8

Cardiology

Cardiovascular disease is the most frequent cause of adult death in the Western world. Although the incidence of ischaemic heart disease is declining in many developed countries, it is rising in Eastern Europe and Asia. Valvular heart disease is also common, but although rheumatic fever still predominates in the Indian subcontinent and Africa, calcific aortic valve disease is now the most common problem in developed countries. Prompt recognition of the development of heart disease is limited by two factors. Firstly, patients often remain asymptomatic despite the presence of advanced disease, and secondly, the diversity of symptoms attributable to heart disease is limited, and so different conditions frequently present similarly.

Presenting problems in cardiovascular disease

A close relationship between symptoms and exercise is a hallmark of cardiovascular disease. The NYHA functional classification is often used to grade disability (Box 8.1).

Chest pain on exertion

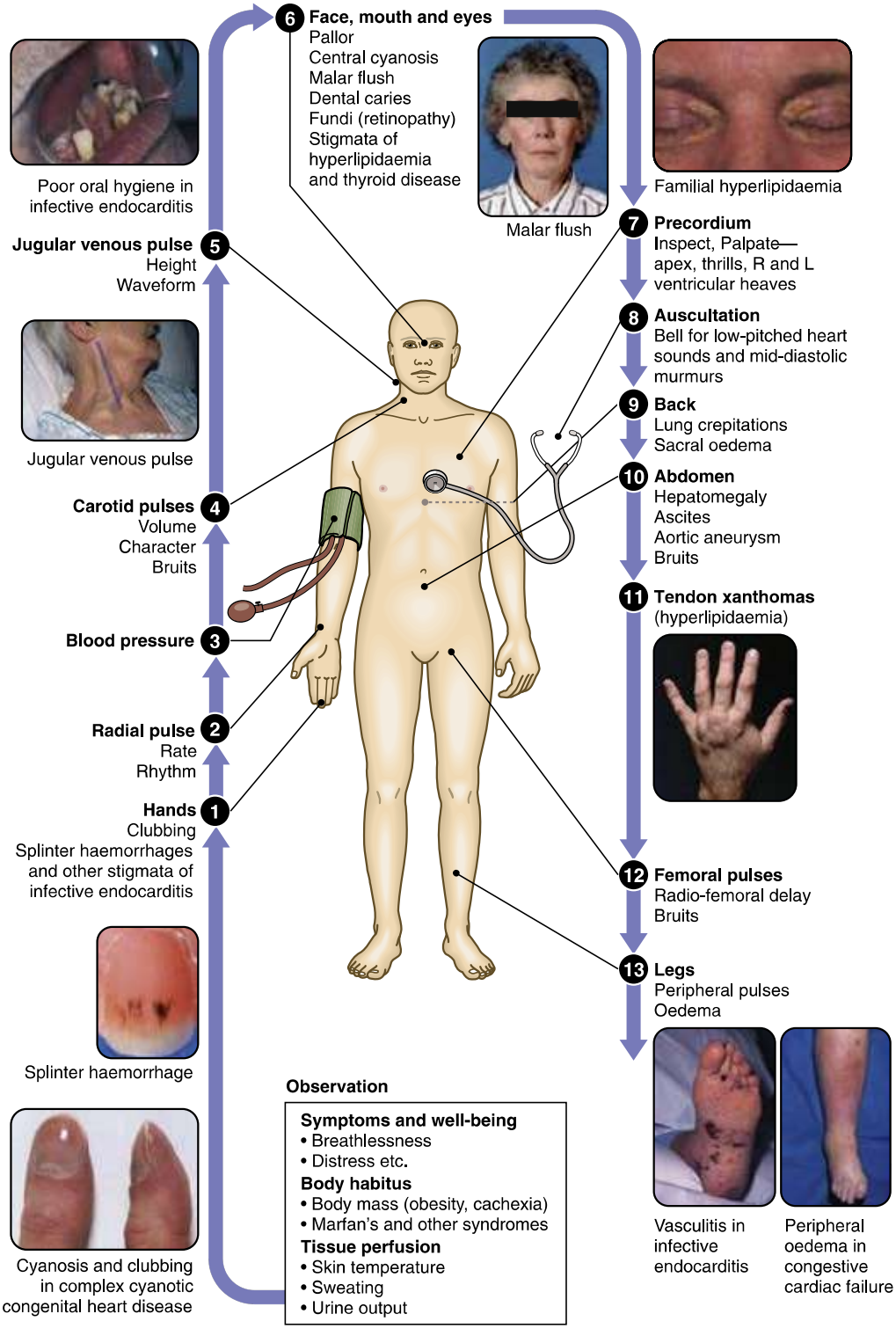
The many noncardiac causes of chest pain are covered in Chapter 4. This section covers exertional chest pain, which is typical of coronary artery disease.

A careful history is crucial in determining whether chest pain is cardiac. The reproducibility and predictability of the relationship between exertion and chest pain are the most important features. The duration is also

i 8.1 NYHA functional classification

Class I	No limitation during ordinary activity
Class II	Slight limitation during ordinary activity
Class III	Marked limitation of normal activities without symptoms at rest
Class IV	Unable to undertake physical activity without symptoms; symptoms may be present at rest

Clinical examination of the cardiovascular system



important; recent-onset angina indicates greater risk than long-standing and unchanged symptoms. Examination is often normal, but may reveal risk factors such as xanthelasma indicating hyperlipidaemia. Signs of anaemia or thyrotoxicosis may be identified, both of which can exacerbate angina. Cardiovascular examination may reveal left ventricular dysfunction or cardiac murmurs in patients with aortic valve disease and hypertrophic

cardiomyopathy. Evidence of arterial disease, such as bruits and loss of peripheral pulses, may also be observed.

Investigations

Blood count, fasting glucose, lipids, thyroid function tests and a 12-lead ECG are the basic investigations. An exercise ECG may identify high-risk patients requiring further investigation, but false-negative and false-positive results can occur. Patients with chest pain suggestive of coronary disease but with a normal exercise ECG should undergo CT coronary angiography. If a murmur is found, echocardiography should be performed to exclude valve disease or hypertrophic cardiomyopathy.

Severe prolonged chest pain

Severe prolonged cardiac chest pain may represent acute myocardial infarction or unstable angina (p. 279)—the acute coronary syndromes.

Clinical assessment

Acute coronary syndrome is often preceded by stable angina, but unheralded severe chest pain at rest can be the first presentation of coronary disease. History and examination may reveal pallor or sweating caused by accompanying autonomic disturbance, arrhythmia, hypotension or heart failure. Patients with symptoms suggesting acute coronary syndrome require hospital admission and urgent investigation.

Investigations

Initial triage is by 12-lead ECG and serum troponin I or T. Acute coronary syndrome is suggested by ST elevation or depression and elevated troponin I or T, indicating myocardial damage.

If the diagnosis remains unclear, repeat ECGs are useful, particularly if recorded during pain. If baseline plasma troponin is normal, repeat measurements should be made 6 to 12 hours after the onset of symptoms or after admission. New ECG changes or elevated troponin confirm the diagnosis of an acute coronary syndrome. If the pain settles, there are no new ECG changes and troponin remains normal, the patient can be discharged, but further investigations may still be indicated (p. 284).

The differential diagnosis and management of acute coronary syndrome are described in more detail on pp. 279 and 282.

Breathlessness

Cardiac causes of breathlessness include arrhythmias, heart failure, acute coronary syndrome, valvular disease, cardiomyopathy and constrictive pericarditis, all discussed later. The differential diagnosis however, includes many noncardiac causes, and is discussed on pp. 61 and 311.

Syncope

This refers to loss of consciousness caused by reduced cerebral perfusion, and is covered on p. 63.

Palpitation

Palpitation is a term used to describe a variety of sensations, including an erratic, fast, slow or forceful heartbeat.

Clinical assessment

Take a detailed history (Box 8.2) and ask the patient to tap out the heartbeat on the table.

Recurrent but short-lived bouts of an irregular heartbeat, such as dropped or missed beats, are usually because of atrial or ventricular extrasystoles. Attacks of a pounding, forceful, fast heartbeat are a common manifestation of anxiety, but may also occur in anaemia, pregnancy and thyrotoxicosis. Discrete bouts of a very rapid (>120/min) heartbeat suggest a paroxysmal arrhythmia. Atrial fibrillation typically presents with a completely irregular tachycardia.

Investigation and management

An ECG during an attack of palpitation (ambulatory monitoring or patient-activated recorder) is necessary to establish a definitive diagnosis. Most cases are attributed to an awareness of the normal heartbeat, sinus tachycardia or benign extrasystoles, in which case an explanation and reassurance will often suffice. Palpitation associated with syncope should be investigated without delay. Arrhythmia management is described on pp. 262-263.

Cardiac arrest

Cardiac arrest describes the sudden, complete loss of cardiac output as a result of asystole, catastrophic arrhythmia or loss of mechanical contraction (pulseless electrical activity). The patient is unconscious and pulseless. Coronary disease is the commonest cause, but valvular disease, cardiomyopathy, drugs and electrolyte abnormalities can all cause catastrophic arrhythmias. Death is inevitable without prompt effective treatment.

8.2 How to evaluate palpitation

- Is the palpitation continuous or intermittent?
- Is the heart beat regular or irregular?
- What is the approximate heart rate?
- Do symptoms occur in discrete attacks?
  - Is the onset abrupt? How do attacks terminate?
- Are there any associated symptoms?
  - Chest pain, lightheadedness, polyuria (a feature of supraventricular tachycardia, p. 266)?
- Are there any precipitating factors, e.g. exercise, alcohol?
- Is there a history of structural heart disease, e.g. coronary artery disease, valvular heart disease?

Clinical assessment and management

Basic life support: The ABCDE approach to management should be followed: restoration of the **A**irway; rescue **B**reathing ('mouth-to-mouth'); maintenance of **C**irculation using chest compressions; **D**isability (assessment of neurological status); and **E**xposure (removal of clothes to enable defibrillation, auscultation, assessment for rash, injuries, etc.).

Chest compression–only ('hands-only') cardiopulmonary resuscitation is simpler to teach and do, and is now advocated for members of the public.

Advanced life support: Advanced life support (Fig. 8.1) aims to restore normal cardiac rhythm by defibrillation when the cause of arrest is tachyarrhythmia, or to restore cardiac output by correcting other reversible causes of cardiac arrest. The initial priority is to assess the cardiac rhythm using a defibrillator or monitor. Treatment is based on the ECG findings.

Ventricular fibrillation (VF) (Fig. 8.2) or pulseless ventricular tachycardia (VT) should be treated with immediate 150 J defibrillation, then a further 2 minutes of CPR, because cardiac output rarely resumes immediately after successful defibrillation. After 2 minutes, if there is still no pulse, a further shock (150–200 J) should be given. Thereafter, additional shocks are given every 2 minutes after each cycle of CPR. Adrenaline (epinephrine, 1 mg IV) should be given every 3 to 5 minutes, and intravenous amiodarone should be considered, especially if VF or VT recurs after successful defibrillation.

VF of low amplitude, or 'fine VF', may mimic asystole. If asystole cannot be confidently diagnosed, the patient should be defibrillated. If the observed ECG rhythm would be expected to produce a cardiac output, 'pulseless electrical activity' is present. This should be treated by continuing CPR and adrenaline (epinephrine) administration while seeking reversible causes. Asystole should be treated similarly, with the additional support of atropine and sometimes external or transvenous pacing in an attempt to generate an electrical rhythm. The main reversible causes of cardiac arrest are listed in Fig. 8.1.

The chain of survival: Survival is most likely if all the key elements of resuscitation happen rapidly: that is the arrest is witnessed, basic life support is administered immediately by a trained individual, and the emergency services deliver defibrillation and advanced life support within a few minutes. Training in life support is essential and should be maintained by regular refresher courses. In recent years, public-access automated defibrillators have been introduced in places of high population density, particularly where congestion may delay the emergency services.

Survivors of cardiac arrest: Patients who survive a cardiac arrest caused by acute MI have a similar prognosis to those recovering from an uncomplicated infarct. Those with reversible causes, such as exercise-induced ischaemia or aortic stenosis, should have the cause treated. Survivors of VT or VF arrest in whom no reversible cause can be identified may be at risk of another episode, and should be considered for an implantable cardiac defibrillator (p. 275) and antiarrhythmic drugs. In these patients, the risk is reduced by treatment of heart failure with β-adrenoceptor antagonists and ACE inhibitors, and by coronary revascularisation.

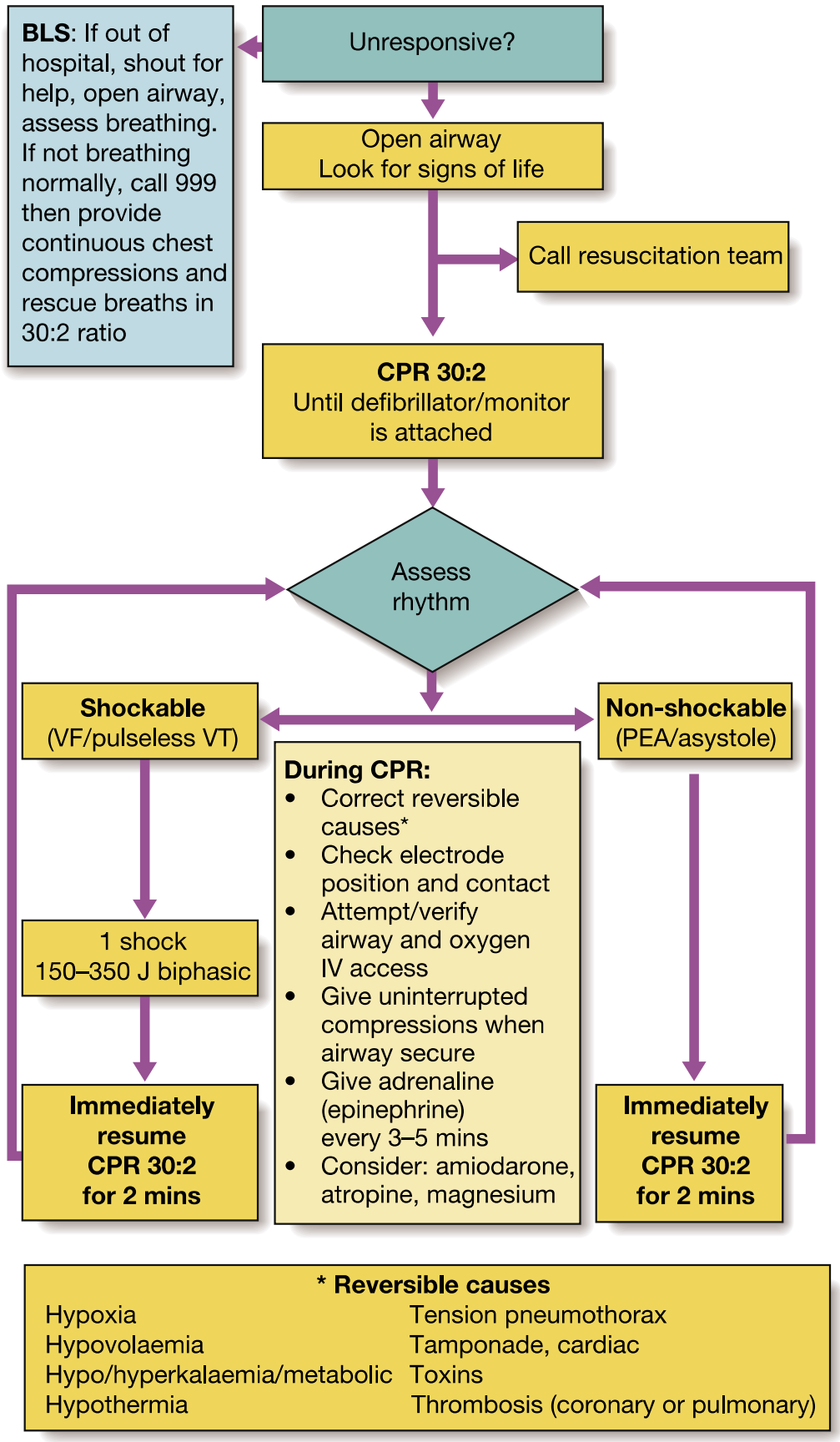


Fig. 8.1 Algorithm for basic and adult advanced life support. For further information see www.resus.org.uk. *BLS*, Basic life support; *CPR*, cardiopulmonary resuscitation; *PEA*, pulseless electrical activity; *VF*, ventricular fibrillation; *VT*, pulseless ventricular tachycardia.

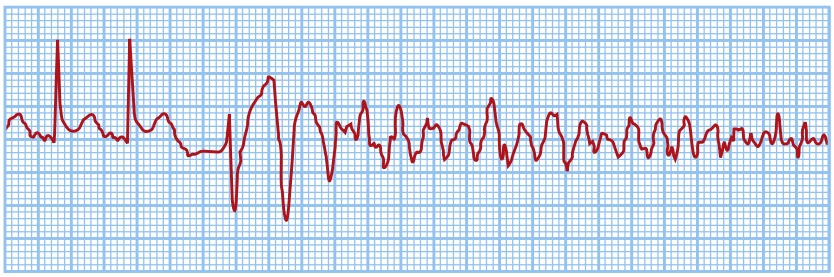


Fig. 8.2 **VF.** A bizarre chaotic rhythm, initiated in this case by two ectopic beats in rapid succession.

8.3 How to assess heart murmurs

When does it occur?

- Time the murmur using heart sounds, carotid pulse and apex beat. Is it systolic or diastolic?
- Does the murmur extend throughout systole or diastole, or is it confined to a shorter part of the cardiac cycle?

How loud is it? (intensity)

- Grade 1 Very soft (only audible in ideal conditions)
- Grade 2 Soft
- Grade 3 Moderate
- Grade 4 Loud with associated thrill
- Grade 5 Very loud
- Grade 6 Heard without stethoscope

N.B. Diastolic murmurs are rarely louder than grade 4.

Where is it heard best? (location)

- Listen over the apex and base of the heart, including the aortic and pulmonary areas

Where does it radiate?

- Evaluate radiation to the neck, axilla or back

What does it sound like? (pitch and quality)

- Pitch is determined by flow (high pitch indicates high-velocity flow)
- Is the intensity constant or variable?

Abnormal heart sounds and murmurs

The first clinical manifestation of heart disease may be the incidental discovery of an abnormal sound on auscultation. Clinical evaluation (Box 8.3) is helpful, but an echocardiogram is often necessary to confirm the nature of an abnormal heart sound or murmur. Some added sounds are physiological but may also occur in pathological conditions; for example, a third sound is common in young people and in pregnancy, but is also a feature of heart failure. Similarly, an ejection systolic murmur may occur in hyperdynamic states (e.g. anaemia, pregnancy) but also in aortic stenosis. Benign murmurs do not occur in diastole, and systolic murmurs that radiate or

are associated with a thrill are almost always pathological. Valvular heart disease is covered on p. 295.

Systolic murmurs: Ejection systolic murmurs occur in ventricular outflow obstruction and have a mid-systolic crescendo–decrescendo pattern. Pansystolic murmurs occur with mitral or tricuspid regurgitation and ventricular septal defect and have constant intensity from the first to beyond the second heart sound.

Diastolic murmurs: Soft, low-pitched mid-diastolic murmurs occur with turbulent flow across stenotic mitral or tricuspid valves, and are best heard with the stethoscope bell. Early diastolic murmurs accompany aortic or pulmonary regurgitation, and have a decrescendo, soft, blowing quality best heard with the diaphragm of the stethoscope.

Heart failure

Heart failure describes the state that develops when the heart cannot maintain an adequate cardiac output or can do so only at the expense of elevated filling pressures. Initially it causes mainly exertional symptoms, but advanced heart failure may cause symptoms at rest.

Left-sided heart failure: This causes a reduction in LV output and an increase in the left atrial or pulmonary venous pressure. An acute increase in left atrial pressure may cause pulmonary oedema; a more gradual increase leads to reflex pulmonary vasoconstriction and pulmonary hypertension.

Right-sided heart failure: This causes a reduction in RV output and an increase in right atrial pressure. The common causes are chronic lung disease and pulmonary embolism.

Biventricular heart failure: This may develop because disease affects both ventricles (e.g. dilated cardiomyopathy), or because left heart failure leads to chronic elevation of left atrial pressure, pulmonary hypertension and right heart failure.

Epidemiology

Heart failure mainly affects older patients, the prevalence rising from around 1% in those aged 50 to 59 years to more than 10% of those aged 80 to 89 years. The prognosis is poor; around 50% of patients with severe heart failure caused by LV dysfunction die within 2 years, either from pump failure or ventricular arrhythmias. Ischaemic heart disease is the most common cause, but most forms of heart disease can cause heart failure (Box 8.4).

Pathophysiology

Cardiac output is determined by preload, afterload and myocardial contractility (Fig. 8.3). Ventricular dysfunction can occur because of impaired systolic contraction or abnormal diastolic relaxation because of a stiff, noncompliant ventricle (usually caused by left ventricular hypertrophy). Systolic and diastolic dysfunction often coexist, particularly in coronary artery disease. Falling cardiac output activates the SNS, causing vasoconstriction, and the RAAS, causing sodium and water retention mediated by

8.4 Mechanisms of heart failure

Cause	Examples
Reduced ventricular contractility	MI (segmental dysfunction) Myocarditis/cardiomyopathy (global dysfunction)
Ventricular outflow obstruction (pressure overload)	Hypertension, aortic stenosis (left heart failure) Pulmonary hypertension, pulmonary valve stenosis (right heart failure)
Ventricular inflow obstruction	Mitral stenosis, tricuspid stenosis
Ventricular volume overload	LV volume overload (e.g. mitral or aortic regurgitation) Ventricular septal defect RV volume overload (e.g. atrial septal defect)
Arrhythmia	Atrial fibrillation Complete heart block Tachycardia-induced cardiomyopathy
Diastolic dysfunction	Constrictive pericarditis Restrictive cardiomyopathy LV hypertrophy and fibrosis Cardiac tamponade

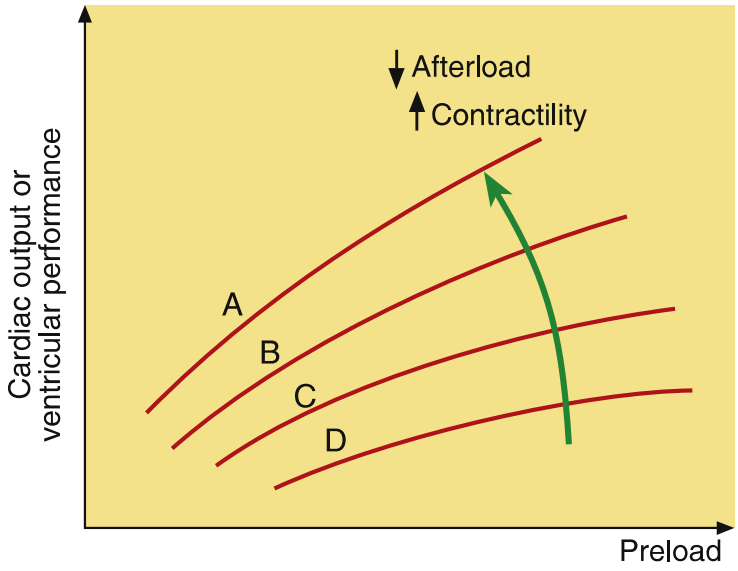


Fig. 8.3 Starling's Law. Normal (A), mild (B), moderate (C) and severe (D) heart failure. Ventricular performance is related to the degree of myocardial stretching. An increase in preload (end-diastolic volume, end-diastolic pressure, filling pressure or atrial pressure) will therefore enhance function; however, overstretching causes marked deterioration. In heart failure, the curve moves to the right and becomes flatter. An increase in myocardial contractility or a reduction in afterload will shift the curve upwards and to the left (green arrow).

angiotensin II, aldosterone, endothelin-1 and antidiuretic hormone. This leads to a vicious cycle of increased afterload and preload.

Although sympathetic activation initially sustains cardiac output through increased contractility and HR, prolonged activation causes cardiac myocyte apoptosis, hypertrophy and focal myocardial necrosis, and predisposes to arrhythmias. Natriuretic peptides are released from the dilated atria and compensate for the sodium-conserving effect of aldosterone, but this mechanism is overwhelmed in heart failure. Pulmonary and peripheral oedema develop, compounded by impairment of renal perfusion and secondary hyperaldosteronism.

High output failure: Heart failure can occur in the absence of heart disease if there is an excessively high cardiac output, for example, with large arteriovenous shunts or thyrotoxicosis.

Clinical features: Heart failure can develop acutely as with MI, or gradually as in valvular disease. 'Compensated heart failure' describes a patient with gradually impaired cardiac function in whom adaptive changes have prevented overt heart failure. An infection or arrhythmia may precipitate acute heart failure in such patients.

Acute left heart failure: This usually presents with sudden-onset dyspnoea at rest with acute respiratory distress, orthopnoea and prostration. A precipitant (e.g. acute MI) may be apparent from the history. The patient appears agitated, pale and clammy. The peripheries are cool to the touch, the pulse is rapid, and the JVP is usually elevated. The apex is not displaced, as there has been no time for ventricular dilatation. Auscultation may reveal a triple 'gallop' rhythm, a systolic murmur if there is mitral regurgitation or septal rupture and crepitations at the lung bases. Acute-on-chronic heart failure will have additional features of long-standing heart failure (see later). Potential precipitants (e.g. arrhythmia, changes in medication, intercurrent infective illness) should be identified.

Chronic heart failure: This commonly follows a relapsing and remitting course, with periods of stability interrupted by episodes of decompensation. A low cardiac output causes fatigue, listlessness and a poor effort tolerance; the peripheries are cold, and BP is low. Pulmonary oedema as a result of left heart failure may present with breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea and pulmonary crepitations. Right heart failure produces a high JVP, with hepatic congestion and dependent peripheral oedema. In ambulant patients the oedema affects the ankles, whereas in bed-bound patients it collects around the thighs and sacrum.

Chronic heart may cause additional complications:

- *Weight loss* (cardiac cachexia) as a result of anorexia and impaired absorption because of GI congestion.
- *Renal failure* from poor renal perfusion as a result of a low cardiac output—exacerbated by diuretics, ACE inhibitors and angiotensin receptor blockers.
- *Hypokalaemia* caused by diuretics and hyperaldosteronism.
- *Hyperkalaemia* caused by the effects of drugs (particularly ACE inhibitors given with spironolactone) and renal dysfunction.

- *Hyponatraemia* caused by diuretic therapy or inappropriate water retention because of high ADH secretion—a poor prognostic sign.
- *Thromboembolism*—either DVT with pulmonary embolism or systemic emboli from cardiac thrombus in atrial fibrillation or complicating MI.
- *Atrial and ventricular arrhythmias* may be related to electrolyte changes (e.g. hypokalaemia, hypomagnesaemia), underlying cardiac disease and accompanying sympathetic activation. Sudden death occurs in up to 50% of patients, probably caused by VF.

Investigations

• CXR: may reveal cardiomegaly, and shows characteristic changes in pulmonary oedema (Fig. 8.4), including distension of upper lobe pulmonary veins, Kerley B lines (horizontal lines near the costal margin indicating interstitial oedema), hazy hilar opacification (alveolar oedema) and pleural effusions. • Echocardiography: consider in all patients with heart failure to determine the aetiology (e.g. valvular disease, regional wall motion defect in MI) and assess LV impairment. • ECG: may reveal LV hypertrophy, evidence of previous MI. • U&Es, LFTs, TFTs and FBC: may identify some of the associated causes and complications listed previously. • Brain natriuretic peptide (BNP): elevated in heart failure and is a prognostic marker, as well as being useful in differentiating heart failure from other causes of breathlessness or peripheral oedema.

Management of acute pulmonary oedema

This is summarised in Box 8.5. For severe or unresponsive patients, treatment of cardiogenic shock is covered on p. 84.

Management of chronic heart failure

General measures

The aim of treatment is to improve cardiac function by increasing contractility, optimising preload or decreasing afterload and controlling cardiac rate and rhythm. In addition to treating the underlying cause, both nondrug and drug therapies are important.

Nondrug measures include:

• Effective education about heart failure. • Maintenance of nutritional status. • Smoking cessation. • Avoidance of excessive salt or alcohol intake. • Regular moderate exercise. • Vaccinations for influenza and pneumococcus.

Drug treatment

Drugs that reduce preload are indicated if there is pulmonary or systemic venous congestion. Drugs that reduce after load and increase contractility are useful if cardiac output is low.

Diuretics: Promote sodium and water excretion, reducing plasma volume and preload, thereby improving pulmonary and systemic venous congestion. In some patients with severe chronic heart failure, IV loop diuretics or combination therapy with a loop and thiazide diuretic may be required. Aldosterone receptor antagonists such as spironolactone are potassium-sparing diuretics that improve long-term outcome in patients with severe heart failure and those with heart failure following MI.

ACE inhibitors: Interrupt the vicious circle of neurohormonal activation in chronic heart failure, preventing salt and water retention, peripheral

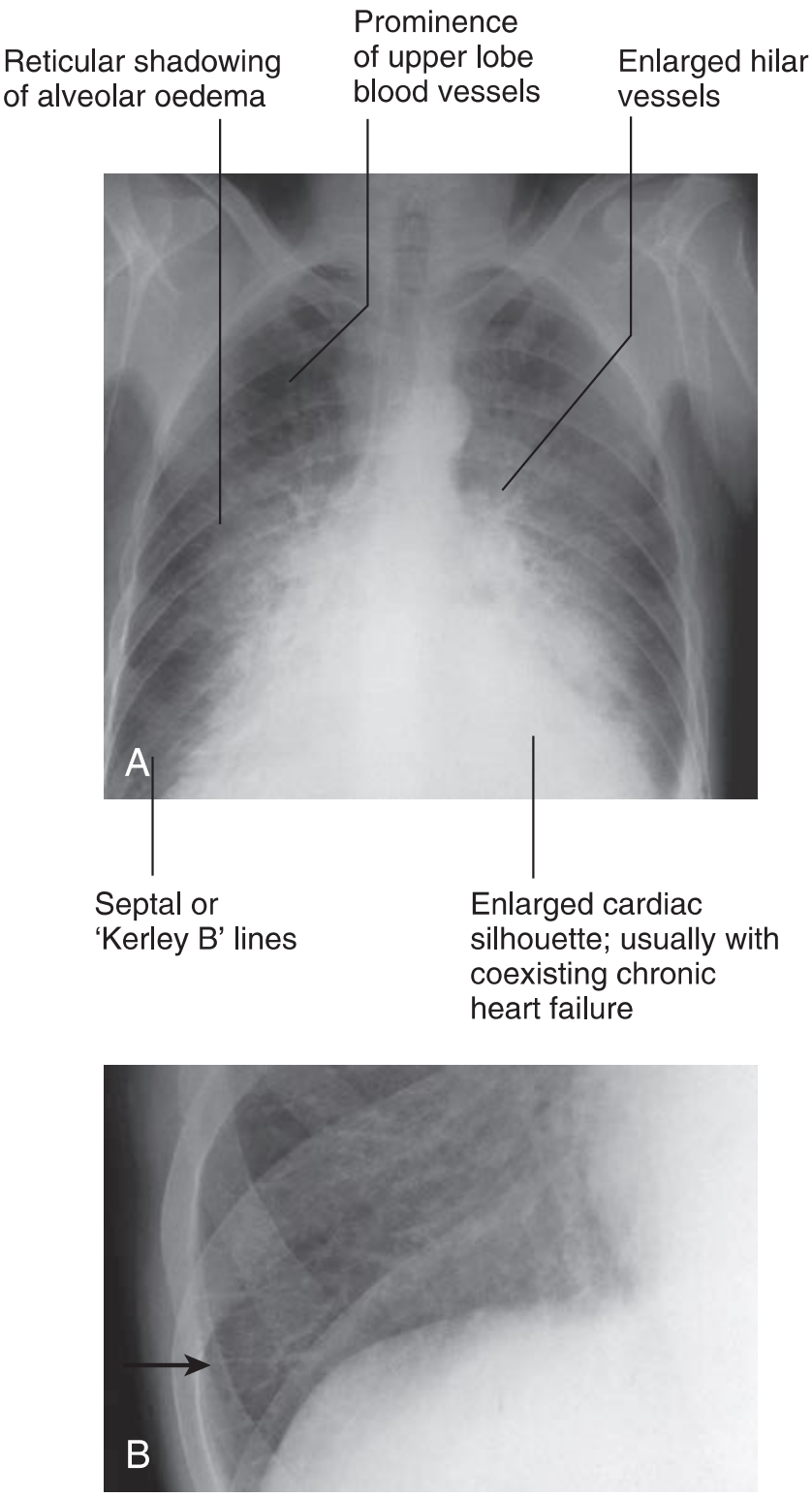


Fig. 8.4 Radiological features of heart failure. (A) CXR of a patient with pulmonary oedema. (B) Enlargement of lung base showing septal or 'Kerley B' lines (arrow).

vasoconstriction, and sympathetic nervous system activation. They improve effort tolerance and mortality in moderate to severe heart failure and following MI. They may cause hypotension and renal impairment, especially in hypovolaemic and elderly patients, and should therefore be started cautiously.

ARBs: Produce haemodynamic and mortality benefits similar to those of ACE inhibitors, and are a useful alternative for patients intolerant of ACE inhibitors.

8.5 Management of acute pulmonary oedema

Action	Effect
Sit the patient up	Reduces preload
Give high-flow oxygen	Corrects hypoxia
Ensure CPAP of 5–10 mmHg by tight-fitting mask	Reduces preload and pulmonary capillary hydraulic gradient
Administer nitrates:[a] IV glyceryl trinitrate (10–200 μg/min) Buccal glyceryl trinitrate 2–5 mg	Reduces preload and afterload
Administer a loop diuretic: Furosemide (50–100 mg IV)	Combats fluid overload

[a]*The dose of nitrate should be titrated upwards every 10 minutes until there is an improvement or systolic blood pressure is less than 110 mmHg.*

Neprilysin inhibitors: Sacubitril inhibits breakdown of the endogenous diuretics ANP and BNP. Combined with the ARB valsartan (sacubitril–valsartan), it improves symptoms and mortality compared with ACE treatment, and is now recommended for resistant heart failure.

Vasodilators: Valuable in chronic heart failure when ACE inhibitors or ARBs are contraindicated. Venodilators (e.g. nitrates) and arterial dilators (e.g. hydralazine) may be used, but may cause hypotension.

β-Blockers: Help to counteract the adverse effects of sympathetic stimulation in chronic heart failure and reduce the risk of arrhythmias and sudden death. They must be introduced gradually to avoid precipitating acute-on-chronic failure, but when used appropriately have been shown to increase ejection fraction, improve symptoms and reduce mortality.

Ivabradine: Acts on the SA node to reduce HR. It reduces mortality and admissions in moderate to severe LV dysfunction, and is useful if β-blockers are not tolerated or not effective.

Digoxin: Can be used for rate control in heart failure with AF. It may reduce episodes of hospitalisation in patients with severe heart failure, but has no effect on long-term survival.

Amiodarone: Useful for controlling arrhythmias in patients with poor LV function because it has little negative inotropic effect.

Nondrug therapies

Implantable cardiac defibrillators (p. 275): Reduce the risk of sudden death in selected patients with chronic heart failure, particularly those with symptomatic ventricular arrhythmia.

Cardiac resynchronisation therapy (p. 275): Restores the normal contraction pattern of the left ventricle, which may be dysynchronous in patients with impaired LV function and left bundle branch block.

Coronary revascularisation: Bypass grafting or percutaneous coronary intervention may improve function in areas of 'hibernating' myocardium with inadequate blood supply, and can be used to treat carefully selected patients with heart failure and coronary artery disease.

Cardiac transplantation: An established and successful form of treatment for patients with intractable heart failure. Coronary artery disease and dilated cardiomyopathy are the most common indications. The use of transplantation is limited by the availability of donor hearts, and so is generally reserved for young patients with severe symptoms. Serious complications include rejection, infection (because of immunosuppressive therapy) and accelerated atherosclerosis.

Ventricular assist devices: Have been employed as a bridge to cardiac transplantation, and more recently as potential long-term therapy. They assist cardiac output by using a roller, centrifugal or pulsatile pump. There is currently a high rate of complication (e.g. haemorrhage, systemic embolism, infection).

Cardiac arrhythmias

Arrhythmias are generally classified as either tachycardias (HR >100/min) or bradycardias (HR <60/min). There are two main mechanisms of tachycardia:

Increased automaticity: Repeated spontaneous depolarisation of an ectopic focus, often in response to catecholamines.

Re-entry: This occurs when there are two alternative pathways with different conducting properties (e.g. a normal and an ischaemic area). In sinus rhythm, each impulse passes down both pathways before entering a common distal pathway. If the refractory periods of the paths differ, a premature impulse may travel down one pathway, then retrogradely up the alternative pathway, establishing a closed loop or re-entry circuit and initiating a tachycardia.

'Supraventricular' (sinus, atrial or junctional) arrhythmias usually produce narrow QRS complexes because the ventricles are depolarised via normal pathways. Ventricular arrhythmias cause broad, bizarre QRS complexes because the ventricles are activated in an abnormal sequence.

Clinical features

Tachycardias can cause palpitation, dizziness, syncope, chest pain or breathlessness, and trigger heart failure or even sudden death. Bradycardias cause fatigue and syncope.

Investigations

A 12-lead ECG will be diagnostic in many cases. If arrhythmias are intermittent, the rhythm should be recorded using an ambulatory ECG or a patient-activated ECG.

Management

This depends on the rhythm.

Sinus arrhythmia: Refers to the normal increase in HR during inspiration and slowing during expiration. It is mediated by the parasympathetic nerves, and may be pronounced in young patients.

Sinus bradycardia: May occur in healthy people at rest, especially athletes. Pathological causes include MI, raised intracranial pressure, hypothermia, hypothyroidism, cholestatic jaundice and drug therapy (e.g. β-blockers, verapamil, digoxin). Asymptomatic sinus bradycardia requires no treatment; symptomatic patients may require IV atropine or a pacemaker.

Sinus tachycardia: Usually because of an increase in sympathetic activity with exercise, emotion or pregnancy. Pathological causes include anaemia, fever, thyrotoxicosis, phaeochromocytoma, cardiac failure, shock and drug therapy (e.g. inhaled β-agonists).

Sick sinus syndrome

Sick sinus syndrome results from degeneration of the sinus node, and is more common in the elderly. It typically presents with palpitation, dizzy spells or syncope, because of intermittent tachycardia, bradycardia or pauses with no atrial or ventricular activity (sinus arrest or sinoatrial block). A permanent pacemaker may benefit patients with symptomatic bradycardias, but is not indicated in asymptomatic patients.

Atrial arrhythmias

Atrial ectopic beats (extrasystoles): Usually cause no symptoms, but can give the sensation of a missed beat or abnormally strong beat. The ECG shows a premature but otherwise normal QRS complex; the preceding P wave has a different morphology because the atria activate from an abnormal site. Treatment is rarely necessary.

Atrial tachycardia: Produces a narrow-complex tachycardia with abnormal P-wave morphology caused by increased atrial automaticity, sinoatrial disease or digoxin toxicity. It may respond to β-blockers, which reduce automaticity, or class I or III antiarrhythmic drugs (Box 8.9). Catheter ablation may be useful for recurrent tachycardias.

Atrial flutter: Results from a large re-entry circuit in the right atrium. The atrial rate is around 300/min, but associated 2:1, 3:1 or 4:1 AV block usually produces a ventricular HR of 150, 100 or 75/min. The ECG shows saw-tooth flutter waves. With regular 2:1 AV block, these may be buried in the QRST complexes, but can be revealed by transiently increasing the AV block through carotid sinus massage (Fig. 8.5) or IV adenosine. Digoxin, β-blockers or verapamil can limit the ventricular rate, but electrical or chemical cardioversion using amiodarone or flecainide is often

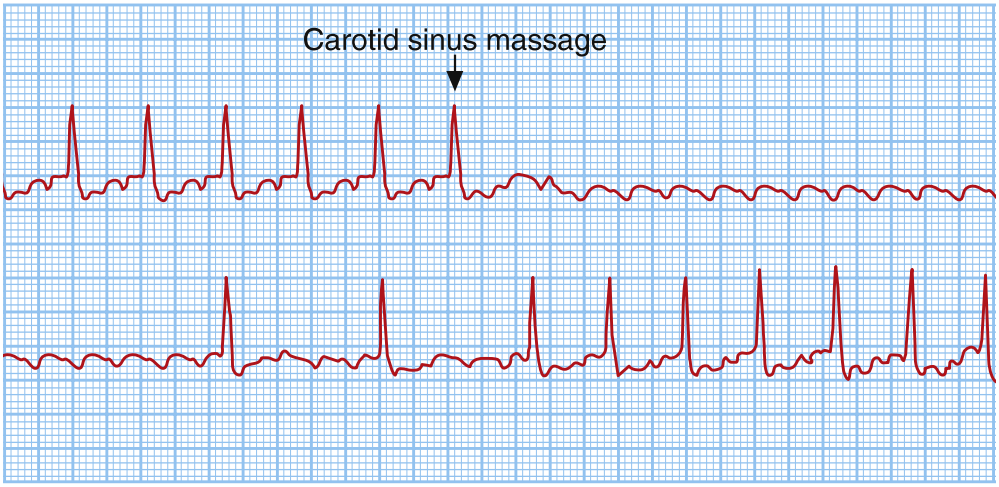


Fig. 8.5 Atrial flutter with 2:1 block: flutter waves revealed by carotid sinus massage.

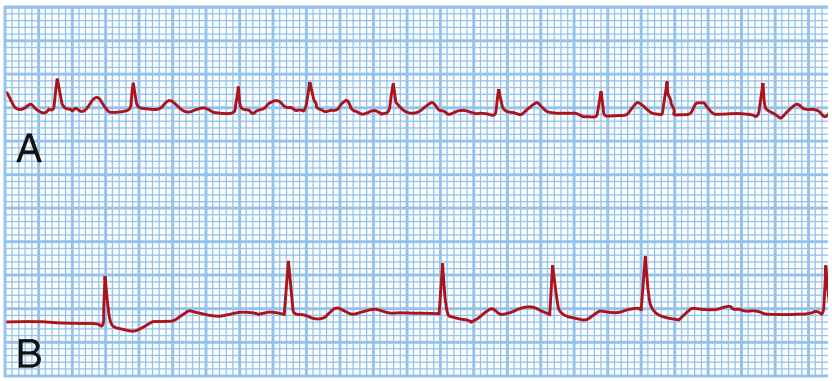


Fig. 8.6 Two examples of AF. The QRS complexes are irregular, and there are no P waves. (A) There is usually a fast ventricular rate, often between 120 and 160/min, at the onset of AF. (B) In chronic AF the ventricular rate may be much slower as a result of the effects of medication and AV nodal fatigue.

preferable. β-Blockers or amiodarone may be used to prevent recurrent atrial flutter, but catheter ablation is now the treatment of choice for patients with persistent symptoms. Anticoagulants are used to manage thrombotic risk around cardioversion as for atrial fibrillation (see below).

Atrial fibrillation

AF is the most common sustained cardiac arrhythmia, and its prevalence rises with age. The atria beat rapidly, but in an uncoordinated and ineffective manner. The ventricles are activated irregularly at a rate determined by conduction through the AV node, giving rise to an 'irregularly irregular' pulse. The ECG (Fig. 8.6) shows normal but irregularly spaced QRS complexes with absent P waves.

AF can be classified as:

• Paroxysmal (intermittent, self-terminating episodes). • Persistent (prolonged episodes that can be terminated by electrical or chemical cardioversion). • Permanent.

Paroxysmal AF often becomes permanent, with progression of underlying disease and electrical and structural remodeling of the atria. Common causes are shown in Box 8.6; however, many patients have 'lone atrial fibrillation', where no underlying cause is identified.

Clinical features

AF is occasionally asymptomatic, but typically presents with palpitation, breathlessness and fatigue. It may provoke angina in patients with coronary disease or cardiac failure in those with poor ventricular function or valve disease. Asymptomatic AF may present with embolic stroke in the elderly.

Investigation and management

All patients should have an ECG, echocardiogram and TFTs.

Paroxysmal AF: When AF complicates an acute illness (e.g. chest infection), treatment of the primary disorder usually restores sinus rhythm. Occasional attacks of paroxysmal AF do not necessarily need treatment. For repeated symptomatic episodes, β-blockers can be used to reduce the

8.6 Common causes of atrial fibrillation

- Coronary artery disease (including acute MI)
- Valvular heart disease, especially rheumatic mitral valve disease
- Hypertension
- Sinoatrial disease
- Hyperthyroidism
- Alcohol
- Cardiomyopathy
- Congenital heart disease
- Chest infection
- Pulmonary embolism
- Pericardial disease
- Idiopathic (lone AF)

ectopics that initiate AF, and are the usual first-line therapy, especially in patients with associated ischaemic heart disease, hypertension or cardiac failure. Flecainide, along with β-blockers, prevents episodes, but should be avoided in coronary disease or LV dysfunction. Amiodarone is also effective, but side effects restrict use. Digoxin and verapamil limit rate in AF but do not prevent episodes. Catheter ablation is useful in drug-resistant cases.

Persistent AF: *Rhythm control*—Successful restoration of sinus rhythm is most likely if AF has been present for less than 3 months and the patient is young and has no structural heart disease. Immediate cardioversion is indicated within 48 hours of onset. In stable patients without structural heart disease, IV flecainide is usually effective; amiodarone by central venous catheter is used in those with structural heart disease, and DC cardioversion is used if drugs fail. Beyond 48 hours, the ventricular rate should be controlled and cardioversion deferred until more than 4 weeks of oral anticoagulation. Prophylactic amiodarone may help to reduce recurrence, and catheter ablation may help in resistant cases.

Rate control—If sinus rhythm cannot be restored, β-blockers and rate-limiting calcium antagonists (e.g. verapamil) are more effective than digoxin at controlling HR during exercise. In exceptional cases, AF can be treated by inducing complete heart block with catheter ablation after first implanting a permanent pacemaker.

Thromboprophylaxis

Left atrial dilatation and loss of contraction may lead to thrombus formation, predisposing patients to stroke and systemic embolism. Patients undergoing cardioversion require temporary anticoagulation with warfarin (INR target 2.0–3.0) or direct-acting oral anticoagulant drugs, which should be started 4 weeks before and maintained for 3 months after successful cardioversion.

In chronic AF, the risk of stroke is balanced against the risk of bleeding complicating anticoagulation. Patients with underlying mitral valve disease should always be anticoagulated; in others, clinical scores (Box 8.7) are

i 8.7 CHA_2DS_2-VAS_c stroke risk score for nonvalvular atrial fibrillation

	Parameter	Score
C	Congestive heart failure	1 point
H	Hypertension history	1 point
A_2	Age ≥75 years	2 points
D	Diabetes mellitus	1 point
S_2	Previous stroke or TIA	2 points
V	Vascular disease	1 point
A	Age 65–74 years	1 point
S_c	Sex category female	1 point
	Maximum total score	9 points

Annual stroke risk
0 points = 0% (no prophylaxis required)
1 point = 1.3% (oral anticoagulant recommended–males only)
2+ points = >2.2% (oral anticoagulant recommended)

European Society of Cardiology Clinical Practice Guidelines: Atrial Fibrillation (Management of) 2010 and Focused Update (2012). Eur Heart J 2012; 33:2719–2747.

used to assess stroke risk. Risk is weakly related to frequency and duration of AF episodes, so guidelines do not distinguish between paroxysmal, persistent and permanent AF.

Directly acting oral anticoagulants (e.g. apixaban, dabigatran) are at least as effective as warfarin at preventing thrombotic stroke and have a lower risk of intracranial haemorrhage. They also do not require monitoring and have fewer drug interactions. Comorbid conditions (e.g. frequent falls) and drug interactions must be considered before anticoagulation is recommended.

Supraventricular tachycardia

This term describes a group of narrow-complex tachycardias (Fig. 8.7) caused by atrial re-entry circuits or abnormal atria foci, including AVNRT and AVRT (see later).

Atrioventricular nodal re-entrant tachycardia

AVNRT is attributed to re-entry in the right atrium and AV node, and tends to occur in structurally normal hearts. It produces episodes of regular tachycardia, with a rate of 120 to 240/min lasting from a few seconds to many hours.

The patient experiences a rapid, forceful, regular heartbeat and may feel faint or breathless. Polyuria may occur. The ECG usually shows a regular tachycardia with normal QRS complexes, but occasionally there is rate-dependent bundle branch block.

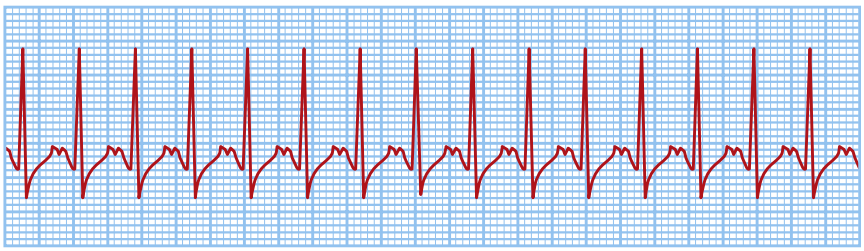


Fig. 8.7 Supraventricular tachycardia. The rate is 180/min, and the QRS complexes are normal.

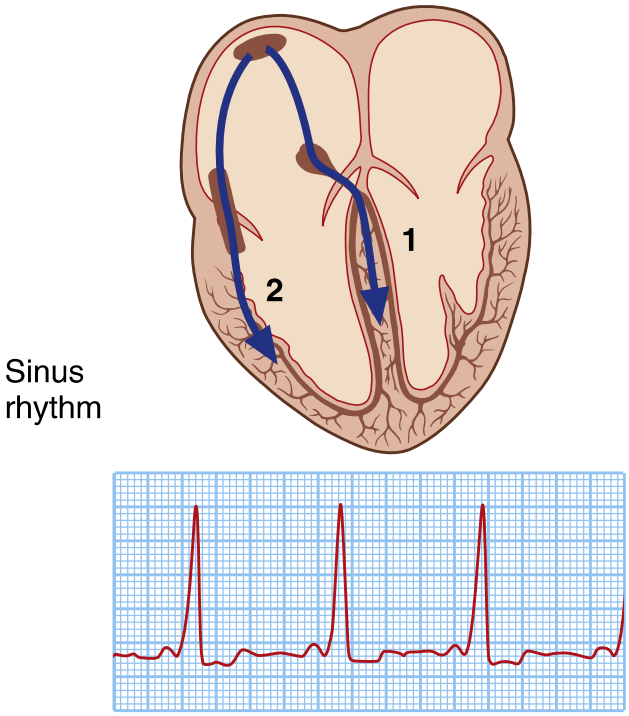


Fig. 8.8 Wolff–Parkinson–White syndrome. A strip of accessory conducting tissue allows electricity to bypass the AV node and spread from atria to ventricles without delay. When ventricular activation occurs through the AV node (1), the ECG is normal; however, when it occurs through the accessory pathway (2), a very short PR interval and a broad QRS complex are seen. In sinus rhythm, ventricular activation occurs by both paths, causing the characteristic short PR and slurring of the upstroke of the QRS complex (delta wave). The proportion of activation occurring via the accessory pathway may vary; therefore, at times, the ECG can look normal.

Management

Attacks may be terminated by carotid sinus pressure or Valsalva manœuvre, but if not, IV adenosine or verapamil will usually restore sinus rhythm. If there is severe haemodynamic compromise, the tachycardia should be terminated by DC cardioversion (p. 273). For recurrent attacks, catheter ablation (p. 275) is the most effective therapy, and is preferable to long-term medication with β-blockers or verapamil.

Atrioventricular re-entrant tachycardia

In this condition an abnormal band of rapidly conducting tissue ('accessory pathway') connects the atria and ventricles (Fig. 8.8). In 50% of cases,

premature ventricular activation via the pathway produces a short PR interval and a 'slurred' upstroke of the QRS complex, called a delta wave. As the AV node and accessory pathway have different conduction speeds and refractory periods, a re-entry circuit can develop, causing tachycardia. When associated with symptoms, this is known as Wolff–Parkinson–White syndrome. The ECG during tachycardia is indistinguishable from that of AVNRT.

Management

Carotid sinus pressure, Valsalva manœuvre or IV adenosine can terminate the tachycardia. If AF occurs, it may produce a dangerously rapid ventricular rate (because the accessory pathway lacks the rate-limiting properties of the AV node) causing syncope. This is treated with emergency DC cardioversion. Catheter ablation (p. 275) of the accessory pathway is first-line treatment in symptomatic patients, and is nearly always curative. Prophylactic flecainide or propafenone can be used, but long-term medication cannot be justified, as ablation is safer and more effective. Digoxin and verapamil shorten the refractory period of the accessory pathway and must be avoided.

Ventricular premature beats

VPBs occur frequently in healthy people at rest, disappearing on exercise. They also occur in subclinical coronary artery disease, cardiomyopathy or following an MI. Most patients are asymptomatic, but some feel irregular or missed beats. The pulse reveals weak or missed beats because VPBs have a low stroke volume. The ECG shows broad and bizarre QRS complexes as depolarization propagates outside the conducting system.

Treatment (β-blockers) is only necessary in highly symptomatic cases. Frequent VPBs in patients with heart failure or those who have survived the acute phase of MI are associated with an adverse prognosis. Treatment should be directed at the underlying cause.

Ventricular tachycardia

VT usually occurs in patients with coronary heart disease or cardiomyopathies, and may cause haemodynamic compromise or degenerate into VF (Fig. 8.4). The ECG shows tachycardia with broad, abnormal QRS complexes and a rate greater than 120/min (Fig. 8.9). VT is by far the most common cause of a broad-complex tachycardia, but may be difficult to distinguish from supraventricular tachycardia with bundle branch block or Wolff–Parkinson–White syndrome. When there is doubt, it is safer to manage the problem as VT.

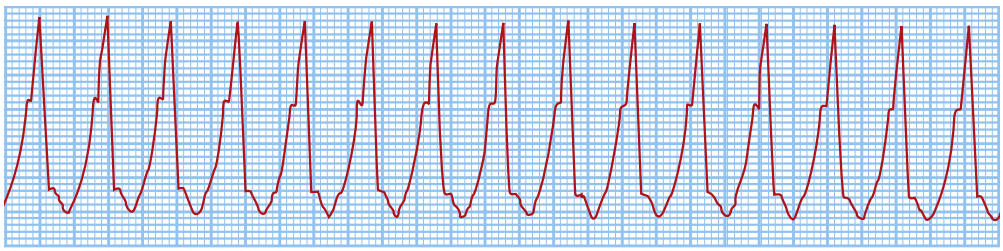


Fig. 8.9 VT: rhythm strip. Typical broad, bizarre QRS complexes with a rate of 160/min.

Management

Prompt DC cardioversion is required if systolic BP is less than 90 mmHg, but if VT is well tolerated, then IV amiodarone may be tried. Hypokalaemia, hypomagnesaemia, acidosis and hypoxaemia must be corrected. β-Blockers and/or amiodarone may be effective for subsequent prophylaxis. Class Ic antiarrhythmic drugs should be avoided because they can provoke dangerous arrhythmia. An implantable cardiac defibrillator is recommended in patients with poor LV function, or those with refractory VT causing haemodynamic compromise. VT occasionally occurs in patients with otherwise healthy hearts; in such cases prognosis is good and catheter ablation can be curative.

Torsades de pointes

This form of VT complicates a prolonged QT interval, which may be congenital or secondary to drugs (e.g. class Ia, Ic and III antiarrhythmics, macrolide antibiotics, tricyclic antidepressants, phenothiazines) or electrolyte disturbance (↓Ca^{2+}, ↓Mg^{2+}, ↓K^{+}). The ECG shows rapid broad complexes that seem to twist around the baseline as the QRS axis changes. It is typically nonsustained but may degenerate into VF. The ECG in sinus rhythm shows a prolonged QT interval (>0.44 seconds in men, >0.46 seconds in women when corrected to a HR of 60/min).

Management

IV magnesium should be given in all cases. Atrial pacing or IV isoprenaline shortens the QT interval by increasing HR. Otherwise, treatment is directed at the underlying cause. Patients with congenital long QT syndrome often require an implantable cardiac defibrillator.

Atrioventricular block

This usually indicates disease affecting the AV node. Block may be intermittent and only apparent when tachycardias stress the conducting tissue.

First-degree AV block

AV conduction is delayed, producing a prolonged PR interval (>0.20 seconds). It rarely causes symptoms.

Second-degree AV block

Here, dropped beats occur because some atrial impulses fail to conduct to the ventricles.

Mobitz type I block ('Wenckebach's phenomenon'): There is progressive lengthening of the PR intervals, culminating in a dropped beat. The cycle then repeats itself. It is sometimes observed at rest or during sleep in athletic young adults with high vagal tone.

Mobitz type II block: The PR interval of conducted impulses remains constant, but some P waves are not conducted. It is usually caused by disease of the His–Purkinje system, and carries a risk of asystole. In 2:1 AV block (Fig. 8.10), alternate P waves are conducted, so it is impossible to distinguish between Mobitz type I and type II block.

Third-degree AV block

AV conduction fails completely, the atria and ventricles beat independently (AV dissociation, Fig. 8.11) and ventricular activity is maintained by an

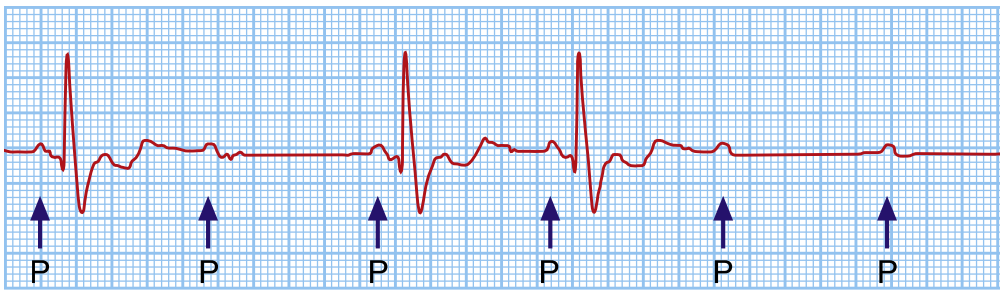


Fig. 8.10 Second-degree atrioventricular block (Mobitz type II). The PR interval of conducted beats is normal, but some P waves are not conducted. The constant PR interval distinguishes this from Wenckebach's phenomenon.

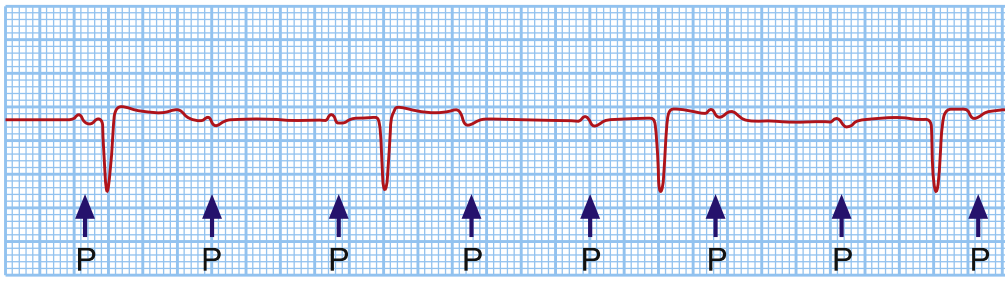


Fig. 8.11 Third-degree atrioventricular block. There is complete dissociation of atrial and ventricular complexes. The atrial rate is 80/min, and the ventricular rate is 38/min

escape rhythm arising in the AV node or bundle of His (narrow QRS) or the distal Purkinje tissues (broad QRS). Distal escape rhythms are slower and less reliable. The pulse is slow, regular and unresponsive to exercise. Cannon waves may be visible in the neck, and the intensity of the first heart sound varies because of loss of AV synchrony.

Clinical features

The typical presentation is with recurrent sudden loss of consciousness, typically without warning ('Stokes–Adams' attacks). Anoxic seizures (because of cerebral ischaemia) may occur if asystole is prolonged. There is pallor and a death-like appearance during the attack, but when the heart starts beating again there is a characteristic flush. In contrast to epilepsy, recovery is rapid.

Management

Acute inferior MI is often complicated by transient AV block because the right coronary artery supplies the AV node. There is usually a reliable escape rhythm, and if the patient remains well, no treatment is required. Symptomatic second-degree or third-degree block may respond to IV atropine or, if this fails, a temporary pacemaker. In most cases the AV block resolves within 7 to 10 days.

Second- or third-degree AV block complicating acute anterior MI indicates extensive ventricular damage involving both bundle branches, and carries a poor prognosis. Asystole may ensue, and a temporary pacemaker

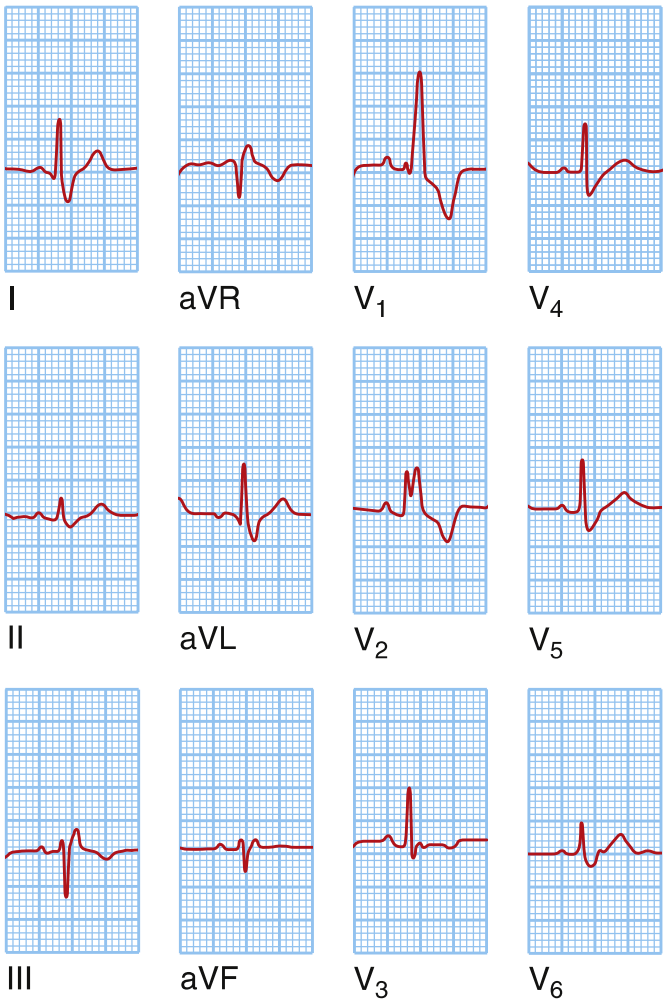


Fig. 8.12 RBBB. Note the wide QRS complexes with 'M'-shaped configuration in leads V_1 and V_2 and a wide S wave in lead I.

should be inserted promptly. If the patient presents with asystole, IV atropine (3 mg) or IV isoprenaline (2 mg in 500 mL 5% dextrose, infused at 10–60 mL/hour) may help to maintain the circulation until a temporary pacing electrode can be inserted.

Patients with symptomatic bradyarrhythmias associated with AV block should receive a permanent pacemaker. Asymptomatic first-degree or Mobitz type I second-degree AV block does not require treatment, but a permanent pacemaker is usually indicated in patients with asymptomatic Mobitz type II second-degree or third-degree heart block on prognostic grounds.

Bundle branch block

Interruption of the right or left branch of the conducting system delays activation of the corresponding ventricle, broadens the QRS complex (≥0.12 seconds) and produces characteristic alterations in QRS morphology (Figs. 8.12 and 8.13). RBBB can be a normal variant, but LBBB usually signifies important underlying heart disease (Box 8.8).

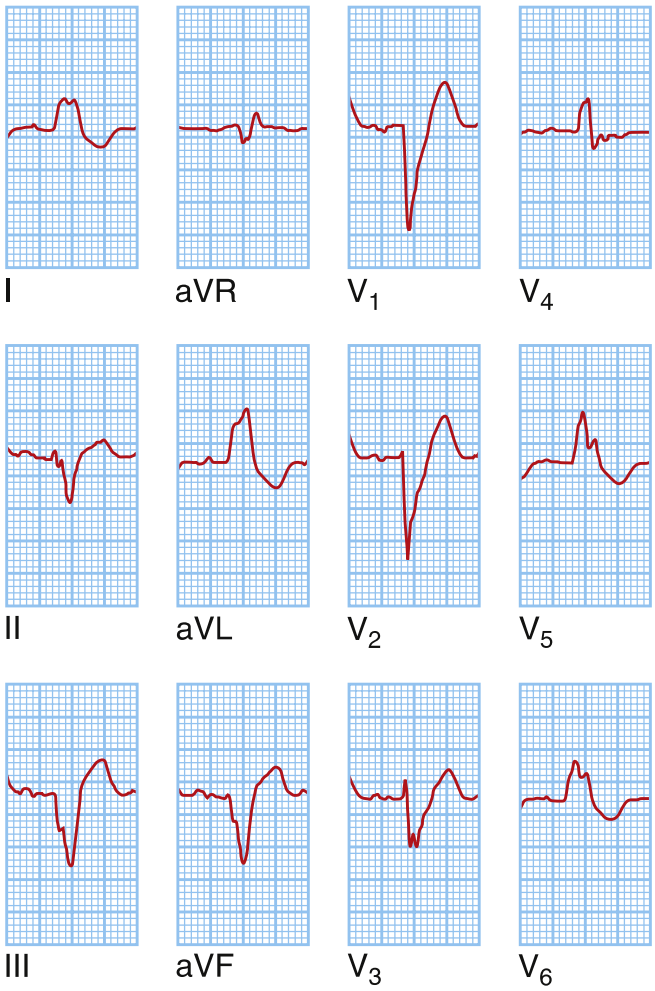


Fig. 8.13 LBBB. Note the wide QRS complexes with the loss of the Q wave or septal vector in lead I and 'M'-shaped QRS complexes in V_5 and V_6.

8.8 Common causes of bundle branch block

Right

- Normal variant
- RV hypertrophy or strain, e.g. PE
- Congenital heart disease, e.g. atrial septal defect
- CAD

Left

- CAD
- Aortic valve disease
- Hypertension
- Cardiomyopathy

Antiarrhythmic drugs

The major classes of antiarrhythmic drugs and their side effects are summarised in Box 8.9.

Nonpharmacological treatment of arrhythmias

Electrical cardioversion

This is useful for terminating rhythms such as AF or VT. The shock interrupts the arrhythmia and produces a brief asystole, followed by the resumption of sinus rhythm. Cardioversion is usually carried out electively under general anaesthesia. The shock is delivered immediately after the R wave, because a shock applied during the T wave may provoke VF. High-energy shocks may cause chest wall pain postprocedure, so it is usual to begin with a shock of 50 J, proceeding to larger shocks if necessary.

Defibrillation

Defibrillators deliver a high-energy DC shock via two large paddles coated with conducting jelly or a gel pad, positioned over the upper right sternal edge and the apex. They are used in the management of cardiac arrest because of VF or VT. Modern units deliver a biphasic shock, during which the shock polarity is reversed mid-shock, reducing the energy required to depolarise the heart. In VF and other emergencies, the energy of the first and second shocks should be 150 J and thereafter up to 200 J.

Temporary pacemakers

Transvenous pacing: Delivered by positioning a pacing electrode at the apex of the right ventricle via the internal jugular, subclavian or femoral vein using fluoroscopic imaging. The electrode is connected to an external pacemaker that delivers an adjustable electrical impulse if the HR falls below a set rate. Temporary pacing may be indicated in the management of transient heart block or of other causes of transient bradycardia (e.g. drug overdose), or as a prelude to permanent pacing. Complications include pneumothorax, brachial plexus or subclavian artery injury, infection or sepsis (usually *Staphylococcus aureus*) and pericarditis.

Transcutaneous pacing: Administered by delivering an electrical stimulus sufficient to induce cardiac contraction through two adhesive gel pad electrodes placed externally over the apex and upper right sternal edge. It is easy and quick to set up, but causes significant discomfort.

Permanent pacemakers

These use the same principles, but the pulse generator is implanted under the skin. Electrodes can be placed in the right ventricular apex, the right atrial appendage or both (dual-chamber). Atrial pacing may be appropriate for patients with sinoatrial disease without AV block. In dual-chamber pacing, the atrial electrode can be used to detect spontaneous atrial activity and trigger ventricular pacing, thereby preserving AV synchrony and allowing the ventricular rate to increase together with the atrial rate during exercise, leading to improved exercise tolerance. A code is used to signify the pacing mode (Box 8.10). Most dual-chamber pacemakers are programmed to DDD mode. Rate-responsive pacemakers trigger a rise in HR in response to

8.9 Classification, use and side effects of antiarrhythmic drugs

Drug	Main uses	Route	Important side effects
Class 1: Membrane stabilizing agents			
Disopyramide	Atrial and ventricular tachyarrhythmias	IV, oral	Myocardial depression
Lidocaine	Ventricular tachycardia and fibrillation	IV	Convulsions
Mexilitine	Atrial and ventricular tachyarrhythmias	IV, oral	Myocardial depression
Flecainide	Atrial and ventricular tachyarrhythmias	IV, oral	Myocardial depression
Class II: Beta adrenoceptor antagonists			
Atenolol Bisoprolol Metoprolol	Treatment and prevention of SVT and AF, prevention of VPBs and exercise induced VT	IV, oral oral IV, oral	Myocardial depression, bronchospasm, cold peripheries
Class III: Drugs prolonging action potential			
Amiodarone	Atrial and ventricular tachyarrhythmias	IV, oral	Thyroid, lung toxicity
Dronedarone	Paroxysmal atrial fibrillation	oral	Renal, liver toxicity
Sotalol[a]	AF, rarely ventricular arrhythmias	IV, oral	Torsades de pointes
Class IV: Slow calcium channel blockers			
Verapamil	Treatment of SVT, control of AF	IV, oral	Myocardial depression
Other			
Atropine	Treatment of vagal bradycardia	IV	Dry mouth, poor vision
Adenosine	Identification/treatment of SVT	IV	Flushing, dyspnea
Digoxin	Treatment of SVT, rate control in AF	IV, oral	GI upset, arrhythmias

[a] *Sotalol also has class II β-blocker activity*

movement or increased respiratory rate and are used in patients unable to raise their HR during exercise. Complications of permanent pacing include:

Early: pneumothorax, cardiac tamponade, lead displacement, infection.

Late: infection, erosion of the generator or lead, lead fracture because of mechanical fatigue.

8.10 International generic pacemaker code

Chamber paced	Chamber sensed	Response to sensing
O = none	O = none	O = none
A = atrium	A = atrium	T = triggered
V = ventricle	V = ventricle	I = inhibited
D = both	D = both	D = both

8.11 Key indications for implantable cardiac defibrillator therapy

Primary prevention

- After MI, if LV ejection fraction <30%
- Mild to moderate symptomatic heart failure, on optimal drug therapy, with LV ejection fraction <35%
- Selected inherited conditions e.g. long QT syndrome, cardiomyopathy

Secondary prevention

- Survivors of VF or VT cardiac arrest not attributed to transient or reversible cause
- VT with haemodynamic compromise or significant LV impairment (LV ejection fraction <35%)

Implantable cardiac defibrillators

In addition to the functions of a permanent pacemaker, ICDs sense rhythm and deliver current through leads implanted in the heart via the subclavian or cephalic vein. They automatically sense and terminate life-threatening ventricular arrhythmias. These devices can treat ventricular tachyarrhythmias using overdrive pacing, synchronised cardioversion or defibrillation. ICD implantation is subject to similar complications as pacemaker implantation (see earlier). Indications for ICDs are shown in Box 8.11.

Cardiac resynchronisation therapy

CRT is a useful treatment for selected patients with LBBB, which causes uncoordinated LV contraction, exacerbating heart failure. CRT systems pace the septum through an RV lead and the epicardial surface of the LV using a lead placed via the coronary sinus into an epicardial vein. Simultaneous septal and epicardial pacing resynchronise LV contraction, improving heart failure and mortality in selected patients.

Catheter ablation therapy

This is the treatment of choice for many patients with AVNRT, AV re-entrant tachycardias and atrial flutter, and is useful for some patients with AF or

ventricular arrhythmias. A series of catheter electrodes are inserted into the heart via the venous system and used to record the activation sequence of the heart in sinus rhythm, during tachycardia and after pacing manœuvres. Once the arrhythmia focus or circuit is identified, a catheter is used to ablate the culprit tissue using radiofrequency current or cryoablation. Serious complications are rare (<1%), but include complete heart block requiring pacemaker implantation, and cardiac tamponade. Successful ablation spares the patient long-term drug treatment.

Coronary artery disease

CAD is the most common cause of angina and acute coronary syndrome and the most common cause of death worldwide. In the UK, 1 in 3 men and 1 in 4 women die from CAD.

Disease of the coronary arteries is almost always caused by atherosclerosis and its complications, particularly thrombosis. Atherosclerosis is a progressive inflammatory disorder of the arterial wall, characterised by focal lipid-rich deposits of atheroma that remain clinically silent until they become large enough to impair arterial perfusion or until disruption of the lesion results in thrombotic occlusion or embolisation of the vessel. Several risk factors have been identified:

Age and sex: Age is the most powerful independent risk factor for athero-sclerosis. Premenopausal women have lower rates of disease than men, but thereafter risk is similar. Hormone replacement therapy has no role in prevention of atherosclerosis, however.

Genetics: A positive family history is common in patients with early-onset disease (age <50 in men and <55 in women). A monozygotic twin of a case has an eightfold risk and a dizygotic twin a fourfold risk of dying from CAD, because of shared genetics, environment and lifestyle. Other risk factors, such as hypertension, hyperlipidaemia and diabetes, have polygenic inheritance.

Smoking: The most important modifiable risk factor, smoking is strongly related to CAD.

Hypertension: The incidence of atherosclerosis increases as BP (systolic and diastolic) rises. Antihypertensive therapy reduces cardiovascular mortality and stroke.

Hypercholesterolaemia: Risk rises with serum cholesterol concentration. Lowering serum total and LDL cholesterol reduces the risk of cardiovascular events.

Diabetes mellitus: This is a potent risk factor for atherosclerosis, and is often associated with diffuse disease. Insulin resistance (normal glucose homeostasis with high levels of insulin) is also a risk factor for CAD.

Lifestyle factors: Alcohol excess is associated with hypertension and cerebrovascular disease. Physical inactivity and obesity are independent risk factors for atherosclerosis; regular exercise appears to have a protective effect. Diets deficient in fresh fruit, vegetables and polyunsaturated fatty acids are associated with an increased risk of cardiovascular disease.

Social deprivation: This is an independent risk factor for cardiovascular disease. Guidelines recommend lower treatment thresholds for socially deprived patients.

Management

Primary prevention: This aims to prevent atherosclerosis in healthy individuals with elevated risk. Public health measures are used to actively discourage risk factors such as obesity and smoking. In addition, scoring systems can identify high-risk individuals for treatment.

Secondary prevention: This means treating patients who already have disease, to prevent subsequent events. Following an event such as an MI, patients are usually receptive to lifestyle advice, such as diet and smoking cessation. Additional interventions are discussed below.

Angina pectoris

Angina pectoris is the symptom complex occurring when an imbalance between myocardial oxygen supply and demand causes transient myocardial ischaemia. Atherosclerosis is by far the most common cause of angina; however, it can also occur with aortic valve disease, hypertrophic cardiomyopathy, vasculitis or aortitis. Angina may accompany coronary vasospasm, and when accompanied by transient ST elevation, this is termed *Prinzmetal's angina*.

Angina on effort with myocardial ischaemia on stress testing but with normal coronary angiography is known as syndrome X. This disorder is poorly understood, but carries a good prognosis.

Clinical features

The history is the most important factor in making the diagnosis (p. 1). Stable angina is characterised by central chest pain, discomfort or breathlessness that is precipitated by exertion or other stress, and is promptly relieved by rest. Examination is frequently negative, but may reveal evidence of:

• Aortic stenosis (an occasional cause of angina). • Risk factors (e.g. hypertension, diabetes; check fundi). • LV dysfunction (e.g. cardiomegaly). • Other arterial disease (e.g. carotid bruits, peripheral vascular disease). • Conditions that exacerbate angina (e.g. anaemia, thyrotoxicosis).

Investigations

Symptoms are a poor guide to the extent of CAD, so stress testing and noninvasive imaging are advisable in patients who are potential candidates for revascularisation.

Exercise ECG: performed using a standard treadmill or bicycle ergometer protocol is the first-line investigation. Horizontal or down-sloping ST segment depression of 1 mm or more is indicative of ischaemia; up-sloping ST depression is less specific. Exercise testing is of value in identifying high-risk individuals with severe coronary disease, but false negatives and positives do occur, the predictive accuracy is lower in women and not all patients can exercise to the required level.

Myocardial perfusion scanning: is helpful if suspicion of CAD is high but the exercise test is equivocal, uninterpretable (e.g. LBBB) or cannot be done. A perfusion defect present during stress but not at rest indicates reversible myocardial ischaemia; a persistent defect suggests previous MI.

CT coronary arteriography: is used increasingly to investigate patients with suspected CAD. It can clarify the diagnosis and (if negative or showing only mild disease) can avoid the need for cardiac catheterisation.

Coronary angiography: provides detailed anatomical information about the extent of CAD. It is usually performed when coronary bypass surgery or percutaneous coronary intervention are being considered.

Management

This should begin with a careful explanation of the problem and a discussion of the lifestyle and medical interventions that can relieve symptoms and improve prognosis. Management then involves:

- Assessment of extent and severity of CAD.
- Identification and control of risk factors (see earlier).
- Symptom control using medication.
- Identification of high-risk patients for treatment to improve life expectancy.

All patients with angina secondary to CAD should receive low-dose (75 mg) aspirin (or clopidogrel 75 mg daily if aspirin causes dyspepsia), continued indefinitely because it reduces the risk of MI. Similarly, all patients should be prescribed a statin, even if cholesterol is normal.

Antianginal drug therapy

The goal is control of angina with minimum side effects and the simplest possible drug regimen. Five groups of drug are used, but there is little evidence that one group is more effective than another. It is conventional to start with glyceryl trinitrate and a β-blocker, adding a calcium channel antagonist or a long-acting nitrate if needed. If two drugs fail to control symptoms, revascularisation should be considered.

Nitrates: Sublingual GTN spray (400 μg) is used for acute attacks and as prophylaxis before exercise. GTN patches have a longer effect. Isosorbide dinitrate or mononitrate can be given by mouth. Headache is a common side effect.

β-Blockers: These limit myocardial oxygen demand by reducing HR, BP and myocardial contractility, but may provoke bronchospasm in asthmatic patients. Cardioselective preparations such as bisoprolol (5–15 mg daily) are widely used.

Calcium channel antagonists: These lower myocardial oxygen demand by reducing BP and myocardial contractility. Nifedipine and amlodipine may cause a reflex tachycardia, so are often combined with a β-blocker. Verapamil and diltiazem can be used as monotherapy. All can aggravate heart failure and cause peripheral oedema and dizziness.

Potassium channel activators: Nicorandil acts as an arterial and venous vasodilator, and has the advantage that it does not exhibit the tolerance seen with nitrates.

I_f channel antagonist: Ivabradine induces bradycardia by modulating ion channels in the sinus node. It does not inhibit contractility or exacerbate heart failure.

Nonpharmacological treatments

Percutaneous coronary intervention: involves passing a fine guidewire across a coronary stenosis under radiographic control and using

it to position a balloon, which is then inflated to dilate the stenosis. This can be combined with deployment of a coronary stent, which is metallic 'scaffolding' impregnated with antiproliferative drugs, used to dilate and maintain a stenosed vessel. PCI is an effective symptomatic treatment, but does not improve survival in patients with chronic stable angina. It is mainly used in single- or two-vessel disease, and can also be used to dilate stenosed bypass grafts. The main acute complication is vessel occlusion by thrombus or dissection, which may lead to myocardial damage (2%–5%) requiring stenting or emergency CABG. The main long-term complication is restenosis. Stenting substantially reduces the risk of restenosis, probably because it allows more complete dilatation. Antiproliferative drug-eluting stents can reduce this risk even further. Adjunctive therapy with a potent platelet inhibitor such as the P2Y12 receptor antagonists (clopidogrel, prasugrel or ticagrelor) in combination with aspirin and heparin improves the outcome following PCI.

Coronary artery bypass grafting: The internal mammary arteries, radial arteries or reversed segments of saphenous vein can be used to bypass coronary artery stenoses, usually under cardiopulmonary bypass. The operative mortality is ~1.5%, but higher in elderly patients and those with poor LV function or significant comorbidity (e.g. renal failure). There is a 1% to 5% risk of perioperative stroke. Approximately 90% of patients are free of angina 1 year after surgery, but less than 60% of patients are asymptomatic 5 years or more after CABG. Arterial grafts have much better long-term patency rates than vein grafts. Long-term aspirin or clopidogrel improves graft patency, whereas intensive lipid-lowering therapy slows progression of disease in the native coronary arteries and grafts. Persistent smokers are twice as likely to die in the 10 years following surgery compared with those who give up at surgery. CABG improves survival in patients with left main stem coronary stenosis and those with symptomatic three-vessel coronary disease; the benefit is greatest in those with impaired LV function or positive stress testing before surgery.

Acute coronary syndrome

This term encompasses unstable angina and MI. Unstable angina refers to new-onset or rapidly worsening (crescendo) angina, and angina on minimal exertion or at rest without myocardial damage. In MI there is evidence of myocardial necrosis in a clinical setting of acute myocardial ischaemia. Criteria for diagnosing an MI are a rise in cardiac biomarker values (e.g. cardiac troponin), to more than the 99th centile and at least one of the following:

1. Symptoms of ischaemia
2. New/presumed new significant ST–T changes or new LBBB
3. Development of pathological Q waves
4. New loss of viable myocardium or new regional wall motion abnormality on imaging
5. Identification of an intracoronary thrombus by angiography or post-mortem

Acute coronary syndrome may present de novo or against a background of chronic stable angina. The underlying pathophysiology is usually a fissured atheromatous plaque with adherent thrombus formation.

Clinical features

The cardinal symptom is severe and prolonged angina-like pain occurring at rest. Other symptoms include:

• Breathlessness. • Vomiting because of vagal stimulation, particularly in inferior MI. • Syncope or sudden death because of arrhythmia.

MI may occasionally be painless, especially in diabetic or elderly patients.

Complications of acute coronary syndromes

Arrhythmias: Arrhythmias are common with acute coronary syndrome, but often transient. The risks can be minimised by pain relief, rest and correction of hypokalaemia. VF occurs in 5% to 10% of hospitalised patients. The prognosis of patients defibrillated for VF in the first 48 hours is identical to that of patients without VF. Ventricular arrhythmias during convalescence signify poor ventricular function, and selected patients may benefit from ICDs (p. 275). AF is common and only requires cardioversion if it causes tachycardia with hypotension, otherwise digoxin or a β-blocker are usually given. Anticoagulation is required if AF persists.

Bradycardia does not require treatment unless there is hypotension, in which case atropine (0.6–1.2 mg IV) is given. Inferior MI may cause AV block, which often resolves following reperfusion. If there is compromise because of second- or third-degree AV block, or block complicating anterior MI, a temporary pacemaker is required.

Recurrent angina: Patients who develop recurrent angina following acute coronary syndrome are at high risk and should be considered for coronary angiography and urgent revascularisation. Angiography is also indicated in all those who have had successful thrombolysis, to treat residual stenosis.

Patients with dynamic ECG changes and ongoing pain should be treated with intravenous glycoprotein IIb/IIIa receptor antagonists.

Acute heart failure: Acute heart failure usually reflects extensive myocardial damage and carries a poor prognosis. The management of heart failure is discussed on p. 259.

Pericarditis: This complicates infarction and is particularly common on the second and third days. A distinct new pain develops, which is often positional or exacerbated by inspiration. A pericardial rub may be heard. Opiate analgesics are preferred over NSAIDs and glucocorticoids because the latter may increase the risk of aneurysm and myocardial rupture.

Dressler's syndrome: This is an autoimmune disorder that occurs weeks to months after the infarct, and is characterised by persistent fever, pericarditis and pleurisy. Severe symptoms may require treatment with an NSAID or glucocorticoids.

Papillary muscle rupture: This causes acute pulmonary oedema and shock with a pansystolic murmur because of the sudden onset of severe mitral regurgitation. Emergency mitral valve replacement may be necessary.

Ventricular septum rupture: Usually presents with sudden haemodynamic deterioration accompanied by a new, loud pansystolic murmur. It may

be difficult to distinguish from acute mitral regurgitation, but tends to cause right heart failure rather than pulmonary oedema. Doppler echocardiography will confirm the diagnosis. Without prompt surgery, the condition is usually fatal.

Ventricular rupture: Leads to cardiac tamponade and is usually fatal.

Other recognised peri-infarct complications

These include:

• Systemic embolism from a cardiac thrombus. • Development of a ventricular aneurysm.

Investigations

ECG: This is the most important investigation in the assessment of acute chest pain, and guides initial therapy. It shows a characteristic series of changes in MI (Fig. 8.14):

The earliest change is ST elevation followed by diminution in the size of the R wave, and development of a Q wave (indicating full-thickness infarction). Subsequently, the T wave becomes inverted, and this change persists after the ST segment has returned to normal. ECG changes are best seen in the leads that 'face' the infarcted area. With anteroseptal infarction, abnormalities are found in one or more leads from V_1 to V_4. Anterolateral infarction produces changes from V_4 to V_6, in aVL and lead I. Inferior infarction is best shown in leads II, III and aVF. Infarction of the posterior wall of the left ventricle does not cause ST elevation or Q waves in the standard leads, but can be diagnosed by the presence of reciprocal changes (ST depression and a tall R wave in leads V_1–V_4).

In non-ST segment elevation acute coronary syndrome, partial or minor coronary occlusion causes unstable angina or subendocardial MI (termed NSTEMI). The ECG shows ST depression and T-wave changes.

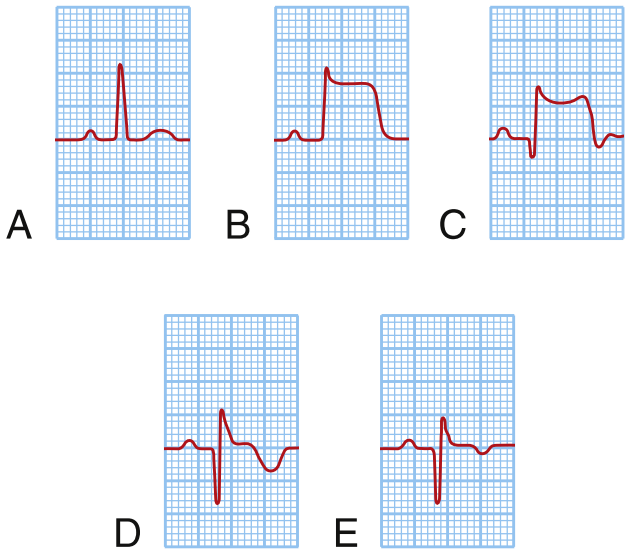


Fig. 8.14 The serial evolution of ECG changes in full-thickness myocardial infarction. (A) Normal ECG complex. (B) (Minutes) Acute ST elevation. (C) (Hours) Progressive loss of the R wave, developing Q wave, resolution of the ST elevation and terminal T-wave inversion. (D) (Days) Deep Q wave and T-wave inversion. (E) (Weeks or months) Old or established infarct pattern; the Q wave tends to persist, but the T-wave changes become less marked.

Occasionally, new-onset LBBB is the only ECG change with infarction.

Patients with ST elevation or new LBBB block require immediate reperfusion therapy. Patients with unstable angina or NSTEMI have a high risk of progression to STEMI or death.

Cardiac biomarkers: Serial measurements of serum troponin should be taken. In unstable angina, there is no rise in troponin, and the diagnosis is made from the history and ECG. In contrast, MI causes a rise in plasma troponin T and I concentrations and other cardiac muscle enzymes (Fig. 8.15). Troponins T and I increase within 3 to 6 hours, peak at about 36 hours and remain elevated for up to 2 weeks.

ECG: This is useful for assessing ventricular function and for detecting complications such as mural thrombus, cardiac rupture, ventricular septal defect, mitral regurgitation and pericardial effusion.

Coronary angiography: Angiography with a view to revascularisation should be considered in patients at moderate or high risk, including those with: • failure to settle on medical therapy • extensive ECG changes • elevated plasma troponin • severe preexisting stable angina

Other investigations: A CXR may reveal pulmonary oedema or cardiomegaly. Lipids should be measured within 24 hours as cholesterol falls following infarction.

Management

Urgent hospital admission is required, as appropriate medical therapy reduces the risk of death and recurrent ischaemia by at least 60%. Initial therapy is summarised in Fig. 8.16.

Clinical risk stratification using defined scores (e.g. the GRACE score; Box 8.12) should be used to select patients for early coronary angiography or early mobilisation and discharge.

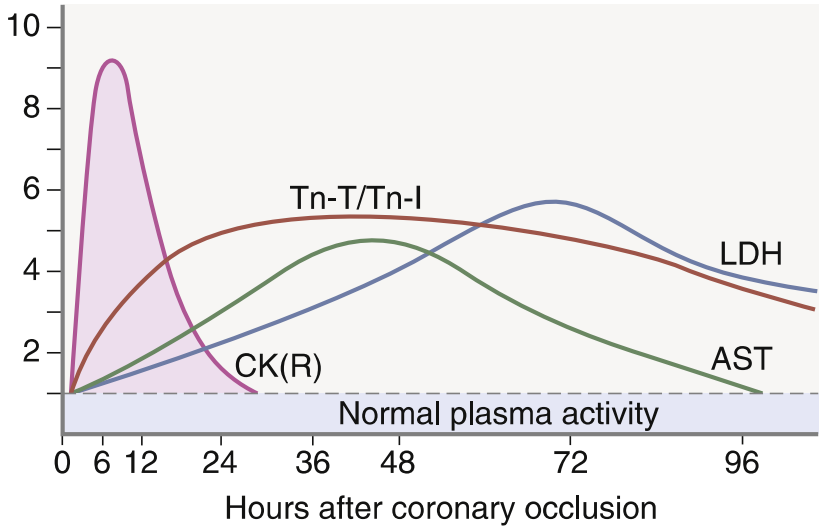


Fig. 8.15 Changes in plasma cardiac biomarker concentrations after myocardial infarction. Creatine kinase (CK) and troponins T (TnT) and I (Tn I) are the first to rise, followed by aspartate aminotransferase (AST) and then lactate (hydroxybutyrate) dehydrogenase (LDH). In patients treated with reperfusion therapy, a rapid rise in plasma creatine kinase (curve CK [R]) occurs, because of a washout effect.

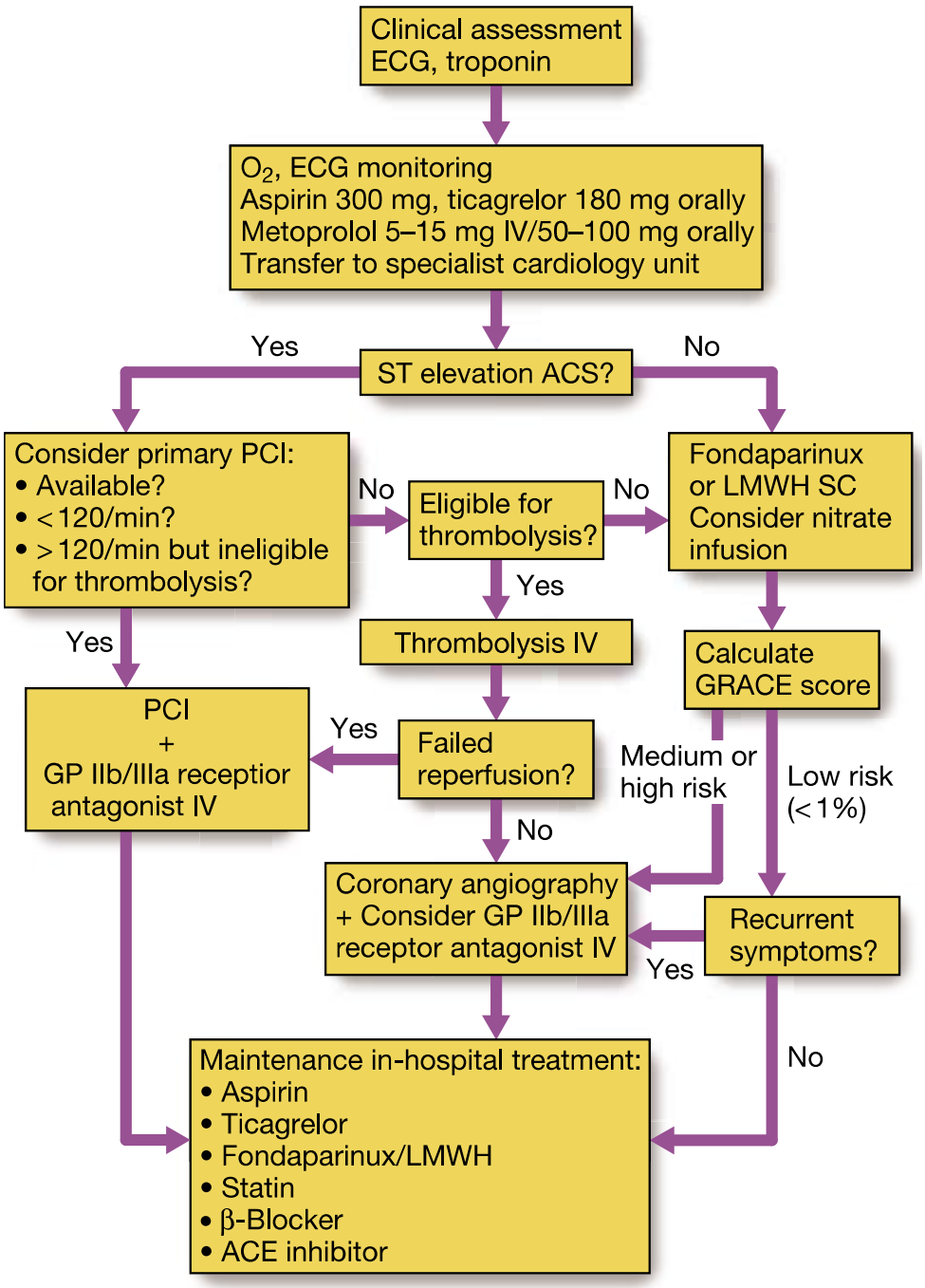


Fig. 8.16 Summary of treatment for acute coronary syndrome. *PCI*, Percutaneous coronary intervention: *GP*, glycoprotein: *LMWH*, low molecular weight heparin.

Analgesia: This is essential to relieve distress, and also to lower adrenergic drive and susceptibility to arrhythmias. IV opiates with an appropriate antiemetic (e.g. metoclopramide) should be titrated until the patient is comfortable.

Reperfusion therapy: Immediate reperfusion therapy is indicated when the ECG shows new bundle branch block or characteristic ST segment elevation of more than 1 mm in the limb leads or 2 mm in the chest leads. PCI is the treatment of choice for those presenting within 12 hours of symptom onset (Fig. 8.16). If PCI cannot be performed within 120 minutes, and thrombolysis is contraindicated, the procedure should

i 8.12 Risk stratification in acute coronary syndrome: GRACE score

Clinical feature	Points range		
Heart failure score (Killip class)	No failure: 0	to	Cardiogenic shock: 59
Systolic BP (mmHg)	≥200: 0	to	≤80: 58
Heart rate	≤50: 0	to	≥200: 46
Age (years)	≤30: 0	to	≥90: 100
Serum creatinine (μmol/L)	0–34: 1	to	≥353: 28
Cardiac arrest at admission	39		
ST-segment deviation	28		
Elevated cardiac enzyme levels	14		

The first five factors score points according to defined ranges (see SIGN Guideline 93; Feb 2007; pp. 42 (annex 1) and 47 (annex 4): http://www.sign.ac.uk/guidelines/fulltext/93/. Sum of points predicts in-hospital death: 0.2% for points ≤60, rising to 52% for points totalling >240

be performed as soon as possible. Patients should be considered for PCI within 24 hours, even after spontaneous reperfusion or thrombolysis. PCI restores coronary patency in more than 95% of patients, with more than 95% 1-year survival and marked reductions in heart failure and recurrent MI. Successful PCI also leads to rapid pain relief, resolution of acute ST elevation and occasional transient arrhythmias. PCI confers no immediate mortality benefit in patients with non-ST segment elevation acute coronary syndrome.

Thrombolysis: If primary PCI cannot be achieved in a timely manner (see Fig. 8.16), thrombolysis should be administered. The survival advantage following thrombolysis is significant, but less than for primary PCI. The benefit is greatest within the first 12 hours, and especially the first 2 hours. Tenecteplase and reteplase, analogues of human tissue plasminogen activator, are given as an IV bolus, assisting emergency treatment including in the prehospital setting. The major hazard of thrombolysis is bleeding. Cerebral haemorrhage causes four extra strokes per 1000 patients treated, and the incidence of other major bleeds is between 0.5% and 1%. Thrombolysis should therefore be withheld if there is a risk of serious bleeding (Box 8.13). PCI should be considered if thrombolysis is contraindicated but there is evidence of cardiogenic shock, and also within 24 hours of successful thrombolysis, to prevent recurrent infarction and improve outcome.

Antithrombotic therapy: Antiplatelet therapy with oral aspirin (300 mg initially, then 75 mg long term) improves survival (25% reduction in mortality). A P2Y12 receptor antagonist such as ticagrelor (180 mg, then 90 mg twice daily) should be given with the aspirin for up to 12 months. Patients intolerant of aspirin should receive clopidogrel (300 mg, then 75 mg daily).

i 8.13 Relative contraindications to thrombolytic therapy (potential candidates for primary percutaneous coronary intervention)

- Active internal bleeding
- Previous subarachnoid or intracerebral haemorrhage
- Uncontrolled hypertension
- Recent surgery (within 1 month)
- Recent trauma (including traumatic resuscitation)
- High probability of active peptic ulcer
- Pregnancy

Glycoprotein IIb/IIIa receptor antagonists (e.g. tirofiban) block platelet aggregation and are given IV to high-risk patients with acute coronary syndromes undergoing PCI.

Anticoagulation: This reduces thromboembolic complications and reinfarction. Fondaparinux (2.5 mg SC daily) has the best safety and efficacy profile, but LMWH is a useful alternative. Anticoagulation should be continued for 8 days or until hospital discharge.

Antianginal therapy: Sublingual GTN (300–500 μg) is valuable first aid in unstable angina, and IV nitrates are useful for the treatment of LV failure and for recurrent or persistent ischaemic pain. Intraveous β-blockers (atenolol or metoprolol) relieve pain, reduce arrhythmias and improve short-term mortality in patients who present within 12 hours of the onset of symptoms, but should be avoided if there is heart failure, hypotension or bradycardia. Nifedipine or amlodipine can be added to the β-blocker if there is persistent chest discomfort. Long-term oral β-blockers reduce mortality by around 25% in survivors of MI.

Renin–angiotensin blockade: Long-term ACE inhibitors (e.g. enalapril 10 mg twice daily or ramipril 2.5–5 mg daily) counteract ventricular remodelling, prevent heart failure, improve survival and reduce recurrent MI and rehospitalisation. Patients with heart failure benefit most, but they should be considered in all patients with acute coronary syndrome. ACE inhibitors may exacerbate hypotension, in which case ARBs (e.g. candesartan) may be better tolerated.

Mineralocorticoid receptor antagonists: Patients with acute MI complicated by heart failure and LV dysfunction, and either pulmonary oedema or diabetes, further benefit from eplerenone (25–50 mg daily) or spironolactone (25–50 mg daily).

Lipid lowering therapy: All patients should receive therapy with HMG CoA reductase enzyme inhibitors (statins) after acute coronary syndrome, irrespective of serum cholesterol. Patients with serum LDL cholesterol concentrations greater than 3.2 mmol/L (~120 mg/dL) benefit from more intensive therapy, such as atorvastatin (80 mg daily). Ezetimibe, fibrates and anion exchange resins may be used in cases resistant to statins alone.

Smoking cessation: Giving up smoking is the single most effective thing a patient can do after acute coronary syndrome, as cessation halves mortality at 5 years. Cessation success rates are improved by supportive advice and pharmacological therapy.

Diet and exercise: Maintaining an ideal weight, eating a Mediterranean-style diet, taking regular exercise, and controlling hypertension and diabetes mellitus all improve the long-term outlook.

Rehabilitation

When there are no complications, the patient can mobilise on the second day, return home in 2 to 3 days and gradually increase activity, aiming to return to work in 4 weeks. Most patients may resume driving after 1 to 4 weeks, but drivers of trucks and buses usually require special assessment. Emotional problems such as anxiety and depression are common, and must be recognised and dealt with accordingly. Formal rehabilitation programmes, based on graded exercise protocols with individual and group counselling, are often very successful.

Prognosis

In almost one-quarter of cases of MI, death occurs within a few minutes without medical care. Half of deaths occur within 24 hours of the onset of symptoms, and around 40% of all affected patients die within the first month. Of those who survive an acute attack, more than 80% live for a further year, around 75% for 5 years and 50% for 10 years. Early death is usually caused by an arrhythmia but, later on, the outcome is determined by the extent of myocardial damage. Unfavourable features include poor LV function, AV block and persistent ventricular arrhythmias. The prognosis is worse for anterior than for inferior infarcts.

Peripheral arterial disease

Around 20% of UK adults aged 55 to 75 years have PAD, but only one-quarter have symptoms, usually intermittent claudication. Almost all PAD is because of atherosclerosis, and it shares the same risk factors as CAD. Some 5% to 10% of patients with PAD have diabetes, but this increases to 30% to 40% in those with severe limb ischaemia. The mechanism of PAD in diabetes is atheroma of medium to large arteries, so diabetes is not a contraindication to lower limb revascularisation.

Clinical features

Symptomatic PAD affects the legs eight times more commonly than the arms. Several vessels may be affected in a variable and asymmetric manner. Box 8.14 lists the clinical signs of chronic PAD.

Intermittent claudication: IC is the most common presentation of CAD and refers to ischaemic pain in the leg muscles. It is usually felt in the calf (superficial femoral artery disease) but may occur in the thigh or buttock (iliac artery disease). Typically, the pain comes on after a reasonably constant distance and resolves rapidly on stopping.

8.14 Examination findings in chronic lower limb ischaemia

- Pulses—diminished or absent
- Bruits—denote turbulent flow but bear no relationship to the severity of the underlying disease
- Reduced skin temperature
- Pallor on elevation and rubor on dependency (Buerger's sign)
- Superficial veins that fill sluggishly and empty ('gutter') upon minimal elevation
- Muscle wasting
- Skin and nails—dry, thin and brittle
- Loss of hair

8.15 Symptoms and signs of ALI

Symptoms/signs	Comment
Pain **P**allor **P**ulselessness	May be absent in complete acute ischaemia, and can be present in chronic ischaemia
Perishing cold	Unreliable, as the ischaemic limb takes on the ambient temperature
Paraesthesia **P**aralysis	Important features of impending irreversible ischaemia

Critical limb ischaemia: CLI is defined as rest pain requiring opiate analgesia and/or ulceration or gangrene, present for more than 2 weeks, in the presence of an ankle BP less than 50 mmHg. Rest pain with ankle pressures greater than 50 mmHg is known as subcritical limb ischaemia (SCLI). Severe limb ischaemia (SLI) comprises both CLI and SCLI. Whereas IC is usually because of single-segment plaque, SLI is always because of multilevel disease. Patients are at risk of losing their limb (or life) in a matter of weeks or months without surgical bypass or endovascular revascularisation, but treatment is difficult because most are elderly with significant multisystem comorbidity and extensive disease.

Acute limb ischaemia: This is most frequently caused by acute thrombotic occlusion of a preexisting arterial stenosis or thromboembolism (often secondary to AF). The typical presentation is with the so-called 'Ps of acute ischaemia' (Box 8.15). Pain on squeezing the calf indicates muscle infarction and impending irreversible ischaemia. All suspected acutely ischaemic

limbs must be discussed immediately with a vascular surgeon. If there are no contraindications, an IV bolus of heparin (3000–5000 U) should be given to limit thrombus propagation and protect the collateral circulation. Distinguishing thrombosis from embolism is frequently difficult. Evidence of chronic lower limb ischaemia (e.g. previous IC symptoms, bruits, diminished contralateral pulses) favours thrombosis, whereas sudden onset and the presence of AF favour embolism.

ALI because of thrombosis can often be treated medically with IV heparin (target APTT 2.0–3.0), antiplatelet agents, high-dose statins, IV fluids and oxygen. ALI because of embolus (no collateral circulation) normally results in extensive tissue necrosis within 6 hours unless the limb is revascularised. Irreversible ischaemia mandates early amputation or palliative therapy.

Investigations

The ankle–brachial pressure index (ABPI, the ratio between the systolic ankle and brachial blood pressures) is over 1.0 in health. In IC, the ABPI is typically 0.5 to 0.9, and in CLI usually less than 0.5. Further investigation with duplex ultrasonography, MRI or contrast CT is used to define the sites of involvement. Intra-arterial digital subtraction angiography is reserved for those undergoing endovascular revascularisation. Other investigations should include a full blood count to exclude anaemia and thrombocythaemia, as well as measurement of lipids and blood glucose.

Management

Medical management consists of smoking cessation, exercise, antiplatelet therapy (aspirin or clopidogrel), statins and treatment of coexisting diabetes, hypertension or polycythaemia. Vorapaxar, an inhibitor of platelet activation, has recently been licensed in combination with either aspirin or clopidogrel in patients with PAD. The peripheral vasodilator cilostazol may improve walking distance in patients who fail to respond to usual therapy. Angioplasty, stenting, endarterectomy or bypass is usually considered in patients who remain severely disabled by symptoms despite 6 months of medical therapy. Subclavian artery disease is usually treated by angioplasty and stenting.

Buerger's disease–thrombangitis obliterans

This inflammatory obliterative arterial disease usually affects male smokers aged 20 to 30 years, causing claudication and finger pain, with absent wrist and ankle pulses. Smoking cessation is essential, and sympathectomy and prostaglandin infusions may help.

Raynauld's syndrome

This disorder affects 5% to 10% of young women aged 15 to 30 years in temperate climates. It is usually benign, so the patient should be reassured and advised to avoid cold. More severe Raynauld's syndrome with digital ulceration occurs with connective tissue disease (p. 770).

Diseases of the aorta

Aortic aneurysms

An aortic aneurysm is an abnormal dilatation of the aortic lumen. Abdominal aortic aneurysms (AAAs) affect men three times more commonly than women, and occur in about 5% of men over the age of 60 years.

The most common cause of aortic aneurysm is atherosclerosis, for which the risk factors are described earlier (p. 276). Additional genetic factors cause aortic aneurysm to run in families. Marfan's syndrome (p. 290) is a rare cause.

Clinical features

The clinical presentation depends on the site of the aneurysm. Thoracic aneurysms may typically present with acute severe chest pain, but other features, including aortic regurgitation, stridor, hoarseness and superior vena cava syndrome, may occur. Erosion into the oesophagus or bronchus may present with massive bleeding.

AAAs can present in a number of ways, including central abdominal or back pain, lower limb thromboemboli and compression of the duodenum or IVC. The usual age is 65 to 75 years for elective presentations and 75 to 85 years for emergency presentations. Many AAAs are asymptomatic and found incidentally or on screening.

Investigation

Ultrasound establishes the diagnosis and is used to monitor asymptomatic AAAs; elective repair is considered if the diameter exceeds 5.5 cm. CT and MRI scanning are used to assess thoracic aneurysms and to plan surgical intervention.

Management

All symptomatic AAAs should be considered for repair, not least because pain often predates rupture. Distal embolisation is a strong indication for repair. Rupture of an AAA produces severe abdominal pain with hypovolaemic shock, and is rapidly fatal. Operative mortality for ruptured AAA is around 50%, but survivors have a good prognosis. Endovascular repair using a stent-graft introduced through the femoral artery is used increasingly to replace open surgery.

Aortic dissection

A breach in the intima of the aortic wall allows arterial blood to enter the media, which is then split into two layers, creating a 'false lumen' alongside the existing or 'true lumen'. Aortic dissection is classified into type A and type B, involving or sparing the ascending aorta, respectively. Aortic atherosclerosis and hypertension are common aetiological factors, but other predisposing conditions include thoracic aortic aneurysm, aortic coarctation, previous aortic surgery, Marfan's syndrome, trauma and pregnancy.

Clinical features

The patient typically presents with sudden-onset, severe, 'tearing' anterior chest pain or interscapular back pain, often associated with collapse. Occlusion of aortic branches may cause stroke, MI or paraplegia, as well as asymmetry of the brachial, carotid or femoral pulses.

Investigation

CT and MRI are the investigations of choice. The CXR may show broadening of the upper mediastinum and distortion of the aortic 'knuckle', but these findings are absent in 10% of cases. Transoesophageal echocardiography is useful; transthoracic echocardiography shows only 3 to 4 cm of the ascending aorta.

Management

Early mortality of acute dissection is 1% to 5% per hour. Initial management comprises pain control and IV labetalol (target systolic BP <120 mmHg). Endoluminal repair with fenestration of the intimal flap or insertion of a stent-graft may be effective.

Marfan's syndrome

This is a rare autosomal dominant connective tissue disorder that is associated with a high risk of aortic aneurysm and dissection.

Clinical features

Aortic and mitral regurgitation, skin laxity, joint hypermobility, long arms, legs and fingers (arachnodactyly), scoliosis, pectus excavatum, high-arched palate, lens dislocation retinal detachment and pneumothorax.

Investigations

The clinical diagnosis is confirmed by genetic testing. Patients should undergo serial echocardiography of the aortic root; if dilatation is observed, elective surgery should be considered.

Management

β-Blockers reduce the risk of aortic dilatation and should be given to all patients. Activities associated with increases in cardiac output are best avoided. Surgery to replace the aortic root can be performed in patients with progressive aortic dilatation.

Hypertension

The risk of cardiovascular diseases such as stroke and CAD is closely related to BP; however, there is no specific cut-off above which the risk of cardiovascular risk suddenly increases. The diagnosis of hypertension is made when BP rises above a specific threshold where the risk of cardiovascular complications and benefits of treatment outweigh the costs and side effects of therapy. The British Hypertension Society defines hypertension as a BP greater than 140/90 mmHg.

In more than 95% of cases, no specific underlying cause of hypertension can be found, and such patients are said to have essential hypertension. Important predisposing factors for essential hypertension include:

• Age. • Ethnicity (higher incidence in African Americans and Japanese). • Genetic factors. • High salt intake. • Alcohol excess. • Obesity. • Lack of exercise. • Impaired intrauterine growth.

In around 5% of cases, hypertension results from a specific underlying disorder (secondary hypertension). Causes include:

8.16 Hypertensive retinopathy

Grade 1	Arteriolar thickening, tortuosity and increased reflectiveness ('silver wiring')
Grade 2	Grade 1 plus constriction of veins at arterial crossings ('arterio-venous nipping')
Grade 3	Grade 2 plus evidence of retinal ischaemia (flame-shaped or blot haemorrhages and 'cotton wool' exudates)
Grade 4	Grade 3 plus papilloedema

• Renal disease (renal vascular disease, glomerulonephritis, polycystic kidney disease; see Chapter 7). • Endocrine disorders (phaeochromocytoma, Cushing's syndrome, Conn's syndrome, acromegaly, thyrotoxicosis, congenital adrenal hyperplasia; see Chapter 10). • Pregnancy. • Drugs (corticosteroids, oestrogen-containing oral contraceptive pill, anabolic steroids). • Coarctation of the aorta.

Clinical features

Hypertension is usually asymptomatic until discovered at a routine examination or when a complication arises. A BP check is therefore advisable every 5 years in adults older than 40 years to detect occult hypertension. The history may reveal familial hypertension, lifestyle factors (exercise, salt intake, smoking, alcohol intake) and potential drug causes. Examination may reveal radiofemoral delay (coarctation of the aorta), enlarged kidneys (polycystic kidney disease), abdominal bruits (renal artery stenosis) or features of Cushing's syndrome. More commonly, there may be evidence of risk factors such as central obesity or hyperlipidaemia, or of complications such as LV hypertrophy (LV heave, fourth heart sound), aortic aneurysm, stroke or retinopathy (Box 8.16).

Investigations

Antihypertensive therapy is commonly lifelong, so it is vital that the BP readings on which the diagnosis is based are accurate. Measurements should be made to the nearest 2 mmHg, sitting with the arm supported, using an appropriately sized cuff and repeated after 5 minutes' rest if initial values are high. Sphygmomanometry, particularly when performed by a doctor, can cause a transient rise in BP ('white coat' hypertension). A series of automated ambulatory BP measurements obtained over 24 hours or longer provides a better profile than a limited number of clinic readings. Home self-measurement is an alternative that is less well established. Ambulatory or home measurements may be particularly helpful in patients with unusually labile or refractory BP, those with symptomatic hypotension and those in whom white coat hypertension is suspected.

All hypertensive patients should also be investigated by urinalysis for blood, protein and glucose, U&Es, blood glucose, serum lipids, thyroid function and 12-lead ECG. Additional investigations are appropriate in selected patients to identify target organ damage (e.g. echocardiography) or potential causes of secondary hypertension (e.g. renal USS, urinary catecholamines).

Management

The objective of antihypertensive therapy is to reduce the incidence of adverse cardiovascular events. The relative benefit of BP reduction (~30% reduction in risk of stroke and 20% reduction in risk of CAD) is similar in all patient groups, so the absolute benefit of treatment is greatest in those at highest risk. Decisions on treatment should therefore be guided by an overall assessment of cardiovascular risk. In practice this is best calculated using risk-prediction charts (Fig. 8.18). The British Hypertension Society management guidelines are summarised in (Box 8.17).

The following lifestyle measures can not only lower BP but also reduce cardiovascular risk:

• Correcting obesity. • Reducing alcohol intake. • Restricting salt intake. • Engaging in regular physical exercise. • Increasing consumption of fruit and vegetables.

Drug therapy

Thiazides: The antihypertensive action of thiazides is incompletely understood, and may take up to a month to take effect. The daily dose of bendroflumethiazide is 2.5 mg.

ACE inhibitors: ACE inhibitors (e.g. lisinopril 10–40 mg daily) are effective, but can precipitate renal failure in patients with renal impairment or renal artery stenosis. U&E should be checked before and 1 to 2 weeks into therapy. Side effects include first-dose hypotension, cough, rash, hyperkalaemia and renal dysfunction.

Angiotensin receptor blockers: ARBs (e.g. irbesartan 150–300 mg daily) have similar efficacy to ACE inhibitors but do not cause cough and are better tolerated.

Calcium channel antagonists: Amlodipine (5–10 mg daily) and nifedipine (30–90 mg daily) are particularly useful in older people. Side effects include flushing, palpitations and fluid retention.

β-Blockers: These are not first-line antihypertensive therapy, except in patients with a second indication such as angina. Atenolol (50–100 mg daily) and bisoprolol (5–10 mg daily) are β_1-selective and less likely than nonselective agents to cause the side effects of poor circulation and bronchospasm.

Combined β- and α-blockers: Labetalol (200 mg–2.4 g daily in divided doses) can be used as an infusion in accelerated hypertension (see below).

Other vasodilators: These include α_1-adrenoceptor antagonists (e.g. doxazosin 1–16 mg daily) and vascular smooth muscle relaxants (e.g. hydralazine 25–100 mg twice daily). Side effects include first-dose and postural hypotension, headache, tachycardia and fluid retention.

Combination therapy is often required to achieve adequate control, and a recommended treatment algorithm is shown in Fig. 8.19. However, comorbid conditions may have an important influence on initial drug selection (e.g. a β-blocker might be the most appropriate treatment for a patient with angina, but should be avoided in asthma).

Accelerated hypertension

This rare complication of hypertension is characterised by rapidly progressive end-organ damage, including retinopathy, renal dysfunction and

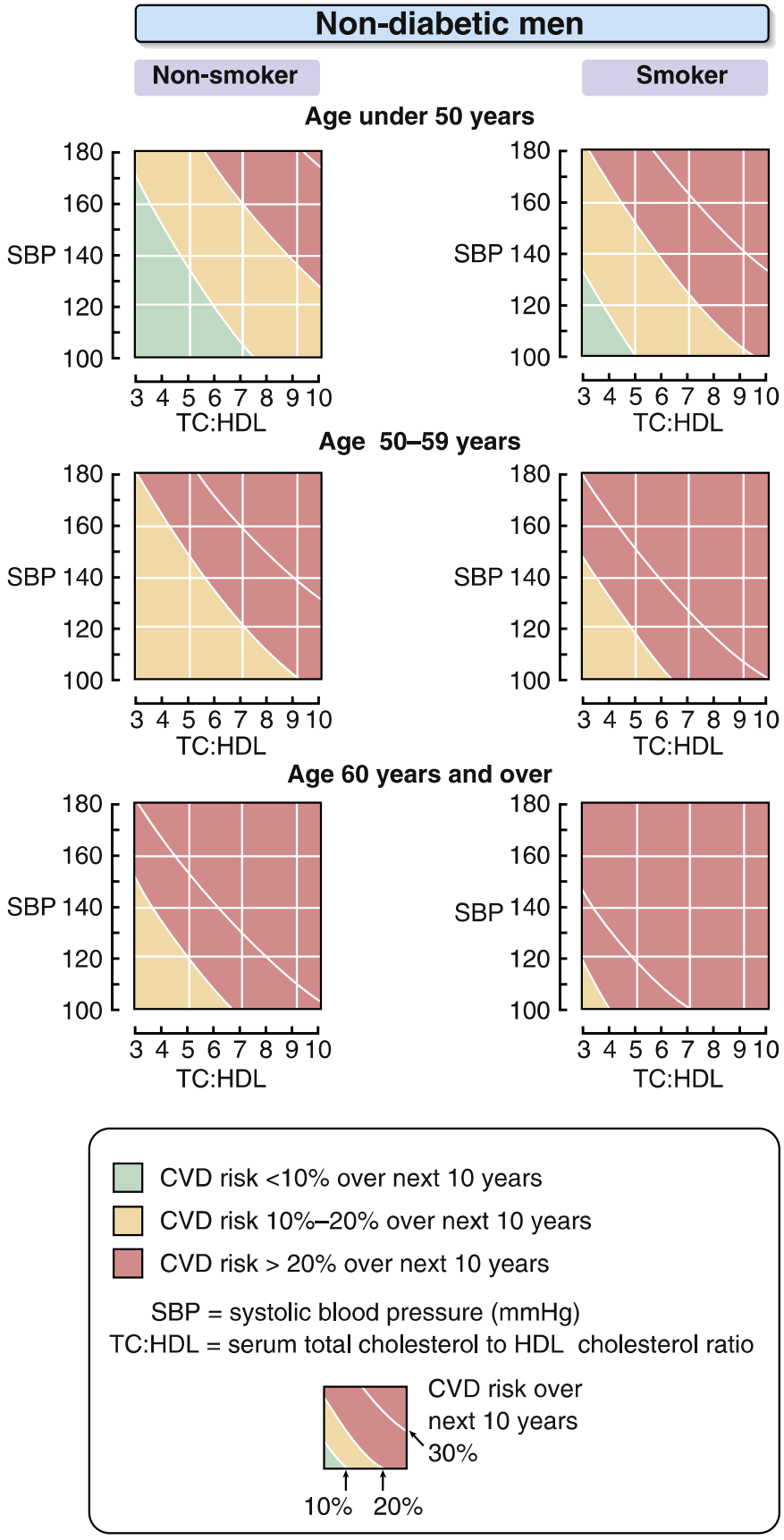


Fig. 8.17 Example of cardiovascular risk prediction chart for nondiabetic men. Cardiovascular risk is predicted from the patient's age, sex, smoking habit, BP and cholesterol ratio.

8

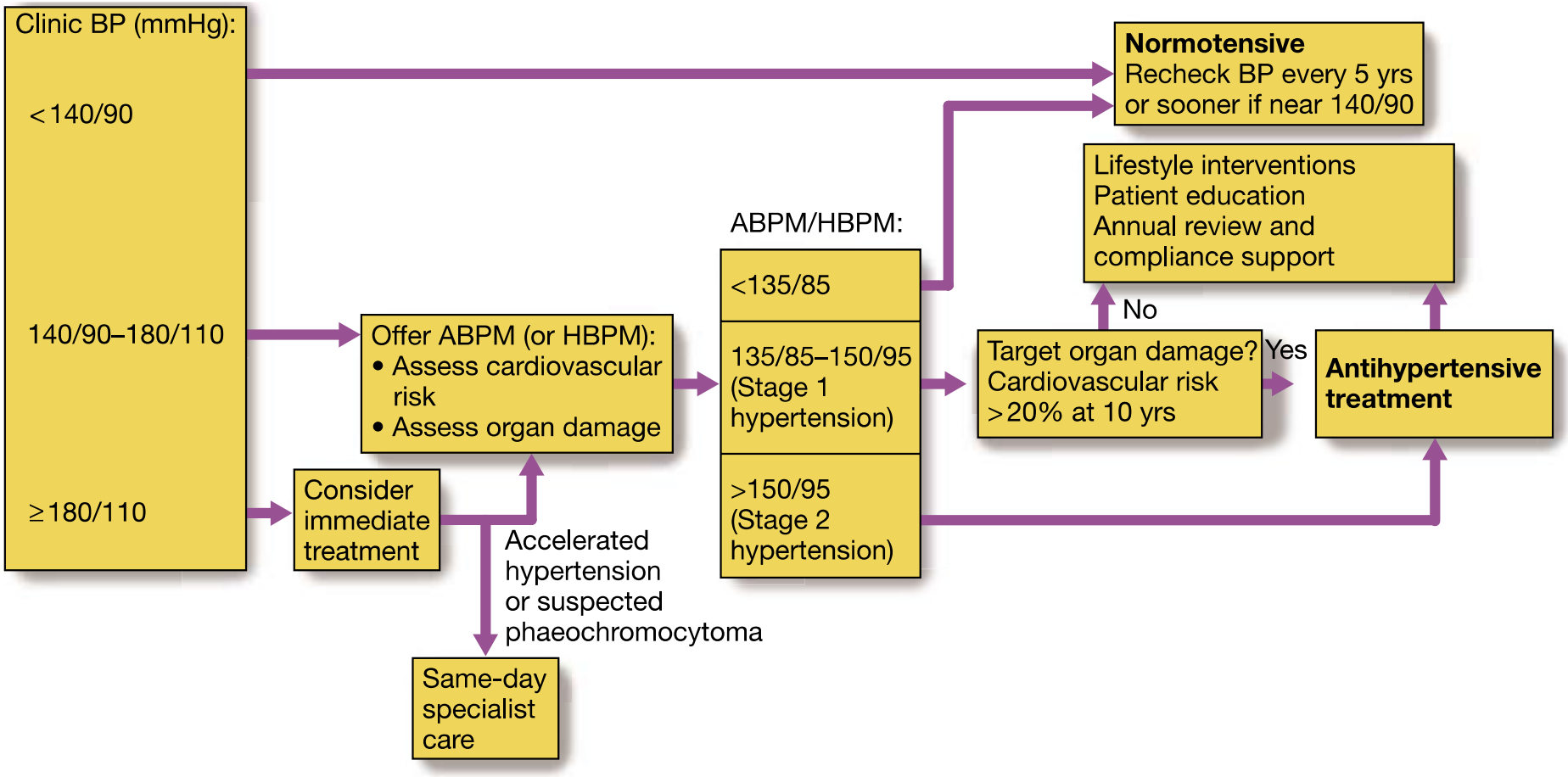


Fig. 8.18 Management of hypertension: British Hypertension Society guidelines. Consider specialist referral for stage 1 hypertension in those aged younger than 40 years. *ABPM*, Ambulatory blood pressure monitoring; *HBPM*, home blood pressure monitoring.

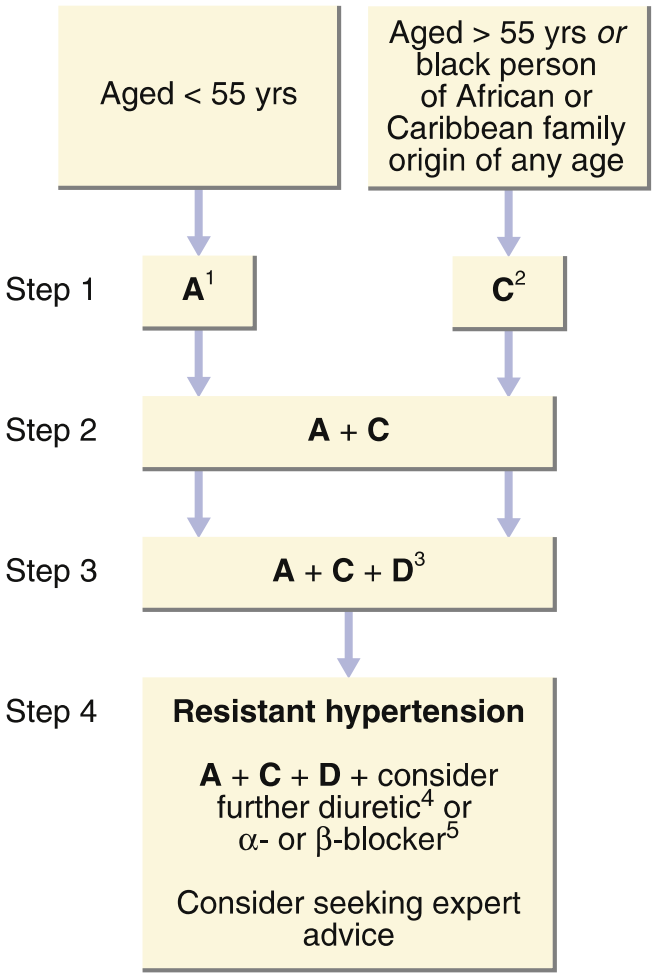


Fig. 8.19 Antihypertensive drug combinations. [1]A = ACE inhibitor or ARB. [2]C = calcium channel blocker (CCB); consider thiazide if CCB not tolerated or in heart failure. [3]D = thiazide. [4]Low-dose spironolactone or higher-dose thiazide. [5]Consider an α- or β-blocker if further diuretics are not tolerated, contraindicated or ineffective. *CCB,* Calcium channel blocker.

encephalopathy. Sudden lowering of BP may compromise perfusion, leading to cerebral, coronary or renal insufficiency. A controlled reduction to around 150/90 mmHg over 24 to 48 hours using oral agents is ideal. Where necessary, IV labetalol, GTN and sodium nitroprusside are effective alternatives, but require careful supervision.

Diseases of the heart valves

A diseased valve may be narrowed (stenosed), or it may fail to close adequately, and thus permit regurgitation of blood. Sudden valve failure can occur with aortic dissection, traumatic rupture, endocarditis or papillary muscle rupture complicating MI. Valve disease may also be congenital or acquired through rheumatic carditis, syphilitic aortitis, ventricular dilatation in heart failure or senile degeneration.

Acute rheumatic fever

This usually affects children or young adults. It is now rare in Western Europe and North America, but remains endemic in the Indian subcontinent,

Africa and South America. It is triggered by an immune-mediated delayed response to infection with specific strains of group A streptococci that have antigens that cross-react with cardiac myosin and sarcolemmal membrane protein. Antibodies produced against the streptococcal antigens mediate inflammation in the endocardium, myocardium and pericardium, as well as the joints and skin.

Clinical features

ARF typically follows 2 to 3 weeks after an episode of streptococcal pharyngitis, and presents with fever, anorexia, lethargy and joint pains. The diagnosis is based on the revised Jones criteria (Box 8.17). Carditis may involve the endocardium, myocardium and pericardium to varying degrees, and manifests as breathlessness (heart failure or pericardial effusion), palpitations or chest pain (pericarditis). Other features include tachycardia, cardiac enlargement, new murmurs (especially mitral regurgitation) or a soft mid-diastolic murmur because of mitral valvulitis (Carey Coombs murmur).

Acute, painful, asymmetric and migratory arthritis of the large joints (knees, ankles, elbows, wrists) is the most common major manifestation.

Erythema marginatum appears as red macules, which fade in the centre but remain red at the edges; they occur mainly on the trunk and proximal extremities, but not the face. Subcutaneous nodules are small, firm, painless and best felt over extensor surfaces of bone or tendons. They usually appear more than 3 weeks after the onset of other manifestations.

i 8.17 Jones criteria for the diagnosis of rheumatic fever

Major manifestations

- Carditis
- Polyarthritis
- Chorea
- Erythema marginatum
- Subcutaneous nodules

Minor manifestations

- Fever
- Arthralgia
- Previous rheumatic fever
- Raised ESR or CRP
- Leucocytosis
- First-degree AV block

Notes

- Diagnosis depends on two or more major manifestations, or one major and two or more minor manifestations PLUS supporting evidence of preceding streptococcal infection: recent scarlet fever, raised ASO or other streptococcal antibody titre, positive throat culture
- Evidence of recent streptococcal infection is particularly important if there is only one major manifestation

Sydenham's chorea (St. Vitus' dance) is a late (>3 months) neurological manifestation characterised by emotional lability and purposeless involuntary choreiform movements of the hands, feet or face; spontaneous recovery usually occurs within a few months.

Investigations

Raised WCC, ESR and CRP indicate systemic inflammation, and are useful for monitoring the disease. Throat swabs are often negative because infection has already resolved. ASO titre indicates preceding streptococcal infection—either rising titres or high titres (children >300 U, adults >200 U). ECG (AV block, pericarditis) and echocardiography (cardiac dilatation, valve abnormalities) may reveal evidence of carditis.

Management

Benzathine benzylpenicillin (1.2 million U IM once) or oral phenoxymethylpenicillin (250 mg four times daily for 10 days) should be given to eliminate residual streptococcal infection. Bed rest lessens joint pain and reduces cardiac workload. Cardiac failure should be treated. High-dose aspirin (60–100 mg/kg up to 8 g per day) usually relieves arthritic pain, and a response within 24 hours helps to confirm the diagnosis. Prednisolone 1 to 2 mg/kg per day produces more rapid symptomatic relief, and is indicated for carditis or severe arthritis until the ESR returns to normal. Patients are susceptible to further attacks of rheumatic fever if subsequent streptococcal infection occurs, and long-term prophylaxis with penicillin should be given, usually until the age of 21 years.

Chronic rheumatic heart disease

This is characterised by progressive valve fibrosis, and develops in at least half of those affected by rheumatic fever with carditis. Some episodes of rheumatic fever may pass unrecognised, and a positive history is only found in about half of patients. The mitral valve is affected in more than 90% of cases, with the aortic valve the next most frequently involved.

Mitral stenosis

Mitral stenosis is almost always rheumatic in origin. The valve orifice is slowly diminished by progressive fibrosis, leaflet calcification and fusion of the cusps and subvalvular apparatus. Restricted blood flow from left atrium to ventricle causes a rise in left atrial pressure, leading to pulmonary venous congestion and breathlessness, whereas low cardiac output may cause fatigue. Patients usually remain asymptomatic until the mitral valve area is less than 2 cm^2 (normal = 5 cm^2). AF occurs frequently because of progressive left atrial dilatation, and the onset of AF often causes rapid decompensation with pulmonary oedema because ventricular filling depends on left atrial contraction. Exercise and pregnancy also increase left atrial pressure and cause decompensation. More gradual rises in left atrial pressure cause pulmonary hypertension, RV hypertrophy and dilatation, tricuspid regurgitation and right heart failure.

Clinical features

Effort-related dyspnoea is usually the dominant symptom and produces a gradual reduction in exercise tolerance over many years, culminating in

dyspnoea at rest. Acute pulmonary oedema or pulmonary hypertension may cause haemoptysis. On examination, the patient is usually in AF, and a malar flush may be apparent. Thromboembolism is a common complication, especially in patients with AF. The apex beat is characteristically tapping in nature. On auscultation there may be a loud first heart sound, an opening snap and a low-pitched mid-diastolic murmur. An elevated JVP, RV heave, loud pulmonary component of the second heart sound and features of tricuspid regurgitation all signify the presence of pulmonary hypertension.

Investigations

• Doppler echocardiography provides the definitive evaluation of mitral stenosis, allowing estimation of valve area, pressure gradient across the valve and pulmonary artery pressure. • ECG may show bifid P waves (P mitrale) because of left atrial hypertrophy, or AF. • CXR may show an enlarged left atrium and features of pulmonary congestion.

Management

Medical management consists of diuretics for pulmonary congestion, digoxin, β-blockers or calcium antagonists for rate limitation, plus anticoagulants if there is AF. For persistent symptoms or pulmonary hypertension, valvuloplasty, valvotomy or valve replacement are indicated. Balloon valvuloplasty or valvotomy are useful in noncalcific pure stenosis; valve replacement is needed for calcific disease or stenosis with regurgitation.

Mitral regurgitation

Causes of mitral regurgitation are shown in Box 8.18. Chronic mitral regurgitation causes gradual dilatation of the LA with little increase in pressure; progressive LV dilatation occurs because of chronic volume overload. Acute mitral regurgitation causes a rapid rise in left atrial pressure, resulting in pulmonary oedema.

Mitral valve prolapse: A common cause of mild mitral regurgitation, this arises from congenital anomalies or degenerative myxomatous changes, and rarely as a feature of Marfan's syndrome. In mild cases, the valve remains competent but bulges back into the atrium during systole, causing a mid-systolic click but no murmur. If the valve becomes regurgitant, the click is followed by a late systolic murmur. Sudden deterioration may occur if the chordae tendinae rupture. The condition is associated with a variety of benign arrhythmias, atypical chest pain and a very small risk of embolic stroke or transient ischaemic attack. Nevertheless, the long-term prognosis is good.

8.18 Causes of mitral regurgitation

- Mitral valve prolapse
- Dilatation of the LV and mitral valve ring (e.g. coronary artery disease, cardiomyopathy)
- Damage to valve cusps and chordae (e.g. rheumatic heart disease, endocarditis)
- Ischaemia or infarction of papillary muscle
- Myocardial infarction

Clinical features

Chronic mitral regurgitation typically causes progressive exertional dyspnoea and fatigue, whereas sudden-onset mitral regurgitation usually presents with acute pulmonary oedema. The regurgitant jet causes an apical pan-systolic murmur that radiates to the axilla. The first heart sound is quiet, and there may be a third heart sound. The apex beat feels hyperdynamic and is usually displaced to the left, indicating LV dilatation. Signs of AF, pulmonary venous congestion and pulmonary hypertension may be present.

Investigations

Doppler echocardiography reveals chamber dimensions, LV function, the severity of regurgitation and structural abnormalities of the valve. ECG commonly shows AF. Cardiac catheterisation is indicated if surgery is being considered. The severity of regurgitation can be assessed by left ventriculography and by the size of the *v* (systolic) waves in the left atrial or pulmonary artery wedge pressure trace.

Management

Medical treatment includes diuretics and afterload reduction with vasodilators (e.g. ACE inhibitors). AF requires digoxin and anticoagulation. Regular review is important to detect worsening symptoms, progressive cardiac enlargement and LV impairment, as these are all indications for surgical intervention. Mitral valve repair is now the treatment of choice for severe mitral regurgitation, even in asymptomatic patients, because early repair prevents irreversible left ventricular damage. Acute severe mitral regurgitation necessitates emergency valve replacement or repair.

Aortic stenosis

The three common causes of aortic stenosis are:
• Rheumatic fever (usually associated with mitral valve disease). • Calcification of a congenitally bicuspid valve. • In the elderly, senile degenerative aortic stenosis.

Cardiac output is initially maintained, but the left ventricle becomes increasingly hypertrophied. Eventually it can no longer overcome the outflow tract obstruction and heart failure develops. Patients with aortic stenosis typically remain asymptomatic for many years but deteriorate rapidly when symptoms develop.

Clinical features

Mild to moderate aortic stenosis is usually asymptomatic, but may be detected incidentally on routine examination. The three cardinal symptoms are angina, syncope and breathlessness.
• Angina: arises because of the increased oxygen demands of the hypertrophied LV working against the high-pressure outflow tract obstruction (or coexisting CAD). • Syncope: usually occurs on exertion when cardiac output fails to rise to meet demand because of severe outflow obstruction, causing a fall in BP. • Exertional breathlessness: suggests cardiac decompensation as a consequence of chronic excessive pressure overload.

The characteristic clinical signs are:
• Harsh ejection systolic murmur radiating to the neck (often with a thrill). • Soft second heart sound. • Slow-rising carotid pulse. • Narrow pulse pressure. • Thrusting but undisplaced apex beat.

Investigations

• Doppler echocardiography is the key investigation. It demonstrates restricted opening and any structural abnormalities, and permits calculation of the systolic pressure gradient. • The ECG: usually shows features of LV hypertrophy, often with down-sloping ST segments and T inversion ('strain pattern'), but can be normal despite severe stenosis. • CT or MRI to assess calcification. • Cardiac catheterisation: is usually necessary to assess the coronary arteries before surgery.

Management

Patients with asymptomatic aortic stenosis have a good prognosis with conservative management, but should be kept under review, as the development of angina, syncope or heart failure are indications for prompt surgery. Old age is not a contraindication to valve replacement, and results are very good, even for those in their eighties. This is especially true for transcatheter aortic valve implantation (TAVI). Balloon valvuloplasty is useful in congenital stenosis but not in calcific stenosis.

Aortic regurgitation

This condition may be caused by disease of the aortic valve cusps (e.g. rheumatic fever, infective endocarditis) or dilatation of the aortic root (e.g. ankylosing spondylitis, Marfan's syndrome, aortic dissection or aneurysm). The LV dilates and hypertrophies to compensate for the regurgitation, producing a large increase in stroke volume. As disease progresses, LV end-diastolic pressure rises, and pulmonary oedema develops.

Clinical features

In mild to moderate aortic regurgitation, patients are frequently asymptomatic, but may experience an awareness of the heartbeat because of the increased stroke volume. Exertional dyspnoea is the dominant symptom in more severe disease. The pulse is typically of large volume and collapsing in nature, the pulse pressure is wide and the apex beat is heaving and displaced laterally. The characteristic soft early diastolic murmur is usually best heard to the left of the sternum with the patient leaning forward, with the breath held in expiration. A systolic murmur because of the increased stroke volume is common. In acute severe regurgitation (e.g. perforation of aortic cusp in endocarditis) there may be no time for compensatory LV hypertrophy and dilatation to develop, and the features of heart failure may predominate.

Investigations

• Doppler echocardiography: confirms the diagnosis and may show a dilated, hyperdynamic left ventricle. • Cardiac catheterisation and aortography: can also be helpful in assessing the severity of regurgitation, aortic dilatation and the presence of coexisting coronary artery disease. • MRI is useful in assessing aortic dilatation if this is suspected on CXR or echocardiography.

Management

Underlying conditions, such as endocarditis and syphilis, should be treated. Replacement of the aortic valve (and aortic root, if dilated) is indicated in

symptomatic regurgitation. Asymptomatic patients should also be followed up annually to detect the development of symptoms or increasing ventricular size on echocardiography; if the end-systolic dimension increases to 55 mm or more, then aortic valve replacement should be undertaken. Systolic BP should be controlled with vasodilating drugs such as nifedipine or ACE inhibitors.

Tricuspid stenosis

This is uncommon, usually rheumatic in origin and almost always associated with mitral and aortic valve disease. It may cause signs and symptoms of right heart failure.

Tricuspid regurgitation

This is common and most frequently secondary to RV dilatation caused by pulmonary hypertension or MI. It may also be caused by endocarditis (especially in IV drug-users), rheumatic fever or carcinoid syndrome. Symptoms result from reduced forward flow (tiredness) and venous congestion (oedema, hepatic enlargement). The most prominent sign is a large systolic *v* wave in the JVP. Other features include a pansystolic murmur at the left sternal edge and a pulsatile liver. Tricuspid regurgitation caused by RV dilatation often improves when the cause of RV overload is corrected, for example, diuretic and vasodilator therapy in congestive cardiac failure.

Pulmonary stenosis

This can occur in the carcinoid syndrome but is usually congenital, when it may be isolated or associated with other abnormalities, such as tetralogy of Fallot (p. 305). On examination there is an ejection systolic murmur, loudest at the left upper sternum and radiating towards the left shoulder. Mild to moderate pulmonary stenosis is nonprogressive and does not require treatment. Severe pulmonary stenosis (gradient >50 mmHg) is treated by percutaneous balloon valvuloplasty or, if this is not available, surgical valvotomy.

Pulmonary regurgitation

Rarely an isolated phenomenon and usually associated with pulmonary artery dilatation caused by pulmonary hypertension of any cause.

Prosthetic valves

Diseased valves can be replaced with mechanical or biological prostheses. Common mechanical prostheses include ball and cage, tilting disc and tilting bi-leaflet valves. All generate audible clicks and require long-term anticoagulation to prevent thromboembolism. Pig or allograft valves are the commonest biological valves. They generate normal heart sounds and do not require anticoagulation.

Infective endocarditis

Infective endocarditis is caused by microbial infection of a heart valve (native or prosthetic) or the lining of a cardiac chamber or blood vessel. It

typically occurs at sites of preexisting endocardial damage, although infection with particularly virulent organisms (e.g. *Staphylococcus aureus*) can cause endocarditis in a previously normal heart. Areas of endocardial damage caused by a high-pressure jet of blood (e.g. VSD, mitral regurgitation, aortic regurgitation) are particularly vulnerable. When the infection is established, vegetations composed of organisms, fibrin and platelets grow and may break away as emboli. Adjacent tissues are destroyed, abscesses may form and valve regurgitation may develop through cusp perforation, distortion or rupture of chordae. Extracardiac manifestations, such as vasculitis and skin lesions, are caused by emboli or immune complex deposition.

Microbiology

S. aureus is the commonest cause of acute endocarditis, originating from skin infections, abscesses or vascular access sites such as intravenous lines or intravenous drug use. *Streptococcus viridans* (from the upper respiratory tract or gums) and enterococci (from the gut or urinary tract) may enter the blood stream, and are common causes of subacute endocarditis. *S. epidermidis*, a normal skin commensal, is the most common organism in endocarditis, complicating cardiac surgery. Rarer causes include the Gram-negative HACEK-group organisms (*Haemophilus* spp., *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella* spp. and *Kingella kingae*). *Coxiella burnetii* (Q fever) and *Brucella* cause occasional cases in patients exposed to farm animals. Yeasts and fungi may be responsible in immunocompromised patients.

Clinical features

Subacute endocarditis: Should be suspected when a patient with congenital or valvular heart disease develops a persistent fever, unusual tiredness, night sweats, weight loss or new signs of valve dysfunction. Other features include embolic stroke, petechial rash, splinter haemorrhages, nonvisible haematuria and splenomegaly. Osler's nodes (painful swellings at the fingertips) are rare, and finger clubbing is a late sign.

Acute endocarditis: Usually presents as a severe febrile illness with prominent and changing heart murmurs and petechiae. Clinical stigmata of chronic endocarditis are usually absent, but embolic events (e.g. cerebral) are common, and cardiac or renal failure may develop rapidly.

Postoperative endocarditis: This presents as unexplained fever in a patient who has had heart valve surgery. The pattern may resemble subacute or acute endocarditis, depending on the virulence of the organism. Morbidity and mortality are high, and revision surgery is often required.

Investigations

Diagnosis is based on the modified Duke criteria (Box 8.19). Blood culture is the key investigation to identify the causative organism and guide antibiotic therapy; 3 to 6 sets should be taken, using scrupulous aseptic technique, before commencing therapy. Echocardiography allows detection of vegetations and abscess formation, as well as assessment of valve damage. Transoesophageal echo has a higher sensitivity than transthoracic echo for detecting vegetations (90% vs. 65%), and is particularly valuable for investigating patients with prosthetic heart valves. Failure to detect vegetations does not exclude the diagnosis. A normochromic, normocytic

8.19 Diagnosis of infective endocarditis (modified Duke's criteria)

Major criteria

- Positive blood culture: typical organism from two cultures; persistent positive blood cultures taken >12 hours apart; three or more positive cultures taken over >1 hour
- Endocardial involvement: positive echocardiographic findings of vegetations; new valvular regurgitation

Minor criteria

- Predisposing valvular or cardiac abnormality
- IV drug misuse
- Pyrexia ≥38°C
- Embolic phenomenon
- Vasculitic phenomenon
- Blood cultures suggestive—organism grown but not achieving major criteria
- Suggestive echocardiographic findings

Definite endocarditis: two major, or one major and three minor, or five minor
Possible endocarditis: one major and one minor, or three minor

anaemia and elevated WCC, ESR and CRP are common. CRP is superior to ESR for monitoring progress. Nonvisible haematuria is usually present. ECG may show the development of AV block (caused by abscess formation). CXR may show evidence of cardiac failure.

Management

Any source of infection (e.g. dental abscess) should be removed immediately. Empirical antibiotic therapy is with vancomycin (1g IV twice daily) and gentamicin (1mg/kg IV twice daily) if the presentation is acute, or with amoxicillin (2 g IV six times daily) with or without gentamicin if subacute. Subsequent antibiotic treatment is guided by culture results and is usually continued for 4 weeks. Indications for surgery (debridement of infected material, valve replacement) include heart failure, abscess formation, failure of antibiotic therapy and large vegetations on left-sided heart valves (high risk of systemic emboli).

Prevention

Until recently, antibiotic prophylaxis was given routinely to people at risk of infective endocarditis undergoing interventional procedures. However, as the link between episodes of infective endocarditis and interventional procedures has not been demonstrated, antibiotic prophylaxis is no longer offered routinely.

Congenital heart disease

This usually presents in childhood, but defects such as atrial septal defect may be asymptomatic until adulthood or discovered incidentally on routine examination or CXR. Defects that were previously fatal in childhood can now be corrected or mitigated, so prolonged survival is the norm. Such patients may re-present as adults with arrhythmia or heart failure.

Persistent ductus arteriosus

During fetal life, most of the blood from the pulmonary artery passes through the ductus arteriosus into the aorta. Normally, the ductus closes soon after birth but in this anomaly it fails to do so. Because the pressure in the aorta is higher than that in the pulmonary artery, there will be a continuous left to right shunt.

Usually there is no disability in infancy, but cardiac failure may eventually ensue, dyspnoea being the first symptom. A continuous 'machinery' murmur is heard, maximal in the second left intercostal space below the clavicle. Closure of the patent ductus is usually performed by catheterisation using an implantable occlusive device in early childhood.

Coarctation of the aorta

This condition is associated with other abnormalities, including bicuspid aortic valve and cerebral 'berry' aneurysms. It is an important cause of cardiac failure in the newborn, but is often asymptomatic in older children or adults. Headaches may occur from hypertension proximal to the coarctation, and occasionally leg weakness or cramps from decreased distal circulation. The BP is raised in the upper body but normal or low in the legs, with weak, delayed femoral pulses. A systolic murmur is heard posteriorly, over the coarctation. CXR may show an altered contour of the aorta and notching of the under-surfaces of the ribs from collaterals. MRI is the investigation of choice. Surgical correction is advisable in all but the mildest cases. If this is done sufficiently early, persistent hypertension can be avoided, but patients repaired in late childhood or adult life often remain hypertensive. Recurrence of stenosis may be managed by balloon dilatation and stenting, which can also be used as the primary treatment in some cases.

Atrial septal defect

This common congenital defect results in shunting of blood from left to right atrium, and then to the RV and pulmonary arteries. As a result, there is gradual enlargement of the right side of the heart and of the pulmonary arteries.

The condition is frequently asymptomatic but may cause dyspnoea, cardiac failure or arrhythmias, for example, AF. Characteristic physical signs include wide, fixed splitting of the second heart sound and a systolic flow murmur over the pulmonary valve. Echocardiography can directly demonstrate the defect, and may show RV dilatation or hypertrophy. The CXR typically shows enlargement of the heart and the pulmonary artery, as well as pulmonary plethora. The ECG usually shows incomplete RBBB. The defect is often first detected when a CXR or ECG is carried out for incidental reasons. Atrial septal defects in which pulmonary flow is increased by 50% above systemic flow should be closed either surgically or by catheter implantation of a closure device.

Ventricular septal defect

This is the most common congenital cardiac defect; it may be isolated or part of complex congenital heart disease. Flow from the high-pressure

LV to the low-pressure RV produces a pansystolic murmur, best heard at the left sternal edge but radiating all over the precordium. VSD may present as cardiac failure in infants, as a murmur with minimal haemodynamic disturbance in older children or adults, or rarely as Eisenmenger's syndrome (see later). Doppler echocardiography helps to identify small, haemodynamically insignificant VSDs that are likely to close spontaneously. With larger defects, the CXR shows pulmonary plethora, and the ECG shows bilateral ventricular hypertrophy. Small VSDs require no treatment. Larger VSDs should be followed with serial ECG and echo. Surgical repair is indicated for those with cardiac failure or developing pulmonary hypertension.

Eisenmenger's syndrome

Persistently raised pulmonary flow (e.g. with left to right shunting) leads to increased pulmonary resistance and pulmonary hypertension. In severe pulmonary hypertension, a left to right shunt may reverse, resulting in right to left shunting and marked cyanosis (Eisenmenger's syndrome). Patients with Eisenmenger's syndrome are at particular risk from changes in afterload that exacerbate right to left shunting, for example, vasodilatation, anaesthesia, pregnancy.

Tetralogy of Fallot

This is the most common cause of cyanotic disease in childhood and comprises:

• Right ventricular outflow obstruction (usually subvalvular). • Right ventricular hypertrophy. • Ventricular septal defect. • Aorta overriding the septum.

Cyanosis is usual, but may be absent in the newborn, until RV pressure rises to above LV pressure. The subvalvular obstruction may increase suddenly after feeding or crying, causing apnoea and unconsciousness ('Fallot's spells'). In older children, Fallot's spells are uncommon, but cyanosis increases as rising RV pressure causes increasing right to left shunting across the VSD, together with stunted growth, clubbing and polycythaemia. A loud ejection systolic murmur is heard in the pulmonary area. Investigation is by echocardiography, which is diagnostic. ECG shows RV hypertrophy, and CXR a 'boot-shaped' heart. Definitive management is by surgical relief of the outflow obstruction and closure of the VSD, and the prognosis is good following childhood surgery.

Adult congenital heart disease

Many patients who would not previously have survived childhood now do so following corrective surgery. These adult survivors may develop problems; for example, those with transposition of the great arteries corrected by 'Mustard' repair, in which blood is redirected at the atrial level, leaving the RV supplying the aorta, may develop right ventricular failure in adulthood. Adults with repaired ventricular defects may develop ventricular arrhythmias as a result of postoperative scarring, and may require an implantable defibrillator. All such patients require careful follow-up through adult life in specialist clinics.

Diseases of the myocardium

Myocarditis

This is an acute inflammatory condition of the myocardium, caused by infection, autoimmune disease (e.g. lupus) or toxins (e.g. cocaine). Viral infection is the most common cause, particularly Coxsackie and influenza viruses A and B. Other causes include Lyme disease (p. 131), Chagas' disease (p. 153) and acute rheumatic fever.

Four presentations occur:

- ***Fulminant myocarditis:*** follows a viral illness, causing severe heart failure or cardiogenic shock.
- ***Acute myocarditis:*** presents more gradually with heart failure; can lead to dilated cardiomyopathy.
- ***Chronic active myocarditis:*** rare, with chronic myocardial inflammation.
- ***Chronic persistent myocarditis:*** can cause chest pain and arrhythmia, sometimes without ventricular dysfunction.

Echocardiography may reveal LV dysfunction, which is sometimes regional (focal myocarditis). MRI may show diagnostic patterns of inflammation. Troponins and CK are elevated in proportion to the extent of damage.

In most patients, treatment is supportive and the prognosis is good; however, death may occur because of ventricular arrhythmia or rapidly progressive heart failure. Some forms of myocarditis (e.g. Chagas' disease) may lead to chronic low-grade myocarditis or dilated cardiomyopathy. Treatment for cardiac failure or arrhythmias may be required, and intense physical exertion should be avoided. Transplantation is occasionally required.

Dilated cardiomyopathy

This condition is characterised by dilatation and impaired contraction of the LV and often the RV. The causes include:

• Alcohol. • Inherited mutations of cytoskeletal proteins. • X-linked muscular dystrophies. • Autoimmune reactions to viral myocarditis.

Most patients present with heart failure. Arrhythmia, thromboembolism and sudden death may occur at any stage, and chest pain also occurs. The differential diagnosis includes CAD, and dilated cardiomyopathy should only be diagnosed when this has been excluded.

Echocardiography and MRI are useful investigations. Treatment is aimed at controlling heart failure and preventing arrhythmias. The prognosis is variable, and cardiac transplantation may be required.

Hypertrophic cardiomyopathy

This is the most common form of cardiomyopathy, and is characterised by elaborate LV hypertrophy with malalignment of the myocardial fibres. The hypertrophy may be generalised or confined largely to the interventricular septum. Heart failure develops because the stiff, noncompliant ventricles impede diastolic filling. Septal hypertrophy may also cause dynamic LV

outflow tract obstruction (hypertrophic obstructive cardiomyopathy). The condition is a genetic disorder with autosomal dominant transmission, a high degree of penetrance and variable expression.

Effort-related symptoms (angina and breathlessness), arrhythmia and sudden death (mainly from ventricular arrhythmias) are the dominant clinical problems. Signs are similar to those of aortic stenosis, except that in hypertrophic cardiomyopathy the character of the arterial pulse is jerky. Echocardiography is usually diagnostic. The ECG is abnormal and may show LV hypertrophy or deep T-wave inversion.

β-Blockers, rate-limiting calcium antagonists and disopyramide can relieve symptoms and prevent syncopal attacks. Arrhythmias often respond to amiodarone, but no drug is definitely known to improve prognosis. Outflow tract obstruction can be improved by partial surgical resection or by iatrogenic infarction of the basal septum using a catheter-delivered alcohol solution. An ICD should be considered in patients with risk factors for sudden death, including previous syncope or ventricular arrhythmias or severe hypertrophy.

Restrictive cardiomyopathy

In this rare condition, ventricular filling is impaired because the ventricles are 'stiff'. This leads to high atrial pressures with atrial hypertrophy, dilatation and later AF. Amyloidosis is the most common cause in the UK.

Diagnosis can be difficult, and requires Doppler echocardiography, CT or MRI, and endomyocardial biopsy. Treatment is symptomatic, but the prognosis is poor and transplantation may be indicated.

Other diseases affecting the myocardium are listed in Box 8.20.

8.20 Specific diseases of heart muscle

Infections

- Viral, e.g. Coxsackie A and B, influenza, HIV
- Bacterial, e.g. diphtheria, *Borrelia burgdorferi*
- Protozoal, e.g. trypanosomiasis

Endocrine and metabolic disorders

- e.g. diabetes, hypo- and hyperthyroidism, acromegaly, carcinoid syndrome, phaeochromocytoma, inherited storage diseases

Connective tissue diseases

- e.g. systemic sclerosis, systemic lupus erythematosus, polyarteritis nodosa

Infiltrative disorders

- e.g. haemochromatosis, haemosiderosis, sarcoidosis, amyloidosis

Toxins

- e.g. doxorubicin, alcohol, cocaine, irradiation

Neuromuscular disorders

- e.g. dystrophia myotonica, Friedreich's ataxia, X-linked muscular dystrophies

Cardiac tumours

Primary cardiac tumours are rare, but metastases can affect the heart and mediastinum. Most primary tumours are benign (75%), and of these, the majority are left atrial polypoid myxomas. Treatment is by surgical excision.

Diseases of the pericardium

Acute pericarditis

This may be attributed to infection (viral, bacterial, TB), immunological reaction (e.g. post-MI, connective tissue disorder), trauma, uraemia or neoplasm. Pericarditis and myocarditis often coexist, and all forms of pericarditis may produce a pericardial effusion (see later).

Clinical features

The characteristic pain of pericarditis is retrosternal, radiates to the shoulders and neck and is aggravated by deep breathing and movement. A low-grade fever is common. A pericardial friction rub is heard; this is a high-pitched, superficial scratching or crunching noise produced by movement of the inflamed pericardium, and is diagnostic of pericarditis.

Investigations

The ECG shows widespread ST elevation with upward concavity over the affected area. PR interval depression is a very sensitive indicator of acute pericarditis.

Management

The pain is usually relieved by aspirin, but a more potent antiinflammatory agent, such as indometacin, may be required. Glucocorticoids may suppress symptoms, but there is no evidence that they accelerate cure. Viral pericarditis usually resolves in a few days or weeks.

Pericardial effusion

This refers to accumulation of fluid within the pericardial sac and often accompanies pericarditis. Cardiac tamponade describes acute heart failure caused by compression of the heart by a large or rapidly developing effusion.

Typical physical findings include hypotension, a markedly raised JVP that rises paradoxically with inspiration, pulsus paradoxus (exaggerated fall in BP during inspiration) and muffled heart sounds. Echocardiography confirms the diagnosis and helps identify the optimum site for aspiration of fluid. The QRS voltages on the ECG are often reduced in the presence of a large effusion. CXR may show an increase in the size of the cardiac shadow, which may have a globular appearance if the effusion is large. The patient usually responds promptly to percutaneous pericardiocentesis or surgical drainage; the latter is safer in cardiac rupture and aortic dissection. Tuberculous pericarditis causes effusion, is diagnosed on periocardiocentesis and responds to antituberculous therapy and glucocorticoids.

Chronic constrictive pericarditis

Constrictive pericarditis is caused by progressive thickening, fibrosis and calcification of the pericardium. In effect, the heart is encased in a solid shell and cannot fill properly. It often follows tuberculous pericarditis, but can also complicate haemopericardium, viral pericarditis, rheumatoid arthritis and purulent pericarditis.

The symptoms and signs of systemic venous congestion are the hallmarks of constrictive pericarditis. AF is common, and there is often dramatic ascites and hepatomegaly. Breathlessness is not prominent because the lungs are seldom congested. The condition should be suspected in any patient with unexplained right heart failure and a small heart. A CXR showing pericardial calcification and echocardiography often help to establish the diagnosis, although it may be difficult to distinguish from restrictive cardiomyopathy.

Management

Surgical resection of the diseased pericardium can lead to a dramatic improvement, but carries a high morbidity and produces disappointing results in up to 50% of patients.