying cause. If necessary, β-blockers may be used to slow the sinus rate, e.g. in hyperthyroidism.

Atrioventricular junctional tachycardias

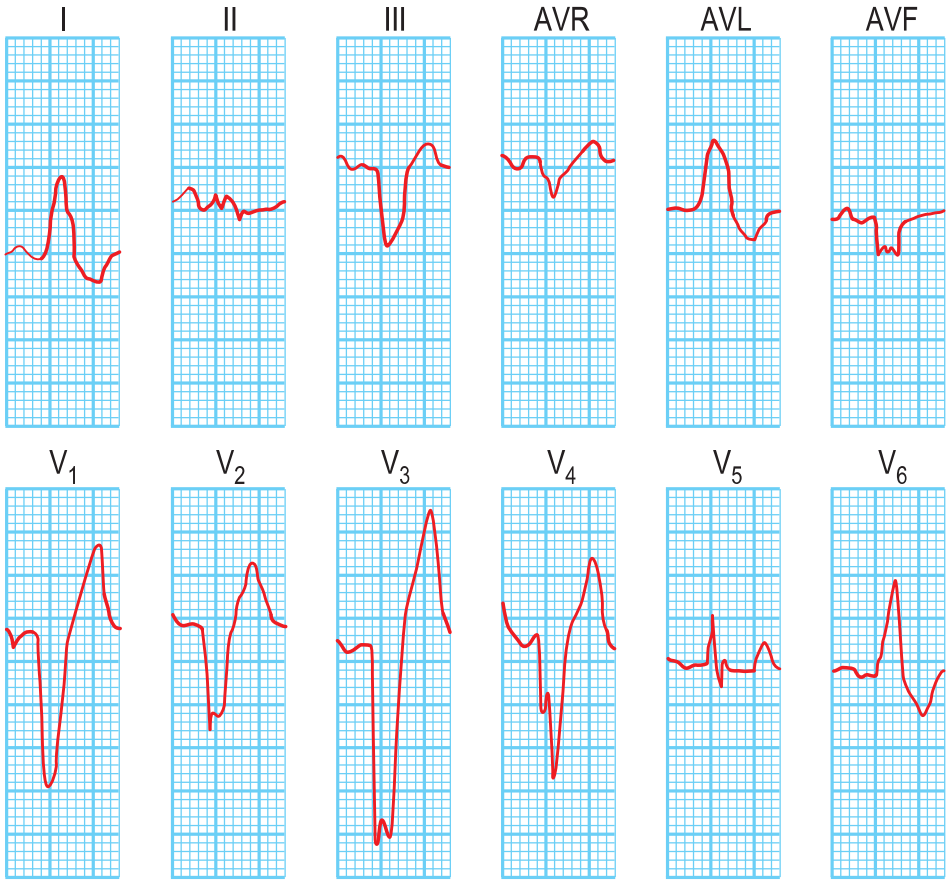
Tachycardia arises as a result of re-entry circuits in which there are two separate pathways for impulse conduction. They are usually referred to as paroxysmal SVTs and are often seen in young patients with no evidence of structural heart disease.

Atrioventricular nodal re-entry tachycardia

AVNRT is the most common type of SVT and is twice as common in women as in men. It is due to the presence of a 'ring' of conducting pathway in the AV node, of which the 'limbs' have differing conduction times and refractory periods. This allows a re-entry circuit and an impulse to produce a circus movement tachycardia. On the ECG, the P waves are either not visible or are seen immediately before or after the QRS complex (Fig. 10.10). The QRS complex is usually of normal shape because the ventricles are activated in the normal way. Occasionally the QRS complex is wide, because of a rate-related bundle branch



(A)



(B)

Fig. 10.9 Bundle branch block. A 12-lead ECG showing (A) right bundle branch block. Note an RSR pattern with the tall R in lead V_1–V_2 and the broad S waves in leads I and V_5 and V_6. (B) Left bundle branch block. The QRS duration is greater than 0.12 s. Note the broad notched R waves with ST depression in leads I, AVL and V_6, and the broad QRS waves in V_1–V_3.

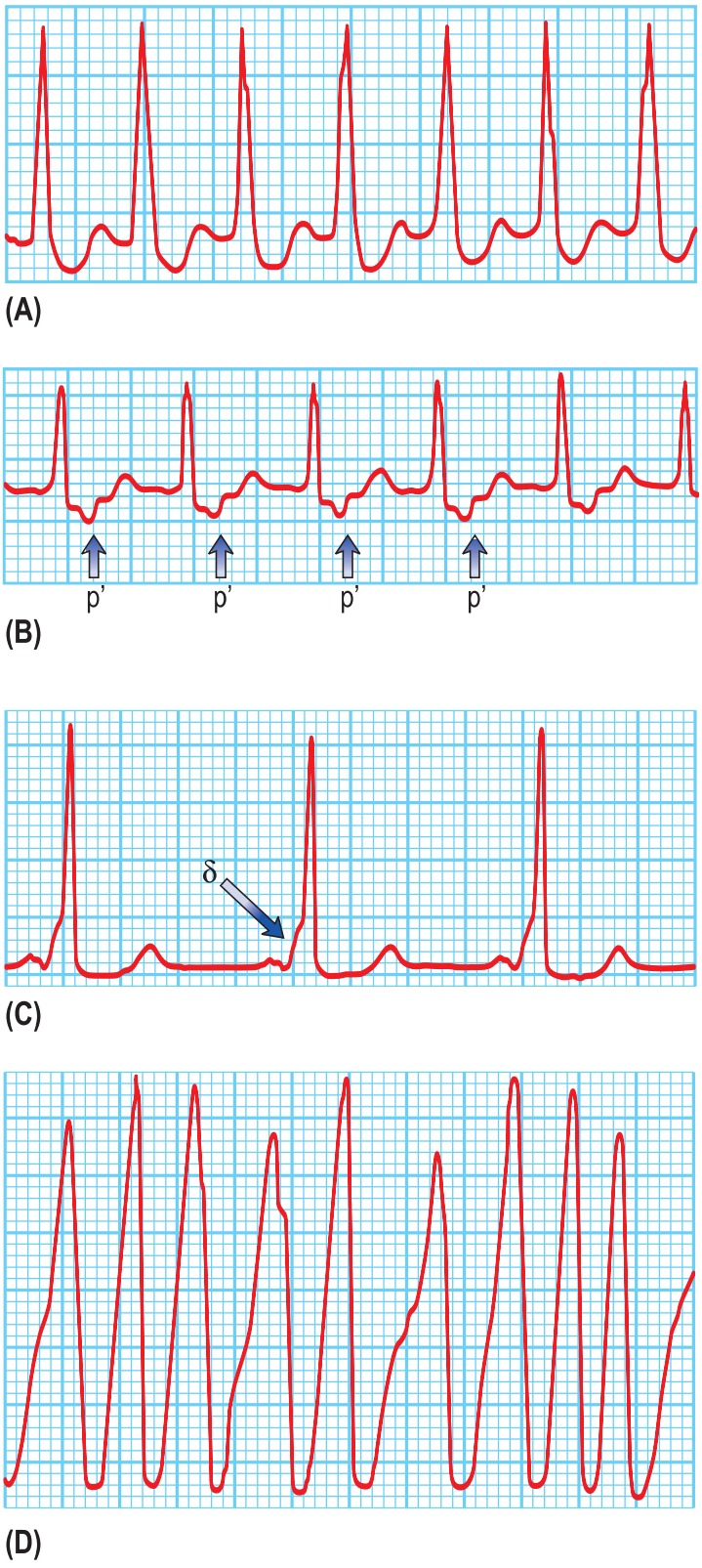


Fig. 10.10 Atrioventricular junctional tachycardia. (A) Atrioventricular nodal re-entry tachycardia. The QRS complexes are narrow and the P waves cannot be seen. (B) Atrioventricular re-entry tachycardia (Wolff–Parkinson–White [WPW] syndrome). The tachycardia P waves (arrows) are clearly seen after narrow QRS complexes. (C) An electrocardiogram taken in a patient with WPW syndrome during sinus rhythm. Note the short PR interval and the δ wave (arrow). (D) Atrial fibrillation in the WPW syndrome. Note tachycardia with broad QRS complexes with fast and irregular ventricular rate.

Table 10.3 Clinical indicators for the identification of sustained ventricular tachycardia (12-lead ECG) in a patient presenting with wide complex tachycardia

Ventricular tachycardia is more likely than supraventricular tachycardia with:
History of ischaemic heart disease
QRS interval > 140 ms
Atrioventricular dissociation – P waves have no relationship to the QRS complexes
Capture complexes – intermittent normal QRS complex
RS interval > 100 ms
Bifid, upright QRS complex with a taller first peak in V_1
Deep S wave in V_6
Concordant QRS direction in leads V_1–V_6, i.e. all positive or all negative complexes

block, and it may be difficult to distinguish from ventricular tachycardia (Table 10.3).

Atrioventricular reciprocating tachycardia

AVRT is due to the presence of an accessory pathway that connects the atria and ventricles and is capable of antegrade or retrograde conduction, or both. In contrast to AVNRT, each part of the circuit is activated sequentially in, so atrial activation occurs after ventricular activation and the P wave is usually clearly seen between the QRS and T wave. Wolff–Parkinson–White syndrome is the best-known type of AVRT in which there is an accessory pathway (bundle of Kent) between atria and ventricles. The resting ECG in Wolff–Parkinson–White syndrome shows evidence of the pathway's existence if the path allows some of the atrial depolarization to pass quickly to the ventricle before it gets through the AV node. The early depolarization of part of the ventricle leads to a shortened PR interval and a slurred start to the QRS (delta wave). The QRS is narrow (Fig. 10.10). These patients are also prone to atrial and occasionally ventricular fibrillation.

Symptoms

The usual history is of rapid regular palpitations, usually with abrupt onset and sudden termination. Other symptoms are dizziness, dyspnoea, central chest pain and syncope. Exertion, coffee, tea or alcohol may aggravate the arrhythmia.

Acute management

The aim of treatment is to restore and maintain sinus rhythm:

- *Unstable patient* – emergency cardioversion is required in patients whose arrhythmia is accompanied by adverse symptoms and signs.

- *Haemodynamically stable patient:*
  - Increase vagal stimulation of the sinus node by the Valsalva manoeuvre (ask the patient to blow into a 20-mL syringe with enough force to push back the plunger) or right carotid sinus massage (contraindicated in the presence of a carotid bruit).
  - Adenosine (p. 491) is a very short-acting AV nodal-blocking drug that will terminate most junctional tachycardias. Other treatments are intravenous verapamil (p. 501) or β-blockers, e.g. metoprolol. Verapamil is contraindicated with β-blockers, if the QRS is wide and therefore differentiation from VT difficult or if there is atrial fibrillation (AF) and an accessory pathway.

Long-term management

Radiofrequency ablation of the accessory pathway via a cardiac catheter is successful in about 95% of cases. Flecainide, verapamil, sotalol and amiodarone are the drugs most commonly used.

Atrial tachyarrhythmias

AF, flutter, tachycardia and ectopic beats all arise from the atrial myocardium. In some cases, automaticity is acquired by damaged atrial cells. They share common aetiologies (Table 10.4). Baseline investigations in a patient with an atrial arrhythmia include an ECG, thyroid function tests and transthoracic echocardiogram.

Table 10.4 Causes of atrial arrhythmias

General
Hypertension, age, obesity
Cardiac
Ischaemic heart disease, rheumatic heart disease, valvular heart disease Cardiomyopathy Lone atrial fibrillation (no cause identified) Wolff–Parkinson–White syndrome Pericarditis, myocarditis Atrial septal defect, cardiac surgery
Pulmonary
Pneumonia, pulmonary embolus, carcinoma of the bronchus, chronic obstructive pulmonary disease
Metabolic
Acute and chronic alcohol use, electrolyte imbalance,
Endocrine
Diabetes mellitus, thyrotoxicosis

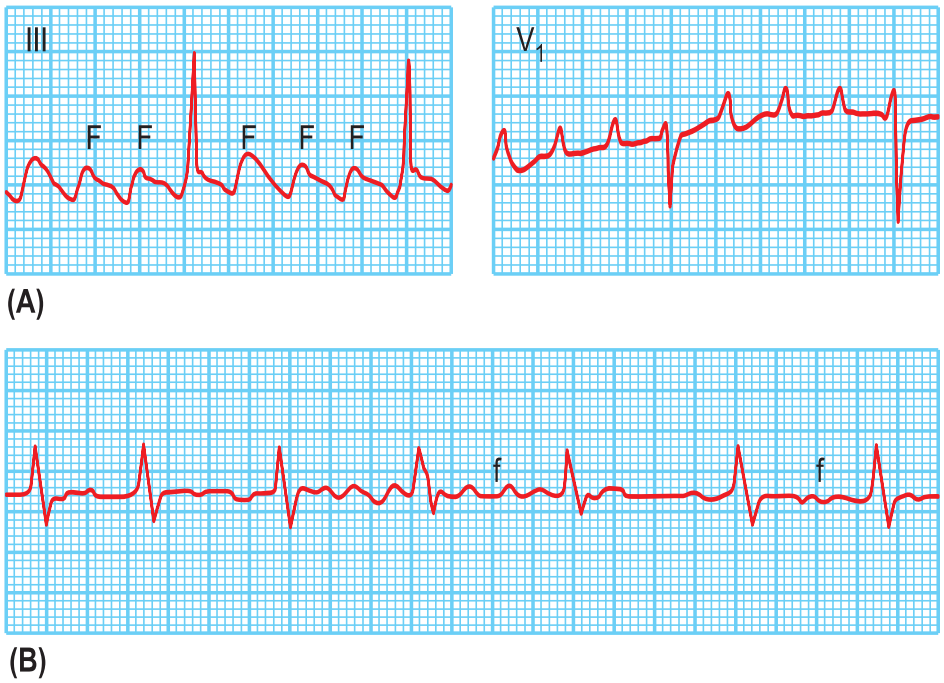


Fig. 10.11 Atrial flutter and atrial fibrillation. (A) Atrial flutter: the flutter waves are marked with an F, only half of which are transmitted to the ventricles. (B) Atrial fibrillation: there are no P waves; the ventricular response is fast and irregular.

Atrial fibrillation

AF is the most common arrhythmia and occurs in 15% of patients over 75 years of age. It also occurs, particularly in a paroxysmal form (stopping spontaneously within 7 days), in younger patients. Atrial activity is chaotic and mechanically ineffective. The AV node conducts a proportion of the atrial impulses to produce an irregular ventricular response – giving rise to an irregularly irregular pulse. In some patients, it is an incidental finding; in others, symptoms range from palpitations and fatigue to acute heart failure. AF is associated with a five-fold increased risk of stroke, primarily as a result of embolism of a thrombus that has formed in the atrium. There are no clear P waves on the ECG (Fig. 10.11), only a fine oscillation of the baseline (so-called fibrillation or f waves).

Management

When AF is caused by an acute precipitating event, the underlying cause should be treated:

- *Haemodynamically unstable patient* (p. 422) – immediate heparinization and attempted *cardioversion with a synchronized DC shock (p. 490).*
  If cardioversion fails or AF recurs, intravenous amiodarone is given (p. 491) before a further attempt at cardioversion. A second dose of amiodarone can be given.
- *Stable patient* – two strategies are available for the long-term management of AF: rate control or rhythm control (i.e. conversion to, and maintaining

sinus rhythm). Randomized studies in heart failure and in older patients have shown that neither strategy has net benefits compared with the other.

- *Rate control* aims to reduce heart rate at rest and during exercise, but the patient remains in AF. β-blockers (p. 495) or calcium antagonists (verapamil, diltiazem, p. 501) are the preferred treatment except in predominantly sedentary people where digoxin (p. 493) is used.
- *Rhythm control* is generally appropriate in patients who are < 65 years of age, highly symptomatic, patients with heart failure and individuals with recent onset AF (<48 h). Conversion to sinus rhythm is achieved by electrical DC cardioversion (p. 490) and then administration of β-blockers to suppress the arrhythmia. Other agents used depend on the presence (use amiodarone) or absence (sotalol, flecainide, propafenone) of underlying heart disease. Catheter ablation techniques such as pulmonary vein isolation are used in patients who do not respond to antiarrhythmic drugs.
  Patients with infrequent symptomatic paroxysms of AF (less than one per month) that are haemodynamically well tolerated and whom have little underlying heart disease are treated on an as-needed basis ('pill in the pocket') with oral flecainide (p. 493) or propafenone.

Assessment for anticoagulation

AF is associated with an increased risk of thromboembolism, and anticoagulation with warfarin or with dabigatran 150 mg twice daily should be given for at least 3 weeks before (with the exception of those who require emergency cardioversion or new-onset AF < 48 h duration) and 4 weeks after cardioversion. Longer-term anticoagulation is indicated in underlying rheumatic mitral stenosis or in the presence of a mechanical heart valve. Otherwise, a scoring system known as $CHADS_2$ (Congestive heart failure, Hypertension, Age ≥75, Diabetes mellitus and previous Stroke or transient ischaemic attack [TIA]) is used to determine the need for anticoagulation. Each factor scores 1 except previous stroke or TIA, which scores 2. A total score of 2 implies that oral anticoagulation is needed. When the score is <2 the $CHADS_2VASc$ scoring system is applied, which adds Vascular disease (aorta, coronary or peripheral arteries), Age 65–74 and female Sex category. Each factor scores 1, except previous age >75 and stroke or TIA, which score 2. A $CHADS_2VASc$ score of 2 requires oral anticoagulation and a score of 1 merits consideration for oral anticoagulation or aspirin. A score of 0 should not require any antithrombotic prophylaxis.

When oral anticoagulation is required, either warfarin (international normalized ratio [INR] 2.0–3.0) or one of the novel oral anticoagulants (NOACs) can be used. These newer agents fall into two classes: direct thrombin inhibitors (e.g. dabigatran) and oral direct factor Xa inhibitors (e.g. rivaroxaban and apixaban). NOACs specifically block a single step in the coagulation cascade in contrast to warfarin, which blocks several vitamin K-dependent factors (II, VII, IX and X). Unlike warfarin, the NOACs have rapid onset of action, shorter half-life, fewer

food and drug interactions and do not require INR testing. Trial data have shown them to be equally effective and safer as compared to warfarin. However, these agents require dose reduction or avoidance in patients with renal impairment, elderly patients or those with low body weight.

Atrial flutter

Atrial flutter is often associated with AF. The atrial rate is typically 300 beats/min and the AV node usually conducts every second flutter beat, giving a ventricular rate of 150 beats/min. The ECG (Fig. 10.11A) characteristically shows 'sawtooth' flutter waves (F waves), which are most clearly seen when AV conduction is transiently impaired by carotid sinus massage or drugs. The treatment of atrial flutter is similar to AF, except that most cases of flutter can be cured by radiofrequency catheter ablation of the re-entry circuit.

Ventricular tachyarrhythmias

Ventricular ectopic premature beats (extrasystoles)

These are asymptomatic or patients complain of extra beats, missed beats or heavy beats. The ectopic electrical activity is not conducted to the ventricles through the normal conducting tissue and thus the QRS complex on the ECG is widened, with a bizarre configuration (Fig. 10.12). Treatment is with β-blockers if symptomatic.

Sustained ventricular tachycardia

Ventricular tachycardia (VT) and ventricular fibrillation (VF) are usually associated with underlying heart disease. The ECG in sustained VT (>30 s) shows a rapid ventricular rhythm with broad abnormal QRS complexes. Supraventricular tachycardia with bundle branch block also produces a broad complex tachycardia, which can sometimes be differentiated from VT on ECG criteria (Table 10.3). However, the majority of broad complex tachycardias are VT and if in doubt treat as such. Urgent DC cardioversion is necessary if the patient

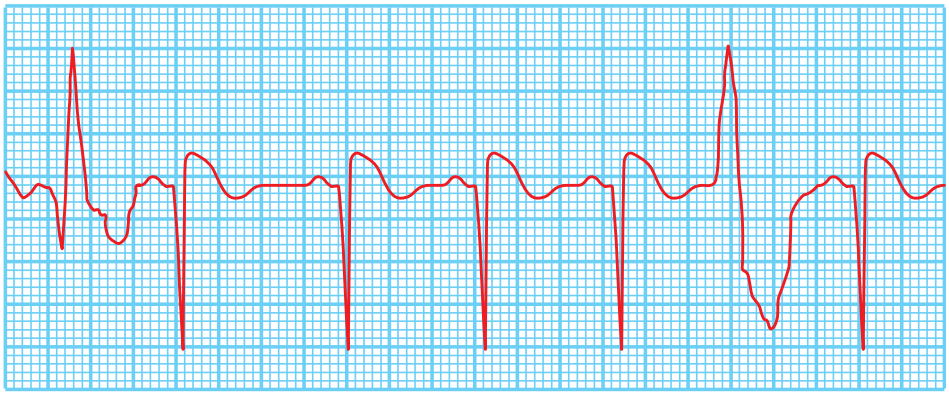


Fig. 10.12 A rhythm strip demonstrating two ventricular ectopic beats of different morphology (multimorphological).

is haemodynamically compromised (p. 422). If there is no haemodynamic compromise, treatment of VT is usually with intravenous β-blockers (esmolol) or amiodarone (p. 491). Recurrence is prevented with β-blockers or an implantable cardioverter–defibrillator (ICD). This is a small device implanted behind the rectus abdominis and connected to the heart; it recognizes VT or VF and automatically delivers a defibrillation shock to the heart.

Non-sustained ventricular tachycardia

This is defined as VT $\geq$ 5 consecutive beats but lasting $<$ 30 s. It is common in patients with heart disease (and in a few individuals with normal hearts). The treatments indicated are β-blockers in symptomatic patients or an ICD in patients with poor left ventricular function (ejection fraction $<$ 30%) in whom it improves survival.

Ventricular fibrillation

VF is a very rapid and irregular ventricular activation (Fig. 10.13) with no mechanical effect and hence no cardiac output. The patient is pulseless and becomes rapidly unconscious, and respiration ceases (cardiac arrest). Treatment is immediate defibrillation (Emergency Box 10.1). Survivors of VF are, in the absence of an identifiable reversible cause (e.g. during the first 2 days of acute MI, severe metabolic disturbance), at high risk of sudden death and treatment is with an ICD.

Long QT syndrome

Ventricular repolarization (QT interval) is greatly prolonged (p. 416). The causes include congenital (mutations in sodium and potassium-channel genes), electrolyte disturbances (hypokalaemia, hypocalcaemia, hypomagnesaemia) and a variety of drugs (e.g. tricyclic antidepressants, phenothiazines and macrolide antibiotics). Symptoms are palpitations and syncope, as a result of a polymorphic VT (torsade de pointes, rapid irregular sharp QRS complexes that

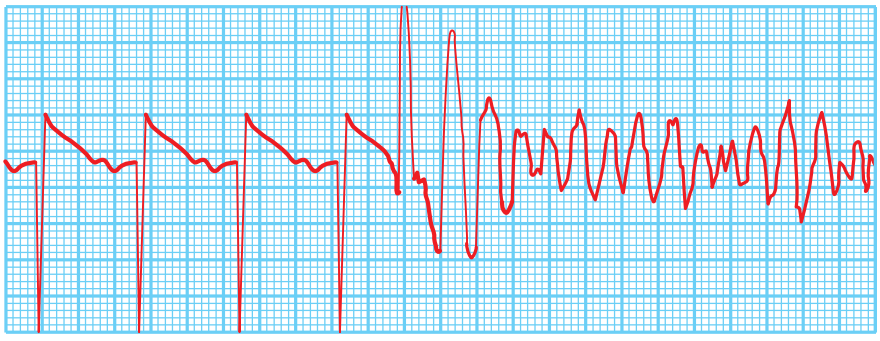


Fig. 10.13 A rhythm strip demonstrating four beats of sinus rhythm followed by a ventricular ectopic beat that initiates ventricular fibrillation. The ST segment is elevated owing to acute myocardial infarction.

Emergency Box 10.1

Basic life support (BLS)

- Assess if patient is responsive – gently shake shoulders and ask loudly 'Are you alright?'
- If there is no response, move onto AIRWAY. Call for help and ask for AED.

Airway

- Turn the victim on his/her back on a firm surface.
- Open the airway using head tilt and chin lift – place your hand on victim's forehead and tilt the head back and with fingertips underneath the point of the chin, lift the chin to open the airway.

Breathing

- Keeping the airway open, look (chest movement), listen (breath sounds) and feel (victim's expired air on your cheek) for normal breathing. Assess for no more than 10 seconds.
- If victim is not breathing normally, start chest compressions (see below).
- After 30 chest compressions, give two rescue breaths: use head tilt and chin lift, pinch the nose closed, take a breath and create a seal with your lips around his mouth, exhale over 1 minute. Watch for the rise and fall of the patient's chest, indicating adequate ventilation.

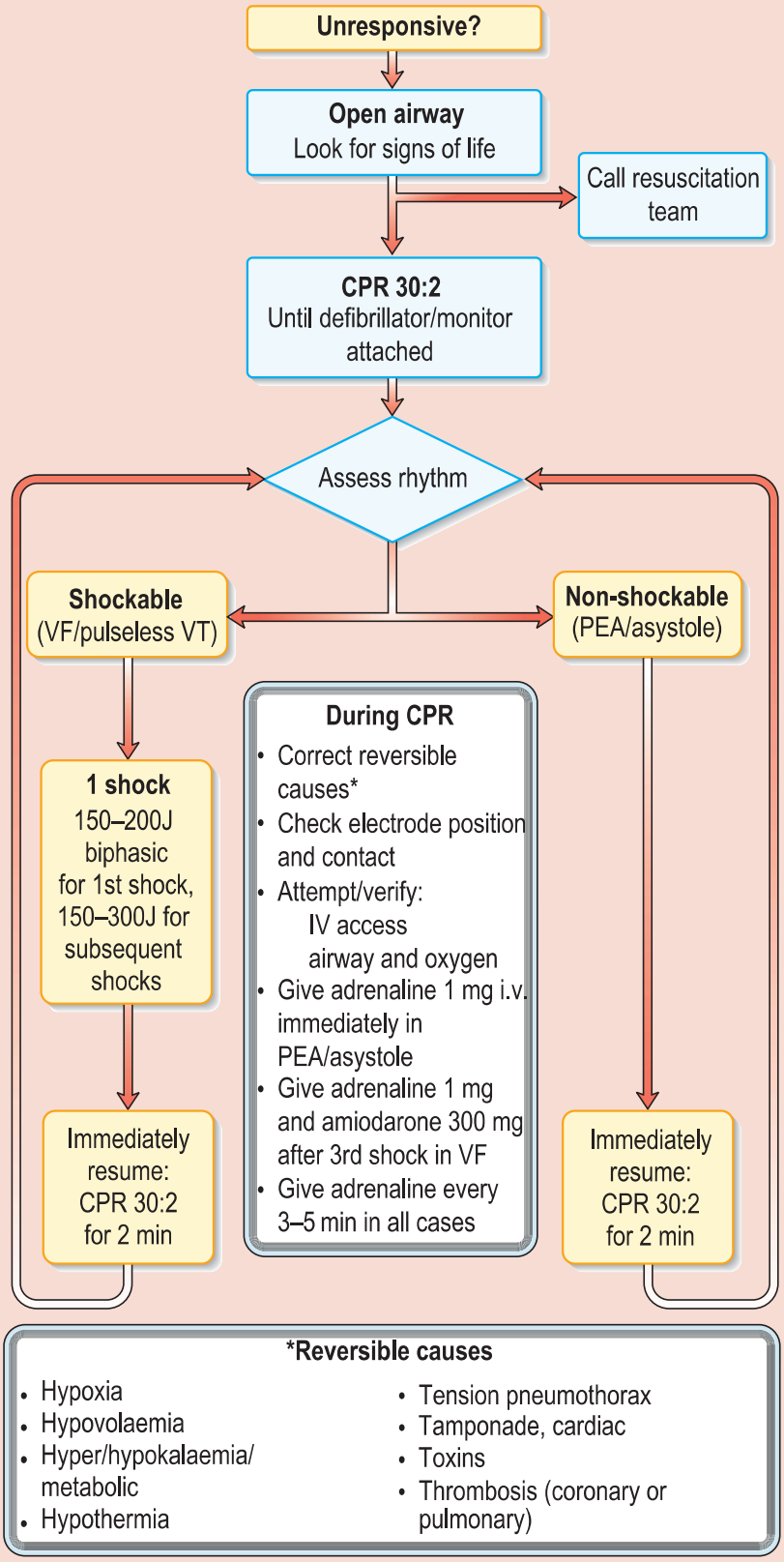
Circulation

- Circulation is assessed by palpation of the carotid pulse at the same time as assessing for respiratory effort.
- Circulation is achieved by external chest compression.
- Place the heel of one hand in the centre of the victim's chest. Place the heel of your other hand on top of the first hand. Interlock the fingers of your hands and with straight arms press down on the sternum 5–6 cm. After each compression, release all the pressure on the chest.
- Continue with chest compressions and rescue breaths in a ratio of 30:2 with 100–120 compressions per minute.
- Attach AED pads. AED assesses rhythm and delivers shock if indicated. Immediately resume CPR.

Advanced life support (ALS)

- Institute as soon as help arrives; continue cardiac massage throughout except during actual defibrillation.
- Give 100% O_2 via Ambu-bag, intubate as soon as possible and initiate positive-pressure ventilation.
- Establish intravenous access and connect ECG leads.
- Drugs administered by the peripheral route should be followed by a flush of 20 mL of 0.9% saline.
- If intravenous access not possible, give drugs by the intraosseous route (tibia and humerus).

Advanced life-support algorithm*



AED, Automated External Defibrillator; CPR, cardiopulmonary resuscitation; EMD, electromechanical dissociation; VF/VT, ventricular fibrillation/ventricular tachycardia; PEA, Pulseless Electrical Activity.

*Reproduced with permission from the Resuscitation Council; http://www.resus.org.uk

continuously change from an upright to an inverted position on the ECG), that usually terminates spontaneously but may degenerate into VF. In acquired cases, treatment is that of the underlying cause and intravenous isoprenaline.

Cardiac arrest

In cardiac arrest there is no effective cardiac output. The patient is unconscious and apnoeic with absent arterial pulses (best felt in the carotid artery in the neck). Irreversible brain damage occurs within 3 minutes if an adequate circulation is not established. Management is described in Emergency Box 10.1. Resuscitation is stopped when there is return of spontaneous circulation and a pulse, or further attempts at resuscitation are deemed futile. Post-resuscitation care centres on maintaining arterial oxygen saturation (94–98%), blood glucose values $<$10 mmol/L and therapeutic hypothermia.

Prognosis In many patients resuscitation is unsuccessful, particularly in those who collapse out of hospital and are brought into hospital in an arrested state. In patients who are successfully resuscitated, the prognosis is often poor because they have severe underlying heart diseases. The exceptions are those who are successfully resuscitated from a VF arrest in the early stages of MI, when the prognosis is much the same as for other patients with an infarct.

Studies suggest that therapeutic hypothermia (32–34°C for 12–24 hours) might improve neurological outcomes in unconscious adult patients with spontaneous circulation after an out-of-hospital cardiac arrest due to ventricular fibrillation.

HEART FAILURE

Heart failure is a complex syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the heart to function as a pump and maintain sufficient cardiac output to meet the demands of the body. It is a common condition, with an estimated annual incidence of 10% in patients over 65 years. The long-term outcome is poor and approximately 50% of patients are dead within 5 years.

Aetiology

Ischaemic heart disease is the most common cause in the developed world and hypertension is the most common cause in Africa (Table 10.5). Any factor that increases myocardial work (arrhythmias, anaemia, hyperthyroidism, pregnancy, obesity) may aggravate existing heart failure or initiate failure.

Pathophysiology

When the heart fails, compensatory mechanisms attempt to maintain cardiac output and peripheral perfusion. However, as heart failure progresses, the mechanisms are overwhelmed and become pathophysiological. These mechanisms involve the following factors.

Table 10.5 Causes of heart failure

Main causes
Ischaemic heart disease
Cardiomyopathy (dilated)
Hypertension
Other causes
Cardiomyopathy (hypertrophic, restrictive)
Valvular heart disease (mitral, aortic, tricuspid)
Congenital heart disease (atrial septal defect, ventricular septal defect)
Alcohol and chemotherapy, e.g. imatinib, doxorubicin
Hyperdynamic circulation (anaemia, thyrotoxicosis, Paget's disease)
Right heart failure (RV infarct, pulmonary hypertension, pulmonary embolism, cor pulmonale, COPD)
Severe bradycardia or tachycardia
Pericardial disease (constrictive pericarditis, pericardial effusion)
Infections (Chagas' disease)

COPD, chronic obstructive pulmonary disease; RV, right ventricle.

Activation of the sympathetic nervous system

Activation of the sympathetic nervous system improves ventricular function by increasing heart rate and myocardial contractility. Constriction of venous capacitance vessels redistributes flow centrally, and the increased venous return to the heart (preload) further augments ventricular function via the Starling mechanism (Fig. 10.14). Sympathetic stimulation, however, also leads to arteriolar constriction; this increases the afterload, which eventually reduces cardiac output.

Renin–angiotensin system

The fall in cardiac output and increased sympathetic tone lead to diminished renal perfusion, activation of the renin–angiotensin system and hence increased fluid retention. Salt and water retention further increases venous pressure and maintains stroke volume by the Starling mechanism (see Fig. 10.14). As salt and water retention increases, however, peripheral and pulmonary congestion causes oedema and contributes to dyspnoea. Angiotensin II also causes arteriolar constriction, thus increasing the afterload and the work of the heart.

Natriuretic peptides

Natriuretic peptides are released from the atria (atrial natriuretic peptide [ANP]), ventricles (brain natriuretic peptide [BNP] – so-called because it was first

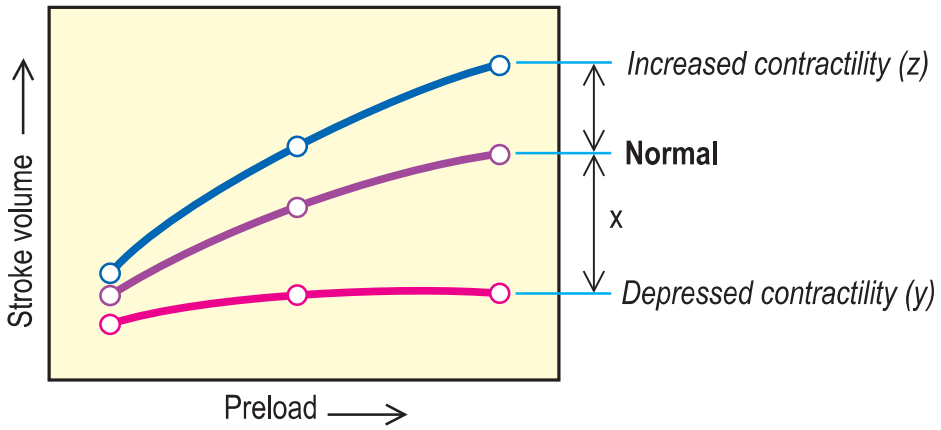


Fig. 10.14 The Starling curve. Starling's law states that the stroke volume is directly proportional to the diastolic filling (i.e. the preload or ventricular end-diastolic pressure). As the preload is increased, the stroke volume rises (normal). Increasing contractility (e.g. increased with sympathetic stimulation) shifts the curve upwards and to the left (z). If the ventricle is overstretched, the stroke volume will fall (x). In heart failure (y) the ventricular function curve is relatively flat, so that increasing the preload has only a small effect on cardiac output.

discovered in the brain) and vascular endothelium (C-type peptide). They have diuretic, natriuretic and hypotensive properties. The effect of their action may represent a beneficial, albeit inadequate, compensatory response leading to reduced cardiac load (preload and afterload). The N terminal fragment released from pro-BNP (NTproBNP) and BNP itself correlate with the severity of heart failure and they are therefore predictors of cardiovascular events and mortality. There is increasing interest in monitoring levels to help guide heart failure therapy.

Ventricular dilatation

Myocardial failure leads to a reduction of the volume of blood ejected with each heartbeat, and thus an increase in the volume of blood remaining after systole. The increased diastolic volume stretches the myocardial fibres and, as Starling's law would suggest, myocardial contraction is restored. Once heart failure is established, however, the compensatory effects of cardiac dilatation become limited by the flattened contour of Starling's curve. Eventually the increased venous pressure contributes to the development of pulmonary and peripheral oedema. In addition, as ventricular diameter increases, greater tension is required in the myocardium to expel a given volume of blood, and oxygen requirements increase.

Ventricular remodelling

This is a process of hypertrophy, loss of myocytes and increased interstitial fibrosis which all contribute to progressive and irreversible pump (contractile) failure. The process is multifactorial and includes apoptosis of myocytes and changes in cardiac contractile gene expression (e.g. myosin).

Clinical features

Most patients with heart failure present insidiously.

The clinical syndromes are:

- *Left ventricular systolic dysfunction (LVSD)* (or heart failure and a reduced ejection fraction) – commonly caused by ischaemic heart disease, but can also occur with valvular heart disease and hypertension.
- *Right ventricular systolic dysfunction (RVSD)* – occurs secondary to LVSD, with primary and secondary pulmonary hypertension, right ventricular infarction and adult congenital heart disease.
- *Diastolic heart failure* (or heart failure with normal ejection fraction) – a syndrome consisting of symptoms and signs of heart failure but with a normal or near-normal left ventricular ejection fraction (above 45–50%) and evidence of diastolic dysfunction on echocardiography (e.g. abnormal left ventricular relaxation and filling, usually with left ventricular hypertrophy). This leads to impairment of diastolic ventricular filling and hence decreased cardiac output. Diastolic heart failure is more common in elderly hypertensive patients but may occur with primary cardiomyopathies.

Symptoms

Symptoms include exertional dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea and fatigue.

Signs

There is one or more of the following: tachycardia, elevated jugular venous pulse (JVP), cardiomegaly with a displaced apex beat, third and fourth heart sounds, bi-basal lung crackles, pleural effusion, ankle oedema (plus sacral oedema in bed-bound patients), ascites and tender hepatomegaly.

The NYHA classification of heart failure (Table 10.6) is useful in the assessment of severity and the response to therapy.

Table 10.6 New York Heart Association classification of heart failure

Class I	No limitation. Normal physical exercise does not cause fatigue, dyspnoea or palpitations
Class II	Mild limitation. Comfortable at rest but normal physical activity produces fatigue, dyspnoea or palpitations
Class III	Marked limitation. Comfortable at rest but less gentle physical activity produces marked symptoms of heart failure
Class IV	Symptoms of heart failure occur at rest and are exacerbated by any physical activity

Investigations

The aim of investigation in a patient with symptoms and signs of heart failure is to objectively show evidence of cardiac dysfunction (usually by echocardiography) and to establish the cause (Fig. 10.15):

- *Chest X-ray* shows cardiac enlargement and features of left ventricular failure (p. 412), but can be normal.
- *ECG* may show evidence of underlying causes, e.g. arrhythmias, ischaemia, left ventricular hypertrophy in hypertension.
- *Blood tests*. Full blood count (to look for anaemia which may exacerbate heart failure), liver biochemistry (may be altered due to hepatic congestion), blood glucose (for diabetes), urea and electrolytes (as a baseline before starting diuretics and angiotensin-converting enzyme inhibitors [ACEIs]), and thyroid function tests (in the elderly and those with atrial fibrillation).

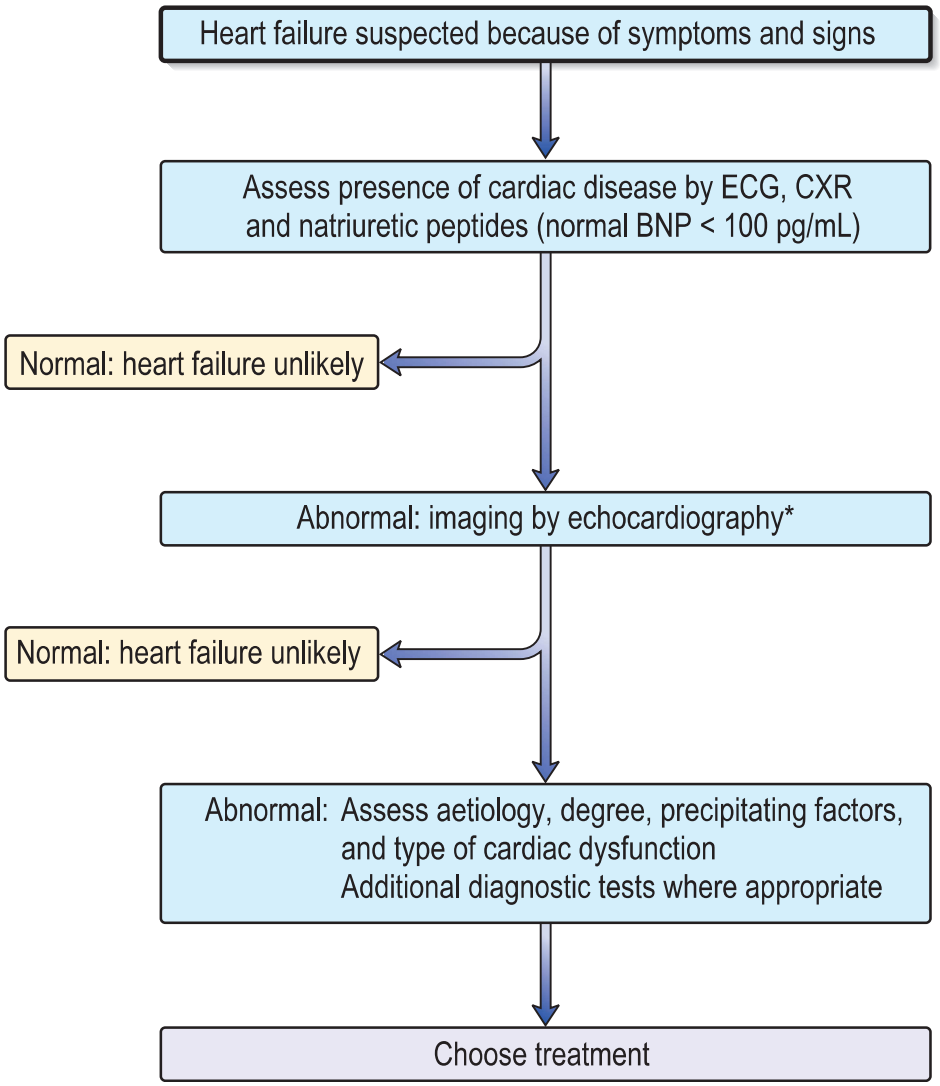


Fig. 10.15 Algorithm for the diagnosis of heart failure. BNP, brain natriuretic peptide; CXR, chest X-ray; ECG, electrocardiogram. Based on the European Society of Cardiology and NICE guidelines. *Prior to BNP testing in patients with previous myocardial infarction.

Normal plasma concentrations of BNP (<100 pg/mL) or NTproBNP (p. 437) exclude heart failure.

- *Echocardiography* is performed in all patients with new-onset heart failure. It allows an assessment of ventricular systolic and diastolic function, shows regional wall motion abnormalities and may reveal the aetiology of heart failure. An ejection fraction of < 0.45 is usually accepted as evidence for systolic dysfunction.
- *Other investigations*. Cardiac catheterization, thallium perfusion imaging, positron emission tomography (PET) scanning, cardiac magnetic resonance imaging (MRI) or dobutamine stress echocardiography (p. 419) may be of benefit in selected patients to identify those with *hibernating myocardium* (a region of impaired myocardial contractility due to persistently impaired coronary blood flow) in whom revascularization will improve left ventricular function and long-term prognosis.

Treatment of chronic heart failure

Treatment is aimed at relieving symptoms, minimising cardiac dysfunction, retarding disease progression and improving quality and length of survival (Table 10.7).

Drug treatment

Vasodilator therapy

- *ACEIs* (p. 497), e.g. perindopril, lisinopril and rampiril, inhibit the production of angiotensin II, a potent vasoconstrictor, and increase concentrations of the vasodilator bradykinin. They enhance renal salt and water excretion and increase cardiac output by reducing afterload. They improve symptoms, limit the development of progressive heart failure and prolong survival, and should be given to all patients with heart failure. The major side effect is first-dose hypotension. ACEI treatment should be introduced gradually with a low initial dose and gradual titration every 2 days to full dose with regular BP monitoring and a check on serum potassium and renal function; creatinine levels normally rise by about 10–15% during ACEI therapy.
- *Angiotensin II type 1 receptor antagonists* (ARAs, p. 498) (e.g. losartan, irbesartan, candesartan and valsartan) block binding of angiotensin II to the type 1 receptor (AT1) and are indicated as second-line therapy in patients intolerant of ACEIs. Unlike ACEIs, they do not affect bradykinin metabolism and do not produce a cough. Both ACEIs and ARAs are contraindicated in patients with bilateral renal artery stenosis.
- *Vasodilators.* Isosorbide mononitrate (vasodilator reduces preload) in combination with hydralazine (arteriolar vasodilator reduces afterload) improves symptoms and survival and is used in patients intolerant of ACEIs and ARAs. Ivabradine is also used.

Table 10.7 Summary of the management of chronic heart failure
General measures*
Education of patients and family
Physical activity: reduce during exacerbations to reduce work of the heart. Encourage low-level (e.g. 20- to 30-minute walks three to five times weekly) with compensated heart failure
Diet and social: weight reduction if necessary, no added salt diet, avoid alcohol (negative inotropic effects), stop smoking (p. 512)
Vaccinate against pneumococcal disease and influenza
Correct aggravating factors, e.g. arrhythmias, anaemia, hypertension and pulmonary infections
Driving: unrestricted, except symptomatic heart failure disqualifies driving large lorries and buses
Sexual activity: tell patients on nitrates not to take phosphodiesterase type 5 inhibitors
Pharmacological treatment
ACEI (or ARA)*
β-Blocker*
Diuretic
Spironolactone/eplerenone
Digoxin
Vasodilators
Inotropic agents
Non-pharmacological treatment (in selected cases)
Revascularization (coronary artery bypass graft)
Cardiac resynchronization therapy (biventricular pacing)
Implantable cardioverter–defibrillator
Replacement of diseased valves
Repair of congenital heart disease
Cardiac transplantation
Left ventricular assist device and artificial heart (bridge to transplantation)
ACEI, angiotensin-converting enzyme inhibitor; ARA, angiotensin II receptor antagonist. **In all patients. ACEI (ARA) and β-blockers improve prognosis.*

β-Blockers Bisoprolol, carvedilol and nebivolol (p. 495) improve symptoms and reduce cardiovascular mortality in patients with chronic stable heart failure. This effect is thought to arise through blockade of the chronically activated sympathetic system. They are started at a low dose and gradually titrated upwards.

Diuretics (see Table 8.4 and p. 351) are used in patients with fluid overload. They act by promoting renal sodium excretion, with enhanced water excretion as a secondary effect. The resulting loss of fluid reduces ventricular filling pressures (preload) and thus decreases pulmonary and systemic congestion.

- *Loop diuretics*, e.g. furosemide (20–40 mg daily, maximum 250–500 mg daily) and bumetanide, are potent diuretics used in moderate/severe heart failure. When given intravenously, they also induce venodilatation, a beneficial action independent of their diuretic effect.
- *Thiazide diuretics*, e.g. bendroflumethiazide (2.5 mg daily, maximum 10 mg daily), are mild diuretics that inhibit sodium reabsorption in the distal renal tubule. The exception is metolazone (2.5 mg daily, maximum 10 mg daily), which causes a profound diuresis and is only used in severe and resistant heart failure.
- *Aldosterone antagonists.* Spironolactone and eplerenone are relatively weak diuretics with a potassium-sparing action. Spironolactone (25 mg daily) in combination with conventional treatment improves survival in patients with moderate/severe heart failure and should be given to all these patients. However, gynaecomastia or breast pain is a common side effect. Eplerenone reduces mortality in patients with acute MI and heart failure.

Digoxin is indicated in patients with heart failure and atrial fibrillation. It is also used as add-on therapy in patients in sinus rhythm who remain symptomatic despite standard treatment (vasodilators, β-blockers, diuretics).

Inotropes (p. 579) are occasionally used in patients not responding to oral medication.

Non-pharmacological treatment

Revascularization Coronary artery disease is the most common cause of heart failure. Revascularization with angioplasty and stenting or surgery can result in improvement in regional abnormalities in wall motion in up to one-third of patients and may thus have a role to play in some individuals.

Cardiac resynchronization therapy (also known as biventricular pacing) aims to improve the coordination of the atria and both ventricles. It is indicated for patients with left ventricular systolic dysfunction who have moderate or severe symptoms of heart failure and a widened QRS on ECG.

Implantable cardioverter–defibrillator (ICD) is indicated for patients with symptomatic ventricular arrhythmias or left ventricular ejection fraction $< 30\%$ on optimal medical therapy. Sudden death from ventricular tachyarrhythmias is reduced.

Cardiac transplantation is the treatment of choice for younger patients with severe intractable heart failure and a life expectancy of < 6 months. The expected 1-year survival following transplantation is over 90%, with 75% alive at 5 years. Death is usually the result of operative mortality, organ rejection and overwhelming infection secondary to immunosuppressive treatment. After this time the greatest threat to health is accelerated coronary atherosclerosis, the cause of which is unknown.

Prognosis

There is usually a gradual deterioration necessitating increased doses of diuretics, and sometimes admission to hospital. The prognosis is poor in those with severe heart failure (i.e. breathless at rest or on minimal exertion), with a 1-year survival rate of 50%.

Acute heart failure

Acute heart failure is a medical emergency, with left or right heart failure developing over minutes or hours. Aetiology is similar to chronic heart failure and initial investigations are similar (ECG, chest X-ray, blood tests, transthoracic echocardiogram) with additional blood tests of serum troponin (for myocardial necrosis) and D-dimer (for evidence of pulmonary embolism).

Clinical features

Several clinical syndromes are defined:

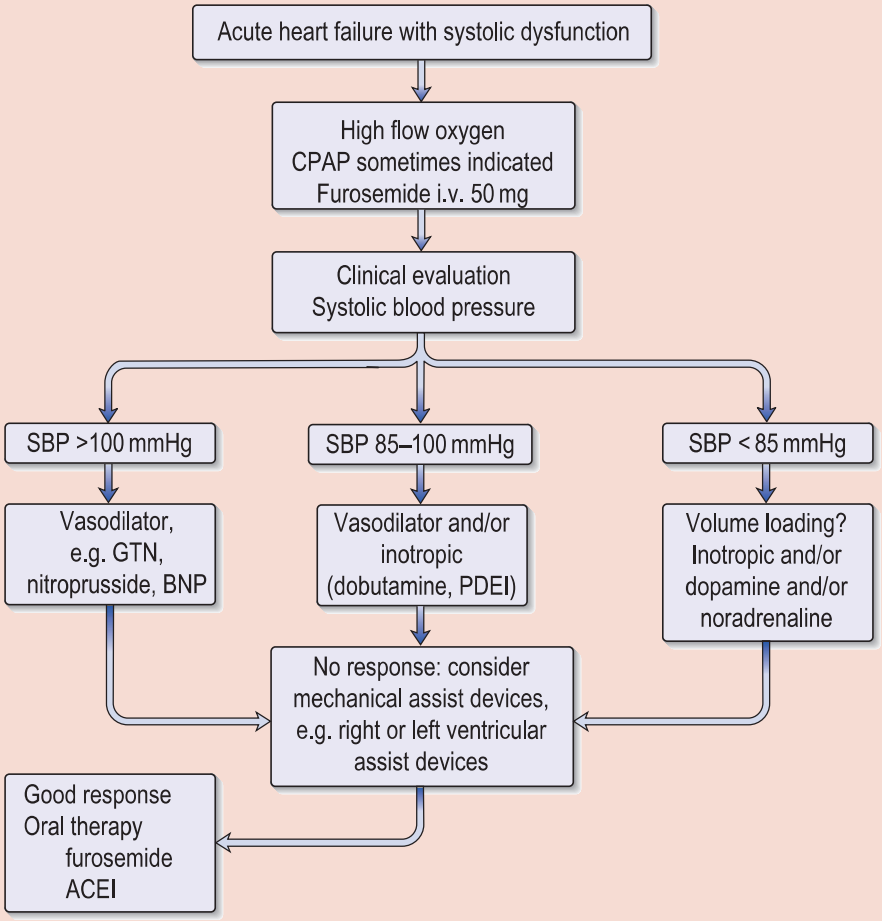
- Acute decompensation of chronic heart failure
- Hypertensive heart failure – high BP, preserved left ventricular function, pulmonary oedema on chest X-ray
- Acute pulmonary oedema – acutely breathless, tachycardia, profuse sweating (sympathetic overactivity), wheezes and crackles throughout the chest, hypoxia, pulmonary oedema on chest X-ray
- Cardiogenic shock – hypotension, tachycardia, oliguria, cold extremities
- High output cardiac failure – e.g. septic shock, warm peripheries, pulmonary congestion, BP may be low
- Right heart failure – low cardiac output, elevated jugular venous pressure, hepatomegaly, hypotension.

Management

In many cases the patient is so unwell that treatment (Emergency Box 10.2) must begin before the investigations are completed. Patients are managed in a high dependency unit. All require prophylactic anticoagulation, e.g. enoxaparin (p. 247). Some patients will require central venous cannulation, arterial lines and pulmonary artery cannulation for monitoring and to direct therapy. Initial therapy includes oxygen, diuretics (furosemide 50 mg i.v.) and vasodilator therapy (glyceryl trinitrate intravenous infusion 50 mg in 50 mL 0.9% saline at 2–10 mL/h) providing systolic BP is $>$ 85 mmHg. Inotropic support can be added in patients who do not respond to initial therapy (p. 579). Mechanical assist devices can be used in patients who fail to respond to standard medical therapy but in whom there is transient myocardial dysfunction with likelihood of recovery.

Emergency Box 10.2

Management of acute heart failure with systolic dysfunction



ACEI, angiotensin-converting enzyme inhibitor; BNP, brain natriuretic peptide; CPAP, continuous positive airway pressure (p. 584); GTN, glyceryl trinitrate; PDEI, phosphodiesterase inhibitor; SBP, systolic blood pressure.

ISCHAEMIC HEART DISEASE

Myocardial ischaemia results from an imbalance between the supply of oxygen to cardiac muscle and myocardial demand. The most common cause is coronary artery atheroma (coronary artery disease), which results in a fixed obstruction to coronary blood flow. Less common causes of myocardial ischaemia are coronary artery thrombosis, spasm or, rarely, arteritis (e.g. polyarteritis). Increased demand for oxygen due to an increase in cardiac output occurs in thyrotoxicosis or myocardial hypertrophy (e.g. from aortic stenosis or hypertension).

Coronary artery disease (CAD) is the single largest cause of death in many parts of the world, including the UK. However, in the last decade the mortality

rate in the UK has fallen. Atheroma consists of atherosclerotic plaques (an accumulation of lipid, macrophages and smooth muscle cells in the intima of arteries) which narrow the lumen of the artery. The risk factors, listed below, contribute to the development of atheroma through vascular endothelial dysfunction, biochemical abnormalities, immunological factors and inflammation. Some of these risk factors cannot be changed, i.e. they are irreversible, and others can be modified.

Irreversible risk factors for coronary artery disease

Age CAD rate increases with age. It rarely presents in the young, except in familial hyperlipidaemia (p. 693).

Gender Men are more often affected than pre-menopausal women, although the incidence in women after the menopause is similar to that in men, possible due to the loss of the protective effect of oestrogen.

Family history CAD is often present in several members of the same family. It is unclear, however, whether family history is an independent risk factor as so many other factors are familial. A positive family history refers to those in whom a first-degree relative has developed ischaemic heart disease before the age of 50 years.

Potentially changeable risk factors

Hyperlipidaemia The risk of CAD is directly related to serum cholesterol levels, but there is an inverse relationship with high-density lipoproteins (HDLs). High triglyceride levels are also independently linked with coronary atheroma. Lowering serum cholesterol slows the progression of coronary atherosclerosis and causes regression of the disease.

Cigarette smoking increases the risk of CAD, more so in men. The risk from smoking declines to almost normal after 10 years of abstention.

Hypertension (systolic and diastolic) is linked to an increased incidence of CAD.

Metabolic factors Diabetes mellitus, an abnormal glucose tolerance, raised fasting glucose, lack of exercise and obesity have all been linked to an increased incidence of atheroma.

Diets high in fats (particularly saturated fat intake) and low in antioxidant intake (fruit and vegetables) are associated with CAD.

Other risk factors Lack of exercise, psychosocial factors (work stress, lack of social support, depression), elevated serum C-reactive protein (CRP) levels (as an inflammatory marker), high alcohol intake and coagulation factors (high levels of fibrinogen, factor VII and homocysteine) are also associated with CAD, while moderate alcohol consumption (one to two drinks per day) is associated with a reduced risk of CAD.

Estimation of cardiovascular risk

Atherosclerotic disease manifest in one vascular bed is often advanced in other territories. Patients with intermittent claudication have a two- to four-fold increased risk of CAD, stroke or heart failure. Following MI, there is a three- to six-fold increase in the risk of heart failure and stroke. Patients with symptomatic cardiovascular disease therefore require intense lifestyle and drug therapy to improve their modifiable risk factors, i.e. secondary prevention. The cardiovascular disease risk for asymptomatic apparently healthy people can be estimated using prediction charts which take into account a number of risk factors, e.g. diabetes mellitus, BP and lipid profile. In the UK, NICE guidelines recommend that primary care should use the QRISK2 risk assessment tool to target high-risk people (10-year risk of cardiovascular disease $\geq$10%) for primary preventative measures.

Angina

Angina pectoris is a descriptive term for chest pain arising from the heart as a result of myocardial ischaemia.

Clinical features

Angina is usually described as a central, crushing, retrosternal chest pain, coming on with exertion and relieved by rest within a few minutes. It is often exacerbated by cold weather, anger and excitement, and it frequently radiates to the arms and neck. Variants of classic angina include:

- *Decubitus angina* – occurs on lying down.
- *Nocturnal angina* – occurs at night and may waken the patient from sleep.
- *Variant (Prinzmetal's) angina* – caused by coronary artery spasm and results in angina that occurs without provocation, usually at rest.
- *Unstable angina* – increases rapidly in severity, occurs at rest, or is of recent onset (less than 1 month) (see Acute coronary syndromes).
- *Cardiac syndrome* X – patients with symptoms of angina, a positive exercise test and normal coronary arteries on angiogram. It is thought to result from functional abnormalities of the coronary microcirculation. The prognostic and therapeutic implications are not known.

Physical examination in patients with angina is often normal, but must include a search for risk factors (e.g. hypertension and xanthelasma occurring in hyperlipidaemia) and underlying causes (e.g. aortic stenosis).

Diagnosis

The diagnosis of angina is largely based on the clinical history. Occasionally, chest wall pain or oesophageal reflux causes diagnostic confusion.

Investigations

- Resting ECG may show ST segment depression and T-wave flattening or inversion during an attack. The ECG is usually normal between attacks.
- Exercise ECG testing is positive (p. 418) in most people with CAD, but a normal test does not exclude the diagnosis. ST segment depression (>1 mm) at a low workload (within 6 minutes of starting the Bruce protocol) or a paradoxical fall in BP with exercise usually indicates severe CAD and is an indication for coronary angiography.
- Other testing protocols (pharmacological stress testing with myocardial perfusion imaging or stress echocardiography [p. 419]) are used in patients who cannot exercise or have baseline ECG abnormalities that can interfere with interpretation of the exercise ECG test. They may also be helpful in patients with an equivocal exercise test.
- Coronary angiography (p. 421) is occasionally used in patients with chest pain where the diagnosis of angina is uncertain. More commonly it is used to delineate the exact coronary anatomy before coronary intervention (p. 449) or surgery is considered. CT coronary angiography and CMR are also being increasingly used to provide information about coronary anatomy.

Management

This is two-fold:

- Identify and treat risk factors for CAD and offer secondary prevention
- Symptomatic treatment of angina.

Secondary prevention Patients with angina are at a high risk of experiencing subsequent cardiovascular events, including MI, sudden death and stroke. Modification of risk factors has a beneficial effect on subsequent morbidity and mortality, and includes smoking cessation, control of hypertension, maintaining ideal body weight, regular exercise and glycaemic control in diabetes mellitus. In addition, aspirin and statins reduce subsequent risk:

- Aspirin (75 mg daily, p. 246) inhibits platelet cyclo-oxygenase and formation of the aggregating agent thromboxane A_2, and reduces the risk of coronary events in patients with CAD. Clopidogrel (75 mg daily, p. 246) is an alternative when aspirin is not tolerated, or is contraindicated.
- Lipid-lowering agents reduce mortality and incidence of MI in patients with CAD and should be used in patients to achieve a cholesterol level of less than 5.0 mmol/L. Guidelines on introduction of lipid-lowering therapy are illustrated on page 694. A statin (p. 701) is used unless the triglycerides are above 3.5 mmol/L, in which case a fibrate is indicated.

Symptomatic treatment Acute attacks are treated with sublingual glyceryl trinitrate tablet or spray (p. 499). Patients should be encouraged to use this before exertion, rather than waiting for the pain to develop. The main side effect is a severe bursting headache, which is relieved by inactivating the tablet either by swallowing or spitting it out.

Most patients will require regular prophylactic therapy. Nitrates, β-blockers or calcium antagonists are most commonly used (p. 501), with treatment being tailored to the individual patient. Some patients will require combination therapy and revascularization for those not controlled on medical therapy:

- *β-Adrenergic blocking drugs* (p. 495), e.g. atenolol and metoprolol, reduce heart rate and the force of ventricular contraction, both of which reduce myocardial oxygen demand.
- *Calcium antagonists* (p. 501), e.g. diltiazem, amlodipine, block calcium influx into the cell and the utilization of calcium within the cell. They relax the coronary arteries and reduce the force of left ventricular contraction, thereby reducing oxygen demand. The side effects (postural dizziness, headache, ankle oedema) are the result of systemic vasodilatation. High-dose nifedipine increases mortality and should not be used in this situation.
- *Nitrates* (p. 499) reduce venous and intracardiac diastolic pressure, reduce impedance to the emptying of the left ventricle, and dilate coronary arteries. They are available in a variety of slow-release preparations, including infiltrated skin plasters, buccal pellets and long-acting oral nitrate preparations, e.g. isosorbide mononitrate, isosorbide dinitrate. The major side effect is headache, which tends to diminish with continued use.
- *Other treatments* are usually reserved for patients where there are contraindications or inadequate response to the above agents. *Nicorandil* combines nitrate-like activity with potassium-channel blockade; it has both arterial and venous vasodilating properties. *Ranolazine* interacts with sodium channels and can improve exercise tolerance but causes QT prolongation. *Ivabradine* inhibits the cardiac pacemaker I_f current and lowers the heart rate. It is used in patients who have a contraindication or intolerance of β-blockers.

When angina persists or worsens in spite of general measures and optimal medical treatment, patients should be considered for coronary artery bypass grafting (CABG) or percutaneous coronary intervention.

Percutaneous coronary intervention (PCI) Localized atheromatous lesions are dilated at cardiac catheterization using small inflatable balloons. Stent placement reduces the risk of restenosis. Studies support an initial strategy of optimal medical management in patients with stable angina symptoms, but revascularization should be considered in patients who remain symptomatic despite two anti-anginals. This technique is most useful for isolated, proximal, non-calcified atheromatous plaques. Complications include death, acute MI, the need for urgent CABG and restenosis. Dual antiplatelet therapy with aspirin and clopidogrel is routinely given (p. 246) for 6–12 months. The addition of the antiplatelet glycoprotein IIb/IIIa antagonists (tirofiban, eptifibatide, abciximab) has further reduced periprocedural complications. Drug-eluting stents which release antiproliferative agents (sirolimus, paclitaxel) reduce restenosis rates still further but there is a risk of late stent thrombosis. Bare metal stents may be preferred in patients requiring anticoagulation and early surgery.

Coronary artery bypass grafting The left or right internal mammary artery is used to bypass stenoses in the left anterior descending or right coronary artery, respectively. Less commonly, the saphenous vein from the leg is anastomosed between the proximal aorta and coronary artery distal to the obstruction. Surgery successfully relieves angina in about 90% of cases and, when performed for left main stem obstruction or three-vessel disease, an improved lifespan and quality of life can be expected. Operative mortality rate is less than 1%. In most patients the angina eventually recurs because of accelerated atherosclerosis in the graft (particularly vein grafts), which can be treated by stenting. CABG is recommended for patients with triple vessel coronary artery disease and impaired left ventricular function (left ventricular ejection fraction [LVEF] 35–49%). Left stem disease with a stenosis of $\geq$ 50% is also an indication for revascularization.

Acute coronary syndromes

Acute coronary syndromes (ACSs) encompass a spectrum of unstable coronary artery disease. The mechanism common to all ACSs is rupture or erosion of the fibrous cap of a coronary artery atheromatous plaque with subsequent formation of a platelet-rich clot and vasoconstriction produced by platelet release of serotonin and thromboxane A_2. Patients with ACS include those whose clinical presentations cover the following diagnoses:

- Unstable angina
- Non-ST-elevation MI (NSTEMI)
- ST-elevation MI (STEMI).

Unstable angina differs from NSTEMI in that in the latter the occluding thrombus is sufficient to cause myocardial damage and an elevation in serum markers of myocardial injury (troponin and creatine kinase). In patients presenting with symptoms suggestive of ACS, serum troponin should be measured on arrival at hospital and at 12 hours after the onset of symptoms; a normal serum troponin at 12 hours suggests unstable angina rather than MI. In both unstable angina and NSTEMI the ECG may be normal or show evidence of ischaemia with T-wave inversion and/or ST segment depression. Both unstable angina and NSTEMI may be complicated by MI with ST segment elevation (STEMI) if treatment is inadequate. In STEMI there is complete occlusion of the coronary artery by thrombus with usually more severe symptoms, typical ECG changes of MI (Fig. 10.16) and elevated troponin and creatine kinase (pp. 453–457).

Clinical features

The diagnosis of ACS is made in a patient with worsening pain on minimal exertion, chest pain at rest, or chest pain unrelieved in the usual time by nitrates or rest. In some patients, chest pain is absent and presentation is with collapse, arrhythmia or new-onset heart failure. Other causes of chest pain must be

considered in all patients, e.g. aortic dissection, musculoskeletal pain, gastro-oesophageal reflux disease.

Treatment of NSTEMI and unstable angina

Emergency Box 10.3 summarizes the initial investigation and management of patients presenting with suspected ACS.

- *Antiplatelet therapy*. In the absence of contraindications, aspirin (300 mg initially, then 75 mg daily, p. 246) is indicated in all patients. It reduces the risk of subsequent vascular events and deaths and is continued indefinitely. Clopidogrel (300 mg initially, then 75 mg daily for 12 months, p. 246) or prasugrel (60 mg initially then 10 mg o.d.) or ticagrelor (180 mg initially then 90 mg b.d.). Platelet glycoprotein IIb/IIIa receptor inhibitors (e.g. abciximab, tirofiban) are added for high-risk patients.
- *Antithrombins.* Heparin interferes with thrombus formation at the site of plaque rupture and reduces the risk of ischaemic events and death. Low molecular weight heparin, e.g. enoxaparin (1 mg/kg s.c. twice daily [p. 247]), has better efficacy than unfractionated heparin. Treatment should be for at least 48 hours. The synthetic pentasaccharide, fondaparinux, inhibits factor Xa of the coagulation cascade. It has a lower risk of bleeding than heparin and may become the antithrombin of choice in ACS. Bivalirudin reversibly binds to and inhibits clot-bound thrombin.
- *Anti-ischaemia agents*. Nitrates (p. 495) are given sublingually or by intravenous infusion with continuing pain for 24–48 hours. β-blockers (p. 495), e.g. metoprolol, are the first-line oral anti-anginal of choice given their secondary preventative effects in CAD.
- *Plaque stabilization*. Statins (p. 701) and an ACEI (p. 497) are continued long term and reduce future cardiovascular events.

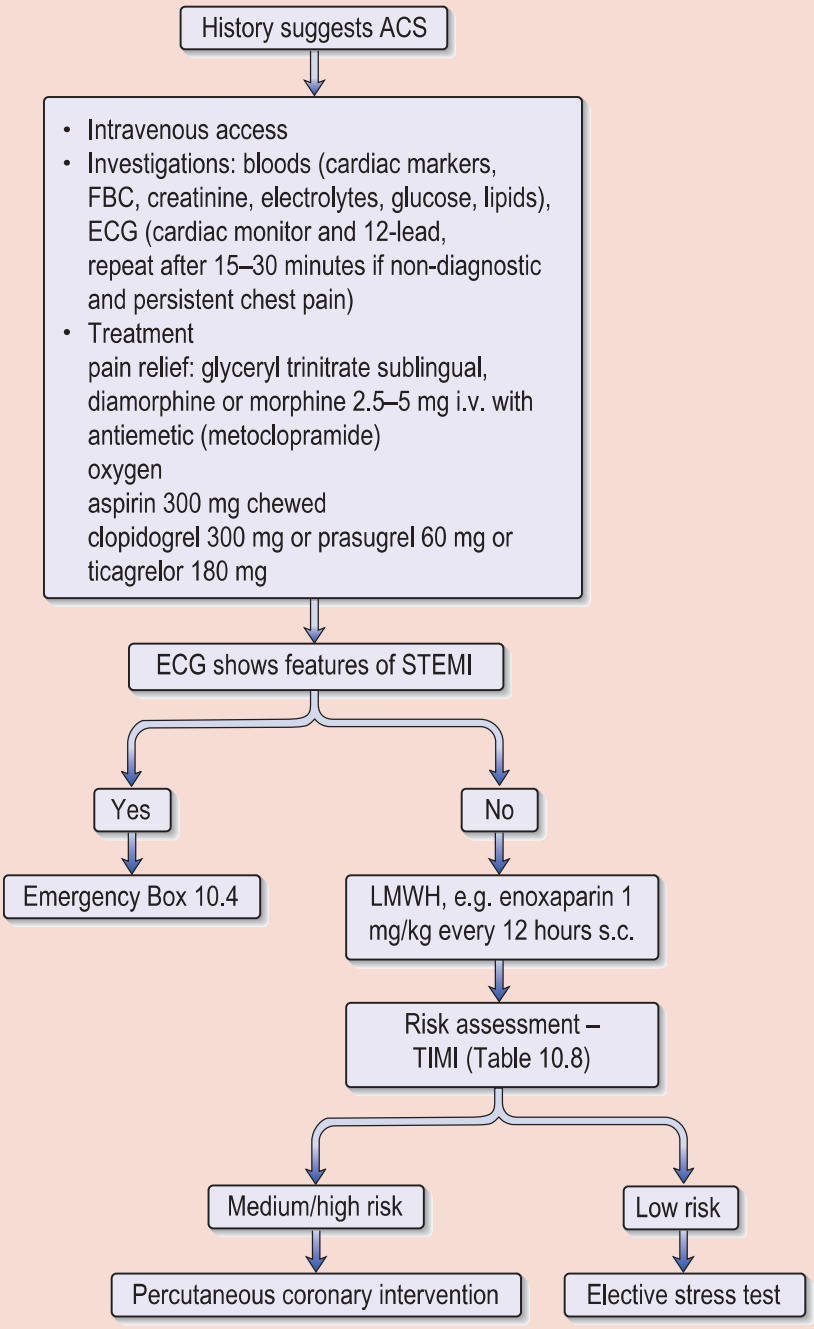
Oral medication is continued indefinitely after hospital discharge, with the exception of clopidogrel, which is stopped after 12 months.

Risk stratification

There are several risk stratification scoring systems (e.g. Thrombolysis in Myocardial Infarction [TIMI] and the Global Registry of Acute Coronary Events [GRACE]) that can predict subsequent risk of STEMI and death in patients with unstable angina/NSTEMI and provide a basis for therapeutic decision-making. The TIMI score is shown in Table 10.8. The GRACE score includes age, heart rate, systolic BP and serum creatinine. Early coronary angiography with a view to surgery or PCI is recommended in patients at intermediate/high risk. Coronary stenting may stabilize the disrupted coronary plaque and reduces angiographic restenosis rates compared to angioplasty alone. Low-risk patients should have a cardiac stress test (p. 448), usually an exercise ECG, if they remain pain-free with no evidence of ischaemia, heart failure or arrhythmias.

Emergency Box 10.3

Immediate management of acute coronary syndrome (ACS)



ECG, electrocardiography; FBC, full blood count; LMWH, low-molecular-weight heparin; STEMI, ST segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.

Table 10.8 The Thrombolysis in Myocardial Infarction (TIMI) risk score in acute coronary syndrome

Risk factor	Score*
Age > 65 years	1
More than three coronary artery disease risk factors – hypertension, hyperlipidaemia, family history, diabetes, smoking	1
Known CAD (stenosis of ≥ 50% on angiography)	1
Aspirin use in the last 7 days	1
At least two episodes of rest pain in the last 24 hours	1
ST deviation on admission ECG (horizontal ST depression or transient ST elevation > 1 mm)	1
Elevated cardiac markers (creatine kinase-myocardial bound or troponin)	1

CAD, coronary artery disease; ECG, electrocardiogram.
**Low risk = score 0–2. Intermediate risk = score 3–4. High risk = score 5–7.*

ST segment elevation myocardial infarction (STEMI)

MI is the most common cause of death in developed countries. It is almost always the result of rupture of an atherosclerotic plaque, with the development of thrombosis and total occlusion of the artery.

Clinical features

Central chest pain similar to that occurring in angina is the most common presenting symptom. Unlike angina, it usually occurs at rest, is more severe and lasts for some hours. The pain may radiate to the left arm, neck or jaw and is often associated with sweating, breathlessness, nausea, vomiting and restlessness. There may be no physical signs unless complications develop (p. 457), although the patient often appears pale, sweaty and grey. About 20% of patients have no pain, and such 'silent' infarctions either go unnoticed or present with hypotension, arrhythmias or pulmonary oedema. This occurs most commonly in elderly patients or those with diabetes or hypertension.

Investigations

The diagnosis is made on the basis of the clinical history and early ECG appearances. Serial changes (over 3 days) in the ECG and serum levels of cardiac markers confirm the diagnosis and allow an assessment of infarct size (on the magnitude of the enzyme and protein rise, and extent of ECG changes). A normal ECG in the early stages does not exclude the diagnosis.

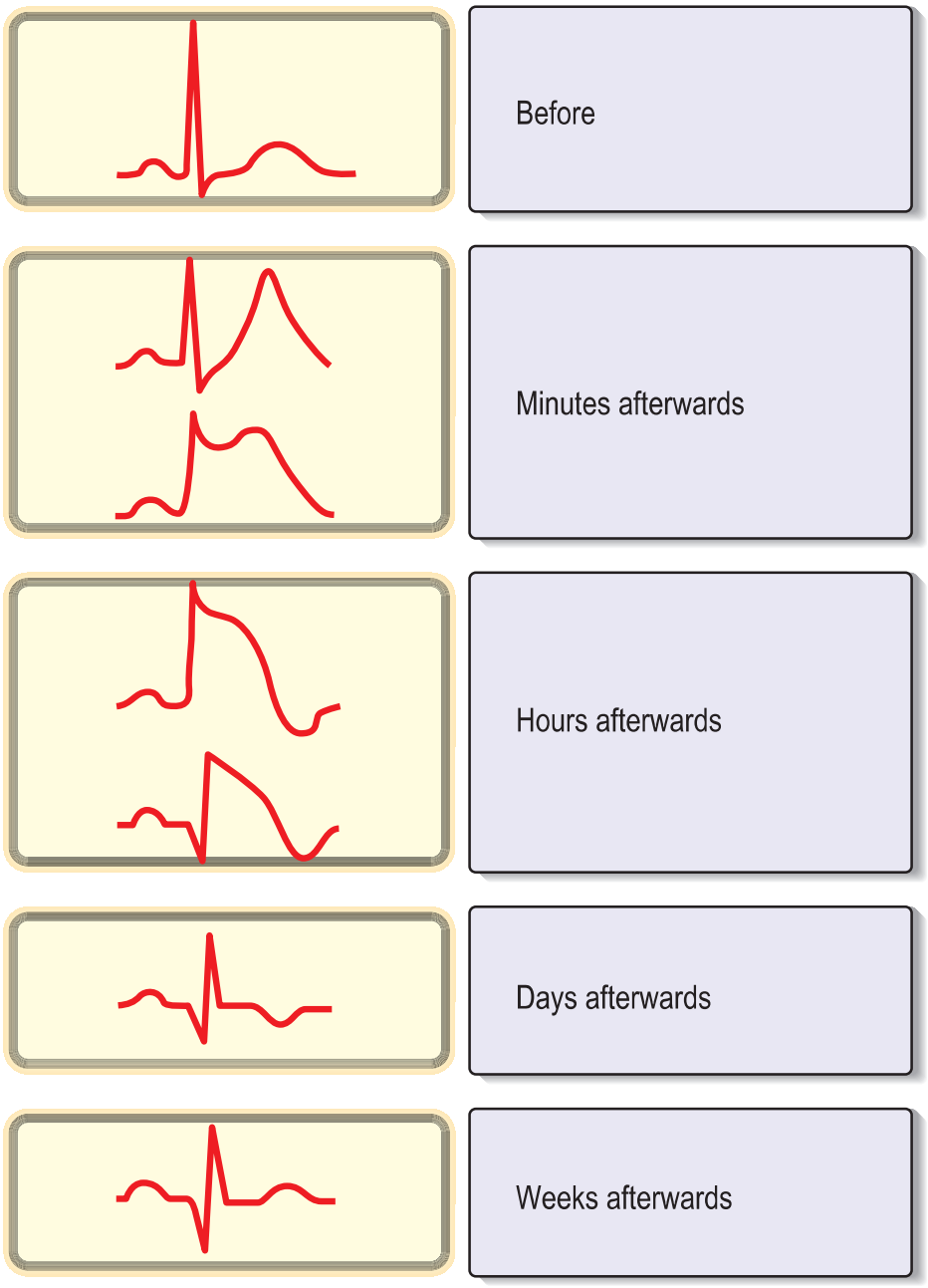


Fig. 10.16 Electrocardiographic evolution of myocardial infarction. After the first few minutes, the T waves become tall, pointed and upright and there is ST segment elevation. After the first few hours, the T waves invert, the R wave voltage is decreased and Q waves develop. After a few days, the ST segment returns to normal. After weeks or months, the T wave may return to upright but the Q wave remains.

The ECG shows a characteristic pattern. Within hours there is ST segment elevation (>1 mm in two or more contiguous leads) followed by T-wave flattening or inversion (Fig. 10.16). Pathological Q waves are broad (>1 mm) and deep (>2 mm, or >25% of the amplitude of the following R wave) negative deflections that start the QRS complex. They develop because the infarcted muscle is electrically silent so that the recording leads 'look through' the

infarcted area. This means that the electrical activity being recorded (on the opposite ventricular wall) is moving away from the electrode and is therefore negative. New LBBB is also an indicator of acute MI.

Typically, ECG changes are confined to the leads that 'face' the infarct. Leads II, III and AVF are involved in inferior infarcts; I, AVL and V_5–V_6 in lateral infarcts; and V_2–V_4 in anterior infarcts. As there are no posterior leads, a posterior wall infarct is diagnosed by the appearance of reciprocal changes in V_1 and V_2 (i.e. the development of tall initial R waves, ST segment depression and tall upright T waves). New or presumed new LBBB is also compatible with a diagnosis of MI.

Cardiac markers Necrotic cardiac muscle releases several enzymes and proteins into the systemic circulation:

- Troponin T and troponin I are regulatory proteins, highly specific and sensitive for cardiac muscle damage. They are released within hours of event onset, persist for several days, and are more sensitive and cardiac specific than CK-MB (the MB isoform of creatine kinase, which is found mainly in heart muscle).

Other investigations These include a chest X-ray, full blood count, serum urea and electrolytes, blood glucose and lipids (lipids taken within the first 12 hours reflect preinfarction levels, but after this time they are altered for up to 6 weeks).

Management

The aims of treatment are relief of pain, limitation of infarct size and treatment of complications. The immediate and subsequent management is summarized in Emergency Boxes 10.3 and 10.4. Treatment is urgent: prolonged times between symptom onset and treatment to recanalize the artery are associated with impaired ST-segment resolution, larger infarct sizes and higher mortality ('time is muscle').

Limitation of infarct size

Immediate primary angioplasty is the optimal treatment for recanalization of the infarct-related arteries (p. 421). When compared with thrombolysis (see below), PCI reduced mortality, re-infarction, recurrent ischaemia, stroke and the need for CABG. However, it is only a therapeutic option when rapid access to a catheterization laboratory is possible, the cardiologist is experienced in interventional cardiology and a full support team is immediately available. PCI is also used as 'rescue' therapy in patients who have received thrombolysis and who seem on clinical grounds not to have reperfused (ongoing chest pain and $<$ 50% resolution of ST elevation 45–60 minutes after start of thrombolysis).

Fibrinolytic agents (thrombolysis) enhance the breakdown of occlusive thromboses by the activation of plasminogen to form plasmin. They are indicated where primary PCI is not available and there are no contraindications to thrombolysis (p. 251). Maximum benefit is derived from thrombolytic agents if they are given early ('time is muscle' – minutes count) and

Emergency Box 10.4

Management of ST elevation myocardial infarction (STEMI)

Immediate management

- Immediate investigations and treatment (see Emergency Box 10.3).
- Reperfusion therapy: preferred therapy for patients presenting within 90 minutes of onset is primary angioplasty with dual antiplatelet therapy. If presenting after 90 minutes and within 12 hours (preferably 6 hours), treat with thrombolysis, e.g. double-bolus reteplase or single-bolus tenecteplase.
- Metoprolol (5 mg slow i.v. injection) if heart rate > 100 beats/min. Repeat every 15 minutes, titrated against heart rate and BP. Do not give if hypotension, heart failure, bradycardia, asthma.
- Insulin infusion if blood glucose > 11 mmol/L; aim for blood glucose of 7–10 mmol/L.
- Treat complications (p. 457).

Subsequent management of uncomplicated infarction

- Repeat ECG, serum cardiac markers and electrolytes at 24 and 48 hours after admission.
- Initiate secondary prevention therapy: aspirin, clopidogrel, statin, metoprolol, ACEI and modification of CAD risk factors (as for ACS).
- Transfer from CCU to medical ward after 48 hours.
- Mobilize gradually and discharge from hospital after 5 days.
- Submaximal exercise ECG test prior to discharge if primary angioplasty not performed.
- Refer to cardiac rehabilitation programme.
- No driving for 1 month; special assessment is required for heavy goods or public service licence holder before driving. Usually return to work in 2 months.

ACS, acute coronary syndrome; BP, blood pressure; CAD, coronary artery disease; CCU, coronary care unit; ECG, electrocardiography.

in some centres pre-hospital thrombolysis is used. There is little benefit of thrombolysis more than 12 hours after the onset of symptoms. Of the four thrombolytic agents available, reteplase and tenecteplase are preferred in the pre-hospital setting because they can be administered as a bolus intravenous injection. Streptokinase and alteplase are given by intravenous infusion. Streptokinase is the cheapest thrombolytic agent available but may induce the development of antistreptokinase antibodies and reduce the effectiveness of subsequent treatment. It should not be used beyond 4 days after first administration.

Mortality is increased in diabetic patients with MI, largely due to the high incidence of heart failure. This is due in part to metabolic changes which occur in the early stages of MI, and is reduced by rigorous control of blood glucose with insulin infusion, and monitoring with 2-hourly BM Stix. This regimen is also indicated in patients not known to be diabetic who have an admission blood glucose of >11 mmol/L. β-Blockers reduce infarct size and the incidence of sudden death. Metoprolol (5–10 mg i.v.) should be given, particularly if the heart rate is greater than 100 beats/min and there is persistent pain.

Subsequent management ACEIs (or angiotensin receptor blocker if intolerant) reduce mortality and prevent the development of heart failure and should be started on the first day after MI. Treatment with ACEIs, aspirin, statin and β-blockers is continued indefinitely (see ACS for doses). Aldosterone antagonist, e.g. eplerenone 25 mg/day (p. 352), is given to patients with clinical evidence of heart failure and reduced ejection fraction on echocardiogram. Gradual mobilization takes place on the second day and if the patient is fully ambulant and pain-free, a submaximal exercise tolerance test is performed (70% of age-predicted maximal heart rate) before hospital discharge on day 5 or 6 in uncomplicated cases. Patients with test results suggesting ischaemia are referred for coronary angiography.

Complications (Table 10.9)

Disturbances of rate, rhythm and conduction (p. 421)

- *Atrial arrhythmias*. Sinus tachycardia is common; treatment is that of the underlying cause, particularly pain, anxiety and heart failure. Sinus

Table 10.9 Complications of myocardial infarction

Heart failure
Rupture of free wall of infarcted ventricle (usually fatal)
Rupture of the interventricular septum (ventricular septal defect)
Mitral regurgitation
Arrhythmias
Heart block
Pericarditis
Thromboembolism
Dressler's syndrome*
Ventricular aneurysm*

**May develop weeks or months after myocardial infarction.*

bradycardia is especially associated with acute inferior wall MI. Treatment is initially with intravenous atropine (p. 422). Atrial fibrillation occurs in about 10% of cases and is usually a transient rhythm disturbance. Treatment with digoxin or β-blockers is indicated if the fast rate is exacerbating ischaemia or causing heart failure.

- *Ventricular arrhythmias*. Ventricular ectopic beats are common and may precede the development of VT or VF. Antiarrhythmic drug treatment has not been shown to affect progression to these more serious arrhythmias. VT may degenerate into VF (p. 433) or may itself produce shock or heart failure. Treatment of VT is with intravenous amiodarone (p. 491) or direct current cardioversion if there is hypotension. VF may be primary (occurring in the first 24–48 hours) or secondary (occurring late after infarction and associated with large infarcts and heart failure). Cardiac arrest requires defibrillation. Recurrences may be prevented with intravenous amiodarone. Late VT/VF is associated with a poor prognosis and a high incidence of sudden death, and is an indication for an implantable cardioverter-defibrillator (ICD).
- *Heart block occurring with inferior infarction* is common and usually resolves spontaneously. Some patients respond to intravenous atropine, but a temporary pacemaker may be necessary if the rhythm is very slow or producing symptoms.
- *Complete heart block occurring with anterior wall infarction* indicates the involvement of both bundle branches by extensive myocardial necrosis, and hence a very poor prognosis. The ventricular rhythm in this case is unreliable and a temporary pacing wire is necessary. Heart block is often permanent and a permanent pacing wire may be necessary.

Heart failure in a mild form occurs in up to 40% of patients following MI. Extensive infarction may cause acute heart failure (p. 444), which may also occur following rupture of the ventricular septum or mitral valve papillary muscle. Both conditions present with worsening heart failure, a systolic thrill and a loud pansystolic murmur. Mortality is high, and urgent surgical correction is often needed. Hypotension with a raised JVP is usually a complication of right ventricular infarction, which may occur with inferior wall infarcts. Initial treatment is with volume expansion, and pericardial effusion (which produces similar signs) should be ruled out on an echocardiogram.

Embolism Patients with severe left ventricular dysfunction, persistent AF or mural thrombus on echocardiography are at risk of embolism from left ventricular or left atrial clot and should be anticoagulated with warfarin to achieve a target INR of 2–3.

Pericarditis is characterized by sharp chest pain and a pericardial rub. Treatment is with non-steroidal anti-inflammatory drugs (NSAIDs) until spontaneous resolution occurs within 1–2 days. Late pericarditis (2–12 weeks after) with fever and a pericardial effusion (Dressler's syndrome) is rare and corticosteroids may be necessary in some patients.

Post-ACS drug therapy and assessment

A range of pharmaceuticals are advantageous in reducing mortality over the years following MI. Therefore post-MI most patients should be taking most of the following medications:

- Aspirin (75 mg o.d.)
- A second anti-platelet agent (e.g. clopidogrel)
- An oral β-blocker to maintain heart rate $<$60 beats/min
- ACEIs or angiotensin receptor blockers, particularly if left ventricular ejection fraction is below 40%
- High-intensity statins with target low-density lipoprotein (LDL) cholesterol $<$ 1.8 mmol/L
- Aldosterone antagonist – post-MI with clinical evidence of heart failure and left ventricular ejection fraction $\leq$ 40% if the serum creatinine is $<$ 221 μmol/L (men) or $<$ 177 μmol/L (women) and the serum potassium $<$ 5.0 mEq/L.

RHEUMATIC FEVER

Rheumatic fever is an inflammatory disease that usually has its first onset between 5 and 15 years of age as a result of infection with group A streptococci. It is a complication of less than 1% of streptococcal pharyngitis, developing 2–3 weeks after the onset of sore throat. It is thought to develop because of an autoimmune reaction triggered by the streptococci rather than direct infection of the heart.

Epidemiology

The incidence in developed countries has decreased dramatically since the 1920s as a result of improved sanitation, a change in the virulence of the organism and the use of antibiotics. The disease is more common in women than in men.

Clinical features

The disease presents suddenly, with fever, joint pains and loss of appetite. The major clinical features are as follows:

- Changing heart murmurs, mitral and aortic regurgitation, heart failure and chest pain, caused by carditis affecting all three layers of the heart
- Polyarthritis – fleeting and affecting the large joints, e.g. knees, ankles and elbows
- Skin manifestations – erythema marginatum (transient pink coalescent rings develop on the trunk) and small non-tender subcutaneous nodules which occur over tendons, joints and bony prominences
- Sydenham's chorea ('St Vitus' dance') indicates involvement of the central nervous system and presents with 'fidgety' and spasmodic, unintentional movements.

Investigations

Blood count shows a leucocytosis and a raised erythrocyte sedimentation rate (ESR).

The diagnosis is based on the revised Duckett Jones criteria, which depend on the combination of certain clinical features and evidence of recent streptococcal infection.

Treatment

Treatment is with complete bed rest and high-dose aspirin. Penicillin is given to eradicate residual streptococcal infection, and then long term to all patients with persistent cardiac damage.

Chronic rheumatic heart disease

More than 50% of those who suffer acute rheumatic fever with carditis will develop chronic rheumatic valvular disease 10–20 years later, predominantly affecting the mitral and aortic valves (pp. 461–467).

VALVULAR HEART DISEASE

Cardiac valves may be incompetent (regurgitant), stenotic or both. The most common problems are acquired left-sided valvular lesions: aortic stenosis, mitral stenosis, mitral regurgitation and aortic regurgitation. Abnormal valves produce turbulent blood flow, which is heard as a murmur on auscultation; a few murmurs are also felt as a thrill on palpation. Murmurs may sometimes be heard with normal hearts ('innocent murmurs'), often reflecting a hyperdynamic circulation, e.g. in pregnancy, anaemia and thyrotoxicosis. Benign murmurs are soft, short, systolic, may vary with posture, and are not associated with signs of organic heart disease.

Diagnosis of valve dysfunction is made clinically and by echocardiography. The severity is assessed by Doppler echocardiography, which measures the direction and velocity of blood flow and allows a calculation to be made of the pressure across a stenotic valve. Transoesophageal echocardiography, cardiac magnetic resonance or invasive cardiac catheterization are usually only necessary to assess complex situations, such as coexisting valvular and ischaemic heart disease, or suspected dysfunction of a prosthetic valve. Treatment of valve dysfunction is both medical and surgical: this may be valve replacement, valve repair (some incompetent valves) or valvotomy (the fused cusps of a stenotic valve are separated along the commissures). The timing of surgery is critical and must not be delayed until there is irreversible ventricular dysfunction or pulmonary hypertension.

Prosthetic heart valves

Prosthetic heart valves are either mechanical or tissue (bioprosthetic). Tissue prostheses are derived from human (homograft), or from porcine or bovine

(xenograft) origin. Tissue valves tend to degenerate after about 10 years but patients do not need long-term anticoagulation. These valves are often used in elderly patients. Mechanical valves last much longer but are thrombogenic and patients need lifelong anticoagulation. There are several types of mechanical valve: a ball-and-cage design (Starr–Edwards), tilting disc (Björk–Shiley) or a double tilting disc (St Jude). All damaged and prosthetic valves carry a risk of infection.

The individual valve lesions are considered separately below, but disease may affect more than one valve (particularly in rheumatic heart disease and infective endocarditis), when a combination of clinical features is produced.

Mitral stenosis

Aetiology

Most cases of mitral stenosis are a result of previous rheumatic heart disease, although a reliable history of rheumatic fever is not always obtained.

Pathophysiology

Thickening and immobility of the valve leaflets leads to obstruction of blood flow from the left atrium to left ventricle. As a result there is an increase in left atrial pressure, pulmonary hypertension and right heart dysfunction. Atrial fibrillation is common due to the elevation of left atrial pressure and dilatation. Thrombus may form in the dilated atrium and give rise to systemic emboli (e.g. to the brain, resulting in a stroke). Chronically elevated left atrial pressure leads to an increase in pulmonary capillary pressure and pulmonary oedema. Pulmonary arterial vasoconstriction leads to pulmonary hypertension and eventually right ventricular hypertrophy, dilatation and failure.

Symptoms

Exertional dyspnoea which becomes progressively more severe is usually the first symptom. A cough productive of blood-tinged sputum is common, and frank haemoptysis may occasionally occur. The onset of atrial fibrillation may produce an abrupt deterioration and precipitate pulmonary oedema. Pulmonary hypertension eventually leads to right heart failure with fatigue and lower limb oedema.

Signs

- Mitral facies or malar flush occurs with severe stenosis. This is a cyanotic or dusky-pink discoloration on the upper cheeks.
- The pulse is low volume and may become irregular if atrial fibrillation develops.
- The apex beat is ‘tapping’ in quality as a result of a combination of a palpable first heart sound and left ventricular backward displacement produced by an enlarging right ventricle.

- Auscultation at the apex reveals a loud first heart sound, an opening snap (when the mitral valve opens) in early diastole, followed by a rumbling mid-diastolic murmur. If the patient is in sinus rhythm the murmur becomes louder when atrial systole occurs (presystolic accentuation), as a result of increased flow across the narrowed valve.

The presence of a loud second heart sound, parasternal heave, elevated JVP, ascites and peripheral oedema indicate that pulmonary hypertension producing right ventricular overload has developed.

Investigations

Investigations are performed to confirm the diagnosis, to estimate the severity of valve stenosis and to look for pulmonary hypertension.

Chest X-ray shows an enlarged left atrium, pulmonary venous hypertension and sometimes a calcified mitral valve. Pulmonary oedema is present in severe disease.

ECG usually shows atrial fibrillation. In patients in sinus rhythm, left atrial hypertrophy results in a bifid P wave ('P mitrale'). With progressive disease there are features of right ventricular hypertrophy.

Echocardiography confirms the diagnosis and assesses severity. A valve area of <2 cm^2 indicates moderate mitral stenosis while an area <1 cm^2 indicates severe stenosis.

Management

General Treatment is often not required for mild mitral stenosis. Complications are treated medically, e.g. β-blockers/digoxin for atrial fibrillation, diuretics for heart failure and anticoagulation in patients with atrial fibrillation to prevent clot formation and embolization.

Specific Mechanical relief of the mitral stenosis is indicated if symptoms are more than mild or if pulmonary hypertension develops. In many cases, percutaneous balloon valvotomy (access to the mitral valve is obtained via a catheter passed through the femoral vein, right atrium and interatrial septum, and a balloon inflated across the valve to split the commissures) provides relief of symptoms. In other cases, open valvotomy (splitting of the valve leaflets) or mitral valve replacement is necessary. The latter is performed if there is associated mitral regurgitation, a badly calcified valve or thrombus in the left atrium despite anticoagulation.

Mitral regurgitation

Aetiology

Prolapsing mitral valve is the most common cause in the developed world but rheumatic heart disease continues to be a common cause in the developing world (Table 10.10).

Table 10.10 Causes of mitral regurgitation
Rheumatic heart disease
Mitral valve prolapse
Infective endocarditis*
Ruptured chordae tendineae*
Rupture of the papillary muscle* complicating myocardial infarction
Papillary muscle dysfunction
Dilating left ventricle disease causing 'functional' mitral regurgitation
Hypertrophic cardiomyopathy
Rarely: systemic lupus erythematosus, Marfan's syndrome
Ehlers–Danlos syndrome
**These disorders may produce acute regurgitation.*

Pathophysiology

The circulatory changes depend on the speed of onset and severity of regurgitation. Long-standing regurgitation produces little increase in the left atrial pressure because flow is accommodated by an enlarged left atrium. With acute mitral regurgitation there is a rise in left atrial pressure, resulting in an increase in pulmonary venous pressure and pulmonary oedema. The left ventricle dilates, but more so with chronic regurgitation.

Symptoms

Acute regurgitation presents as pulmonary oedema. Chronic regurgitation causes progressive exertional dyspnoea, fatigue and lethargy (resulting from reduced cardiac output). In the later stages the symptoms of right heart failure also occur and eventually lead to congestive cardiac failure. Thromboembolism is less common than with mitral stenosis, although infective endocarditis is much more common.

Signs

The apex beat is displaced laterally, with a diffuse thrusting character. The first heart sound is soft. There is a pansystolic murmur (palpated as a thrill), loudest at the apex and radiating widely over the precordium and into the axilla. A third heart sound is often present, caused by rapid filling of the dilated left ventricle in early diastole.

Investigations

- Chest X-ray and ECG changes are not sensitive or specific for the diagnosis of mitral regurgitation. On both, evidence of enlargement of the left atrium, the left ventricle or both, is seen late in the course of the disease.

- Echocardiography can establish the aetiology and haemodynamic consequences of mitral regurgitation. Doppler and colour flow Doppler is used to measure the severity of mitral regurgitation. Cardiac magnetic resonance or cardiac catheterization is rarely needed for further evaluation.

Management

Mild mitral regurgitation in the absence of symptoms can be managed conservatively by following the patient with serial echocardiograms every 1–5 years. Medical management involves diuretics and ACEIs. Surgical intervention is recommended in patients with symptomatic severe mitral regurgitation, left ventricular ejection fraction >30% and end-diastolic dimension of under 55 mm; and in asymptomatic patients with left ventricular dysfunction (end-systolic dimension >45 mm and/or ejection fraction of under 60%). Patients with asymptomatic severe mitral regurgitation and preserved left ventricular function should be considered for surgery in the presence of atrial fibrillation and/or pulmonary hypertension. Emergency valve replacement is necessary with acute severe mitral regurgitation.

Prolapsing ('floppy') mitral valve

This is a common condition that occurs mainly in young women. One or more of the mitral valve leaflets prolapses back into the left atrium during ventricular systole, producing mitral regurgitation in a few cases.

Aetiology

The cause is unknown, but it is associated with Marfan's syndrome, hyperthyroidism and rheumatic or ischaemic heart disease.

Clinical features

Most patients are asymptomatic. Atypical chest pain is the most common symptom. Some patients complain of palpitations caused by atrial and ventricular arrhythmias. The typical finding on examination is a mid-systolic click, which may be followed by a murmur. Occasionally, there are features of mitral regurgitation.

Investigation

Echocardiography is diagnostic and shows the prolapsing valve cusps.

Management

Chest pain and palpitations are treated with β-blockers. Anticoagulation to prevent thromboembolism is indicated if there is significant mitral regurgitation and atrial fibrillation.

Aortic stenosis

Aetiology

There are three main causes of aortic valve stenosis:

- Degeneration and calcification of a normal valve – presenting in the elderly
- Calcification of a congenital bicuspid valve – presenting in middle age
- Rheumatic heart disease.

Pathophysiology

Obstruction to left ventricular emptying results in left ventricular hypertrophy. In turn this results in increased myocardial oxygen demand, relative ischaemia of the myocardium and consequent angina and arrhythmias. Left ventricular systolic function is typically preserved in aortic stenosis (cf. aortic regurgitation).

Symptoms

There are usually no symptoms until the stenosis is moderately severe (aortic orifice reduced to a third of its normal size). The classic symptoms are angina, exertional syncope and dyspnoea. Ventricular arrhythmias may cause sudden death.

Signs

The carotid pulse is slow rising (plateau pulse) and the apex beat thrusting. There is a harsh systolic ejection murmur (palpated as a thrill) at the right upper sternal border and radiating to the neck. The second heart sound may become soft or inaudible when the valve becomes immobile.

Investigations

- Chest X-ray shows a normal heart size, prominence of the ascending aorta (post-stenotic dilatation) and there may be valvular calcification.
- ECG shows evidence of left ventricular hypertrophy and a left ventricular strain pattern when the disease is severe (depressed ST segment and T-wave inversion in the leads orientated to the left ventricle, i.e. I, AVL, V_5 and V_6).
- Echocardiography is diagnostic in most cases. Doppler examination of the valve allows an assessment of the pressure gradient across the valve during systole.
- Cardiac catheterization is used to exclude coronary artery disease prior to recommending surgery.

Management

Aortic valve replacement is indicated in symptomatic patients, as the onset of symptoms is associated with 75% mortality at 3 years. Some would

recommend valve replacement for asymptomatic patients with a critically stenotic valve (valve area ≤ 0.6 cm^2 or the valve gradient exceeds 50 mmHg on echocardiography) or with a left ventricular ejection fraction of $<50\%$. Balloon aortic valvotomy is sometimes used in childhood or adolescence but aortic valve replacement will usually be needed a few years later. If patients are unsuitable for open valve replacement, transcatheter aortic valve implantation (TAVI) with a balloon expandable stent valve may be considered.

Aortic regurgitation

Aetiology

Aortic regurgitation results from either disease of the valve cusps or dilatation of the aortic root and valve ring. The most common causes are rheumatic fever and infective endocarditis complicating an already damaged valve (Table 10.11).

Pathophysiology

Chronic regurgitation volume loads the left ventricle and results in hypertrophy and dilatation. The stroke volume is increased, which results in an increased pulse pressure and the myriad of clinical signs described below. Eventually, contraction of the ventricle deteriorates, resulting in left ventricular failure. The adaptations to the volume load entering the left ventricle do not occur with acute regurgitation and patients may present with pulmonary oedema and a reduced stroke volume (hence many of the signs of chronic regurgitation are absent).

Table 10.11 Causes and associations of aortic regurgitation

Acute aortic regurgitation	Chronic aortic regurgitation
Infective endocarditis	Chronic rheumatic heart disease
Acute rheumatic fever	Bicuspid aortic valve
Dissection of the aorta	Aortic endocarditis
Ruptured sinus of Valsalva aneurysm	Arthritides:
Failure of prosthetic heart valve	• Reiter's syndrome • Ankylosing spondylitis • Rheumatoid arthritis
	Severe hypertension
	Marfan's syndrome
	Syphilis
	Osteogenesis imperfecta

Symptoms

In chronic regurgitation, patients remain asymptomatic for many years before developing dyspnoea, orthopnoea and fatigue as a result of left ventricular failure.

Signs

- A 'collapsing' (water-hammer) pulse with wide pulse pressure is pathognomonic.
- The apex beat is displaced laterally and is thrusting in quality.
- A blowing early diastolic murmur is heard at the left sternal edge in the fourth intercostal space. It is accentuated when the patient sits forward with the breath held in expiration. Increased stroke volume produces turbulent flow across the aortic valve, heard as a mid-systolic murmur.
- A mid-diastolic murmur (Austin Flint murmur) may be heard over the cardiac apex and is thought to be produced as a result of the aortic jet impinging on the mitral valve, producing premature closure of the valve and physiological stenosis.

Investigations

- Chest X-ray shows a large heart and occasionally dilatation of the ascending aorta.
- ECG shows evidence of left ventricular hypertrophy (see aortic stenosis).
- Echocardiography with Doppler examination of the aortic valve helps estimate the severity of regurgitation.
- Cardiac catheterization is needed to assess for coronary artery disease in patients undergoing surgery.

Management

Mild symptoms may respond to the reduction of afterload with vasodilators and diuretics. ACEIs are useful in patients with left ventricular dysfunction. The timing of surgery and aortic valve replacement is critical and must not be delayed until there is irreversible left ventricular dysfunction.

Tricuspid and pulmonary valve disease

Tricuspid and pulmonary valve disease is uncommon. Tricuspid stenosis is almost always the result of rheumatic fever and is frequently associated with mitral and aortic valve disease, which tends to dominate the clinical picture.

Tricuspid regurgitation is usually functional and secondary to dilatation of the right ventricle (and hence tricuspid valve ring) in severe right ventricular failure. Much less commonly it is caused by rheumatic heart disease, infective endocarditis or carcinoid syndrome (p. 100). On examination there is a pansystolic

murmur heard at the lower left sternal edge, the jugular venous pressure is elevated, with giant 'v' waves (produced by the regurgitant jet through the tricuspid valve in systole), and the liver is enlarged and pulsates in systole. There may be severe peripheral oedema and ascites. In functional tricuspid regurgitation these signs improve with diuretic therapy.

Pulmonary regurgitation results from pulmonary hypertension and dilatation of the valve ring. Occasionally it is the result of endocarditis (usually in intravenous drug abusers). Auscultation reveals an early diastolic murmur heard at the upper left sternal edge (Graham Steell murmur), similar to that of aortic regurgitation. Usually there are no symptoms and treatment is rarely required. Pulmonary stenosis is usually a congenital lesion but may present in adult life with fatigue, syncope and right ventricular failure.

Infective endocarditis

Infective endocarditis is an infection of the endocardium or vascular endothelium of the heart. It may occur as a fulminating or acute infection, but more commonly runs an insidious course and is known as subacute (bacterial) endocarditis (SBE).

Infection occurs in the following:

- On valves which have a congenital or acquired defect (usually on the left side of the heart). Right-sided endocarditis is more common in intravenous drug addicts.
- On normal valves with virulent organisms such as *Streptococcus pneumoniae* or *Staphylococcus aureus*.
- On prosthetic valves, when infection may be 'early' (within 60 days of valve surgery and acquired in perioperative period) or 'late' (following bacteraemia). Infected prosthetic valves often need to be replaced.
- In association with a ventricular septal defect or persistent ductus arteriosus.

Aetiology

Streptococcus viridans, *Staphylococcus aureus* and enterococci are common causes (Table 10.12). Blood cultures remain negative in 5–10% of patients, especially in the context of prior antibiotic therapy. Culture-negative endocarditis is particularly likely with organisms which are difficult to isolate in culture: *Coxiella burnetii* (the cause of Q fever), *Chlamydia* spp., *Bartonella* spp. (organisms that cause trench fever and cat scratch disease) and *Legionella*.

Pathology

A mass of fibrin, platelets and infectious organisms form vegetations along the edges of the valve. Virulent organisms destroy the valve, producing regurgitation and worsening heart failure.

Table 10.12 Modified Duke criteria for the diagnosis of infective endocarditis

Major criteria
Positive blood cultures for infective endocarditis
Typical microorganism for infective endocarditis from two separate blood cultures in the absence of a primary focus: e.g. *Streptococcus viridans, Streptococcus bovis,* community-acquired *Staphylococcus aureus* or enterococci
Persistently positive blood cultures, defined as recovery of a microorganism consistent with infective endocarditis from blood cultures drawn more than 12 hours apart *or* all of three or the majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart
Single positive blood culture for *Coxiella burnetii* or antiphase IgG antibody titre > 1:800
Evidence for endocardial involvement
TTE (TOE in prosthetic valve) showing oscillating intracardiac mass on a valve or supporting structures, in the path of regurgitant jet or on implanted material, in the absence of an alternative anatomic explanation, *or*
Abscess
New partial dehiscence of prosthetic valve
New valvular regurgitation
Minor criteria
Predisposition, e.g. prosthetic valve, intravenous drug use
Fever – 38°C
Vascular phenomena (e.g. major arterial emboli, septic pulmonary infarcts)
Immunological phenomena (e.g. Osler's nodes, glomerulonephritis)
Echocardiogram – findings consistent with infective endocarditis but not meeting major criteria
Microbiological evidence – positive blood culture but not meeting major criteria

TTE, transthoracic echocardiogram; TOE, transoesophageal echocardiogram.

Clinical features

Symptoms and signs result from:

- Systemic features of infection, such as malaise, fever, night sweats, weight loss and anaemia. Slight splenomegaly is common. Clubbing is rare and occurs late.
- Valve destruction, leading to heart failure and new or changing heart murmurs (in 90% of cases).

- Vascular phenomena due to embolization of vegetations and metastatic abscess formation in the brain, spleen and kidney. Embolization from right-sided endocarditis causes pulmonary infarction and pneumonia.
- Immune complex deposition in blood vessels producing a vasculitis and petechial haemorrhages in the skin, under the nails (splinter haemorrhages) and in the retinae (Roth's spots). Osler's nodes (tender subcutaneous nodules in the fingers) and Janeway lesions (painless erythematous macules on the palms) are uncommon. Immune complex deposition in the joints causes arthralgia and, in the kidney, acute glomerulonephritis. Microscopic haematuria occurs in 70% of cases but acute kidney injury is uncommon.

Endocarditis should always be excluded in any patient with a heart murmur and fever.

Investigation

- Blood cultures must be taken before antibiotics are started. Three sets (i.e. six bottles) taken over 24 hours will identify the organism in 75% of cases. Special culture techniques are occasionally necessary if blood cultures are negative.
- Transthoracic echocardiography (TTE) identifies vegetations and underlying valvular dysfunction. Small vegetations may be missed and a normal echocardiogram does not exclude endocarditis. Transoesophageal echocardiography (TOE) is more sensitive (but not 100%) particularly in cases of suspected prosthetic valve endocarditis.
- Serological tests may be helpful if unusual organisms are suspected, e.g. *Coxiella, Bartonella, Legionella*.
- Chest X-ray may show heart failure or evidence of septic emboli in right-sided endocarditis.
- ECG may show MI (emboli to the coronary circulation) or conduction defects (due to extension of the infection to the valve annulus and adjacent septum).
- Blood count shows a normochromic, normocytic anaemia with a raised ESR and often a leucocytosis.
- Urine Stix testing shows haematuria in most cases.
- Serum immunoglobulins are increased and complement levels decreased as a result of immune complex formation.

Diagnostic criteria

The Duke classification for diagnosis of endocarditis relies upon major and minor criteria (see Table 10.12). A definite diagnosis of endocarditis requires one of the following:

- Direct evidence of infective endocarditis by histology or culture of organism, e.g. from a vegetation
- Two major criteria

- One major and any three minor criteria
- Five minor criteria.

Possible endocarditis is diagnosed if there is one major and one minor criterion or three minor.

Management

Drug therapy Treatment is with bactericidal antibiotics, given intravenously for the first 2 weeks and by mouth for a further 2–4 weeks. While awaiting the results of blood cultures, a combination of intravenous benzylpenicillin and gentamicin is given unless staphylococcal endocarditis is suspected, when vancomycin should be substituted for penicillin. Subsequent treatment depends on the results of blood cultures and the antibiotic sensitivity of the organism. Antibiotic doses are adjusted to ensure adequate bactericidal activity (microbiological assays of minimum bactericidal concentrations).

Surgery

Surgery to replace the valve should be considered when there is severe heart failure, early infection of prosthetic material, worsening renal failure and extensive damage to the valve.

PULMONARY HEART DISEASE

Pulmonary hypertension

The lung circulation offers a low resistance to flow compared to the systemic circulation and the normal mean pulmonary artery pressure (PAP) at rest is 10–14 mmHg (compared to mean systemic arterial pressure of about 90 mmHg). Pulmonary hypertension is characterized by an elevated PAP (>25 mmHg at rest) and secondary right ventricular failure.

Aetiology

Pulmonary hypertension occurs due to an increase in pulmonary vascular resistance or an increase in pulmonary blood flow. Specific causes are listed in Table 10.13.

Clinical features

Exertional dyspnoea, lethargy and fatigue are the initial symptoms due to an inability to increase cardiac output with exercise. As right ventricular failure develops there is peripheral oedema and abdominal pain from hepatic congestion. On examination there is a loud pulmonary second sound, and a right parasternal heave (caused by right ventricular hypertrophy). In advanced disease there are features of right heart failure (cor pulmonale): elevated jugular venous pressure with a prominent V wave if tricuspid regurgitation is present,

Table 10.13 Causes of pulmonary hypertension

Pulmonary arterial hypertension:
Idiopathic (no cause identified)
Autoimmune rheumatic diseases, e.g. systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis
Congenital heart disease with systemic-to-pulmonary communication (atrial septal defect, ventricular septal defect)
Portal hypertension (portopulmonary hypertension)
Drugs: long-term use of cocaine and amphetamines, dexfenfluramine
HIV infection
Hereditary
Schistosomiasis
Chronic haemolytic anaemia
Pulmonary veno-occlusive disease
Pulmonary hypertension secondary to:
Left heart disease: valvular, systolic dysfunction, diastolic dysfunction
Lung disease and/or hypoxia, e.g. chronic obstructive pulmonary disease, obstructive sleep apnoea, lung fibrosis
Thromboembolic occlusion of proximal or distal pulmonary vasculature
Multifactorial mechanisms: myeloproliferative disorders, sarcoidosis, glycogen storage disease

hepatomegaly, a pulsatile liver, peripheral oedema, ascites and a pleural effusion. There are also features of the underlying disease.

Investigations

The aim of investigation is to confirm the presence of pulmonary hypertension and demonstrate the cause:

- Chest X-ray shows enlarged proximal pulmonary arteries which taper distally. It may also reveal the underlying cause (e.g. emphysema, calcified mitral valve).
- ECG shows right ventricular hypertrophy and P pulmonale (p. 412).
- Echocardiography shows right ventricular dilatation and/or hypertrophy and may also reveal the cause of pulmonary hypertension, e.g. intracardiac shunt. It is possible to measure the peak PAP with Doppler echocardiography.
- Right heart catheterization may be indicated to confirm the diagnosis (elevated PAP), to determine the pulmonary wedge pressure (PWP), to calculate the cardiac output and to assess for pulmonary vascular resistance and reactivity.

Management

The initial treatment is oxygen, warfarin (due to a higher risk of intrapulmonary thrombosis), diuretics for oedema and oral calcium-channel blockers as pulmonary vasodilators, together with treatment of the underlying cause. In more advanced disease, treatment is aimed at decreasing pulmonary vascular resistance and includes oral endothelin receptor antagonists (bosentan, sitaxentan), prostanoid analogues (inhaled iloprost, treprostinil, beraprost), intravenous epoprostenol and oral sildenafil or tadalafil. In primary pulmonary hypertension there is a progressive downhill course and many patients ultimately require heart and lung transplantation.

Pulmonary embolism

Pulmonary embolism (PE) is a common and potentially lethal condition. Unfortunately, the diagnosis is often missed because the presenting symptoms are vague or non-specific. Emboli usually arise from thrombi in the iliofemoral veins (deep venous thrombosis, p. 488). The risk factors for thromboembolism are listed on p. 241. Rarely, PE results from clot formation in the right heart.

Pathology

A massive embolism obstructs the right ventricular outflow tract and therefore suddenly increases pulmonary vascular resistance, causing acute right heart failure. A small embolus impacts in a terminal, peripheral pulmonary vessel and may be clinically silent unless it causes pulmonary infarction. Lung tissue is ventilated but not perfused, resulting in impaired gas exchange. It is important to consider PE in the differential diagnosis of chest pain with elevated troponin. The rise in troponin reflects right ventricular ischaemia and is associated with adverse outcomes.

Clinical features

- Small/medium PEs present with breathlessness, pleuritic chest pain, and haemoptysis if there is pulmonary infarction. On examination the patient may be tachypnoeic and have a pleural rub and an exudative (occasionally bloodstained) pleural effusion can develop.
- Massive PE presents as a medical emergency: the patient has severe central chest pain and suddenly becomes shocked, pale and sweaty, with marked tachypnoea and tachycardia. Syncope and death may follow rapidly. On examination the patient is shocked, with central cyanosis. There is elevation of the jugular venous pressure, a right ventricular heave, accentuation of the second heart sound and a gallop rhythm (acute right heart failure).
- Multiple recurrent PEs present with symptoms and signs of pulmonary hypertension (pp. 471–472), developing over weeks to months.

Investigations

A clinical pre-test probability score of PE is used prior to investigation (Table 10.14), which helps to decide on the most appropriate first-line diagnostic test and interpretation of the results (Emergency Box 10.5):

- Chest X-ray, ECG and blood gases may all be normal with small/medium emboli and any abnormalities with massive emboli are non-specific. The chest X-ray and ECG are useful to exclude other conditions that may present similarly. The chest X-ray may show decreased vascular markings and a raised hemidiaphragm (caused by loss of lung volume). With pulmonary infarction, a late feature is the development of a wedge-shaped opacity adjacent to the pleural edge, sometimes with a pleural effusion. The most

Table 10.14 Revised Geneva score for the clinical prediction of a pulmonary embolism

	Score
Risk factors	
Age > 65 years	+1
Previous deep venous thrombosis or pulmonary embolism	+3
Surgery or fracture within 1 month	+2
Active malignancy	+2
Symptoms	
Unilateral leg pain	+3
Haemoptysis	+2
Clinical signs	
Heart rate (beats/min)	
75–94	+3
≥95	+5
Pain on leg deep vein palpation and unilateral oedema	+4
Clinical probability	**Total score**
Low	0–3
Intermediate	4–10
High	≥11

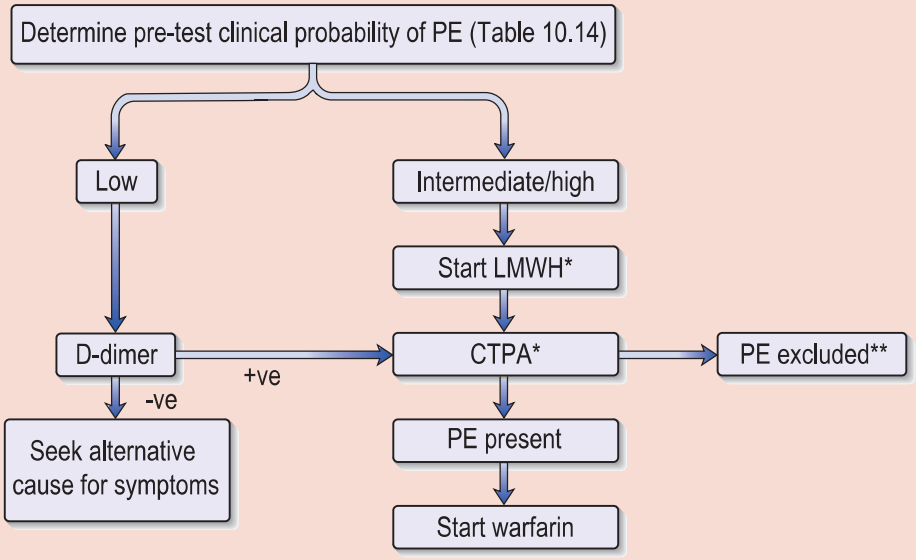
NB: diagnosis of pulmonary embolism (PE) is not excluded on this basis alone; about 8% of patients with a low clinical score will have a PE.
(After Righini M, Le Gal G, Aujesky D, et al. (2008) Lancet 371: 1343–1352, with permission from Elsevier.)

Emergency Box 10.5

Management of suspected and confirmed pulmonary embolism (PE)

Investigation and diagnosis

Investigation and diagnosis



- D dimer, arterial blood gas, ECG, CXR, CTPA or echo
- High flow oxygen if hypoxaemic
- Thrombolysis (p. 251) for massive embolism with persistent hypotension
- Analgesia: morphine (5–10 mg i.v.) relieves pain and anxiety
- Prevention of further thrombi: LMWH and oral warfarin (p. 248). NOACs (p. 250) are also used in patients with VTE (dabigatran, rivaroxaban and apixaban).
- Intravenous fluids (to raise the filling pressure) for patients presenting with moderate/severe embolism.

CTPA, CT pulmonary angiogram; CXR, chest X-ray; ECG, electrocardiogram; LMWH, low-molecular-weight heparin; NOACs, novel oral anticoagulants; VTE, venous thromboembolis.

*Patients with massive PE and persistent hypotension should be treated with thrombolysis. In these cases, bedside echocardiography is an alternative diagnostic test to CTPA if CT is not immediately available or the patient is too unstable for transfer to the radiology department.

**Rarely, CTPA is inconclusive and high pre-test clinical probability patients may need further imaging, e.g. repeat CTPA (if poor quality initially), Doppler ultrasound of legs (to look for a source thrombus) or $\dot{V}/\dot{Q}$ scan.

common ECG finding is sinus tachycardia or there may be new-onset atrial fibrillation. The features of acute right heart strain may be seen: tall peaked P waves in lead II, right axis deviation and right bundle branch block. Arterial blood gases show hypoxaemia and hypocapnia with massive emboli.

- Plasma D-dimers are a subset of fibrinogen degradation products released into the circulation when a clot begins to dissolve. D-dimers are, however, elevated in many other conditions (e.g. cancer, pregnancy, post-operatively) and a positive result is not diagnostic of thromboembolic disease. The value of D-dimer testing is in patients with a low pre-test clinical probability score (Table 10.14 and Emergency Box 10.5).
- Spiral CT with *intravenous* contrast (CT pulmonary angiography, CTPA) images the pulmonary vessels directly and is highly sensitive for the detection of large proximal pulmonary emboli. It is increasingly being used as the diagnostic test of choice for patients with suspected PE. Subsegmental emboli may be missed and occasionally patients may need further imaging (Emergency Box 10.5). One of the benefits over $\dot{V}/\dot{Q}$ scan is the ability to detect an alternative pathology that may explain the clinical presentation.
- Radionuclide lung scan ($\dot{V}/\dot{Q}$ scan) demonstrates areas of ventilated lung with perfusion defects (ventilation-perfusion defects). Pulmonary embolism is excluded in patients with a normal scan. However, there is high incidence of non-diagnostic scans, especially in patients with coexistent chronic lung disease, who will then need further imaging.
- Ultrasound will detect clots in the pelvic or iliofemoral veins.
- MRI gives similar results and is used if CT is contraindicated.
- Echocardiography is diagnostic in massive PE and can be performed at the bedside. It demonstrates proximal thrombus and right ventricular dilatation.

Management

Management of PE is summarized in Emergency Box 10.5. Patients are classed as *high risk* and *not high risk* based on the presence of shock or hypotension *High-risk* patients should proceed to CTPA. A negative test should lead to investigations for other causes of haemodynamic instability. Echocardiography may be useful if patients are too unstable for CTPA. In *not high-risk* patients, the clinical probability of pulmonary embolus should be determined using a scoring system such as the revised Geneva rules (Table 10.14) and D-dimer assay. The only definite indication for thrombolysis in acute massive embolism is persistent arterial hypotension. Surgical embolectomy is occasionally undertaken if thrombolysis is contraindicated or ineffective. In contrast, patients who are cardiovascularly stable and who have no coexistent serious medical pathology can be treated at home once the diagnosis is confirmed. Anticoagulation is continued for 6 weeks to 6 months (p. 248), depending on the likelihood of recurrence of thromboembolism, and lifelong treatment is indicated for recurrent emboli. Insertion of a vena caval filter is used to prevent further emboli when emboli recur despite adequate anticoagulation or in high-risk individuals where anticoagulation is contraindicated.

Pulmonary embolism in pregnancy

Pulmonary embolism occurs more frequently in pregnancy and is the leading cause of maternal death in the developed world. Compression ultrasonography of the legs is the initial investigation. CTPA is required if ultrasound is normal and delivers a lower dose of radiation to the fetus than $\dot{V}/\dot{Q}$ scanning. Warfarin is teratogenic and confirmed PE is treated with low-molecular-weight heparin (LMWH).

MYOCARDIAL DISEASE

Myocarditis

Myocarditis is an inflammation of the myocardium. The most common cause in the UK is viral, particularly Coxsackie virus infection, but it may also occur with diphtheria, rheumatic fever, radiation injury and some drugs. Myocarditis in association with human immunodeficiency virus (HIV) infection is seen at post-mortem in up to 20% of cases but causes clinical problems in less than 10% of cases.

Clinical features

Patients present with an acute illness characterized by fever and varying degrees of biventricular failure. Cardiac arrhythmias and pericarditis may also occur.

Investigations

- Chest X-ray may show cardiac enlargement.
- ECG shows non-specific T-wave and ST changes and arrhythmias.
- The diagnosis is supported by demonstration of an increase in serum viral titres. Cardiac biopsy is not usually performed as the findings rarely influence management. Cardiac enzymes are elevated.

Management

Treatment is with bed rest and treatment of heart failure. The prognosis is generally good.

CARDIOMYOPATHY

Cardiomyopathies comprise a group of diseases of the myocardium that affect the mechanical (hypertrophic, arrhythmogenic right ventricular, dilated and restrictive cardiomyopathy) or electrical function (conduction system disease and ion channelopathies, e.g. long QT syndrome) of the heart. Diagnosis of myocardial disease is usually by imaging (echocardiogram and CMR).

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is characterized by marked ventricular hypertrophy in the absence of abnormal loading conditions such as hypertension and valvular disease. There is usually disproportionate involvement of the interventricular septum. The hypertrophic non-compliant ventricles impair diastolic filling, so that stroke volume is reduced. Most cases are familial, autosomal dominant and caused by mutations in genes encoding sarcomeric proteins, e.g. troponin T and β-myosin. It is the most common cause of sudden cardiac death in young people.

Clinical features

Patients may be symptom-free (and detected through family screening) or have breathlessness, angina or syncope. Complications include sudden death, atrial and ventricular arrhythmias, thromboembolism, infective endocarditis and heart failure. The carotid pulse is jerky because of rapid ejection and sudden obstruction to the ventricular outflow during systole. An ejection systolic murmur occurs because of left ventricular outflow obstruction, and the pansystolic murmur of functional mitral regurgitation may also be heard.

Investigations

- ECG is almost always abnormal. A pattern of left ventricular hypertrophy with no discernible cause is diagnostic.
- Cardiac imaging shows ventricular hypertrophy (on echo and magnetic resonance [MR]) and fibrosis (on MR).
- Genetic analysis may confirm the diagnosis and provide prognostic information.

Management

Amiodarone reduces the risk of arrhythmias and sudden death. Individuals at highest risk are fitted with an ICD. Chest pain and dyspnoea are treated with β-blockers and verapamil. Vasodilators should be avoided because they may aggravate left ventricular outflow obstruction or cause refractory hypotension. In selected cases, outflow tract gradients are reduced by surgical resection or alcohol ablation of the septum, or by dual-chamber pacing.

Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is characterized by a dilated left ventricle which contracts poorly. Inheritance is autosomal dominant in the familial disease.

Clinical features

Shortness of breath is usually the first complaint; less often, patients present with embolism (from mural thrombus) or arrhythmia. Subsequently, there is progressive heart failure with the symptoms and signs of biventricular failure.

Investigations

- Chest X-ray may show cardiac enlargement.
- ECG is often abnormal. The changes are non-specific and include arrhythmias and T-wave flattening.
- Cardiac imaging shows dilated ventricles with global hypokinesis. Cardiac MR may show other aetiologies of left ventricular dysfunction, e.g. previous MI.

Other tests such as coronary angiography, viral and autoimmune screen and endomyocardial biopsy may be needed to exclude other diseases (Table 10.15) that present with the clinical features of DCM.

Management

Heart failure and atrial fibrillation are treated in the conventional way (pp. 436, 430). Cardiac resynchronization therapy and ICDs are used in patients with NYHA III/IV grading. Severe cardiomyopathy is treated with cardiac transplantation.

Primary restrictive cardiomyopathy

The rigid myocardium restricts diastolic ventricular filling and the clinical features resemble those of constrictive pericarditis (pp. 481–482). In the UK the most common cause is amyloidosis. The ECG, chest X-ray and echocardiogram are often abnormal, but the findings are non-specific. Diagnosis is by cardiac catheterization, which shows characteristic pressure changes. An endomyocardial biopsy may be taken during the catheter procedure, thus providing histological diagnosis. There is no specific treatment and the prognosis is poor, with most patients dying less than a year after diagnosis. Cardiac transplantation is performed in selected cases.

Table 10.15 Heart muscle disease presenting with features of dilated cardiomyopathy

Ischaemia
Hypertension
Congenital heart disease
Peripartum cardiomyopathy
Infections, e.g. cytomegalovirus, HIV
Alcohol excess
Muscular dystrophy
Amyloidosis
Haemochromatosis

Arrhythmogenic right ventricular cardiomyopathy

There is progressive fibro-adipose replacement of the wall of the right ventricle. The typical presentation is ventricular tachycardia or sudden death in a young man.

PERICARDIAL DISEASE

The normal pericardium is a fibroelastic sac containing a thin layer of fluid (50 mL) that surrounds the heart and roots of the great vessels.

Acute pericarditis

Aetiology

In the UK, acute inflammation of the pericardium is most commonly secondary to viral infection (Coxsackie B, echovirus, HIV infection) or MI. Other causes include uraemia, autoimmune rheumatic diseases, trauma, infection (bacterial, tuberculosis, fungal) and malignancy (breast, lung, leukaemia and lymphoma).

Clinical features

There is sharp retrosternal chest pain which is characteristically relieved by leaning forward. Pain may be worse on inspiration and radiate to the neck and shoulders. The cardinal clinical sign is a pericardial friction rub, which may be transient.

Diagnosis

The ECG is diagnostic. There is concave upwards (saddle-shaped) ST segment elevation across all leads and return towards baseline as inflammation subsides. ST segment elevation is convex upwards in MI and limited to the leads that face the infarct.

Management

Treatment is of the underlying disorder plus NSAIDs. Systemic corticosteroids are used in resistant cases. NSAIDs should not be used in the few days following MI as they are associated with a higher rate of myocardial rupture. Complications of acute pericarditis are pericardial effusion and chronic pericarditis (>6–12 months).

Pericardial effusion and tamponade

Pericardial effusion is an accumulation of fluid in the pericardial sac which may result from any of the causes of pericarditis. Hypothyroidism also causes a pericardial effusion which rarely compromises ventricular function. Pericardial tamponade is a medical emergency and occurs when a large amount of

pericardial fluid (which has often accumulated rapidly) restricts diastolic ventricular filling and causes a marked reduction in cardiac output.

Clinical features

The effusion obscures the apex beat and the heart sounds are soft. The signs of pericardial tamponade are hypotension, tachycardia and an elevated jugular venous pressure, which paradoxically rises with inspiration (Kussmaul's sign). There is invariably pulsus paradoxus (a fall in BP of more than 10 mmHg on inspiration). This is the result of increased venous return to the right side of the heart during inspiration. The increased right ventricular volume thus occupies more space within the rigid pericardium and impairs left ventricular filling.

Investigations

- Chest X-ray shows a large globular heart.
- ECG shows low-voltage complexes with sinus tachycardia.
- Echocardiography is diagnostic, showing an echo-free space around the heart.
- Invasive tests to establish the cause of the effusion may only be necessary with a persistent effusion, if a purulent, tuberculous or malignant effusion is suspected, or if the effusion is not known to be secondary to an underlying illness. Pericardiocentesis (aspiration of fluid under echocardiographic guidance) and pericardial biopsy for culture, cytology/histology and polymerase chain reaction (PCR) (for tuberculosis) give a greater diagnostic yield with large effusions.

Management

Most pericardial effusions resolve spontaneously. Tamponade requires emergency pericardiocentesis. Pericardial fluid is drained percutaneously by introducing a needle into the pericardial sac. If the effusion recurs, despite treatment of the underlying cause, excision of a pericardial segment allows fluid to be absorbed through the pleural and mediastinal lymphatics.

Constrictive pericarditis

In the UK, most cases of constrictive pericarditis are idiopathic in origin or result from intrapericardial haemorrhage during heart surgery.

Clinical features

The heart becomes encased within a rigid fibrotic pericardial sac which prevents adequate diastolic filling of the ventricles. The clinical features resemble those of right-sided heart failure, with jugular venous distension, dependent oedema, hepatomegaly and ascites. Kussmaul's sign (JVP rises paradoxically with inspiration) is usually present and there may be pulsus paradoxus, atrial

fibrillation and, on auscultation, a pericardial knock caused by rapid ventricular filling. Clinically, constrictive pericarditis cannot be distinguished from restrictive cardiomyopathy (p. 479).

Investigations

A chest X-ray shows a normal heart size and pericardial calcification (best seen on the lateral film). Diagnosis is made by CT or MRI, which shows pericardial thickening and calcification.

Management

Treatment is by surgical excision of the pericardium.

SYSTEMIC HYPERTENSION

The level of BP is said to be abnormal when it is associated with a clear increase in morbidity and mortality from heart disease, stroke and renal failure. This level varies with age, sex, race and country. The definition of hypertension is over 140/90 mmHg, based on at least two readings on separate occasions. The validity of a single BP measurement is unclear (BP rises acutely in certain situations, e.g. visiting the doctor). In the UK, NICE recommends that ambulatory BP monitoring (ABPM) is offered to patients with a clinic BP of $\geq$ 140/90 mmHg to confirm the diagnosis of hypertension. Home BP monitoring (HBPM) can also be used.

Aetiology

Essential hypertension Most patients with hypertension (80–90%) have no known underlying cause, i.e. 'primary' or 'essential' hypertension. Essential hypertension has a multifactorial aetiology:

- Genetic component
- Low birthweight
- Obesity
- Excess alcohol intake
- High salt intake
- The metabolic syndrome (p. 165).

Secondary hypertension Secondary hypertension is the result of a specific and potentially treatable cause:

- Renal disease accounts for over 80% of cases of secondary hypertension. The common causes are diabetic nephropathy, chronic glomerulonephritis, adult polycystic kidneys, chronic tubulointerstitial nephritis and renovascular disease.
- Endocrine disease (p. 645): Conn's syndrome, adrenal hyperplasia, phaeochromocytoma, Cushing's syndrome and acromegaly.

- Coarctation of the aorta is a congenital narrowing of the aorta at, or just distal to, the insertion of the ductus arteriosus, i.e. distal to the left subclavian artery. There is hypertension due to decreased renal perfusion, delayed (radiofemoral delay) pulses in the legs, a mid-late systolic murmur and 'rib notching' (collateral arteries erode the undersurface of ribs) on X-ray.
- Pre-eclampsia occurring in the third trimester of pregnancy.
- Drugs, including oestrogen-containing oral contraceptives, other steroids, NSAIDs and vasopressin.

Clinical features

Hypertension is generally asymptomatic. Secondary causes of hypertension may be suggested by specific features, such as attacks of sweating and tachycardia in phaeochromocytoma. Malignant or accelerated hypertension describes a rapid rise in BP with severe hypertension (diastolic BP $>$ 120 mmHg). The characteristic histological change is fibrinoid necrosis of the vessel wall and untreated it will result in end-organ damage in the kidneys (haematuria, proteinuria, progressive kidney disease), brain (cerebral oedema and haemorrhage), retina (flame-shaped haemorrhages, cotton wool spots, hard exudates and papilloedema) and cardiovascular system (acute heart failure and aortic dissection).

Examination In most patients the only finding is high BP, but in other patients, signs relating to the cause (e.g. abdominal bruit in renal artery stenosis, delayed femoral pulses in coarctation of the aorta) or the end-organ effects of hypertension may be present: e.g. loud second heart sound, left ventricular heave, fourth heart sound in hypertensive heart disease, and retinal abnormalities. The latter are graded according to severity:

- Grade 1 – increased tortuosity and reflectiveness of the retinal arteries (silver wiring)
- Grade 2 – grade 1 plus arteriovenous nipping
- Grade 3 – grade 2 plus flame-shaped haemorrhages and soft 'cotton wool' exudates
- Grade 4 – grade 3 plus papilloedema.

Risk assessment and investigations

Patients with hypertension should have their cardiovascular risk assessed using an appropriate calculator – NICE recommends QRISK2-2014 (http://www.qrisk.org/index.php). Investigations are carried out to identify end-organ damage and those patients with secondary causes of hypertension. Routine investigation should include:

- Serum urea and electrolytes, which may show evidence of renal impairment, in which case more specific renal investigations (e.g. renal ultrasound, renal angiography) are indicated. Hypokalaemia occurs in Conn's syndrome.

- Urinalysis for protein and blood, which may indicate renal disease (either the cause or the effect of hypertension).
- Blood glucose.
- Serum lipids.
- ECG, which may show evidence of left ventricular hypertrophy or myocardial ischaemia.

Patients under 40 years old with no risk factors or those where an underlying cause is suspected (e.g. from clinical examination or abnormal baseline investigations) should undergo further investigation for secondary causes of hypertension.

Management

Treatment is begun immediately in patients with malignant or severe hypertension (BP $\geq$ 180/110 mmHg). In other patients, treatment is started if repeated measurements confirm sustained hypertension (Table 10.16). For most patients, target BP during treatment is 140/90 mmHg. For patients with diabetes, chronic kidney disease or cardiovascular disease, a lower target of 130/80 mmHg is recommended.

Non-pharmacological measures in the treatment of hypertension include:

- Weight reduction (aim for body mass index [BMI] $<$ 25 kg/m^2)
- Low-fat and low saturated fat diet

Table 10.16 Indications for treatment based on sustained blood pressure recordings

Severity	BP (mmHg)	Intervention
Stage 1 hypertension	Clinic BP $\geq$ 140/90 and daytime average ABPM or HBPM $\geq$ 135/85	Offer treatment to everyone under 80 years old with at least one of the following risk factors: • Target organ damage • Cardiovascular disease • Renal disease • Diabetes • 10-year cardiovascular risk $\geq$ 20%
Stage 2 hypertension	Clinic BP $\geq$ 160/100 and daytime average ABPM or HBPM $\geq$ 150/95	All patients should be offered treatment
Severe hypertension	>180/110	Treat immediately

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; HBPM, home blood pressure monitoring.

- Low-salt diet (<6 g sodium chloride per day)
- Limited alcohol consumption (<21 units and <14 units per week for men and women, respectively)
- Dynamic exercise (at least 30 minutes brisk walk per day)
- Increased fruit and vegetable consumption
- Reduce cardiovascular risk by stopping smoking and increasing oily fish consumption.

In most hypertensive patients, statins (p. 701) are also given to reduce the overall cardiovascular risk burden. Glycaemic control should be optimized in diabetics ($HbA_{1c} < 53$ mmol/mol). For each class of antihypertensive there will be indications and contraindications in specific patient groups. A single antihypertensive drug is used initially, but combination treatment will be needed in many patients to control BP. In patients without compelling reasons for a particular drug class, a treatment algorithm such as the one advocated by NICE (Fig. 10.17) is used to advise on the sequencing of drugs and logical drug combinations. This algorithm is based on the observation that younger people and Caucasians tend to have higher renin levels compared to older people or the black population. Thus the 'A' drugs which reduce BP at least in part by suppression of the renin–angiotensin system are more effective as initial blood-pressure-lowering therapy in younger Caucasian patients.

Group A: ACE inhibitors (p. 497), e.g. captopril, enalapril, lisinopril and ramipril, block the conversion of angiotensin I to angiotensin II, which is a potent vasoconstrictor, and block degradation of bradykinin, which is a vasodilator. Side effects include first-dose hypotension and cough, proteinuria, rashes and leucopenia in high doses. ACEIs are contraindicated in renal artery stenosis because inhibition of the renin–angiotensin system in this instance may lead to loss of renal blood flow and infarction of the kidney.

Group B: Angiotensin II receptor antagonists (p. 498), e.g. losartan, valsartan, irbesartan and candesartan, selectively block receptors for angiotensin II. They share some of the actions of ACEIs and are useful in patients who cannot tolerate ACEIs because of cough.

Group C: Calcium antagonists (p. 501), e.g. amlodipine and nifedipine, act predominantly by dilatation of peripheral arterioles. Side effects include bradycardia and cardiac conduction defects (verapamil and diltiazem), headaches, flushing and fluid retention.

Group D: Diuretics increase renal sodium and water excretion and directly dilate arterioles (p. 351). Loop diuretics, e.g. furosemide, and thiazide diuretics, e.g. bendroflumethiazide (bendrofluazide), are equally effective in lowering BP, although thiazides are usually preferred, as the duration of action is longer, the diuresis is not so severe and they are cheaper. Thiazide diuretics cause hypercholesterolaemia, hypokalaemia, hyponatraemia, hyperuricaemia (may precipitate gout) and impairment of glucose tolerance.

β-Adrenergic blocking agents (p. 495) are no longer a preferred initial therapy for hypertension. They are used in younger patients, particularly those

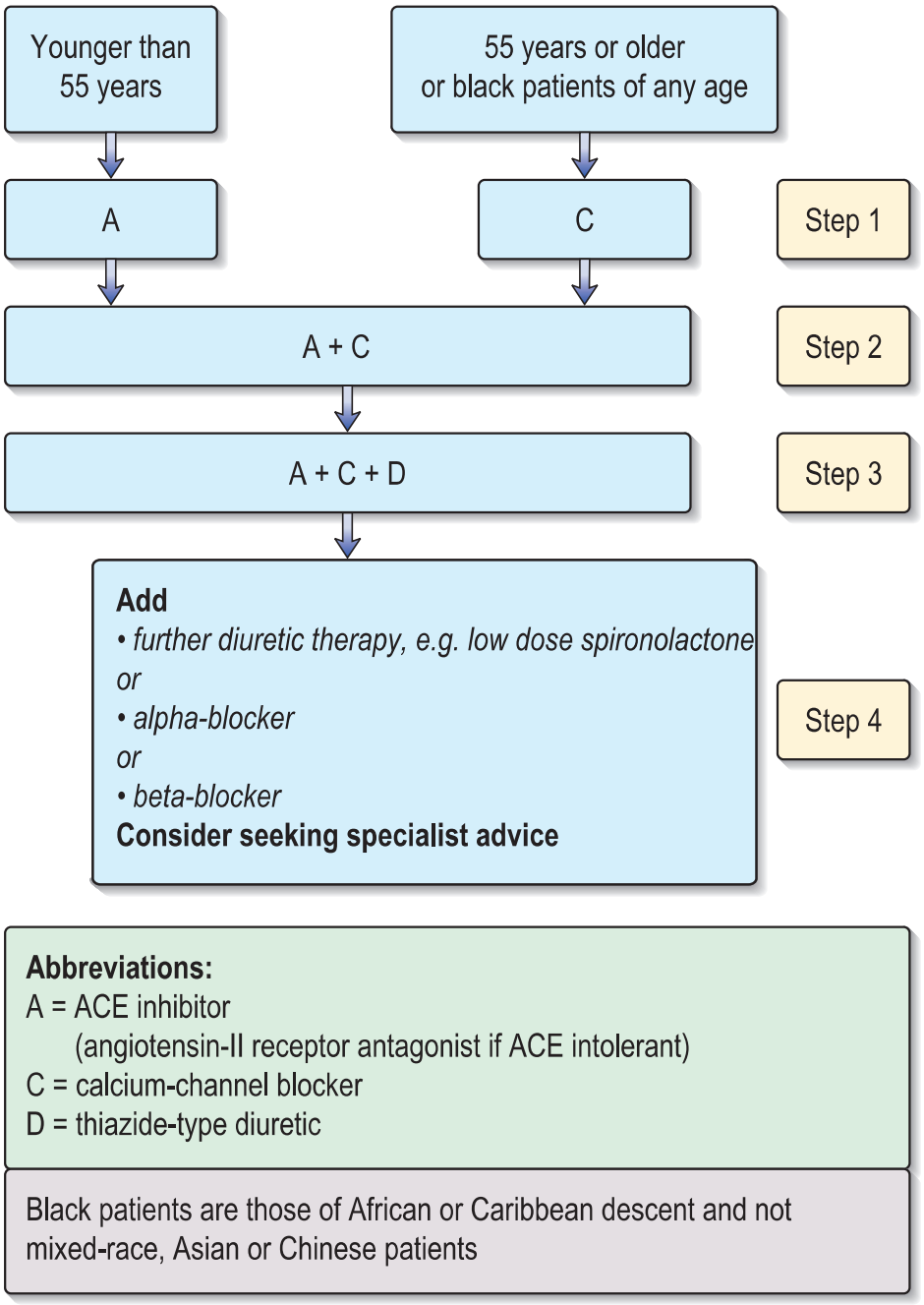


Fig. 10.17 Choosing drugs for patients newly diagnosed with hypertension.
National Institute for Health and Clinical Excellence (2016). NICE pathway: treatment steps for hypertension. http://pathways.nice.org.uk/pathways/hypertension. Pathway last updated 26/4/16.

with an intolerance or contraindication to ACEIs and angiotensin-II receptor antagonists; women of child-bearing potential; or patients with evidence of increased sympathetic drive. β-Blockers reduce renin production and sympathetic nervous system activity. Complications include bradycardia, bronchospasm, cold extremities, fatigue and weakness.

Other agents α-Blocking agents (e.g. doxazosin), hydralazine, an aldosterone antagonist (spironolactone) and centrally acting agents (e.g. clonidine, moxonidine) may be indicated in specific circumstances.

Management of severe hypertension

Patients with malignant (p. 483) or severe hypertension (diastolic BP > 140 mmHg) should be admitted to hospital for treatment. The aim should be to reduce the diastolic BP slowly (over 24–48 hours) to about 100–110 mmHg and this is usually achieved with oral antihypertensives, e.g. atenolol or amlodipine. Sublingual and intravenous antihypertensives are not recommended because they may produce a precipitous fall in BP, leading to cerebral infarction. When rapid control of BP is required (e.g. aortic dissection), the agent of choice is intravenous sodium nitroprusside (starting dose 0.3 μg/kg/min, i.e. 100 mg nitroprusside in 250 mL saline at 2–5 mL/h) or labetalol.

ARTERIAL AND VENOUS DISEASE

Aortic aneurysms

An aneurysm is a permanent localized dilatation of an artery. They may be asymptomatic or cause symptoms by pressure effects or vessel rupture, occasionally with fistula formation, or they may be a source of emboli. Aortic aneurysms (vessel diameter > 3 cm) are usually abdominal and most result from a degenerative process and present in elderly men. Some are the result of connective tissue disease.

Abdominal Abdominal aortic aneurysms can be asymptomatic (e.g. found as a pulsating mass on abdominal examination). In the UK, ultrasound screening should be offered to men aged 65–74 years. Aneurysms may also cause symptoms due to pressure effects (epigastric or back pain) or rupture. The latter is a surgical emergency presenting with epigastric pain radiating to the back, and hypovolaemic shock. Diagnosis is by ultrasonography or CT scan. Surgical replacement of the aneurysmal segment with a prosthetic graft is indicated for a symptomatic aneurysm or large asymptomatic aneurysms (>5.5 cm). In patients who are poor surgical risks, endovascular repair with insertion of an aortic stent is being increasingly employed.

Thoracic Cystic medial necrosis and atherosclerosis are the usual causes of thoracic aneurysms. Cardiovascular syphilis is no longer a common cause. Thoracic aneurysms may be asymptomatic, cause pressure on local structures (causing back pain, dysphagia and cough) or result in aortic regurgitation if the aortic root is involved.

Dissecting aortic aneurysm Aortic dissection results from a tear in the intima: blood under high pressure creates a false lumen in the diseased media. Typically there is an abrupt onset of severe, tearing central chest pain, radiating through to the back. Involvement of branch arteries may produce neurological signs, absent pulses and unequal BP in the arms. The chest X-ray shows a

widened mediastinum and the diagnosis is confirmed by CT scanning and transoesophageal echocardiography or MRI. Management involves urgent control of BP (p. 487) and surgical repair for proximal aortic dissection.

Raynaud's disease and phenomenon

Raynaud's phenomenon consists of intermittent spasm in the arteries supplying the fingers and toes. It is usually precipitated by cold and relieved by heat. There is initial pallor (resulting from vasoconstriction) followed by cyanosis and, finally, redness from hyperaemia. Raynaud's disease (no underlying disorder) occurs most commonly in young women and must be differentiated from secondary causes of Raynaud's phenomenon, e.g. autoimmune rheumatic disease and β-blocker therapy. Treatment is by keeping the hands and feet warm, stopping smoking and stopping β-blockers. Medical treatment includes oral nifedipine and occasionally prostacyclin infusions. Lumbar sympathectomy may help lower limb symptoms.

Venous disease

Superficial thrombophlebitis This usually occurs in the leg. The vein is painful, tender and hard, with overlying redness. Treatment is with simple analgesia, e.g. NSAIDs. Anticoagulation with fondaparinux can limit the extension of superficial thrombosis. Thromboembolic events are uncommon.

Deep venous thrombosis Thrombosis can occur in any vein, but those of the pelvis and leg are the most common sites. The risk factors for deep venous thrombosis (DVT) are listed on page 241.

Clinical features

DVT is often asymptomatic but the leg may be warm and swollen, with calf tenderness and superficial venous distension. The differential diagnosis includes ruptured Baker's cyst (p. 278), oedema from other causes and cellulitis.

Investigations

Measurement of serum D-dimer is the initial investigation in patients with a low clinical probability score (Table 10.17) and no further investigation is indicated if D-dimers are normal. In all other patients, venous compression ultrasonography, which is a reliable test for iliofemoral thrombosis, is indicated. It is not reliable for calf vein thrombosis, and repeat scanning 1 week later with interim heparin treatment is indicated if the initial scan is negative and there is high index of clinical suspicion.

Management

This is discussed on page 242.

Table 10.17 Wells score for the clinical probability of a deep venous thrombosis (DVT)

History			Score if present
Lower limb trauma or surgery or immobilization in a plaster cast			+1
Bedridden for more than 3 days or surgery within the last 4 weeks			+1
Malignancy (including treatment up to 6 months previously)			+1
Tenderness along deep venous system			+1
Clinical findings			
Entire limb swollen			+1
Calf swelling more than 3 cm compared to asymptomatic side, measured at 10 cm below tibial tuberosity			+1
Pitting oedema (greater in symptomatic leg)			+1
Dilated collateral superficial veins (non-varicose)			+1
Possible alternative diagnosis			
Alternative diagnosis (e.g. musculoskeletal injury, haematoma, chronic oedema, cellulitis of the leg, arthritis of the leg, Baker's cyst) as likely or greater than that of DVT			–2
Total score	≤0	1–2	≥3
Risk of DVT	3% (low)	17% (moderate)	75% (high)

The main aim of therapy is to prevent pulmonary embolism. Anticoagulation is initially with LMWH and subsequently with warfarin, usually continued for 3 months in above-knee DVTs. Anticoagulation of below-knee DVTs is recommended for 6 weeks, as 30% of patients will have proximal extension of the clot. Thrombolytic therapy is occasionally used for patients with a large iliofemoral thrombosis.

The main complications of DVT are pulmonary embolus, post-thrombotic syndrome (permanent pain, swelling, oedema and sometimes venous eczema may result from destruction of the deep-vein valves) and recurrence of thrombosis. Elastic support stockings are used for the post-thrombotic syndrome.

Prevention

Hospital-acquired venous thromboembolism is largely preventable. All patients should be assessed on admission to hospital and those at risk should be considered for pharmacological prophylaxis (fondaparinux, LMWH or unfractionated heparin if renal impairment) unless they have a risk factor for bleeding.

THERAPEUTICS FOR THE CARDIOVASCULAR SYSTEM

Electrical cardioversion

Cardioversion is the delivery of energy that is synchronized to the QRS complex, whereas defibrillation is non-synchronized delivery of energy, i.e. the shock is delivered randomly during the cardiac cycle (Table 10.18). In the patient who has had a cardiac arrest and is not responding to repeated defibrillation, a difficult decision is when to stop resuscitation and defibrillation efforts. This depends on the patient, the circumstances of the arrest and how long the patient has had a non-perfusing cardiac rhythm. In general, if a patient arrests in hospital and resuscitation has not resulted in a perfusing cardiac rhythm after 30 minutes, then further attempts are unlikely to be successful. The prognosis is poorer in patients who arrest outside hospital. There are exceptions: resuscitation is continued for longer in a hypothermic patient.

Indications

- Elective cardioversion:
  - atrial tachyarrhythmias.
- Emergency cardioversion:
  - atrial tachyarrhythmias causing haemodynamic compromise, e.g. hypotension, pulmonary oedema, myocardial ischaemia, impaired conscious level
  - VT
  - VF.

Contraindications

- Digitalis toxicity (relative contraindication) – induction of ventricular arrhythmias by cardioversion is more likely
- Atrial fibrillation with onset more than 24 hours previously (due to risk of embolism) unless patient has high-risk symptoms and signs (p. 430).

Table 10.18 Energy levels for biphasic defibrillators

Arrhythmia	Initial shock energy (J)
Broad-complex tachycardia	120–150
Atrial flutter and narrow-complex tachycardia	70–120
Atrial fibrillation	120–150
Ventricular arrhythmias	150–200

DRUGS FOR ARRHYTHMIAS

Adenosine

Mechanism of action

Adenosine is a purine nucleotide. It acts on adenosine receptors and enhances the flow of potassium out of myocardial cells; it produces hyperpolarization of the cell membrane and stabilizes the cell membrane. It has potent effects on the sinus (SA) node, causing complete heart block for a fraction of a second after i.v. administration and producing sinus bradycardia.

Indications

The main indication is reversion to sinus rhythm of atrioventricular junctional tachycardia.

Preparations and dose

3 mg/mL.

Intravenous injection By rapid i.v. injection into a central or large peripheral vein, 6 mg over 2 seconds with cardiac monitoring and resuscitation equipment available; if necessary, followed by 12 mg after 1–2 minutes, and then 12 mg after a further 1–2 minutes; increments should not be given if high-level AV block develops at any dose.

Side effects

Unwanted effects are common; however, they are usually transient. Patients should be warned before drug administration of side effects usually lasting less than 1 minute:

- Bradycardia and AV block
- Facial flushing, headache, chest pain or tightness
- Bronchospasm, sense of impending doom.

Cautions/contraindications

Contraindicated in asthma, second- or third-degree AV block and sick sinus syndrome (unless pacemaker fitted).

Amiodarone hydrochloride

Mechanism of action

Class III (Vaughan Williams' classification) drug action, which prolongs the duration of the action potential, thus increasing the absolute refractory period. Inhibits the potassium channels involved in repolarization.

Indications

Intravenous injection of amiodarone is used in cardiopulmonary resuscitation for ventricular fibrillation or pulseless tachycardia unresponsive to other interventions. Oral and i.v. amiodarone is used in the treatment of arrhythmias (supraventricular and ventricular tachycardia, atrial fibrillation and flutter), particularly when other drugs are ineffective or contraindicated. In the non-emergency setting it should only be initiated under specialist supervision. Unlike many other antiarrhythmic drugs, amiodarone causes little or no myocardial depression.

Preparations and dose

Tablets: 100 mg, 200 mg. Injection: 30 mg/mL or concentrate 50 mg/mL.

Oral Oral administration is 200 mg three times daily for 1 week reduced to 200 mg twice daily for a further week; the maintenance dose is usually 200 mg daily or the minimum required to control the arrhythmia.

Intravenous Intravenous administration is via central line catheter (in an emergency, e.g. ventricular tachycardia, can be given via a large peripheral line, but is a vesicant drug and therefore requires caution), initially 5 mg/kg in 250 mL glucose 5% (drug incompatible with sodium chloride) over 20–120 minutes with ECG monitoring. This may be repeated if necessary to a maximum of 1.2 g in 24 hours in 500 mL. As soon as an adequate response has been obtained, oral therapy should be initiated and the i.v. therapy phased out.

Side effects

Amiodarone therapy can be proarrhythmogenic in patients with significant structural heart disease. Amiodarone contains iodine and can cause both hypothyroidism and hyperthyroidism. Thyroid function tests including T_3 should be measured before treatment and then every 6 months of treatment. Liver toxicity can also occur, so liver biochemistry should be measured before and then every 6 months of treatment. Other side effects are reversible corneal microdeposits (drivers may be dazzled by headlights at night), phototoxic skin reactions (advise use of sunblock creams), slate-grey skin pigmentation, pneumonitis and peripheral neuropathy.

Cautions/contraindications

It is contraindicated in sinus bradycardia or sinoatrial heart block, unless pacemaker fitted, iodine sensitivity and thyroid dysfunction.

Many drugs interact with amiodarone, including warfarin and digoxin (check *British National Formulary* for full list). It has a very long half-life (extending to several weeks) and many months may be required to achieve steady-state concentrations; this is also important when drug interactions are considered.

Flecainide

Mechanism of action

Class Ic (Vaughan Williams' classification) antiarrhythmic drug. It is a membrane-depressant drug that reduces the rate of entry of sodium into the cell (sodium channel blocker). This may slow conduction, delay recovery or reduce the spontaneous discharge rate of myocardial cells.

Indications

AV nodal reciprocating tachycardia, arrhythmias associated with accessory conducting pathways (e.g. Wolff–Parkinson–White syndrome), paroxysmal atrial fibrillation. Occasionally it is used in ventricular tachyarrhythmias resistant to other treatments.

Preparations and dose

SVT – 50 mg twice daily, increased to maximum 300 mg daily.
'On demand' treatment for AF – 200 mg or 300 mg if weight greater than 70 kg, at the onset of paroxysm.

Side effects

Side effects include dizziness, visual disturbances, dyspnoea, palpitations, proarrhythmic effects, headache, fatigue and nausea in 5–10% of patients. Rarely, bronchospasm, heart block, bone marrow suppression and increased ventricular rate in AF/flutter are seen.

Cautions/contraindications

Class Ic agents increase mortality in post-MI patients with ventricular ectopy and should therefore be reserved for patients who ***do not*** have significant coronary artery disease, left ventricular dysfunction, or other forms of significant structural heart disease. Interactions with other drugs, including β-blockers and calcium-channel blockers, can occur (check *British National Formulary* for full list).

β-Blockers

See page 495.

Digoxin

Mechanism of action

This drug blocks AV conduction and reduces heart rate by enhancing vagal nerve activity and inhibiting sympathetic activity. It is positively inotropic (enhancing strength of cardiac contraction) by inhibition of Na^+/K^+-ATPase

and secondary activation of the Na^+/Ca^{2+} membrane exchange pump, thereby increasing intracellular calcium levels.

Indications

Digoxin is used in heart failure with atrial fibrillation or patients in sinus rhythm who remain symptomatic despite ACEI, β-blocker and diuretic uses. It is also used for rate control in sedentary patients with atrial fibrillation/flutter.

Preparations and dose

Tablets: 62.5, 125 and 250 μg. Injection: 250 μg/mL.

Check renal function and electrolytes before starting therapy; reduce dose in the elderly and in renal impairment.

Oral Rapid digitalization for atrial fibrillation/flutter 0.75–1.5 mg in divided doses over 24 hours and then maintenance of 125–250 μg once daily according to heart rate and renal function. For heart failure (sinus rhythm) 62.5–125 μg once daily is given.

Intravenous infusion Intravenous infusion for emergency loading dose for atrial fibrillation or flutter 0.75–1 mg (diluted in glucose 5% or sodium chloride 0.9% to a concentration of not more than 62.5 μg/mL) over at least 2 hours and then maintenance dose the next day by mouth.

Side effects

Side effects include nausea, vomiting, diarrhoea, conduction disturbances, blurred or yellow vision and ventricular arrhythmias. Side effects are common because of the narrow therapeutic index (the margin between effectiveness and toxicity). Hypokalaemia and renal impairment (reduce dose) increase the risk of toxicity. In suspected toxicity, measure plasma potassium concentration first and correct if hypokalaemia is evident. Plasma digoxin concentrations should be measured if toxicity is suspected; concentrations of >2 mmol/L usually suggest toxicity. In severe toxicity, give anti-digoxin antibodies.

Contraindications

Digoxin is contraindicated in arrhythmias associated with accessory conduction pathways, e.g. Wolff–Parkinson–White syndrome, because the accessory pathway is not affected. Blocking the normal pathway can increase the speed of conduction in the abnormal pathway and lead to ventricular arrhythmias. Caution should be demonstrated in left ventricular outflow tract obstruction. Diltiazem, verapamil, spironolactone and amiodarone inhibit renal excretion of digoxin; avoid with amiodarone and measure plasma levels with other drugs (see *British National Formulary* for full interaction list). Tetracycline, erythromycin and possibly other macrolides enhance the effect of digoxin. Rifampicin reduces serum concentrations.

DRUGS FOR HEART FAILURE

Diuretics

See Table 7.4 and pages 351–353.

β-Blockers

Mechanism of action

The β-adrenoceptors in the heart, peripheral vasculature, bronchi, pancreas and liver are blocked. They decrease heart rate, reduce the force of cardiac contraction and lower BP. These effects reduce myocardial oxygen demand and give more time for coronary perfusion. β-Blockers improve functional status and reduce cardiovascular morbidity and mortality in patients with heart failure.

Indications

The main indicators are angina, MI, arrhythmias, stable heart failure, hypertension, alleviation of symptoms of anxiety, prophylaxis of migraine, prevention of variceal bleeding and symptomatic treatment of hyperthyroidism (no effect on thyroid function tests).

Preparations and dose

Most β-blockers are equally effective, but there are differences between them which may affect the choice in particular diseases or individual patients, e.g. atenolol and metoprolol are used in angina; sotalol in the management of supraventricular and ventricular arrhythmias; propranolol in the treatment of hyperthyroidism, prevention of variceal bleeding and prophylaxis of migraine (usually); bisoprolol and carvedilol in the management of heart failure (usually specialist initiated) and nebivolol in the treatment of stable mild–moderate heart failure in patients over 70 years old.

Propranolol

Tablets: 10 mg, 40 mg, 80 mg, 160 mg. Oral solution: 5 mg/mL. Injection 1 mg/mL.

Oral

- Portal hypertension: initially 40 mg twice daily, increased according to heart rate; maximum 160 mg twice daily
- Angina: initially 40 mg two to three times daily; maintenance dose 120–240 mg daily
- Arrhythmias: anxiety, hyperthyroidism, migraine prophylaxis, essential tremor, 10–40 mg three times daily
- Hypertension: initially 80 mg twice daily, increased at weekly intervals as required; maintenance 160–320 mg daily.

Intravenous Arrhythmias and thyrotoxic crisis: 1 mg over 1 minute; if necessary, repeat at 2-minute intervals; maximum 10 mg.

Atenolol

Tablets: 25 mg, 50 mg, 100 mg.

Oral

- Angina: 25–100 mg daily in one or two doses
- After MI: 25–100 mg daily
- Hypertension: 25–50 mg daily.

Intravenous For arrhythmias: 2.5 mg at a rate of 1 mg/min, repeated at 5-minute intervals to a maximum of 10 mg, or by infusion 150 μg/kg over 20 minutes, repeated every 12 hours if required.

Bisoprolol

Tablets: 1.25 mg, 2.5 mg, 3.75 mg, 5 mg, 7.5 mg, 10 mg.

- Hypertension and angina, usually 5–10 mg once daily; maximum 20 mg daily
- Heart failure, initially 1.25 mg daily titrated up at weekly intervals over 8–10 weeks to maximum 10 mg daily.

Metoprolol

Tablets: 50 mg, 100 mg. Injection: 1 mg/mL.

Oral

- After MI: 100 mg twice daily
- Angina, arrhythmias, anxiety, thyrotoxicosis, migraine prophylaxis, essential tremor: 50–100 mg two to three times daily
- Hypertension: 50–100 mg twice daily.

Intravenous For arrhythmias: up to 5 mg at a rate of 1–2 mg/min, repeated after 5 minutes to a maximum of 10–15 mg.

Sotalol Tablets: 40 mg, 80 mg, 160 mg, Injection: 10 mg/mL.

Sotalol use is limited to the treatment of ventricular arrhythmias or the prevention of supraventricular arrhythmias.

Oral 80 mg daily in one to two divided doses, increased gradually at intervals of 2–3 days to usual dose of 160–320 mg daily.

Intravenous Over 10 minutes: 20–120 mg with ECG monitoring repeated at 6-hourly intervals if necessary.

Side effects

Side effects include bradycardia, exacerbation of intermittent claudication, lethargy, nightmares, hallucinations, deterioration of glucose tolerance and interference with metabolic and autonomic responses to hypoglycaemia in diabetics.

Contraindications

These comprise asthma, severe peripheral arterial disease, second- or third-degree heart block, marked bradycardia, hypotension, phaeochromocytoma (apart from specific use with α-blockers).

DRUGS AFFECTING THE RENIN–ANGIOTENSIN SYSTEM

Renin produced by the kidney in response to glomerular hypoperfusion catalyses cleavage of angiotensinogen (produced by the liver) to angiotensin (AT), which in turn is cleaved by angiotensin-converting enzyme (ACE) to angiotensin II, which acts on two receptors. The AT_1 receptor mediates the vasoconstrictor effects of AT. The actions of the AT_2 receptor are less well defined.

Angiotensin-converting enzyme inhibitors

Mechanism of action

These drugs inhibit the conversion of angiotensin I to angiotensin II and reduce angiotensin II-mediated vasoconstriction.

Indications

ACEIs improve symptoms and significantly improve survival in all grades of heart failure. They are also recommended in patients at risk of developing heart failure (e.g. ischaemic heart disease). Other indications are hypertension and diabetic nephropathy.

Preparations and dose

Perindopril

Tablets: 2 mg, 4 mg, 8 mg.

- Hypertension, initially 4 mg once daily (use 2 mg if in addition to diuretic, in the elderly, in renal impairment) subsequently adjusted according to response to maximum 8 mg daily
- Heart failure: initially 2 mg once daily, increased after at least 2 weeks to maintenance usually 4 mg daily
- Ischaemic heart disease, diabetic nephropathy: 4 mg daily increased after 2 weeks to 8 mg daily.

Lisinopril

Tablets: 2.5 mg, 5 mg, 10 mg, 20 mg.

- Hypertension: initially 10 mg once daily (2.5–5 mg if in addition to diuretic, in the elderly, in renal impairment), usual maintenance 20 mg daily, maximum 80 mg daily

- Heart failure: initially 2.5 mg once daily, increased by 10 mg every 2 weeks if tolerated to maintenance 35 mg daily
- Ischaemic heart disease, diabetic nephropathy: 5–10 mg daily. Immediately post-STEMI start at 2.5 mg if systolic BP 100–120 mmHg and gradually increase to maintenance dose of 5–10 mg. Do not give if systolic BP $<$ 100 mmHg.

Ramipril

Tablets: 1.25 mg, 2.5 mg, 5 mg, 10 mg.

- Hypertension: initially 1.25 mg daily, increased weekly to maintenance 2.5–5 mg daily, maximum 10 mg once daily
- Heart failure: initially 1.25 mg daily, increased if necessary to maximum 10 mg daily
- Ischaemic heart disease, diabetic nephropathy: 2.5 mg twice daily, maintenance 2.5–5 mg daily.

Side effects

After the first dose, side effects can include hypotension (use small initial doses) in heart failure and patients taking diuretics, dry cough, hyperkalaemia, sudden deterioration in renal function in patients with renal artery stenosis and in patients taking NSAIDs (check urea and electrolytes 1–2 weeks after starting treatment), loss of taste, rashes and hypersensitivity reactions.

Cautions/contraindications

These include bilateral renal artery stenosis, pregnancy, angio-oedema, severe renal failure, severe or symptomatic mitral or aortic stenosis and hypertrophic obstructive cardiomyopathy (risk of hypotension).

Angiotensin II receptor antagonists

Mechanism of action

These are antagonists of the type 1 subtype of the angiotensin II receptor (AT_1 receptor).

Indications

Indications include hypertension, heart failure or diabetic nephropathy in patients intolerant to ACE inhibitors because of cough.

Preparations and dose

Candesartan

Tablets: 2 mg, 4 mg, 8 mg, 16 mg, 32 mg.

- Hypertension: initially 8 mg daily, increased as necessary to 32 mg daily
- Heart failure: initially 4 mg once daily increased at intervals of at least 2 weeks to target dose of 32 mg.

Valsartan

Capsules: 40 mg, 80 mg, 160 mg.

- Hypertension: 80 mg once daily (40 mg in caution groups) and increased if necessary after 4 weeks to 160 mg daily
- Ischaemic heart disease: 20 mg twice daily increased gradually to 160 mg twice daily.

Side effects

These include postural hypotension, rash, abnormalities in liver biochemistry and hyperkalaemia.

Caution/contraindications

Lower doses should be given in liver and renal impairment, patients taking high-dose diuretics and the elderly (over 75 years). Caution should be applied in renal artery stenosis, aortic or mitral valve stenosis and in obstructive hypertrophic cardiomyopathy.

NITRATES, CALCIUM-CHANNEL BLOCKERS AND POTASSIUM-CHANNEL ACTIVATORS

Nitrates, calcium-channel blockers and potassium-channel activators have a vasodilating effect, leading to a reduction in venous return, which reduces left ventricular work and dilatation of the coronary circulation.

Nitrates

Mechanism of action

An increase in cyclic guanosine monophosphate (cGMP) in vascular smooth muscle cells causes a decrease in intracellular calcium levels and smooth muscle relaxation with dilatation of veins and arteries, including the coronary circulation. Nitrates reduce venous return, which reduces left ventricular work.

Indications

These drugs are used as a prophylaxis for and in the treatment of angina, as an adjunct in congestive heart failure and intravenously in the treatment of acute heart failure and acute coronary syndrome.

Preparations and dose

Glyceryl trinitrate – short acting

Sublingual tablets: 300 μg, 500 μg, 600 μg (expire after 8 weeks once bottle opened). Spray: 400 μg/dose.

- Angina: one or two tablets or sprays under the tongue (sublingual use avoids hepatic first-pass metabolism) repeated as required. More effective if taken before exertion known to precipitate angina. Tablets (unlike spray) can be spat out if side effects occur (headache, hypotension).

Glyceryl trinitrate – transdermal

Patches releasing approx: 5 mg, 10 mg, 15 mg/24 h.

- Angina: apply patch to chest or outer arm and replace at different site every 24 hours. If tolerance (with reduced therapeutic effect) is suspected, the patch should be left off for 4–8 consecutive hours – usually at night as this is the least symptomatic period.

Glyceryl trinitrate – long-acting tablets

Buccal tablets: 2 mg, 3 mg, 5 mg.

- Angina: 1–5 mg three times daily
- Heart failure: 5 mg (increased to 10 mg in severe cases) three times daily.

Glyceryl trinitrate injection

5 mg/mL, diluted to 100 μg/mL, i.e. 5 mg in 50 mL, in glucose 5% or sodium chloride 0.9% administered via a syringe pump.

- 0.6–0.9 mg/h i.v., then increase dose cautiously until response is achieved, keeping systolic BP > 100 mmHg. Usual range 2–10 mg/h.

Isosorbide mononitrate

Tablets: 10 mg, 20 mg, 40 mg.

- 10–40 mg twice daily, 8 hours apart rather than 12 to prevent nitrate tolerance.

Isosorbide mononitrate (modified release)

Tablets: 25 mg, 50 mg, 60 mg.

- 25–60 mg once daily. Reserve for patients where twice-daily dosing (above) has proved unacceptable. Build up dose gradually to avoid headaches. Up to 120 mg daily may be required.

Side effects

These are mainly due to vasodilating properties and are minimized by initiating therapy with a low dose. They include flushing, headache, postural hypotension, and methaemoglobinaemia with excessive dosage.

Cautions/contraindications

Nitrates are contraindicated in hypotension and hypovolaemia, hypertrophic obstructive cardiomyopathy, aortic stenosis, mitral stenosis, cardiac tamponade and constrictive pericarditis. Nitrates potentiate the effect of other vasodilators and hypotensive drugs. Sildenafil is contraindicated in patients taking nitrates.

Calcium-channel blockers

This group of drugs includes different modified-release preparations of calcium-channel blockers that have different bioavailabilities, and so the brand should be stated on the prescription.

Mechanism of action

These drugs block calcium channels and modify calcium uptake into myocardium and vascular smooth muscle cells. The dihydropyridine calcium-channel blockers (e.g. amlodipine, nifedipine, nimodipine) are potent vasodilators with little effect on cardiac contractility or conduction. In contrast, verapamil, and to a lesser extent diltiazem, are weak vasodilators but depress cardiac conduction and contractility.

Indications

Indicators for use are hypertension and prophylaxis for angina. Verapamil is used in the treatment of some arrhythmias. Nimodipine is for the prevention of ischaemic neurological deficits following aneurysmal subarachnoid haemorrhage.

Preparations and dose

Amlodipine

Tablets: 5 mg, 10 mg.

- 5–10 mg once daily.

Verapamil

Tablets: 40 mg, 80 mg, 120 mg, 160 mg. Oral solution: 40 mg/5 mL. Modified-release (slow-release, SR) tablets: 120 mg, 240 mg; injection: 2.5 mg/mL.

- Angina: 80–120 mg three times daily. SR 240 mg once or twice daily
- Hypertension: 240–480 mg daily in two to three divided doses. SR 120–240 mg once or twice daily
- Supraventricular arrhythmias: oral 40–120 mg three times daily, i.v. 5–10 mg over 10 minutes, further 5 mg after 5–10 minutes if required.

Nifedipine modified release

Adalat LA tablets: 20 mg, 30 mg, 60 mg.

- Angina: initially 30 mg once daily, increased if necessary to 90 mg once daily
- Hypertension: initially 20 mg once daily, increased if necessary.

Diltiazem

Tablets: 60 mg.

- Angina: 60 mg three times daily.

Diltiazem slow release

Capsules for twice daily use: 90 mg, 120 mg, 180 mg. Capsules for once daily use: 120 mg, 180 mg, 240 mg, 300 mg.

- Hypertension: 120 mg twice daily
- Angina: 90 mg twice daily, increased to 180 mg twice daily if required
- Angina and hypertension: 240 mg once daily, increased to 300 mg once daily.

Side effects

These are mainly due to vasodilator properties: flushing, dizziness, tachycardia, hypotension, ankle swelling and headache. Side effects are minimized by starting with a low dose and increasing slowly. Constipation occurs with verapamil. Worsening heart failure can be seen with verapamil and diltiazem.

Cautions/contraindications

The major contraindication is aortic stenosis. Verapamil and diltiazem diminish cardiac contractility and slow cardiac conduction; thus they are relatively contraindicated in patients taking β-blockers, left ventricular failure, sick sinus syndrome and heart failure. Verapamil is contraindicated for treatment of arrhythmias complicating Wolff–Parkinson–White syndrome. Short-acting calcium antagonists increase mortality and are contraindicated immediately after MI.

Potassium-channel activators

Mechanism of action

The mechanism of action here is a hybrid of nitrates (p. 499) and calcium-channel blockers. Potassium-channel activators cause an increase in potassium flow into the cell, which indirectly leads to calcium-channel blockade and arterial dilatation.

Indications

Use is indicated in cases of refractory angina in patients who are uncontrolled on standard regimens of aspirin, β-blockers, nitrates, calcium antagonists and statins.

Preparations and dose

Nicorandil

Tablets: 10 mg, 20 mg.

- 5–30 mg twice daily.

Side effects

These include headache (often temporary), flushing, nausea, vomiting, dizziness, hypotension, tachycardia.

Cautions/contraindications

Nicorandil use is contraindicated in left ventricular failure and cardiogenic shock. Sildenafil is contraindicated in patients taking nicorandil.