76 Chronic heart failure

In the year 1775 my opinion was asked concerning a family recipe for the cure of the dropsy. I was told that it had long been kept a secret by an old woman in Shropshire who had sometimes made cures after the more regular practitioners had failed—this medicine was composed of twenty or more different herbs and the active herb could be no other than the Foxglove.

WILLIAM WITHERING (1741–1799), *ON THE USE OF FOXGLOVE (DIGITALIS) IN THE TREATMENT OF HEART DISEASE*

Heart failure occurs when the heart is unable to maintain sufficient cardiac output to meet the demands of the body for blood supply during rest and activity.

Chronic heart failure (CHF) remains a very serious problem with a poor prognosis. It has a 50% mortality within 3 years of the first hospital admission.[1] Australian and overseas data indicate that 1.5% of the adult population have heart failure. The prevalence of CHF has been shown to increase from approximately 1% in those aged 50–59 years to over 5% in those 65 and older, to over 50% in those 85 years and older.[2] Australian research suggests that undertreatment with the all-important ACE inhibitors continues to be a problem. ACE inhibitors (or ARBs) and beta blockers are the gold standard for treating systolic heart failure, with aldosterone antagonists providing added benefit if symptoms persist.[3] The clinical diagnosis is based on a careful history and examination. A major goal of management of CHF is the identification and reversal where possible of underlying causes and/or precipitating factors. CHF is characterised by two pathophysiological factors: fluid retention and reduction in cardiac output.

Diagnosis

The clinical diagnosis is based on a careful history and examination. The classic symptom of CHF is dyspnoea on exertion but symptoms may be reported relatively late, particularly with a sedentary lifestyle. Dyspnoea can progress as follows: exertional dyspnoea → dyspnoea at rest → orthopnoea → paroxysmal nocturnal dyspnoea.

Symptoms in summary

Fluid accumulation:

- Dyspnoea and orthopnoea (as above)
- Dry irritating cough (especially at night)
- Lethargy/fatigue
- Weight change: gain (mainly) or loss
- Ankle oedema
- Abdominal discomfort: hepatic congestion

Poor cardiac output:

- Dizzy spells/syncope
- Weakness
- Fatigue

Note: The irritating cough due to left ventricular failure can be mistaken for asthma, bronchitis or ACE-inhibitor-induced cough. Poor cardiac output causes fatigue and weakness.

Examination

The physical examination is very important for the initial diagnosis and evaluation of progress. The signs are as follows.

Signs

There may be no abnormal signs initially. It is helpful clinically to differentiate between the signs of right and left heart failure:

Left heart failure

- Tachycardia
- Low volume pulse (pulse pressure <25 mmHg)
- Tachypnoea
- Laterally displaced apex beat
- Bilateral basal crackles
- Gallop rhythm (3rd heart sound)

- Pleural effusion
- Poor peripheral perfusion—cool, pale extremities

Right heart failure

- Elevated jugular venous pressure
- Right ventricular heave
- Peripheral/ankle oedema
- Hepatomegaly
- Ascites

Auscultation is important to identify adventitious sounds, a third heart sound and possible underlying valvular disease.

Systolic versus diastolic heart failure

The classic heart failure is systolic failure due to an inadequate pumping action of the heart. The ventricle is dilated and contracting poorly (left ventricular ejection fraction <40%).[4]

Diastolic heart failure is due to impairment of left ventricular filling with preserved systolic function. A substantial proportion of heart failure presentations are due to diastolic heart failure (impaired ventricular relaxation).[2] It should be suspected in the elderly with hypertension and a normal heart size on chest X-ray who present with dyspnoea or pulmonary oedema.[3] It is particularly common in elderly females.

Note: Patients can have simultaneous systolic and diastolic failure.

The oedema of heart failure

Peripheral oedema appears initially on the lower legs as ‘pitting’. To assess pitting, which is usually graded on a four-point scale, press firmly yet gently with the thumb for 5–10 seconds over the dorsum of the feet, behind each medial malleolus and over the shins. With increasing severity of failure the oedema extends proximally to involve the abdomen. In the recumbent position it may be apparent over the sacrum.[5]

Determining severity of heart failure

The severity of heart failure can be considered from three different perspectives: the severity of the symptoms, the degree of impairment of cardiac function and the severity of the congestive state. The severity of the symptoms or the degree of functional disability is usually described according to the New York Heart Association criteria (see TABLE 76.1).[6] The left ventricular

ejection fraction provides an indication of cardiac function.

Table 76.1 New York Heart Association (NYHA) functional classification of CHF symptoms[2,6]

Class	Disability	Approximate 1-year mortalities
I (asymptomatic)	No limitation: cardiac disease present, but ordinary physical activity causes no symptoms such as fatigue, dyspnoea or palpitation, or rapid forceful breathing	5%
II (mild)	Slight limitation: ordinary activity (moderate exertion) causes symptoms but patients comfortable at rest	10%
III (moderate)	Marked limitation: symptoms with less than ordinary physical activity (mild exertion) although patients still comfortable at rest	20%
IV (severe)	Unable to carry out any physical activity without symptoms; may have symptoms at rest	50%

Causes of heart failure

Causes of CHF can be classified under systolic heart failure (impaired ventricular contraction) and diastolic heart failure (impaired ventricular relaxation and filling despite normal contractions). Diagnosis is based on echocardiography.

Ejection fraction—reduced or preserved

With the increased uptake of echocardiography testing, an increasing proportion of adults (particularly older, with diabetes or atrial fibrillation) with heart failure symptoms and signs are found to have normal or near normal (>50%) ventricular ejection fraction. This is called heart failure with preserved ejection fraction (HFpEF), which can result from numerous pathologies, including poorly controlled hypertension, myocardial ischaemia and infiltrative cardiomyopathies.[7] Echocardiography may show a stiff, hypertrophied left ventricle and/or diastolic dysfunction. Serum B-type natriuretic peptide (BNP) is often raised.

HFpEF has similar mortality to heart failure with reduced ejection fraction (HFrEF). A 2018

Cochrane review[8] found that medications including ACE inhibitors, ARBs and beta blockers did not have a significant impact on mortality or other clinical outcomes. Management focuses on optimising treatment of comorbidities, especially hypertension, diabetes, atrial fibrillation and symptomatic fluid overload.

Systolic heart failure

Ischaemic heart disease, including previous myocardial infarction, is the most common cause, accounting for approximately two-thirds. There is often a history of at least one myocardial infarction.[2] Essential hypertension is the other common cause.

Other causes:

- valvular heart disease, mainly aortic and mitral incompetence
- high output states (e.g. anaemia, hyperthyroidism, Paget disease)
- non-ischaemic idiopathic dilated cardiomyopathy
- viral cardiomyopathy
- alcoholic cardiomyopathy
- other cardiomyopathies—diabetic, familial
- persistent arrhythmias, especially atrial fibrillation
- other systemic illness (e.g. sarcoidosis, SLE, scleroderma, myxoedema)
- chemotherapy
- peripartum

Diastolic heart failure

- Obesity, hypertension and diabetes significant risk factors
- Familial: more common in women and the elderly
- Common causes include ischaemic heart disease, systemic hypertension, aortic stenosis, atrial fibrillation (inadequate filling), hypertrophic cardiomyopathy, pericardial disease
- Significant morbidity and difficult to diagnose

Investigations

The following should be considered:

- Echocardiography[2]—the transthoracic echocardiogram is the investigation of choice to measure ventricular function. It can differentiate between systolic dysfunction and those with normal systolic function but abnormal diastolic filling. It gives information about left and right ventricular systolic and diastolic function, left and right ventricular size, volumes, thickness, structure and function. It also provides information about cardiac valves, congenital heart defects and pericardial disease.
- Electrocardiogram—a key investigation to look for evidence of ischaemia, conduction abnormalities, arrhythmias and LV hypertrophy
- Chest X-ray to look for:

  cardiomegaly and interstitial oedema

  upper lobe blood diversion

  fluid in fissures

  oedema in perihilar area with prominent vascular markings

  small basal pleural effusions

  Kerley B lines = raised pulmonary venous pressure

  frank pulmonary oedema

  Note: A normal CXR does not exclude CHF.
- Spirometry/respiratory function testing—to detect associated airways dysfunction
- B-type natriuretic peptide—a hormone secreted from the ventricular myocardium is an indicator of severity of CHF and prognosis

Peripheral markers

- FBE and ESR: anaemia can occur with CHF; severe anaemia may cause CHF
- Serum electrolytes: usually normal in CHF, important to monitor management
- Kidney function tests: for monitoring drug therapy
- Liver function tests: congestive hepatomegaly gives abnormal LFTs
- Urinalysis
- Thyroid function tests, especially if atrial fibrillation
- Viral studies: for suspected viral myocarditis

Specialised cardiac investigation (specialist directive)

- Coronary angiography—for suspected and known ischaemia. CT angiography and cardiovascular MRI preferred
- Haemodynamic testing
- Endomyocardial biopsy
- Nuclear cardiology

Treatment of heart failure

The treatment of heart failure includes determination and treatment of the cause, removal of any precipitating factors, appropriate patient education, general non-pharmaceutical measures and drug treatment. Studies have shown the benefit of an integrated, multidisciplinary approach to management.

Prevention of heart failure

The emphasis on prevention is very important since the onset of heart failure is generally associated with a poor prognosis. Approximately 50% of patients with heart failure die within 5 years of diagnosis.[9]

The scope for prevention includes the following measures:[10]

- dietary advice (e.g. achievement of ideal weight, optimal nutrition)
- emphasising the dangers of smoking and excessive alcohol
- control of hypertension

- control of other risk factors (e.g. hyperlipidaemia)
- early detection and control of diabetes
- early intervention during myocardial infarction to preserve myocardial function (e.g. thrombolytic therapy)
- secondary prevention after the occurrence of myocardial infarction (e.g. beta blockers, ACE inhibitors and aspirin)
- appropriate timing of surgery or angioplasty for ischaemic or valvular heart disease

Treatment of causes and precipitating factors

Any underlying cause should be identified and treated, if possible. Precipitating factors that should be treated include:

- arrhythmias (e.g. atrial fibrillation)
- electrolyte imbalance, especially hypokalaemia
- anaemia
- myocardial ischaemia, especially myocardial infarction
- dietary factors (e.g. malnutrition, excessive salt or alcohol intake)
- adverse drug reactions (e.g. fluid retention with NSAIDs and COX-2 agents) (see TABLE 76.2)[11]
- infection (e.g. bronchopneumonia, endocarditis)
- hyper- and hypothyroidism
- lack of adherence to therapy
- fluid overload

Table 76.2 Drugs that can aggravate CHF

NSAIDs including COX-2 inhibitors
Corticosteroids
Tricyclic antidepressants
Calcium-channel blockers (verapamil and diltiazem)
Selected antiarrhythmics (e.g. quinidine)
Macrolide antibiotic
Macrogol
Type 1 antihistamines
Clozapine
H_2-receptor antagonists
Thiazolidinediones (glitazones)
TNF-alpha inhibitors (e.g. etanercept, infliximab)
Ethanol or illicit drug (e.g. cocaine) use

Note: Be mindful of complementary medications.

General non-pharmacological management

- Education and support
- Smoking: encourage no smoking
- Refer for a rehabilitation program with interdisciplinary care
- Encourage physical activity especially when symptoms absent or mild
- Rest while symptoms are severe
- Weight reduction, if patient obese
- Advice on food supplementation—dietitian
- Salt restriction: advise no-added-salt diet (<2 g or 60–100 mmol/day)
- Water restriction: water intake should be limited to 1.5–2 L/day or less in patients with advanced heart failure, especially when the serum sodium level falls below 130 mmol/L[9]
- Limit caffeine to 1–2 cups coffee/tea a day
- Limit alcohol to 1 standard drink a day
- Fluid aspiration—if pleural or pericardial effusion present
- Daily weighing—check significant weight gain or loss
- Comprehensive information can be found at Heart Online (see: https://www.heartonline.org.au/)

Other general measures[1]

- Optimise cardiovascular risk factors (e.g. BP, lipids, HbA1c)
- Monitor emotional factors including depression
- Regular review
- Vaccination: annual influenza, 5-yearly pneumococcus
- 2-yearly echocardiography (or more) as indicated
- Pleurocentesis or pericardiocentesis (if applicable)

- Treat coexisting obstructive sleep apnoea

Drug therapy of heart failure due to left ventricular systolic dysfunction

Any identified underlying factor should be treated.

Evidence from RCTs shows the beneficial results from ACE inhibitors[2,11] (or angiotensin II receptor blockers), digoxin (improves outcome in people already receiving diuretics and ACE inhibitors), beta blockers and spironolactone (in severe heart failure).

Atrial fibrillation should be treated with digoxin. Vasodilators are widely used for heart failure and angiotensin converting enzyme inhibitors (ACEI) are currently the most favoured vasodilator.

Note: Monitor and maintain normal potassium level in all patients.

ACE inhibitors improve prognosis in all grades of heart failure and should be employed as the initial therapy in all patients, except where contraindicated (e.g. kidney artery stenosis, angioedema).

Diuretics have an important place in fluid overload. As a rule they should be added to an ACEI to achieve euvolaemia. Diuretics should be used in moderation and excessive doses of a single drug avoided. In patients with systolic LV dysfunction they should not be used as monotherapy.[10] Close monitoring of weight, kidney function and electrolytes is required. Loop diuretics such as frusemide, bumetanide or ethacrynic acid are commonly used, especially for heart failure of moderate severity.[10] Thiazide and related diuretics produce a gradual diuresis and are recommended for mild heart failure. Examples include hydrochlorothiazide, bendrofluazide, chlorthalidone or indapamide.

Initial therapy of heart failure[9,12]

1. ACE inhibitor (start low, aim high)
   Dosage of ACE inhibitor: commence with ¼ to ½ lowest recommended therapeutic dose and then adjust it for the individual patient by gradually increasing it to the maintenance or maximum dose (see TABLE 76.3). Once-daily agents are preferred. Use an ARB if cough is problematic.

Table 76.3 Some ACE inhibitors in common usage[6]

ACE inhibitor	Initial daily oral dose	Usual maintenance dose
Captopril	6.25 mg	25 mg tds
Enalapril	2.5 mg	10 mg bd

Fosinopril	5 mg	20 mg daily
Lisinopril	2.5 mg	5–20 mg daily
Perindopril	2 mg*	4 mg* daily
Quinapril	2.5 mg	20 mg daily
Ramipril	1.25 mg	5 mg daily
Trandolapril	0.5 mg	2–4 mg daily

*2 mg perindopril erbumine = 2.5 mg perindopril arginine

ACE inhibitors

- ACE inhibitors are regarded as the agents of first choice because they correct neuroendocrine abnormalities and reduce cardiac load by their vasodilator action.
- Every effort should be made to up-titrate to the highest tolerated dose.
- Consider giving the first dose at bedtime if there is a risk of orthostatic hypotension.
- If the ACEI is not tolerated (e.g. due to cough) consider an angiotensin II receptor blocker (ARB) as they have proven benefit in CHF.[13]
- In practice the usual initial treatment of heart failure is an ACE inhibitor plus diuretic. This combination optimises response and improves diuretic safety.
- Consider stopping any diuretic for 24 hours before starting treatment with an ACEI.
- Potassium-sparing diuretics or supplements should not be given with ACEI (or should at least be used with caution) because of the danger of hyperkalaemia.
- Kidney function and potassium levels should be monitored in all patients.

2. Add a diuretic (if congestion):

   loop diuretic (preferred)

   frusemide 20–40 mg (o) once or twice daily

   or

   ethacrynic acid 50 mg (o) daily

   or

   (thiazide-type diuretic)

hydrochlorothiazide 25–50 mg (o) daily (or other thiazide)

or

indapamide 1.5–2.5 mg (o) daily

3. Add an aldosterone antagonist diuretic (if fluid overload not controlled):

spironolactone 12.5–50 mg (o) daily

or

eplerenone 25–50 mg (o) daily

Some authorities are concerned about the over-reliance on diuretics and also about compliance as well as side effects. Once the diuretic effect has been achieved, diuretics may be withdrawn and fluid restriction advised. The ACEI is then used alone or with a beta blocker.

Beta blockers

Selective beta blockers have been shown to prolong survival of patients with mild to moderate CHF taking ACE inhibitors who are stabilised. Start with extremely low doses (see TABLE 76.4). Commence when patient stable and euvolaemic.

Table 76.4 Beta blockers approved to treat heart failure

Beta blocker	Initial daily dose	Target dose
Bisoprolol	1.25 mg (o) daily	10 mg (o) daily
Carvedilol	3.125 mg (o) bd	25 mg (o) daily
Metoprolol extended release	23.75 mg (o) daily	190 mg (o) daily
Nebivolol	1.25 mg (o)	10 mg (o) daily

Digoxin

Digoxin was the mainstay of treatment of heart failure for decades prior to the use of ACE inhibitors. It was an effective agent but limited. The two indications for its current use are in patients with atrial fibrillation to control rapid ventricular rate and in patients with sinus rhythm not adequately controlled by the other agents above it in FIGURE 76.1 . Most patients are started on a low dose digoxin:

62.5–250 mcg (o) daily

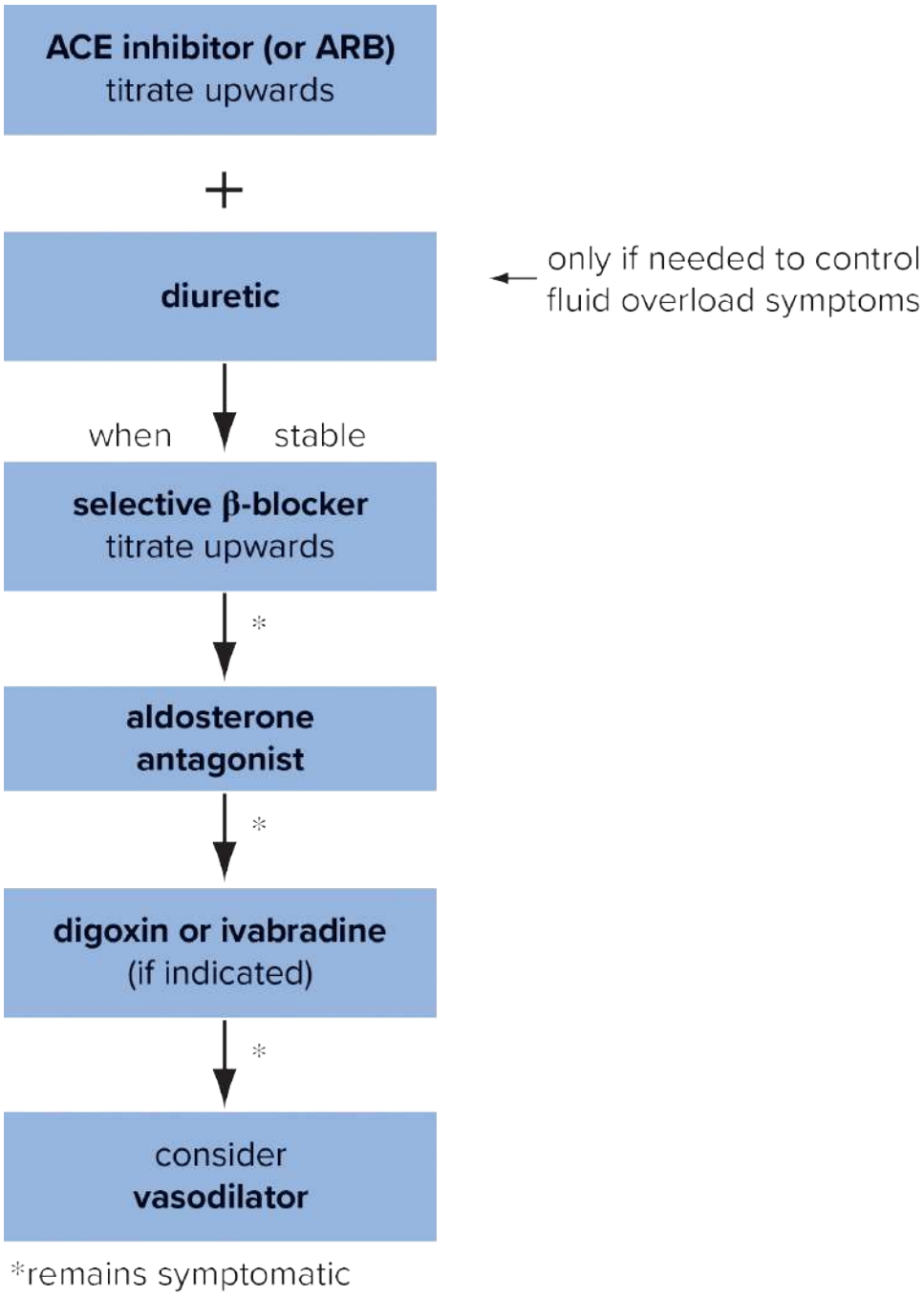

FIGURE 76.1 A stepwise pharmacological management approach to systolic heart failure[12,14]

New agents[9]

Ivabradine is a direct sinus node inhibitor which can be added to a beta blocker in patients with continuing symptoms of moderate to severe failure, or where beta blockers are contraindicated or

not tolerated. Other new agents to consider for optimal treatment include sacubitril/valsartan (Entresto)—an angiotension/neprilysin inhibitor.

Heart failure (unresponsive to first-line therapy)—stepwise strategy[2,9]

ACE inhibitor

plus

frusemide 40–80 mg (o) bd

plus

spironolactone 12.5 (starting)—25 mg (o) daily (monitor potassium and RFTs), if still congestion

plus

a selective beta blocker (if patient euvolaemic)

plus

digoxin (if not already taking it):[9] loading dose:

0.5–0.75 mg (o) statim (depending on kidney function)

then 0.5 mg (o) 4 hours later

then 0.5 mg the following day

then individualise maintenance

Severe heart failure[9,12]

Seek specialist advice.

Hospital with bed rest.

ACE inhibitor to maximum tolerated dose

plus

frusemide to max. 500 mg/day

plus

spironolactone (low dose) 25 mg/day

If poorly controlled, consider adding:

- thiazide diuretic
- spironolactone—doses up to 100–200 mg daily
- a beta blocker
- digoxin
- heparin (if confined to bed)

Vasodilators

If still uncontrolled, consider vasodilators other than ACEIs or ARBs:

isosorbide dinitrate 20–40 mg (o) 6 hourly

plus

hydralazine 50–100 mg (o) 6 hourly

A glyceryl nitrate patch can be used for the relief of symptoms, especially nocturnal dyspnoea.

Consider cardiac transplantation for appropriate patients with end-stage heart failure (e.g. patients under 50 with no other major disease). Other surgical options include heart valvular surgery, coronary artery bypass surgery and surgical ventricular restoration (surgical reduction of an enlarged left ventricle).

A flow chart for the basic management of heart failure is presented in FIGURE 76.1 .

Diastolic heart failure[2,10]

Management is based on treating the cause such as hypertension, ischaemia and diabetes. The basic treatment is with inotropic agents such as calcium-channel blockers (verapamil or diltiazem) and beta blockers. If possible avoid diuretics (except for congestion), digoxin, nitrates/vasodilators and nifedipine. Excessive diuresis from overzealous diuretic therapy can cause severe consequences for cardiac output. ACE inhibitors can be used with caution.

Pitfalls in management

- The most common treatment error—excessive use of diuretics[3]
- Giving an excessive loading dose of ACE inhibitor
- Failure to correct remedial causes or precipitating factors
- Failure to measure left ventricular function

- Failure to monitor electrolytes and kidney function

ACE inhibitors, beta blockers and spironolactone have been shown to improve survival in heart failure with reduced ejection fraction (HFrEF).[11]

Acute severe heart failure

For the treatment of acute pulmonary oedema refer to CHAPTER 120 .

Device-based heart failure treatments[1]

The use of mechanical devices to treat patients with severe failure is gaining momentum. Devices include:

- implantable cardiac defibrillators
- biventricular pacemakers
- left ventricular assist devices (definitive VentrAssist)

The evidence for the efficacy of these devices is good, but limitations include cost and infection. Biventricular pacing or cardiac resynchronisation therapy resynchronises cardiac contraction in patients with systolic CHF and left branch bundle block. VentrAssist is based on a continuous flow rotary blood pump that is surgically implanted in the abdominal wall and attached to the apex of the ventricle.

When to refer

- Age <65 years
- Uncertainty of diagnosis, especially diastolic heart failure
- Complex management issues (especially with beta blockers, digoxin)
- Familial screening (where appropriate)
- Acute decompensation
- Refractory symptoms
- Device implantation or cardiac transplantation

Practice tips

- Echocardiography is the gold standard for diagnosing CHF.
- Early diagnosis and then optimal therapy is the key to prevent or slow progression.
- Use a multidisciplinary team approach for the patient with CHF and refer early and readily for specialist advice.
- ACE inhibitors, if tolerated, are recommended for all patients with heart failure, whether symptoms are mild, moderate or severe.[1]
- The primary reason for prescribing an ACE inhibitor is to reduce the risk of death or hospitalisation.
- Diuretics are very effective in the presence of fluid overload, but should be used in combination with an ACE inhibitor—not as monotherapy.
- Drug treatment should include an ACE inhibitor and selective beta blocker wherever possible.[1]
- Beware of hyperkalaemia with the combination of an ACEI or ARB with an aldosterone antagonist.
- Device-based heart failure therapy is an expanding field and includes three major groups of devices: biventricular pacemakers (cardiac resynchronisation therapy), implantable cardiac defibrillators and left ventricular assist devices.[1]

Patient education resource

Hand-out sheet from *Murtagh's Patient Education* 8th edition:

- Heart failure

Resource

Heart Online: https://www.heartonline.org.au/.

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77 Hypertension

The greatest danger to a man is that someone will discover hypertension and some fool will try to reduce it.

JOHN HAY 1931

Hypertension is a serious community disorder and the most common condition requiring long-term drug therapy in Australia. It is a silent killer because most people with hypertension are asymptomatic and unaware of their problem. Epidemiological studies have demonstrated the association between hypertension and stroke, coronary heart disease, kidney disease, heart failure and atrial fibrillation. Treatment may be lifelong, hence the need for careful work-up.

- Target organs that can be damaged by hypertension include the heart (failure, LVH, ischaemic disease), kidney (kidney insufficiency), retina (retinopathy), blood vessels (peripheral vascular disease, aortic dissection) and brain (cerebrovascular disease).
- Almost 6% of the Australian disease burden is due to hypertension.[1]
- Factors increasing the chances of dying in hypertensive patients are: male, onset at a young age, family history, increased diastolic pressure.[2]

Definitions and classification

- The various categories of BP are arbitrarily defined (and change over time in different guidelines) according to BP values for both diastolic and systolic readings (see TABLE 77.1).[3,4]

Table 77.1 Definition and classification of blood pressure in adults aged 18 years and older measured as sitting blood pressure (mmHg)[4,5]

Category	Systolic	Diastolic

Optimal	<120	<80
Normal	120–129	80–84
High normal	130–139	85–89
Grade 1 hypertension (mild)	140–159	90–99
Grade 2 hypertension (moderate)	160–179	100–109
Grade 3 hypertension (severe)	≥180	≥110
Isolated systolic hypertension	≥140	<90

Note: When a patient's systolic and diastolic BPs fall into different categories, the higher category should apply.

For adults aged 18 years and older, hypertension is repeated measurements of:

- diastolic pressure >90 mmHg, and/or
- systolic pressure >140 mmHg

- Isolated systolic hypertension is that of ≥140 mmHg in the presence of a diastolic pressure <90 mmHg.
- Hypertension is either essential or secondary (see TABLE 77.2).

Table 77.2 Causes of hypertension

Essential (90–95%)
Secondary (approx. 5–10%)
Kidney <3%
- glomerulonephritis
- reflux nephropathy
- kidney artery stenosis (see later in this chapter)
- other renovascular disease

Endocrine: 0.3–1%
- primary aldosteronism (Conn syndrome) (see CHAPTER 14)
- Cushing syndrome (see CHAPTER 14)
- phaeochromocytoma (see CHAPTER 14)
- oral contraceptives

- other endocrine factors

Coarctation of the aorta

Immune disorder (e.g. polyarteritis nodosa)

Drugs (e.g. NSAIDs, corticosteroids)

Pregnancy

- Essential hypertension is the presence of sustained hypertension in the absence of underlying, potentially correctable kidney, adrenal or other factors.
- Malignant hypertension is that with a diastolic pressure >120 mmHg and exudative vasculopathy in the retinal and kidney circulations.
- Refractory hypertension is a BP >140/90 mmHg despite maximum dosage of 2 drugs for 3–4 months.

Risk stratification and calculation of cardiovascular risk[3,4]

Treatment of hypertension is generally indefinite, with the uncommon exception of marked lifestyle change rendering treatment unnecessary, or the more common late-life deprescribing when age and frailty render the risks of treatment greater than the benefits.

It is important to establish the risk status and the prognosis prior to commencing therapy, especially if hypertension is an isolated factor. The World Health Organization–International Society of Hypertension (WHO–ISH) recommendation is that decisions about management of patients with hypertension should not be based on BP alone but also on the presence or absence of other risk factors, including age, diabetes and smoking. This is because the benefits of treatment are less in those with low cardiovascular risk. CV risk should be stratified according to the BP level and the presence of:

- absolute cardiovascular risk factors
- associated clinical conditions
- target organ damage (see TABLE 77.3)

Table 77.3 Factors influencing prognosis in hypertension[3]

Risk factors for cardiovascular disease used for stratification	Associated clinical condition	Target organ damage

Levels of systolic and diastolic BP Male >55 years Female >65 years Smoking Diabetes mellitus Dyslipidaemia (total cholesterol >6.5 mmol/L, or LDL-cholesterol >4.0 mmol/L, or HDL-cholesterol M <1.0, F <1.2 mmol/L) Family history of premature cardiovascular disease (at age <55 years M, <65 years F) Abdominal obesity (abdominal circumference M ≥102 cm, F ≥88 cm)	Cerebrovascular disease: • ischaemic stroke • cerebral haemorrhage • transient ischaemic attack Heart disease: • myocardial infarction • angina • coronary revascularisation • congestive heart failure Kidney disease: • diabetic nephropathy • kidney impairment • proteinuria (>300 mg/24 h) Peripheral vascular disease Advanced retinopathy: • haemorrhages or exudates • papilloedema	Left ventricular hypertrophy Microalbuminuria and/or proteinuria and/or eGFR <60 mL/minute Ultrasound or angiographic evidence of atherosclerotic disease Hypertensive retinopathy (grade II or more)
Other factors affecting prognosis		
Excessive alcohol intake Specific complementary medicines, e.g. containing tyramine Sedentary lifestyle High-risk socioeconomic group High-risk ethnic group		

A practical approach to stratifying total cardiovascular risk is proposed in TABLE 77.4 . The terms ‘low’, ‘moderate’ (medium), ‘high’ and ‘very high’ added risk are calibrated to indicate an absolute 5-year risk of cardiovascular disease of <10%, 10–15%, 15–20% and >20% respectively

(based on Framingham criteria).[5] For example, ‘low risk’ indicates consideration of treatment and monitoring; ‘high risk’ indicates treating immediately.

Table 77.4 Stratification of cardiovascular risk to quantify prognosis[4]

Other risk factors and disease history	Normal BP	High normal BP	Mild hypertension	Moderate hypertension
No other risk factors	Low risk	Low risk	Average risk	Moderate risk
1 or 2 risk factors but not diabetes	Low risk	Low risk	Moderate risk	Moderate risk
3 or more risk factors or target organ damage or diabetes	Moderate risk	High risk	High risk	High risk
Associated clinical conditions	High risk	Very high risk	Very high risk	Very high risk

Risk estimation can be determined by referring to various cardiovascular risk tables on the website (and in CHAPTER 75). A commonly used tool in Australasia is the modified New Zealand Cardiovascular Risk Charts (see: www.heartfoundation.com.au). See CHAPTERS 11 and 75 .

It is important to collaborate with patients in decision making, and thus discussing cardiovascular risk assessment and blood pressure (BP) level should be the starting point when discussing the risks and benefits of treatment.

Secondary hypertension

Secondary hypertension may be suggested by onset below 40 years, or by the history (see TABLE 77.5), physical examination, severity of hypertension or the initial laboratory findings. It is also more likely where BP is responding poorly to drug therapy, and in accelerated or

malignant hypertension.[4]

Table 77.5 Clinical features suggesting secondary hypertension[6]

Clinical features	Likely cause
Abdominal systolic bruit	Renal artery stenosis
Proteinuria, haematuria, casts	Glomerulonephritis
Bilateral kidney masses with or without haematuria	Polycystic disease
History of claudication and delayed femoral pulse	Coarctation of the aorta
Progressive nocturia, weakness	Primary aldosteronism (check serum potassium)
Obesity, snoring, daytime sleepiness	Sleep apnoea
Recreational drugs, complementary or prescribed therapies	Stimulants, diet pills, OCP, energy drinks
Paroxysmal hypertension with headache, pallor, sweating, palpitations	Phaeochromocytoma

The most common causes of secondary hypertension are various kidney diseases, such as renovascular disease, chronic glomerulonephritis and chronic pyelonephritis (often associated with reflux nephropathy).[7] There will often be no physical findings to suggest the existence of such kidney diseases, but an indication will generally be obtained by the presence of one or more abnormalities when the urine is examined. Clinical pointers include proteinuria, an abnormal urine sediment, general atheroma, abdominal bruit and being a smoker. Consider sleep apnoea, and take a comprehensive medication history, including illicit drugs and alternative remedies.

Physical findings that may suggest secondary hypertension include epigastric bruits (possible kidney artery stenosis) and abdominal aortic aneurysm. Less common findings include abdominal flank masses (polycystic kidneys), delayed or absent femoral pulses (coarctation of the aorta), truncal obesity with pigmented striae (Cushing syndrome) and tachycardia, sweating and pallor (phaeochromocytoma). Endocrine causes are presented in CHAPTER 14 .

Further investigation will be required to confirm or reveal secondary hypertension.

Renal artery stenosis

Atherosclerotic kidney artery stenosis accounts for the majority of cases, while fibromuscular dysplasia remains an important cause. Doppler ultrasound is a highly sensitive and specific

investigation.

Detection of hypertension[7]

Hypertension can only be detected when BP is measured. Therefore, frequent opportunities should be taken to measure BP: every 6–12 weeks in high-risk patients; every 6–12 months in moderate-risk patients.[8]

Diagnosis should not be made on the basis of a single visit. Initial raised BP readings should be confirmed on at least two other visits within the space of 3 months; average levels of 90 mmHg diastolic or more, or 140 mmHg systolic or more, are needed before hypertension can be diagnosed. This will avoid the possibility of an incorrect diagnosis, committing an asymptomatic, normotensive individual to unjustified, lifelong treatment.

Measurement guidelines[3,4]

BP varies continuously and can be affected by many outside factors. Care should therefore be taken to ensure that readings accurately represent the patient's usual pressure.

BP measurement recommendations[5]

- All people aged 18 years and over
- Frequency—every 2 years

Office BP measurement guidelines[4]

- May be done manually or using an automated machine.
- Allow the patient to sit quietly for several minutes.
- Use a validated (calibrated) device—manual or automated.
- Take at least two measurements spaced by 60 seconds.
- Use a standard bladder (12–13 × 35 cm), but a larger one for big arms.
- Have the cuff at the heart level (see FIG. 77.1).
- For manual measurements, deflate the cuff slowly (2 mmHg/s).

- Measure BP also in standing position in the elderly and those with diabetes.

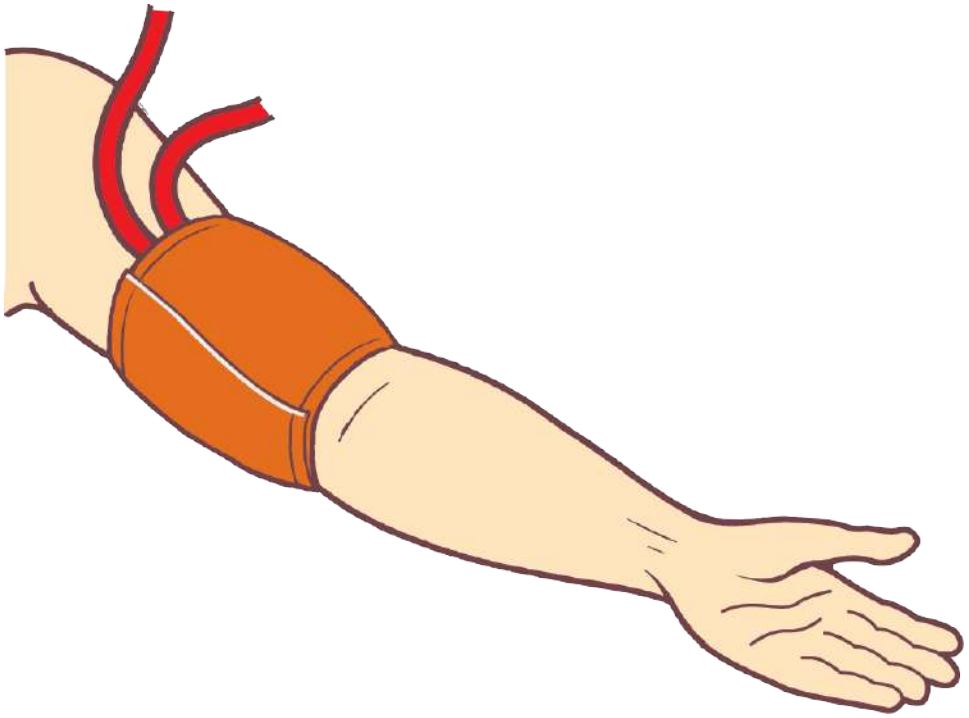

FIGURE 77.1 Correct placement of the cuff

Recording

On each occasion when the BP is taken, two or more readings should be averaged. Wait at least 30 seconds before repeating the procedure. If the first two readings differ by more than 6 mmHg systolic or 4 mmHg diastolic, more readings should be taken.

Both systolic and diastolic levels should be recorded. For the diastolic reading the disappearance of sound (phase 5)—that is, the pressure when the last sound is heard and after which all sound disappears—should be used.[9] This is more accurate than the muffling of sounds (phase 4) (see FIG. 77.2), which should only be used if the sound continues to zero.

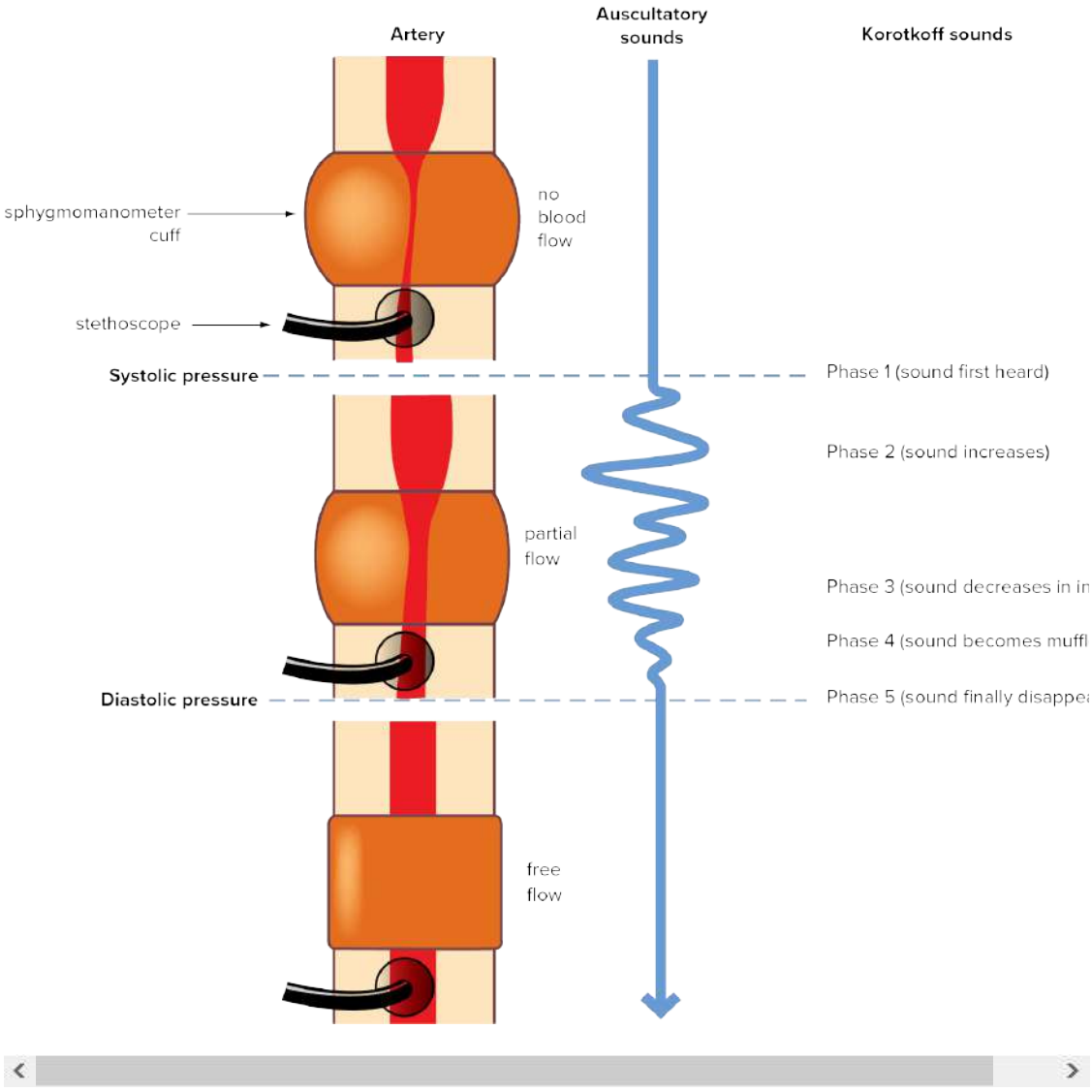

FIGURE 77.2 Illustration of blood pressure measurement in relation to arterial blood flow, cuff pressure and auscultation

Heart rate and pulse

At the same time the BP is measured, record the heart rate and rhythm. A high heart rate may indicate undue stress that is causing the associated elevated BP reading. An irregular heart rhythm may cause difficulty in obtaining an accurate BP reading.

BP modifying factors

Apprehension	Patient should be rested for at least 5 minutes and made as relaxed as possible.
Caffeine	Patients should not take caffeine for 4–6 hours before

	measurement.
Smoking	Patients should avoid smoking for 2 hours before measurement.
Eating	Patients should not have eaten for 30 minutes.

Strategies for high initial readings

If the initial reading is high (DBP >90 mmHg, SBP >140 mmHg), repeat the measures after 10 minutes of quiet rest. The 'white coat' influence in the medical practitioner's office may cause higher readings so a home automated device or Holter monitor may be very useful.

Confirmation and follow-up[7]

Repeated BP readings will determine whether initial high levels are confirmed and need attention, or whether they return to normal and need only periodic checking. Particular attention should be paid to younger patients to ensure that they are regularly followed up.

Initial diastolic BP readings of 115 mmHg or more, particularly for patients with target organ damage, may need immediate drug therapy.

Once an elevated level has been detected, the timing of subsequent readings should be based on the initial pressure level, as shown in TABLE 77.6 .

Table 77.6 Follow-up criteria for initial blood pressure measurement for adults 18 years and older[10]

Systolic (mmHg)	Diastolic (mmHg)	Action/recommended follow-up*
<120	<80	Recheck in 2 years
120–139	80–89	Recheck in 1 year—lifestyle advice
140–159	90–99	*Confirm within 2 months—lifestyle advice
160–179	100–109	*Evaluate (or refer) within 1 month—lifestyle advice
≥180	≥110	*Further evaluate and refer within 1 week (or immediately depending on clinical situation) If BP has been confirmed at ≥180 mmHg systolic and/or ≥110 diastolic mmHg (after multiple readings and

	excluding ‘white coat’ hypertension), commence drug treatment

If systolic and diastolic categories are different, follow recommendations for shorter follow-up (e.g. for BP 160/86 mmHg evaluate or refer within 1 month).
**Note:* Earlier initiation of drug therapy may be indicated for some patients.

If mild hypertension is found, observation with repeated measurement over 3–6 months should be followed before beginning therapy. This is because levels often return to normal.

Ambulatory 24-hour monitoring

This is required for the diagnosis and follow-up of patients with fluctuating levels, borderline hypertension or refractory hypertension (especially where the ‘white coat’ effect may be significant). Studies have shown that this method provides a more precise estimate of BP variability than casual recordings.

An evidence-supported alternative is home BP monitoring, where the patient purchases or borrows an automated machine and takes multiple readings over a number of days.

Guidelines for ambulatory BP measurement:

- unusual variability of office BP
- marked discrepancy between office and home BP
- resistance to drug treatment
- suspected sleep apnoea
- when two BP readings >140/90

‘White coat’ hypertension

This group may comprise up to 25% of patients presenting with hypertension. These people have a type of conditioned response to the clinic or office setting, yet their home BP and ambulatory BP profiles are normal. They appear to be at low risk of cardiovascular disease but may progress to sustained hypertension. Ambulatory 24-hour monitoring can be useful.

Masked hypertension

This is where office measurements are normal but ambulatory BP is elevated. Prognosis is relatively poor. Suspect it if evidence of end organ damage but normal office BP.

Isolated systolic hypertension

Isolated systolic hypertension is most frequently seen in elderly people. It is not benign.

Definition

SBP ≥ 140 mmHg with a DBP <90 mmHg

If a trial of non-pharmacological therapy fails, then drugs are used to cautiously reduce the systolic BP to between 140 and 160 mmHg.

Evaluation

As well as defining the BP problem, the clinical evaluation for suspected hypertension should also determine:

- whether the patient has potentially reversible secondary hypertension
- whether target organ damage is present
- whether there are other potentially modifiable cardiovascular risk factors present, and
- what comorbid factors exist

These factors markedly influence the weighing up of benefit versus risk when deciding whether to commence (or increase) antihypertensive medication. That decision needs to take into account more than just the BP reading.

Medical history

The following should be included in the medical history.

History of hypertension

- Method and date of initial diagnosis
- Known duration and levels of elevated BP
- Symptoms that may indicate the effects of high BP on target organ damage, such as headache, dyspnoea, chest pain, claudication, ankle oedema and haematuria
- Symptoms suggesting secondary hypertension (see TABLE 77.5)
- The results and side effects of all previous antihypertensive treatments

Presence of other diseases and risk factors

- A history of cardiovascular, cerebrovascular or peripheral vascular disease, kidney disease, diabetes or recent weight gain
- Other cardiovascular risk factors, including obesity, hyperlipidaemia, carbohydrate intolerance, smoking, salt intake, alcohol consumption, exercise levels and analgesic intake
- Other relevant conditions, such as asthma or psychiatric illness (particularly depressive illness)

Family history

Particular attention should be paid to the family history of hypertension, cardiovascular or cerebrovascular disease, hyperlipidaemia, obesity, diabetes, kidney disease, alcohol abuse and premature sudden death.

Medication history

A history of all medications, including over-the-counter products, should be obtained because some can raise BP or interfere with antihypertensive therapy. Prohypertensive substances include:

- alcohol
- oral and depot contraceptives
- hormone replacement therapy
- steroids/corticosteroids
- NSAIDs/COX–2 inhibitors
- sympathomimetics, nasal decongestants and other cold remedies, pseudoephedrine
- appetite suppressants
- stimulants, e.g. amphetamines
- irreversible monoamine oxidase inhibitors
- analgesics
- ergotamine
- cyclosporin
- tacrolimus
- natural liquorice

- bupropion/clozapine
- SNRIs, e.g. venlafaxine (dose-related)

Alcohol intake[7]

Alcohol has a direct pressor effect that is dose-related. An assessment of the average daily number of standard drinks is important—more than two standard drinks (20 g alcohol) per day is significant.

Examination

The approach to the physical examination is to detect possible target organ damage and possible causes of secondary hypertension. The main features to consider are illustrated in FIGURE 77.3 .

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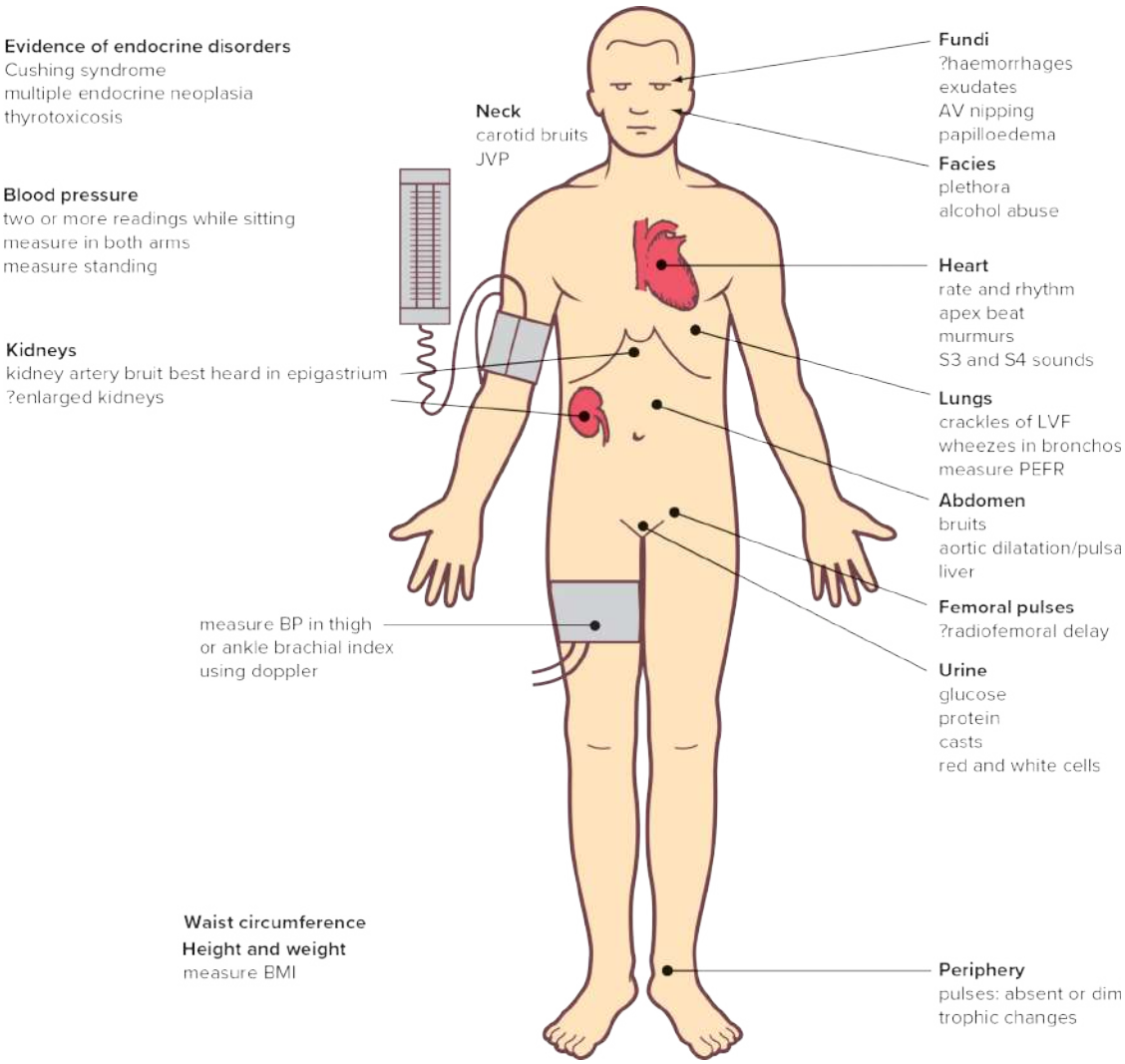

FIGURE 77.3 Examination of patient with hypertension: what to look for

The four grades of hypertensive retinopathy are illustrated in FIGURE 77.4 .

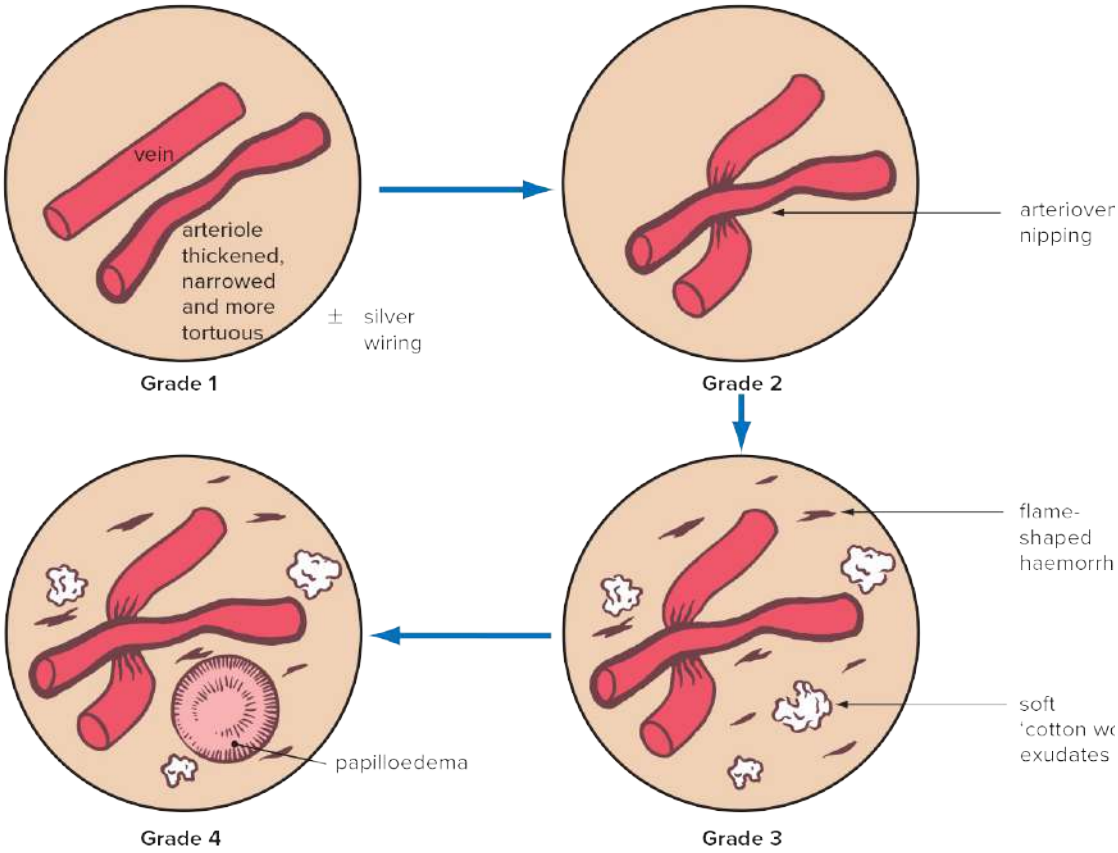

FIGURE 77.4 The four grades of hypertensive retinopathy

Leg pulses and pressure

To assess the remote possibility of coarctation of the aorta in the hypertensive patient, perform at least one observation comparing:

1. the volume and timing of the radial and femoral pulses
2. the BP in the arm and leg
3. comparison of BP in the two arms

An alternative screening test for both coarctation of the aorta and peripheral vascular disease is the ankle brachial index (ABI), using an office doppler ultrasound to compare blood pressures in

the arm (brachial artery) and ankle (dorsalis pedis and posterior tibial arteries). See CHAPTER 55 .

Blood pressure measurement in the leg

- Place the patient prone.
- Use a wide, long cuff at mid-thigh level.
- Position the bladder over the posterior surface and fix it firmly.
- Auscultate over the popliteal artery.

Investigations[4,6,8]

Recommended tests

- Chest X-ray
- Plasma glucose (preferably fasting)
- Serum total and high-density lipoprotein (HDL) cholesterol, triglycerides (fasting if convenient)
- Serum creatinine/eGFR/ACR
- Serum uric acid
- Serum potassium and sodium
- Haemoglobin and haematocrit
- Urinalysis (dipstick test and urinary microscopy for sediment)
- Electrocardiogram

Other tests to consider

- Echocardiogram
- Carotid (and femoral) ultrasound
- HbA1c (when fasting glucose ≥6.1 mmol/L or 110 mg/dL)
- Fundoscopy (in severe hypertension)

These other investigations, including echocardiography, kidney imaging studies (especially kidney doppler ultrasound), 24-hour urinary catecholamines, aldosterone and plasma renin, are not routine and should be performed if specifically indicated (e.g. suspected primary hyperaldosteronism). A chest X-ray may serve as a baseline against which to measure future changes. However, if a chest X-ray shows the heart is enlarged, it is more likely to represent chamber dilatation than increased ventricular wall thickness.[7] Specific kidney studies now favoured include isotope scans, duplex ultrasound studies of kidney arteries and kidney arteriography.

Treatment

A correct diagnosis is the basis of management. Assuming that the uncommon secondary causes are identified and treated, treatment will focus on essential hypertension.

Benefits of treatment

Trials have shown that lowering BP reduces:

- cardiovascular and total mortality
- stroke
- coronary events

Benefits have been proven:

- in those with systolic/diastolic hypertension
- in elderly patients with isolated systolic hypertension

Principles of management[6]

- The overall goal is to improve long-term survival and quality of life.
- Promote an effective physician–patient working relationship.
- Aim to reduce the levels to 140/90 mmHg or less (target varies with circumstance).
- Undertake a thorough assessment of all cardiovascular risk factors.
- Instruct all patients in the use of non-drug treatment strategies and their potential benefits. The benefits of exercise and healthy diet go far beyond what will be measurable by merely observing their effect on hypertension.
- In patients with mild-to-moderate hypertension and no target organ damage, consider ambulatory or home BP monitoring before deciding to start medication.

- Drug therapy should be given to those with:

  sustained high initial readings (e.g. DBP 100 mmHg)

  target organ damage

  failed non-drug measures

  high CV risk where BP is above hypertensive guideline thresholds

- Make a careful selection of an antihypertensive drug and an appraisal of the side effects against the benefits of treatment.
- Avoid drug-related problems such as postural hypotension.
- Avoid excessive, rapid lowering of BP—aim for steady and graduated control.
- Engage the patient to help counter the problem of non-adherence.

Patient education

Patient education should include appropriate reassurances, clear information and easy-to-follow instructions. It is important to establish patients' understanding of the concept of hypertension and its consequences by quizzing them about their knowledge and feelings.

Correction of patients' misconceptions[7]

Patients are likely to have several misconceptions about hypertension that may adversely affect their treatment.

For example, they might believe that:

- hypertension can be cured
- they do not need to continue treatment once BP is controlled
- they do not have a problem because they do not have symptoms
- they need to take additional pills, or stop treatment in response to symptoms they believe are caused by high or low BP levels
- they need not take prescribed pills if they attend to lifestyle factors such as exercise and diet (this is occasionally the case, but needs careful oversight by the GP)
- they can gauge their BP by how they feel

Tips for optimal compliance

- Establish a good, caring rapport.
- Give advice about pill-taking times. A 2019 trial suggests that bedtime dosing may reduce cardiovascular events,[11] but the best routine is one the patient remembers reliably.
- Set therapeutic goals.
- Establish a recall system.
- Provide patient education material.

On review:

- Ask if any pills were missed by accident.
- Review all cardiovascular risk factors.
- Enquire about any side effects.

Non-pharmacological (lifestyle) management measures

If the average diastolic BP at the initial visit is 90–100 mmHg, and there is no evidence of end organ damage, non-pharmacological therapy is indicated for a 3-month period without use of antihypertensive drugs. Remember to remove, revise or substitute drugs that may be causing hypertension (e.g. NSAIDs, corticosteroids, oral contraceptives, hormone replacement therapy).

Behaviour intervention measures

- *Weight reduction*

  There is considerable evidence that weight loss and gain are linked to a corresponding fall and rise in BP. Hovell has estimated that for every 1 kg of weight lost, BP dropped by 2.5 mmHg systolic and 1.5 mmHg diastolic.[12] The BMI should be calculated for all patients and where appropriate a weight-loss program organised to target waist measurement to <94 in males and <80 in females or reduce the BMI to around 25.

- *Reduction of excessive alcohol intake*[7]

  The direct pressor effect of alcohol is reversible. Drinking more than 20 g of alcohol a day raises BP and makes treatment of established hypertension more difficult. People with hypertension should limit their alcohol intake to one or two standard drinks (10–20 g) per day. Reduction or withdrawal of regular alcohol intake reduces BP by 5–10 mmHg.

- *Reduction of sodium intake to ≤4 g/day*

Some individuals seem to be more sensitive to salt restriction. Advise patients to put away the salt shaker and use only a little salt with their food. Reduction of sodium intake to less than 100 mmol sodium per day is advised. Special care should be taken with processed and take-away foods.

- *Increased exercise and regular physical activity*

  Regular aerobic or isotonic exercise helps to reduce BP.[10] Hypertensive patients beginning an exercise program should do so gradually. Walking is an appropriate exercise, ideally 150–300 minutes each week.

- *Reduction of particular stress*

  If avoiding stress or overwork is difficult, recommend relaxation and/or meditation therapy.

- *Other dietary factors for a healthy eating plan*

  There is evidence that lacto–vegetarian diets and diets high in vegetables, fruits and whole grains can reduce BP.[6] A diet high in calcium, and low in fat and caffeine, may also be beneficial. Avoid or minimise liquorice.

- *Smoking*

  Smoking causes acute rises in BP but does not appear to cause sustained hypertension. However, the elimination of smoking is important as it is a strong risk factor for cardiovascular disease and continuing to smoke may negate any cardiovascular benefits of antihypertensive therapy.[7]

- *Management of sleep apnoea*

  A 2014 systematic review found that CPAP reduces BP in those with obstructive sleep apnoea and hypertension, although only by a small amount (2–3 mmHg).[13]

Pharmacological therapy

The benefits of drug therapy appear to outweigh any known risks to individuals with a persistently raised diastolic pressure >95 mmHg. Although the ideal antihypertensive drug has yet to be discovered, there are many effective drugs available from all the major classes of antihypertensive drugs.[14] Deciding which one to use first involves an assessment of the patient's general health, the medication's known side effects, the simplicity of its administration and its cost. A useful plan is outlined in FIGURE 77.5 .

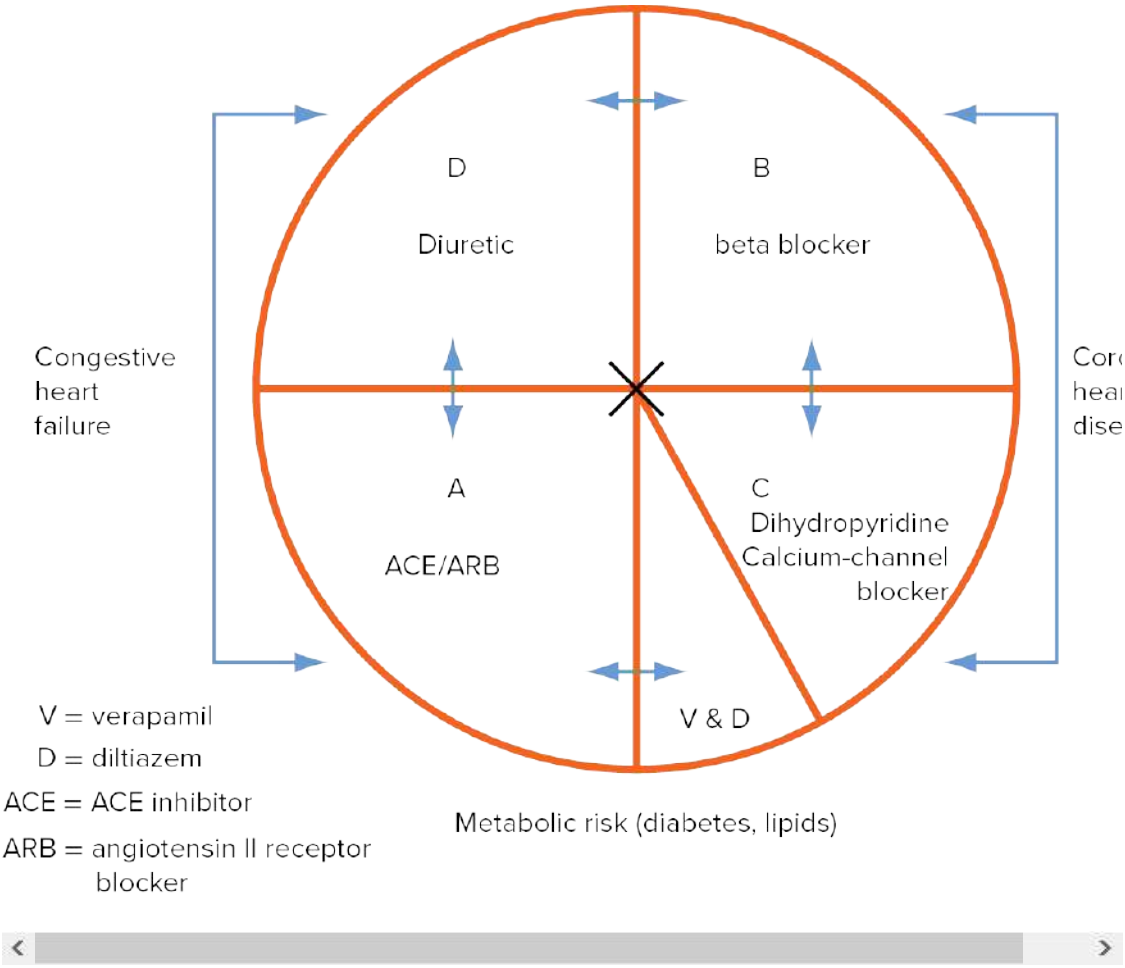

FIGURE 77.5 Common combinations of the therapeutic drug classes used for first-line therapy of hypertension

- Adjacent drug classes are useful combinations in that effects on BP are additive but adverse effects are no more likely than with either drug used alone.
- Non-dihydropyridine CCBs: verapamil (V) and diltiazem (D) generally should not be used with β_2-antagonists (beta blockers).
- Drug groups that are diametrically located on the diagram may be used together, but may not have fully additive effects.
- Drugs on the left side should be combined in patients with hypertension and heart failure, and those on the right side are useful in patients with hypertension and coexisting coronary disease.
- Drug groups in the lower half lack metabolic effects and may be preferred combinations in the presence of diabetes or lipid abnormalities as well as hypertension.

- Do not combine ACE with ARB (increased side effects for little benefit).
- β_2-antagonists are not routine first-line treatment unless they will also be useful for a coexisting condition.
- Prazosin and other α-antagonists are also sometimes used as monotherapy and may be combined with any of the above drug groups.
- Small doses of centrally acting anti-adrenergic drugs (e.g. methyldopa, clonidine) can probably also be used with any of the other agents although data on their use in combination are scarce with the newer drug groups.

Source: Adapted from Management of hypertension: a consensus statement, Med J Aust, 1994; 160: Supplement 21 March. © Copyright 1994. The Medical Journal of Australia. Reproduced with permission.

Various disorders such as diabetes, asthma, COPD, Raynaud phenomenon, heart failure and elevated serum urate and/or lipid levels may restrict the use of some classes of drugs.

Who to treat[6]

- Failed genuine non-pharmacological trial
- Treat those at high CV risk (>15% 5-year CV risk, established CV disease, diabetes with either age >60 or persistent proteinuria)
- For those with >10% 5-year CV risk, treat if SBP >140 mmHg or DBP >90 mmHg
- For those with <10% 5-year CV risk, treat if SBP >160 mmHg or DBP >100 mmHg (For treatment targets, see TABLE 77.7)

Table 77.7 BP treatment targets for adults (mmHg)[6,15]

People with proteinuria >1 g/day (with or without diabetes)	<125/75
People with associated condition(s) or end-organ damage: • coronary heart disease • diabetes • chronic kidney disease • proteinuria (>300 mg/day) • stroke/TIA	<130/80
People with none of the above	<140/90 or lower if tolerated

Guidelines[15]

- Start with a single drug at low dose.
- A period of 4–6 weeks is needed for the effect to become fully apparent.
- If ineffective, consider increasing the drug to its maximum recommended dose, or add an agent from another compatible class, or substitute with a drug from another class.
- Use only one drug from any one class at the same time.
- A summary of first-line therapy options and the uses of the various pharmacological agents is shown in TABLE 77.8 .
- Measure the BP at the same time each day.
- Consider asking patients to self-measure.
- Patients commonly require two or more agents to reach BP targets.

-line pharmacological options for the management of hypertension[6,15,16] (standard

	Drug class			
	Beta blocker	Calcium-channel blocker	ACE inhibitor	ARB (sartans)
s and starting dose (oral therapy)				
	Atenolol 25–50 mg daily	*Dihydropyridine CCBs*	Enalapril 5 mg daily	Candesartan 8 mg daily
de	Metoprolol 50 mg daily	Amlodipine 2.5 mg daily	Lisinopril 5 mg daily	Eprosartan 600 mg daily
	Pindolol 5 mg daily	Felodipine SR 2.5 mg daily	Perindopril 2.5 mg daily	Irbesartan 150 mg daily
	Propranolol 40 mg daily	Lercanidipine 10 mg daily	Ramipril 2.5 mg daily	Losartan 50 mg daily
		Nifedipine CR 20 mg daily	Fosinopril 10 mg daily	Olmesartan 10 mg daily
		Non-dihydropyridine	Quinapril 5 mg daily	Telmisartan 40 mg daily
		Diltiazem CD 180 mg daily	Trandolapril 1 mg daily	Valsartan 80 mg daily

		Verapamil SR 120–180 mg daily		
n				
l)	Pregnancy Glaucoma Stable angina Postmyocardial infarction Migraine	Asthma Stable angina PVD Raynaud phenomenon	Left ventricular heart failure PVD Diabetes Raynaud Post AMI	Left ventricular heart failure Diabetes PVD ACEI-induced cough Post AMI
s				
out	Asthma/COPD History of wheeze Heart failure Heart block (2nd and 3rd degree) PVD Brittle type I diabetes	Heart block 2nd and 3rd degree Heart failure (verapamil, diltiazem) Tachyarrhythmias	Bilateral kidney artery stenosis Pregnancy Hyperkalaemia Angioedema	Pregnancy Severe kidney failure Hyperkalaemia
	Avoid abrupt cessation with angina Caution using with verapamil, NSAIDs and in smokers	Caution using with beta blockers, digoxin and in CCF	Chronic kidney disease Caution using with K-sparing diuretics and NSAIDs	Electrolyte imbalance Renal impairment Hepatic impairment
ffects				
on	Fatigue Insomnia Vivid dreams Bronchospasm Cold extremities Sexual dysfunction	Headache Flushing Ankle oedema Palpitations Dizziness Nausea Constipation (verapamil)	Cough Weakness Rash Dysgeusia (taste) Hyperkalaemia First dose hypotension	Headache Dizziness Orthostatic hypotension Fatigue Weakness Hyperkalaemia Allergies

Lipid metabolism effect	Nocturia, urinary frequency Gum hyperplasia	Angioedema	Angle closure glaucoma

Starting regimens

In patients with uncomplicated hypertension, ACE inhibitors or ARBs, calcium-channel blockers and thiazides are all suitable first-line antihypertensive drugs, either as monotherapy or in some combinations unless contraindicated. Page 911

The traditional method has been to use stepwise therapy until ideal control has been reached, commencing with:

Starting medication

1. ACE inhibitor or ARB especially if ≥55 years

   or
   calcium-channel blocker (CCB)
   or
   low-dose thiazide diuretic
   (if aged ≥65 years)

2. If target not reached after 3 months: combination

   ACEI or ARB + CCB (best evidence)[17]
   or
   ACEI or ARB + thiazide
   or
   ACEI or ARB + beta blocker

3. If target not reached:

   ACEI/ARB + CCB + thiazide

4. If still not reached use spironolactone or seek specialist advice

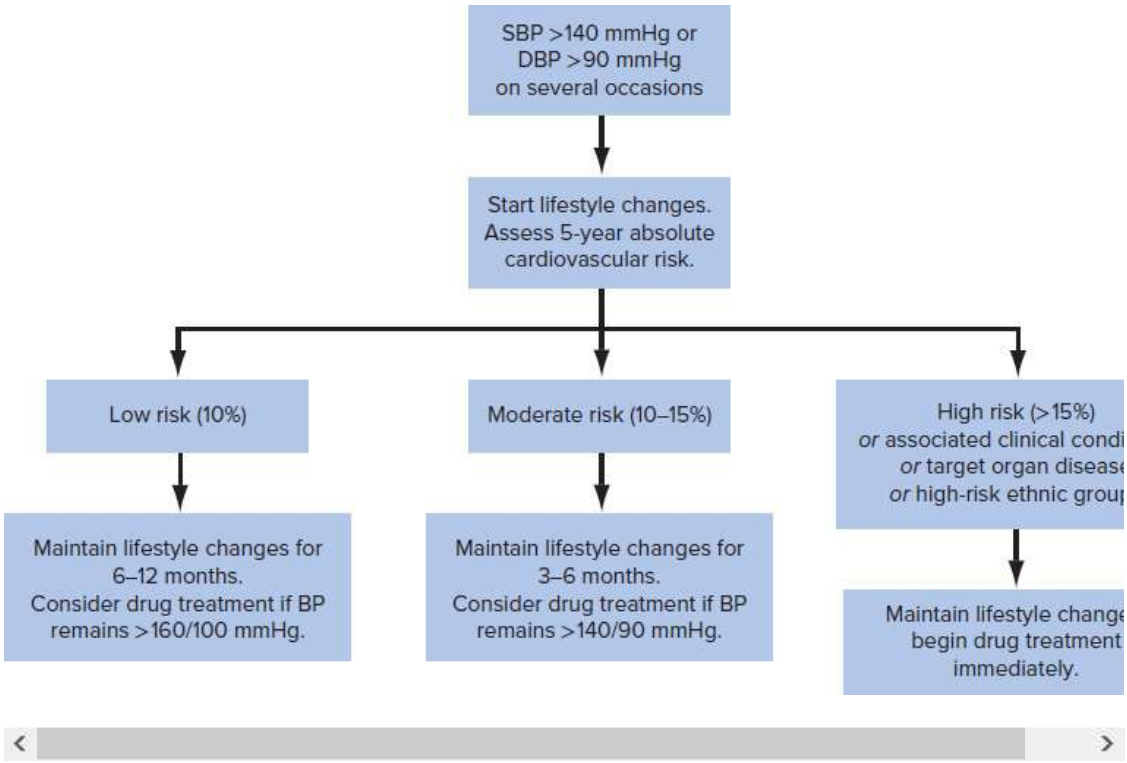

FIGURE 77.6 Decision tree for managing hypertension[2]

As recommended by the National Heart Foundation

The following are useful combinations:[10,18]

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Initial agent	Additional drugs
Thiazide diuretic	ACEI/ARB *or* CCB *or* beta blocker
Beta blocker	Diuretic *or* dihydropyridine calcium-channel blocker
ACE inhibitor or ARB	Diuretic *or* beta blocker *or* calcium-channel blocker

Relatively ineffective combinations[10]

- Diuretic and calcium-channel blocker
- Beta blockers and ACE inhibitors

Undesirable combinations[10,15]

- More than one drug from a particular pharmacological group:

  beta blockers and verapamil (heart block, heart failure)

  potassium-sparing diuretics and ACE inhibitors or ARB (hyperkalaemia)

  ACEI and ARB

Diuretics[10,16]

- Thiazides are good first-line therapy for hypertension.
- Hypokalaemia can be corrected with potassium-sparing diuretics or by changing to another first-line drug.
- Loop diuretics (e.g. frusemide) are less potent as antihypertensive agents but are indicated where there is concomitant cardiac or kidney failure and in resistant hypertension.
- Thiazides are less effective where there is kidney impairment.
- Thiazides may precipitate acute gout.
- NSAIDs may antagonise the antihypertensive and natriuretic effectiveness of diuretics.
- A diet high in potassium and magnesium should accompany diuretic therapy (e.g. lentils, nuts, high fibre).
- Avoid use if significant dyslipidaemia.
- Indapamide has different properties to the thiazide and loop diuretics and has less effect on serum lipids.

Beta blockers

- NSAIDs may interfere with the hypotensive effect of beta blockers.
- If BP is not reduced by one beta blocker it is unlikely to be reduced by changing to another.

- Verapamil plus a beta blocker may unmask conduction abnormalities causing heart block.
- In patients with ischaemic heart disease, or susceptibility to it, treatment must not be stopped suddenly—this can precipitate angina at rest.

Calcium-channel blockers

- These drugs reduce BP by vasodilatation.
- The properties of individual drugs vary, especially their effects on cardiac function.
- The dihydropyridine compounds (nifedipine and felodipine) tend to produce more vasodilatation and thus related side effects.
- Unlike verapamil or diltiazem (which slow the heart), dihydropyridine drugs can be used safely with a beta blocker.
- Verapamil is contraindicated in second and third degree heart block.
- Verapamil and diltiazem should be used with caution in patients with heart failure.
- These drugs are efficacious with ACE inhibitors, beta blockers, prazosin and methyldopa.

ACE inhibitors

Angiotensin-converting enzyme (ACE) is responsible for converting angiotensin I to angiotensin II (a potent vasoconstrictor and stimulator of aldosterone secretion) and for the breakdown of bradykinin (a vasodilator). ACE inhibitors are effective in the elderly; improve survival and performance status in cardiac failure; are protective of kidney function in diabetes; and are cardioprotective after myocardial infarction.

Disturbance in taste is usually transitory and may resolve with continued treatment. Cough, which occurs in about 15% of patients, may disappear with time or a reduction in dose but it often persists and may require a change in drug. Angioedema, a potentially life-threatening condition, may occur in 0.1–0.2% of subjects. Like cough, it is a class effect and will mitigate against the use of any ACE inhibitor. The Heart Outcomes Prevention Evaluation (HOPE)[19] trial demonstrated that ramipril reduces the number of cardiovascular deaths, non-fatal myocardial infarctions, non-fatal strokes and instances of new onset heart failure in a high-risk population. The data also indicated that people with diabetes, microalbuminuria or pre-existing vascular disease can benefit from ACEI treatment, even if normotensive.[18,19]

Angiotensin II receptor antagonists (sartans)

These agents competitively block the binding of angiotensin II to type I angiotensin receptors and block the effects of angiotensin more selectively than the ACE inhibitors. This reduces angiotensin-induced vasoconstriction, sodium reabsorption and aldosterone release. The action

of the ACEIs and ARBs on the renin–angiotensin–aldosterone pathway system is illustrated in FIGURE 77.7 . They have a similar adverse kidney and other effects to the ACE inhibitors but cough does not appear to be a significant adverse effect. This group is used for mild-to-moderate hypertension alone or with other antihypertensive agents. They are useful alternatives for patients who discontinue an ACE inhibitor because of cough. They may be used in combination with thiazide diuretics.

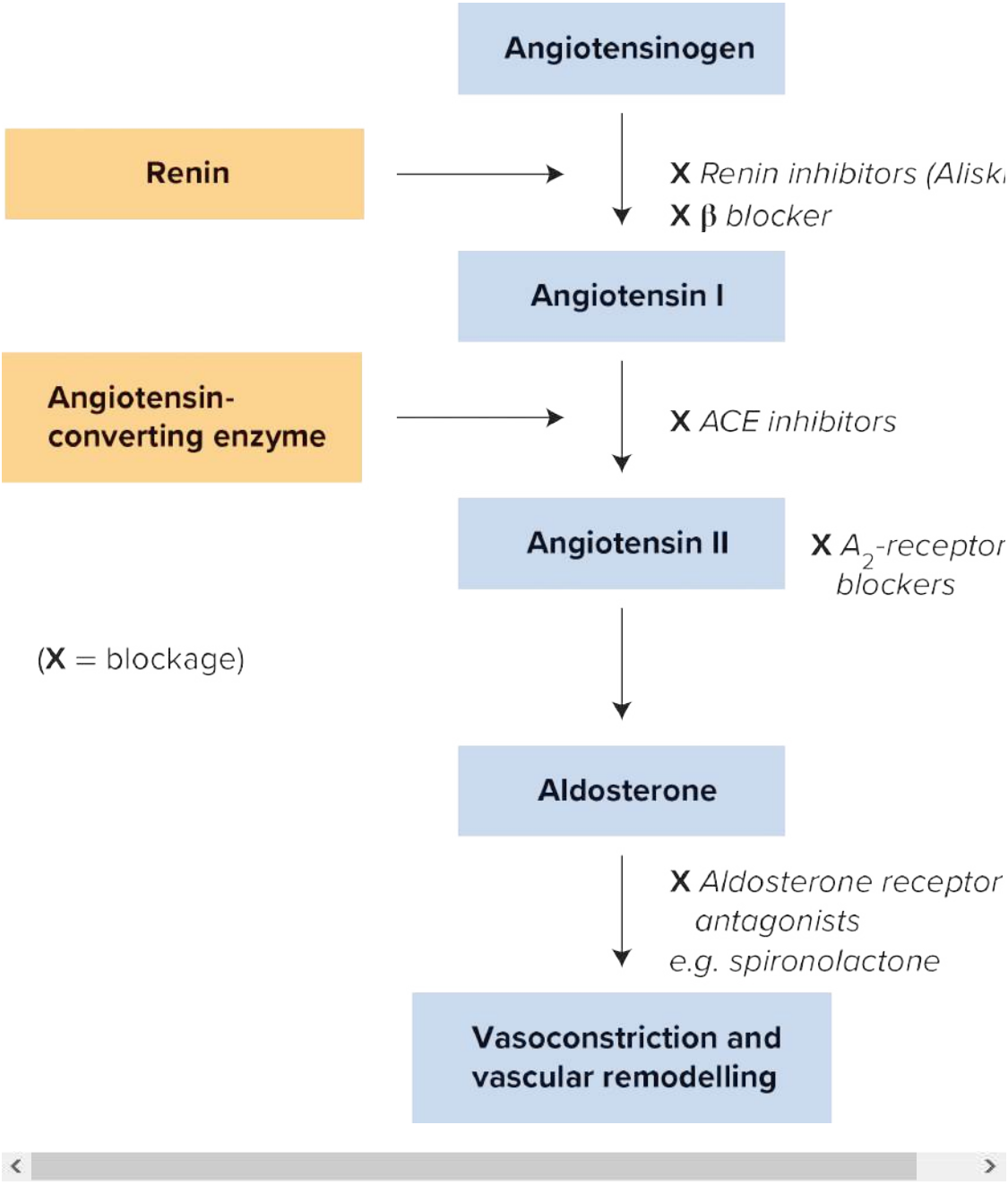

FIGURE 77.7 Drugs targeting the renin–angiotensin–aldosterone system

Alpha blockers: prazosin and terazosin

Not recommended as first-line therapy.

A specific problem of alpha blockers is the ‘first-dose phenomenon’; this involves acute syncope about 90 minutes after the first dose, hence treatment is best initiated at bedtime. Prazosin potentiates beta blockers and works best if used with them. It is a useful second-line therapy in patients who are unsuitable for diuretic or beta blocker therapy (e.g. those with diabetes, asthma or hyperlipidaemia).

Vascular smooth muscle relaxants

Other than calcium-channel blockers, these include hydralazine, minoxidil and diazoxide, which are not used for first-line therapy but for refractory hypertensive states and hypertensive emergencies.

Sympathetic nervous system inhibitors

These reduce peripheral sympathetic activity by inhibiting the sympathetic nervous system. Methyldopa and clonidine may be used during pregnancy.

Hypertensive emergencies[15]

A hypertensive emergency occurs when high BP causes the presenting cardiovascular problem. Typical presentations of hypertensive emergencies (which are rare) include hypertensive encephalopathy, acute stroke, heart failure, dissecting aortic aneurysm and eclampsia. Symptomatically patients may present with headache and confusion.

In all such cases referral to hospital via the emergency department is essential for urgent monitoring and treatment. Treatment must be individualised, mindful of the nature of the underlying problem and associated disorders.

The BP lowering must be gradual because a sudden fall can precipitate a stroke. Aim to reduce the BP by no more than 25% within the first 2 hours, then towards 160/100 mmHg within 2 to 6 hours.[15]

Treatment is with a dihydropyridine CCB and/or an ACE inhibitor. Otherwise, sodium nitroprusside IV in an intensive care setting is the optimal treatment.

Magnesium sulphate (in addition to antihypertensives) reduces the risk of eclampsia and maternal death in women with pre-eclampsia (see CHAPTER 100).

Refractory hypertension

Refractory hypertension exists where control has not been achieved despite reasonable treatment for 3–4 months. A review of possible secondary causes is appropriate. Consider non-adherence, sleep apnoea, hypertensive effects of other drugs, undisclosed use of alcohol and recreational drugs, and also spurious factors (e.g. instrument factors such as small cuff, ‘white coat’ hypertension).

When adequate control is not possible and the cause is not obvious, refer to a specialist. Measurement outside the clinic may help in the assessment of such people, as may 24-hour ambulatory monitoring.

Hypertension in children and adolescents

BP is less frequently measured in children for a number of reasons, including the lower chances of finding any abnormality, the unavailability of an appropriately sized cuff or difficulty in measuring BP in the infant or toddler.

The children of parents with hypertension should be closely watched. Those at risk of secondary hypertension (e.g. kidney or cardiovascular disease, urological abnormalities and diabetes mellitus) should have routine measurements. Children with visual changes, recurrent headache or abdominal pain, seizures and those on drugs such as corticosteroids or oral contraceptives should have their BP checked regularly.

Although secondary causes of hypertension are proportionally more common in children than in adults, young people are still more prone to developing essential rather than secondary hypertension. Kidney parenchymal disease and kidney artery stenosis are the major secondary causes.

The upper limits of normal BP for children in different age groups are:[7]

Age (in years)	Arterial pressure (mmHg)
5 or less	110/75
6–9	120/80
10–13	125/85
14–18	135/90

The proper cuff size is very important to avoid inaccurate readings and a larger rather than a smaller cuff is recommended. The width of the bladder should cover 75% of the length of the upper arm. In infants and toddlers, use of an electronic unit may be necessary. Although cessation of sound (phase 5) is the better reflection of true diastolic pressure, there is often no disappearance of sound in children and so estimation of the point of muffling (phase 4) is recorded instead.

Diagnostic evaluation and drug treatment for children are similar to those for adults. Strongly

consider specialist referral. When a child is obese, reduction in weight may adequately lower BP. ACE inhibitors or calcium-channel blocking agents are preferable in children, with diuretics a second agent. ACE inhibitors should be avoided in postpubertal females.

Hypertension in the elderly

BP shows a gradual increasing linear relationship with age.

Guidelines for treatment

- Isolated systolic hypertension is worth treating.[20]
- Older patients may respond to non-pharmacological treatment.
- Reducing dietary sodium is more beneficial than with younger patients.
- If drug treatment is necessary, commence with half the normal recommended adult dosage —'start low and go slow'.
- Patients over 75 years and in good health should be treated the same as younger patients. Studies indicate that benefits are still significant. However, weigh this against the fact that harms (e.g. falls risk) may be greater.
- Reduce BP gradually.
- Drug reactions are a limiting factor.
- Drug interactions are also a problem: these include NSAIDs, antiparkinson drugs and phenothiazines.

Specific treatment

- *First-line choice:* indapamide (preferred) or thiazide diuretic (low dose);[7] check electrolytes in 2–4 weeks: if hypokalaemia develops, add a K-sparing diuretic rather than K supplements. Diuretics may aggravate bladder difficulties (e.g. incontinence).
- *Second-line choice:* ACE inhibitors (or ARB) especially with heart failure.

Other effective drugs (especially for isolated systolic hypertension):

- beta blockers (low dose) where diuretic cannot be prescribed or if angina
- calcium-channel blockers

Both these classes are generally well tolerated but constipation may be a problem with verapamil.

Kidney function and electrolytes should be monitored when ACE inhibitors are started.

Special management problems

These conditions are summarised in TABLE 77.9 .

Table 77.9 Choice of drugs in patients with coexisting conditions[7]

	Diuretic	ACE inhibitors/ARBs	Calcium-channel blockers	Beta blockers
Asthma/COPD	✓	✓	✓	✗ Caution
Bowel disease/constipation	✗	✓	✗	✗
Bradycardia/heart block	✓	✓	Care	✗
Cardiac failure	✓*	✓*	Care	✗
Depression	✓	✓	✓ Care	✗
Diabetes	✗	✓*	✓	✗ Care
Dyslipidaemia	✗	✓	✓	✗
Hyperuricaemia/gout	✗	✓*	✓*	✗
Impotence	✗	✓	✓	✗
Ischaemic heart disease	✓	✓	✓*	✓*
Peripheral vascular disease	✓	✓	✓*	✗
Pregnancy	✗	✗	✓	✓ Not in late term
Raynaud phenomenon	✓	✓	✓*	✗
Kidney artery stenosis	✓	✗	✓* Care	✓* Care
Kidney failure	✓	Care	✓	✓
Tachycardia (resting)	✗	✗	Care	✓*

*Drugs of choice

Note: Calcium-channel blockers need to be selected with care—some are suitable, others not.

Step-down treatment of mild hypertension[10]

This is an important concept that recognises that drug treatment need not necessarily be lifelong. If BP has been well controlled for several months to years it is often worth reducing the dosage or the number of drugs.

The general ‘deprescribing’ rule of thumb is that a drug (or its specific dosage) should only be continued if the expected benefits justify its continuation.

A ‘drug holiday’ (cessation of treatment) can be hazardous, however, because satisfactory control may be temporary and hypertension will re-emerge. Careful monitoring under such circumstances is mandatory.

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When to refer

- Refractory hypertension—adequate control not possible and cause not obvious
- Suspected ‘white coat’ hypertension—refer for ambulatory BP monitoring
- Severe hypertension—diastolic BP >115 mmHg
- Hypertensive emergency
- Evidence of ongoing target organ impairment and BP inadequately controlled
- Significant kidney impairment eGFR <30 mL/min
- A treatable cause of secondary hypertension is found

Practice tips

- Hypertension should not be diagnosed on a single reading.
- At least two follow-up measurements with average systolic pressure >140 mmHg or diastolic pressures >90 mmHg are required for the diagnosis.
- Beware of using beta blockers in a patient with a history of wheezing.
- Add only one agent at a time and wait about 4 weeks between dosage adjustments.
- Excessive intake of alcohol can cause hypertension and make treatment difficult.
- If hypertension fails to respond to therapy, an underlying kidney or adrenal lesion may have been missed.

- The low-pitched bruits of kidney artery stenosis are best heard by placing the diaphragm of the stethoscope firmly in the epigastric area.
- Older patients may respond better to diuretics, calcium-channel blockers and ACE inhibitors.
- Younger patients may respond better to beta blockers or ACE inhibitors.

Patient education resource

Hand-out sheet from *Murtagh's Patient Education* 8th edition:

- Hypertension

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78 Dyslipidaemia

The landmark Scandinavian Simvastatin Survival Study (4S) published in 1994, may well be remembered as the study that finally put to rest many of the apprehensions and misconceptions regarding lipid-lowering therapy.

DUFFY AND MEREDITH 1996[1]

Dyslipidaemia is the presence of an abnormal lipid/lipoprotein profile in the serum and can be classified as:

- predominant hypertriglyceridaemia
- predominant hypercholesterolaemia
- mixed pattern with elevation of both cholesterol and triglyceride (TG)

Modern epidemiological studies have established the facts that elevated plasma cholesterol causes pathological changes in the arterial wall leading to CAD, and that lipid-lowering through lifestyle factors or drug therapy results in reduction of coronary and cerebrovascular events with improved survival.

A Cochrane systematic review[2] of 18 large RCTs found high-quality evidence that statins reduce all-cause mortality and major vascular events. The number needed to treat (NNT) with statins varies markedly depending on the risk category the person falls into (see TABLE 78.1).

Table 78.1 Number needed to treat (NNT) with a statin for 1 year to prevent 1 death[2]

Risk level	NNT
<5% five-year CV risk	835
5–10% five-year CV risk	335
Previous cardiovascular event—high risk[3]	165

As with other cardiovascular risk factors, focussing on any one measure (in this case, lipid profile) is only part of the whole-person approach to reducing risk.

The main focus of treatment will be on primary dyslipidaemia but secondary causes (see TABLE 78.2) also need to be addressed. LDL-C is the lipid with the highest correlation with CHD and its level remains the primary target of lipid-modifying therapy. The statins are the first-line therapy for a raised level. Like total cholesterol measurement, LDL-C should not be used in isolation.

Table 78.2 Common causes of secondary dyslipidaemia

Hypothyroidism
Nephrotic syndrome
Type 2 diabetes
Cholestasis
Anorexia nervosa
Obesity
Kidney impairment
Smoking
Alcohol excess
Oestrogen therapy
Obstructive liver disease

Established facts[4,5,6]

- Major risk factors for CAD include:

  increased LDL cholesterol + reduced HDL cholesterol

  ratio LDL-C:HDL-C >4

- Risk increases with increasing cholesterol levels
- TG level >10 mmol/L increases risk of pancreatitis
- Management depends on other cardiovascular risk factors
- 10% reduction of total cholesterol gives 20% reduction in CAD after 3 years

- LDL-C reduction with statin therapy reduces heart attacks, stroke, the need for revascularisation and death
- Screening is recommended 5 yearly from age 45 years (Aboriginal and Torres Strait Islander people from 35 years)

Investigations[5]

The following fasting tests are recommended in patients every 5 years, starting at age 45 years:

- serum cholesterol level, HDL-C, LDL-C and triglyceride (TG)

Confirm an initial high result with a second test at 6–8 weeks. Those at moderate risk (5-year CV risk >10%) should have a screening test every two years. Commence testing at 35 years of age if Aboriginal or Torres Strait Islander.

All patients should receive advice and support regarding lifestyle risk management. Patients requiring pharmacological treatment are summarised in TABLE 78.3 .

Table 78.3 Patients requiring treatment (PBS guidelines)[4]

Risk category	Initiate drug therapy if lipid level (mmol/L) is
Patients with existing symptomatic coronary heart disease, peripheral vascular disease and cerebrovascular disease Patients with diabetes PLUS one of microalbuminuria; age >60; Aboriginal or Torres Strait Islander Family history of coronary heart disease (one first-degree relative <45 years of age, or two <55 years)	Any level
Aboriginal and Torres Strait Islander patients with hypertension Family history of coronary heart disease (one first-degree relative <60 years of age, or one second-degree relative <50 years)	Cholesterol >6.5 mmol/L *or* Cholesterol >5.5 mmol/L *and* HDL <1 mmol/L
Patients with HDL <1 mmol/L	Cholesterol >6.5 mmol/L
Patients not eligible under the above:	Cholesterol

• men 35–75 years • postmenopausal women up to 75 years	>7.5 mmol/L *or* Triglyceride >4 mmol/L
Patients not otherwise included in the above	Cholesterol >9 mmol/L *or* Triglyceride >8 mmol/L

Recommended treatment goals[7]

- Total cholesterol <4.0 mmol/L
- LDL-C <2.0 mmol/L*
- HDL-C ≥1.0 mmol/L
- Non-HDL-C <2.5 mmol/L
- TG <2 mmol/L

NVDPA guidelines[7] note there appears to be no major difference between dose titration regimens or use of a fixed dose in studies of longer duration. The majority of benefit from statins results at the lower doses, with less added benefit as doses are increased towards maximum. Therefore treatment should aim towards these targets rather than consider them definitive.

Non-pharmacological measures[6]

- Dietary measures:

  keep to ideal weight (as for cardiovascular disease, see CHAPTER 75)

  reduce saturated and trans fat intake, especially dairy products and meat

  avoid fast foods and deep-fried foods

  replace saturated fats with mono or polyunsaturated fats

use approved cooking methods (e.g. steaming, grilling)

trim fat off meat, remove skin from chicken

avoid biscuits and cakes between meals

high-fibre diet, especially fruit and vegetables (to increase soluble fibre)

introduce plant sterol-enriched milk, margarine or cheeses

alcohol intake 0–2 standard drinks/day

drink more water

- Encourage physical activity: regular exercise program
- Cease smoking
- Cooperation of family is essential
- Exclude secondary causes (e.g. kidney disease, type 2 diabetes, hypothyroidism, obesity, alcohol excess—especially ↑ TG), specific diuretics

Checkpoints

- Diet therapy effective (TG ↓, LDL-C ↓) within 6–8 weeks
- If dietary change is successful, continue at least 6 months before considering drug therapy in all but the highest-risk category

Pharmacological measures

The choice of the lipid-lowering agent depends on the pattern of the lipid disorder.[5,6] See TABLE 78.4 . Use the following agents in addition to diet.

Table 78.4 Lipid-lowering drugs

Drug	Dose (average)	Usage	Adverse effects	Safety monitorin
The statins	**Dose range from starting**			

Atorvastatin Pravastatin Simvastatin Fluvastatin Rosuvastatin	10–80 mg 20–80 mg 10–80 mg 20–80 mg 5–40 mg	↑ cholesterol (total or LDL-C)	Muscle pains, raised liver enzymes	Liver enzymes: creatine kinase an ALT
Bile acid binding resins				
Cholestyramine Colestipol	4–8 g daily–bd 5–10 g daily–bd	↑ cholesterol	GIT dysfunction, drug interactions	
Fibrates				
Gemfibrozil Fenofibrate	600 mg bd 145 mg daily	↑ triglycerides, mixed hyperlipidaemia	GIT dysfunction, myositis; Gemfibrozil relatively contraindicated with statins	Liver enzymes, coagulatic
Other agents				
Ezetimibe	10 mg daily	↑ cholesterol	Arthralgia, myalgia, myositis, liver dysfunction	Liver enzymes
Nicotinic acid	250 mg bd to 1000 mg bd–tds	↑ cholesterol and triglycerides	Flushing (common), raised glucose, urate and liver enzymes	Glucose urate Liver enzymes Increase dose slowly
Fish oils n-3 fatty acids	2 g daily	↑ triglycerides	Minimal	Bleeding time

Treatment should commence with a statin. If LDL-C levels are not reduced to target levels or a maximally tolerated dose on a statin, add one of ezetimibe,[5,8] bile acid binding resin or nicotinic acid. These agents can be used as monotherapy if statins cannot be tolerated.

Hypercholesterolaemia especially ↑ LDL-C

Choose from the following.[6,9]

First-line agent

1. HMG-CoA reductase inhibitors (statins—see TABLE 78.4): supported by evidence but be cautious in patients with muscle or hepatobiliary disease. Typical reduction is 30–50%.[9]

   - Adverse effects: GIT side effects, myalgia, abnormal liver function (uncommon)
   - Monitor: measure LFTs (ALT and CPK) and CK as baseline
   - Repeat LFTs after 4–8 weeks. It is no longer recommended to continue to monitor these unless patient becomes symptomatic.[5]

   Additional drug therapy (options):

2. Ezetimibe 10 mg daily (especially if statin-intolerant). Reduces LDL by about 18%.[9]
3. Combination: ezetimibe + statin (consider if cholesterol above target)[8]
4. Bile acid binding resins (typically reduce LDL by 15–24%):

   - e.g. cholestyramine 4 g daily in fruit juice increasing to maximum tolerated dose (often poorly tolerated)
   - adverse effects: GIT side effects (e.g. constipation, offensive wind)

5. Fibrates: consider if above drugs not tolerated (e.g. fenofibrate 145 mg (o) daily—special care with renal impairment)
6. Nicotinic acid

   - nicotinic acid 250 mg (o) bd with food daily, increase gradually to max. 1000 mg tds if necessary (effective lipid reduction)
   - adverse effects: flushing (common), gastric irritation, gout
   - minimise side effects with gradual introduction; take with food

7. Evolocumab: an injectable PCSK9 monoclonal antibody agent for familial hypercholestoerolaemia and muscle-related statin intolerance[10]

Resistant LDL-C elevation

1. Combination statin + ezetimibe

2. Combined statin and resincholestyramine 4–8 g (o) mane
   plus
   a statin

Moderate to severe (isolated or predominant) TG elevation[6]

Fibrate:

gemfibrozil 600 mg (o) bd

or

fenofibrate 145 mg (o) daily

Note: Slow response; monitor LFTs; predisposes to gallstones and myopathy

and/or

n-3 fish oil concentrate 6 g (o) daily in divided doses to max. 15 g/day

add

nicotinic acid if insufficient response

Note: Statins are not effective at reducing triglycerides, but may be indicated to reduce overall CV risk. Reduction in alcohol intake is important.

Massive hypertriglyceridaemia (TG) 10 mmol/L

- Fibrate plus fish oil plus (if necessary) nicotinic acid

Mixed hyperlipidaemia (↑ TG + ↑ LDL-C)

- If TG <4: a statin
- If TG >4: a fibrate

Consider combination therapy, e.g.:

- fish oil + statin
- fibrate + resin

Note: Statin + gemfibrozil increases risk of myopathy and should ideally be avoided.

Familial hypercholesterolaemia[11]

This is a dominant inherited condition causing accelerated cardiovascular disease by 20–40 years. Diagnosis requires exclusion of secondary causes, e.g. nephrotic syndrome. Refer to Dutch lipid diagnostic criteria.[11]

Special considerations

The decision to commence drug therapy should be based on at least two separate measurements at an accredited laboratory.

Be careful with beta blockers and diuretics affecting lipid levels.

Length of treatment

Possibly lifelong, although the need to consider deprescribing may become the priority with age over 75 years and increasing frailty or reduced life expectancy.

Follow-up investigations

- Serum lipids (overly frequent testing is widespread—for those on therapy, don't monitor levels more often than 6–12 monthly without good reason)
- LFTs (ALT and CPK)
- Possibly CK
- Biochemical monitoring

Special groups

Children

In general there is little justification for using lipid-regulating drugs in children, especially as the drugs have been shown to reduce heart disease within 2–5 years in adults.[6] Initial dietary advice and avoidance of smoking is recommended. Bile acid binding resins are safe to use.

The elderly

A 2019 cohort study based in primary care looked at statins for primary prevention in those aged >74 years.[12] It suggested statins were *not* associated with a reduction in mortality or cardiovascular disease, and this was confirmed in a 2019 meta-analysis.[13] There was a small reduction in CVD in those with diabetes up until age 85 years. Statins remain useful in secondary

prevention regardless of age.

Pregnancy[6]

As a general rule the increase in cholesterol level associated with pregnancy subsides after delivery. Systemically absorbed lipid-lowering agents may be unsafe during pregnancy and should be avoided.

Complementary therapy

Claims have been made for the cholesterol-lowering properties of policosanol (derived from sugar cane), fish oils, plant sterols, vitamin E, garlic and lecithin.

A 2018 Cochrane systematic review[14] found good evidence that taking fish oil supplements does *not* reduce cardiovascular or all-cause mortality, so they should no longer be recommended for that purpose. It found lower quality evidence that eating more foods containing omega-3 fats (fish, nuts, seeds) in the diet may be slightly protective.

The evidence from RCTs to date indicates a possible modest benefit on cholesterol from policosanol[15] and plant sterols[16] but there is insufficient evidence to recommend vitamin E, garlic and lecithin.[17]

Patient education resources

Hand-out sheets from *Murtagh's Patient Education* 8th edition:

- Cardiovascular (including coronary) risk factors
- Cholesterol: how to lower cholesterol

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79 Chronic kidney disease

I have never yet examined the body of a patient dying with dropsy attended by albuminous urine, in whom some obvious derangement was not discovered in the kidneys.

RICHARD BRIGHT 1827

In the diagnostic model the problem of chronic kidney disease (CKD) as a masquerade has been highlighted. The reason for this is that the dysfunction associated with progressive CKD can be difficult to diagnose as there may be no or minimal symptoms. The underlying cause needs to be identified. In some cases it may present as a subtle terminal illness. It is important that all general practitioners are aware of the seriousness of the problem and keep it in mind when the patient presents with apparent minor problems such as fatigue or weakness. Sometimes the kidneys can develop acute failure over days (acute kidney injury) which may recover or progress to chronicity.

> If CKD is detected early and managed appropriately then the otherwise inevitable deterioration in kidney function can be reduced by as much as 50% and may even be reversible.[1]

Key facts and checkpoints

- The definition of CKD has broadened over the years, particularly with the introduction of estimated glomerular filtration rate (eGFR) thresholds, leading to an increase in the percentage of the population defined as having CKD.
- 10% of adults attending Australian general practice[1] have CKD but most do not know it.
- At least 95 people per million of the world's population are treated for end-stage kidney disease (ESKD) each year.
- Two-thirds of these are under 60 years of age.
- Important causes are glomerulonephritis (25%), diabetes mellitus (35%), polycystic kidney disease (8%), reflux nephropathy (8%) and hypertension (13%) (see TABLE 79.1).[2]

- The commonest cause of ESKD in Australia is diabetes.
- The commonest cause of nephritis leading to kidney failure in Australia is IgA nephropathy.
- In children the incidence of chronic kidney failure is low (1 to 2 per million of the population).[2]
- Warmer climates, poorer living conditions and certain genetic predispositions are associated with a higher prevalence of kidney disease.
- Kidney failure should be considered in the diagnosis of patients with unexplained anaemia, unexplained poor health and unusually high analgesic intake.[2]
- CKD is an important risk factor for (and marker of) cardiovascular disease.
- Uraemic symptoms are non-specific and usually are not recognised until the creatinine clearance is less than 20% of normal.
- CKD is characterised by the accumulation of uraemic toxins and a deficiency of kidney hormones that cause dysfunction of organs other than kidneys.
- This interaction can cause phosphate retention, secondary hyperparathyroidism and bone disorders such as osteomalacia.
- Age is an issue—we lose 1% of renal function per year.
- CKD is classified into stages (see TABLE 79.2).

Table 79.1 Significant causes of chronic kidney failure (approximate order of prevalence)

Diabetes mellitus

Glomerulonephritis

- IgA nephropathy (commonest)

Hypertension

Vascular

- atherosclerosis, including kidney artery stenosis

Polycystic kidneys

Obstructive nephropathy/reflux

- bilateral ureteric obstruction
- bladder outflow obstruction: prostatic enlargement

Drugs, including analgesic nephropathy

Lupus and other connective tissue disorders

Vasculitides, e.g. polyarteritis nodosa (PAN)

Gout

Amyloidosis

Multiple myeloma

Hypercalcaemia

Table 79.2 Classification of chronic kidney disease stages[1,3]

Note: A low glomerular filtration rate (GFR) and high urinary albumin–creatinine ratio (ACR) should be repeated 3 months later, to confirm the definition of 'chronic' kidney disease.

CKD stage	GFR (mL/min)	Description	Clinical action plan
1	>90 plus proteinuria	Evidence of kidney damage (e.g. scarring on ultrasound, proteinuria/haematuria)	
2	60–89 plus proteinuria	Evidence of kidney damage Mild kidney failure	Further investigation for those at risk: • Assess proteinuria • Urinalysis • BP Cardiovascular risk reduction: • BP, cholesterol, blood glucose, smoking, obesity
3 3a 3b	30–59 45–59 30–44	Moderate kidney failure	As above, plus • Avoid nephrotoxic drugs • Monitor eGFR 3 monthly

			• Prescribe antiproteinuric drugs, ACE inhibitors or ARBs if appropriate • Address anaemia, acidosis, hyperparathyroidism • Ensure drug dosages are appropriate for level of kidney function Consider referral to nephrologist
4	15–29	Severe kidney failure	As above, plus • Referral to nephrologist • Prepare for dialysis or transplantation (if appropriate)
5	<15	End-stage kidney failure	As above, plus • Institute dialysis or transplantation (if appropriate)

Acute kidney injury

Acute kidney injury (AKI, also called acute kidney failure) is defined as a sudden (hours to weeks) decrease in kidney function (azotaemia) with or without oliguria. It results in dysfunctional fluid and electrolyte balance and nitrogenous waste excretion with a sudden increase in serum urea and creatinine levels. It can be a forerunner of CKD.

AKI is usually classified into:

- prerenal (e.g. acute circulatory failure → kidney hypoperfusion)
- postrenal (e.g. obstruction)
- kidney (intrinsic) (e.g. acute glomerulonephritis)

Early diagnosis with hospital admission is important and this is achieved by being aware of the patient at risk and the early detection of hypovolaemia, hypertension or hypotension, oliguria or urine abnormalities.

Treatment options include renal dialysis, blood filtration and fluid and electrolyte restriction.

 **DxT** malaise (extreme) + a/n/v + confusion (± oliguria) → AKI

Chronic kidney disease

Chronic kidney disease (CKD) is diagnosed as:[1]

- an estimated or measured glomerular filtration rate (GFR)[1] <60 mL/min/1.73m[2] that is present for ≥3 months with or without evidence of kidney damage
  or
- evidence of kidney damage that is present for ≥3 months with or without decreased GFR, as evidenced by the following (irrespective of the underlying cause):

  albuminuria

  haematuria after exclusion of urological causes

  structural abnormalities (e.g. on kidney imaging tests)

  pathological abnormalities (e.g. renal biopsy)

CKD can present surreptitiously and be a real master of disguise in clinical practice. It may be discovered on routine health screening, as a chance finding in a hospitalised or hypertensive patient, or during follow-up of patients with known kidney disease.[4] Symptoms only manifest when stage 4 is reached.

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Important clinical associations[5]

The possibility of CKD should be monitored in patients with:

- diabetes
- hypertension
- established cardiovascular disease
- severe gout
- a history of urinary tract abnormality (e.g. vesicoureteric reflux, bladder outflow obstruction) or kidney failure

The possibility of CKD should be considered and investigated in patients presenting with:

- unexplained poor health

- hypertension
- anaemia
- pruritus
- hyperparathyroidism
- pericarditis
- urinary tract symptoms or signs: proteinuria, haematuria, oedema, nocturia, loin pain, prostatic obstruction
- neurological disturbances: confusion, coma, peripheral neuropathy, seizures

Patients with CKD may present with features of acute kidney failure in the presence of complicating factors such as:

- drug toxicity
- infection
- fluid imbalance

Urgent treatment of the following conditions, which can lead to rapid kidney failure, is essential:

- progressive nephritis
- systemic lupus erythematosus
- vasculitides (see CHAPTER 21), for example, polyarteritis nodosa, Wegener granulomatosis

Risk factors for chronic kidney disease[5]

Non-modifiable	**Modifiable**
Age >60	Diabetes
Family history	Hypertension
Aboriginal or Torres Strait Islander origin >30 years	Smoking
History of acute injury	Obesity—BMI ≥30

The clinical approach

History

A hallmark of early-stage CKD is a non-specific history and examination, and the diagnosis is very difficult in the absence of a known past history of kidney disease. Inquire about drugs, UTIs, LUT symptoms, systemic disease and family history. The diagnosis can be established only by kidney function tests. Symptoms from CKD are rare unless the creatinine clearance is less than 20% of normal and only become common when less than 10% of normal.

In CKD, symptomatic uraemia may be precipitated by prerenal factors, such as fluid loss from vomiting or diarrhoea, infection, antibiotic therapy especially tetracyclines, or increasing hypertension.

Symptoms and signs

The symptoms and signs of CKD are summarised in FIGURE 79.1 .

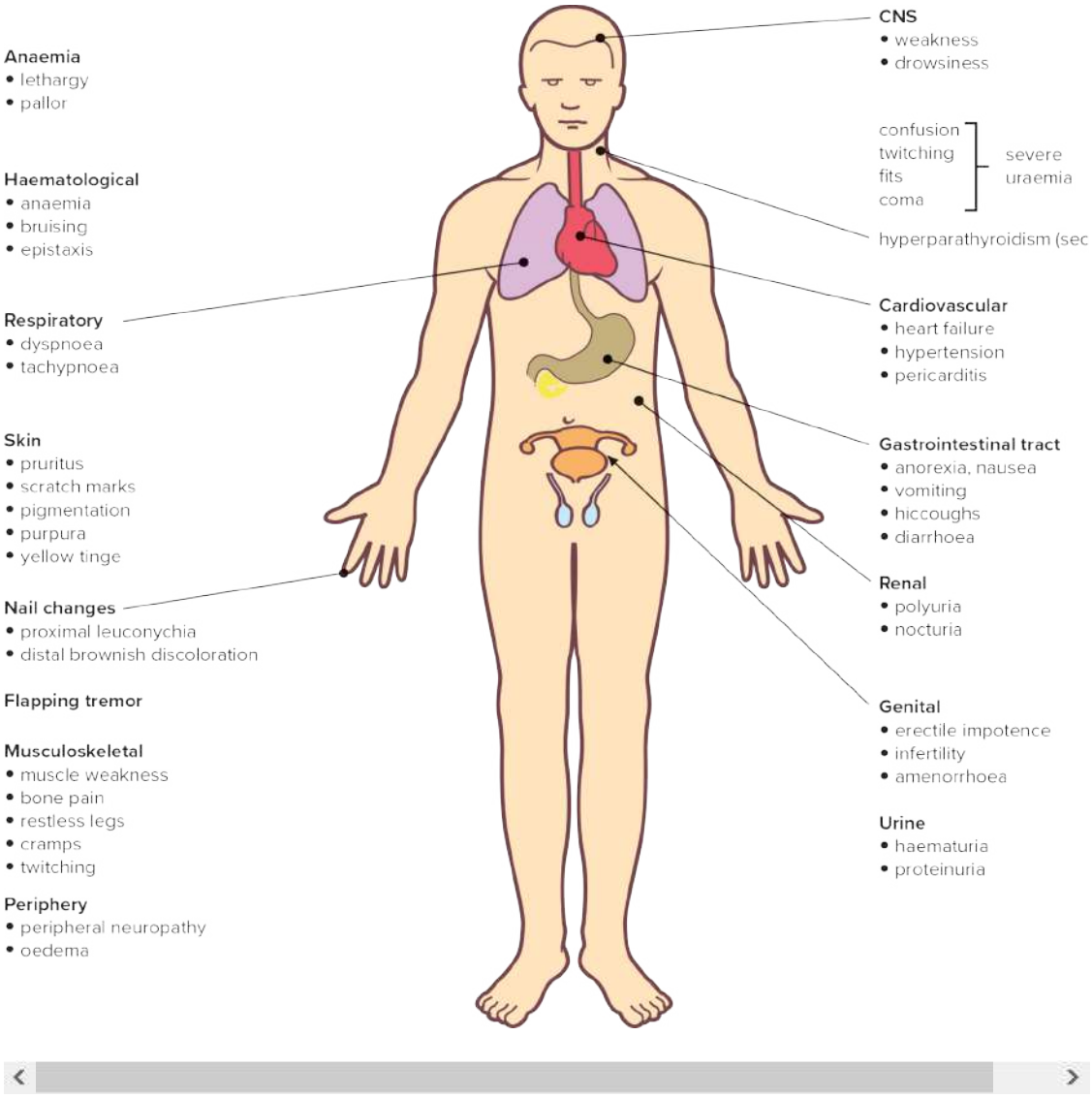

FIGURE 79.1 Clinical features of chronic kidney failure

The common early presenting symptoms are generally non-specific and referable to the GIT, presumably due to the formation of ammonia in the upper GIT. However, anaemia is the main cause of symptoms.

Symptoms that indicate uraemia include:

- malaise
- anorexia, nausea, vomiting
- tiredness/lethargy
- nocturia

- restless legs (esp. if eGFR <15)
- pruritus
- dyspnoea

If someone presenting with these symptoms and has a sallow ‘lemon’ tinge appearance due to a combination of anaemia and brownish pigmentation, CKD should be highly suspected.

DxT fatigue + a/n/v + sallow skin → CKD

Physical examination[6]

General inspection of the patient with CKD will usually reveal a sallow complexion with yellow-brown pigmentation in the skin, which is often dry and pruritic. The patient’s mental state should be noted. The respiratory and pulse rates are usually rapid because of anaemia and metabolic acidosis. Other findings may include bruising, uraemic fetor, reduced mental status, pericarditis and peripheral neuropathy. The abdomen should be carefully palpated, especially in the renal angles. A rectal examination is indicated to detect prostatomegaly or other rectal or pelvic pathology. Ophthalmoscopic examination may show hypertensive or diabetic retinopathy. Urinalysis may indicate glucose, blood and protein. This involves a dipstick testing on the first morning specimen. Proteinuria should be confirmed with an albumin–creatinine ratio (ACR), whereas 24-hour urine protein estimation is usually reserved for hospital inpatients.

ACR guidelines

Normoalbuminuria

Men: <2.5 mg/mmol
Women: <3.5 mg/mmol

Microalbuminuria

Men: 2.5−25 mg/mmol
Women: 3.5−35 mg/mmol

Macroalbuminuria (if persistent, indicates moderate to severe CKD)

Men: >25 mg/mmol
Women: >35 mg/mmol

Investigations

- Urine dipstick (poor sensitivity and specificity)[1]
- Albumin–creatinine ratio (24-hour urine protein occasionally required)
- Microculture of urine
- ESR and FBE (?anaemia)
- Kidney function tests (most appropriate for the GP):
    - plasma urea
    - plasma creatinine
    - creatinine clearance (more precise)
    - eGFR (the new standard)
- Plasma electrolytes:
    - sodium, potassium, chloride, bicarbonate
    - calcium and phosphate
- Consider:
    - magnesium, urate, glucose
    - lipids
    - prescribed drug level
    - cardiac studies
    - protein electrophoresis (?myeloma)
    - ANA for lupus
    - ANCA for vasculitis
- Determination of underlying cause:
    - imaging of urinary tract—ultrasound
    - immunological tests
    - kidney biopsy (nephrologist will assess need)
- Biochemical changes—elevation of:

potassium

phosphate

creatinine and urea

urinary protein

hydrogen ions → acidosis; anion group

Monitoring CKD

The traditional test in identifying and monitoring CKD is the serum creatinine level.[7] The normal range is about 40–120 µmol/L (0.04–0.12 mmol/L) but the laboratory will indicate their appropriate reference level. However, serum creatinine is an unreliable and insensitive marker of CKD, so laboratories report on estimated glomerular filtration rate (eGFR) using the CKP-EPI (chronic kidney disease epidemiology collaboration) formula, which is required to calculate GFR.

Although common in older people, an eGFR <60 is associated with increased risks of adverse clinical outcomes, especially renal and cardiovascular.

Guiding rule

eGFR = 140 − age

Drug prescribing in CKD[3,8]

Drugs that can damage the kidneys include:

- classic nephrotoxic drugs, e.g. gentamicin, vancomycin
- NSAIDs, COX-2 inhibitors
- aminoglycosides
- cephalosporins (various)
- tetracyclines
- lithium
- colchicine

Beware of the ‘triple whammy’

- NSAIDs/COX-2 inhibitors
- ACE inhibitors
- Diuretics

These three agents individually or in combination are implicated in over 50% of cases of iatrogenic acute kidney injury.[9]

Diuretics should be used with care.

Drugs causing hyperkalaemia

- NSAIDs/COX-2
- ACE inhibitors
- ARBs
- Aldactone
- Amiloride
- Trimethoprim
- Digoxin

Increased risk of adverse reaction in CKD

- Allopurinol:
  - vasculitis
  - liver dysfunction
- Statins:
  - liver dysfunction
  - myopathy
  - rhabdomyolysis
- Gemfibrozil: rhabdomyolysis. *Note:* Do not use statins and gemfibrozil together in CKD

- Beta lactams: interstitial nephritis
- LMW heparin: bleeding
- Aspirin/NSAID: GIT bleeding
- Omeprazole and related agents: interstitial nephritis

Dangerous drug accumulation is presented in TABLE 79.3 .

Table 79.3 Dangerous drug accumulation in kidney impairment[7]

Drug	Problem
Aciclovir	Confusion, encephalopathy
Cotrimoxazole	Stevens-Johnson syndrome
Metronidazole (long term)	Peripheral neuropathy
Penicillin (high dose IV)	Seizures
Quinolones: • ciprofloxacin • norfloxacin	Seizures
Metformin	Lactic acidosis
Sulfonylureas	Prolonged hypoglycaemia
Insulin	Hypoglycaemia
Atenolol	Bradycardia/heart block
Digoxin	Nausea, bradycardia
Sotalol	Ventricular tachycardia (Mg required before conversion)
Codeine	Confusion, acute brain syndrome
Methotrexate	Liver dysfunction Bone marrow depression
Lithium	Tremor—confusion Thyroid dysfunction

Management

The basic object is to slow progression of disease. Managing cardiovascular risk factors becomes more urgent, both to slow progression and also because the presence of CKD is a sign of increased CV morbidity and mortality risk. In particular, aggressively managing hypertension achieves both aims.

The underlying disease and any abnormalities causing progressive kidney damage must be corrected where possible. The management of CKD is based on a team approach involving specialists and allied health, including a dietitian. Attention to lifestyle, especially nutrition and fluid control, is fundamental. The patient is usually faced with years of ongoing care so that an empathic support team based around the GP is very important to the patient, who will require considerable psychosocial support. The common problem of depression necessitates surveillance.

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Optimum treatment includes:

- regular review
- good blood pressure control (the most effective way to slow progression)
- maintaining effective fluid and electrolyte balance
- prompt treatment of intercurrent illness
- judicious use of drugs
- avoid treatment errors, especially with drugs

    avoid potassium-sparing diuretics

    avoid nephrotoxic medications

    other drugs that may cause problems include digoxin, tetracyclines, gentamicin, NSAIDs and nitrofurantoin
- rapid treatment of complications, especially salt and water depletion and acute urinary tract infection
- diet: low protein, sodium and potassium
- avoid toxins: nicotine, excessive alcohol or caffeine
- treat anaemia with human recombinant erythropoietin and iron (iron infusions)
- attention to an advanced care plan

Targets: goals of management[1,5]

The following are optimal targets for patients with chronic kidney disease:

- blood pressure
  - <140/90 mmHg if proteinuria
  - ≤130/80 mmHg if albuminuria, diabetes
- cholesterol: total <4.0 mmol/L; LDL <2.5 mmol/L
- blood glucose: pre-prandial 4.4–6.8 mmol/L
- HbA1c: ≤7%
- haemoglobin: 100–115 g/L
- serum potassium: ≤6 mmol/L
- BMI: 20–25 kg/m^2
- serum albumin: >35 g/L
- albuminuria: ≥50% reduction of baseline value
- acidosis: HCO_3^- >22 mmol/L
- phosphate: PO_4^{3-} ≤1.75 mmol/L
- no smoking
- alcohol: ≤2 standard drinks/day

The main goal is to treat blood pressure, achieve resolution of proteinuria and reduce CVD risk. Recommend an advanced care plan.

Blood pressure control

- No added salt diet (with care)
- Drug control: none of the antihypertensive agents is specifically contraindicated but those eliminated mainly by the kidney (e.g. ACE inhibitors, atenolol, sotalol) should be given in lower dosage. ACE inhibitors should not be used in the presence of renal artery stenosis; loop diuretics (e.g. frusemide) are effective in larger doses.[2] The first-line agents are ACEIs or ARBs, which should not be used together. Evidence is equivocal about whether they should be ceased in advanced stages of CKD,[10] but cease them if the serum K exceeds 6 mmol/L (despite dose reduction).[4] The non-dihydropyridine calcium-channel blockers are next choice. Beta blockers can be used. Diuretics have a vital role in individuals with diastolic heart failure (see CHAPTER 76).[8] Control the blood pressure to the lowest tolerable level, to protect GFR.

Anaemia

- Exclude chronic infection and iron deficiency.
- Give iron for iron deficiency and erythropoietin for Hb <100 g/L, as guided by a nephrologist.
- Avoid transfusions where possible.

Hyperphosphataemia control

- Balanced nutrition to reduce dietary phosphate
- Protein restriction
- Calcium carbonate tablets (to bind phosphate)

Hyperkalaemia treatment

(A concern if >6.5 mmol/L.)

- Low potassium diet
- Cease ACEI/ARB/spironolactone (if applicable)
- Nebulised salbutamol (increases intracellular K^+)
- IV insulin and dextrose
- IV calcium gluconate

- Oral resonium A
- Then dialysis

Dialysis

Dialysis is indicated when all other methods fail. It is time-consuming and costly. About two-thirds of patients receive haemodialysis and about 22% are on continuous ambulatory peritoneal dialysis and automated overnight peritoneal dialysis (nocturnal dialysis).

The preferred access is via an AV fistula usually between the radial artery and a cephalic vein. Never take bloods from, or use a sphygmomanometer on, an arm that has an AV fistula.

Transplantation

Transplantation is the treatment of choice for kidney failure except where contraindicated, such as with active malignancy or tuberculosis and perhaps the elderly. However, a critical shortage of donors remains a problem. Rejection and infection are problems, occurring especially in the first 6 months. As a rule, never stop the immunosuppressants. With time there is a high rate of malignancy especially of skin, lymphoma × 5−10 and solid organs × 2−3 (except breast and prostate).

Chronic kidney failure in children

The incidence of CKF in children is about two per million of the total population per year. The commonest causes include chronic glomerulonephritis, obstructive nephropathy and reflux nephropathy. Identification of structural kidney abnormalities by obstetric ultrasound and early investigation of urinary tract infections may decrease the incidence of CKF. Dialysis and transplantation are normally considered for children over 2 years of age with end-stage CKF. For children under 2 years there are complex ethical, psychological and technical problems.[7] Regardless, the prognosis for such treatment is poor.

Chronic kidney failure in elderly

An eGFR <60 is common but still predictive of significant increased risk of adverse clinical outcomes. Individualise management according to how evidence-based risks and benefits apply to that particular person, taking into account both quantity and quality of life and patient preference.

When to refer[4]

- (Glomerular) haematuria
- eGFR <30 (stage 4 or 5 CKD)

- Rapidly declining kidney function
- Significant proteinuria >1 g/24 hours or ACR >30
- Glomerular haematuria with macroalbuminuria
- Kidney impairment + hypertension (poor control)
- Diabetes with kidney impairment: eGFR <60 or albuminuria/proteinuria

Experienced GPs may be comfortable managing some of these circumstances if no complex investigation (such as renal biopsy) is indicated.

Any person with rapidly declining eGFR and/or signs of acute nephritis (oliguria, haematuria, oedema and acute hypertension) should be regarded as a medical emergency.

Patient education resource

Hand-out sheet from *Murtagh's Patient Education* 8th edition:

- Kidney disease

Resources

Kidney Health Australia: www.kidney.org.au

Renal Drug Reference Guide: www.renaldrugreference.com.au

National Aboriginal Community Controlled Health Organisation: www.naccho.org.au

Australian absolute cardiovascular disease risk calculator: www.cvdcheck.org.au

NICE guidelines, chronic kidney disease: www.nice.org.uk

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80 Obesity

Persons who are naturally very fat are apt to die earlier than those who are slender.

HIPPOCRATES

A century ago, infectious diseases were the health scourge of humanity (particularly in childhood) so efforts in public health and medicine focussed on measures such as hygiene, vaccinations and antibiotics. Every four years since then, on average, the life expectancy in many developed nations increased by one full year. By the 1980s mortality due to chronic diseases began to outstrip that of infections. The 21st century has seen many other nations follow suit—notably China and India, which together comprise more than a third of the world's population.

Obesity is prime among the emerging chronic conditions, whether viewed as a disease in its own right, or as a risk factor for other diseases: particularly cardiovascular disease, diabetes and cancer. Almost a third of Australian adults (5.8 million people) are obese, and another 6.7 million people are classified as being overweight.[1]

Obesity is a complex, chronic, recurring health condition. In other words, a condition ideally suited to management in general practice. Australian patients, consistent with international surveys, indicate that they would appreciate more involvement from their GP in the management of obesity.[2] Maintaining substantial weight loss is important—it may even be life-saving—but it is not easy.

The general practitioner's skills may be tested over a long period of time: encouraging initial weight loss, sustaining that weight loss and helping to overcome setbacks. Helpful 'tools' include brief motivational intervention, advice, encouragement, recommending support groups, coordinating allied health (dietitian, exercise physiologist, psychologist) and occasionally using medication or a surgical referral. All the while, attention must be paid to managing related risk factors and comorbidities.

The causative interaction between obesity and medical conditions can be a two-way street; for example, mechanical problems such as osteoarthritis and sleep apnoea are both caused by, and worsen, obesity. A third factor (particularly the 'lifestyle choices'—nutrition and physical activity) can independently lead to both obesity and to a medical condition, notably cardiovascular disease. The causative pathway has implications for treatment, because reversing obesity does not always improve health, and health may be improved without losing a gram in

weight.

That being said, the usual medical goal for people with obesity is a sustained weight reduction through improvements in lifestyle, thereby improving quality of life and reducing morbidity and mortality risks.

Table 80.1 Health conditions caused by obesity

Cardiovascular

- increased mortality (stroke, ischaemic heart disease, etc.)
- hypertension*
- varicose veins

Metabolic

- dyslipidaemia*
- type 2 diabetes*
- hyperuricaemia/gout
- infertility
- PCOS

Mechanical

- osteoarthritis
- obstructive sleep apnoea*
- restrictive pulmonary disease
- spinal dysfunction
- back pain
- urinary incontinence

Other

- hiatus hernia/GORD
- gall bladder disease*
- fatty liver
- cancer (various)
- kidney disease (check for microalbuminuria)
- excessive daytime sleepiness
- erectile dysfunction/subfertility
- psychological problems/depression/anxiety

*Indicates relative risk > 3

Obesity is responsible for 80% of type 2 diabetes, 35% of ischaemic heart disease and 55% of hypertension in European adults.

Measuring obesity

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m}^2\text{)}}$$

- Screen using Body Mass Index (BMI) and waist circumference every two years in adults.[3]
- 'Healthy' adult BMI is 18.5–25 kg/m^2 (see TABLE 80.2)
- BMI is a handy but rough guide to cardiovascular risk and ideal weight targets. Bear in mind that the 'J-shaped' risk curve (see FIG. 80.1) varies according to ethnicity and age, the presence of established disease and muscle–fat ratio.
- Many professional sportspeople have a BMI above 25, but this does not make them 'unhealthy'. In people aged over 70 years, the curve is shifted to the right, with the lowest point on the mortality curve lying within the 'overweight' range.[4]
- A BMI of >40 confers a threefold mortality risk.
- Children's BMI must be interpreted using age-specific ranges.
- For waist circumference, place a stretch-resistant tape on bare skin at the level mid-way between the lateral rib margin and iliac crest, and measure at the end of normal respiration.

  Thresholds for increased mortality risk (and high mortality risk respectively) in females are >80 cm (>88 cm), and in males >94 cm (>102 cm).

Table 80.2 Classification of adult obesity (based on WHO guidelines)[5]

BMI	Grading	Suggested therapy
<18.5	Underweight	Diet and counselling
18.5–25	Healthy weight	
25–30	Overweight	More exercise Diet: less alcohol
30–35	Class I: mildly obese	Combined program: • behaviour modification • diet • exercise

35–40	Class II: moderately obese	Consider medical therapy if >35
≥40	Class III: severely obese	Combined program plus medical therapy Consider gastric surgery

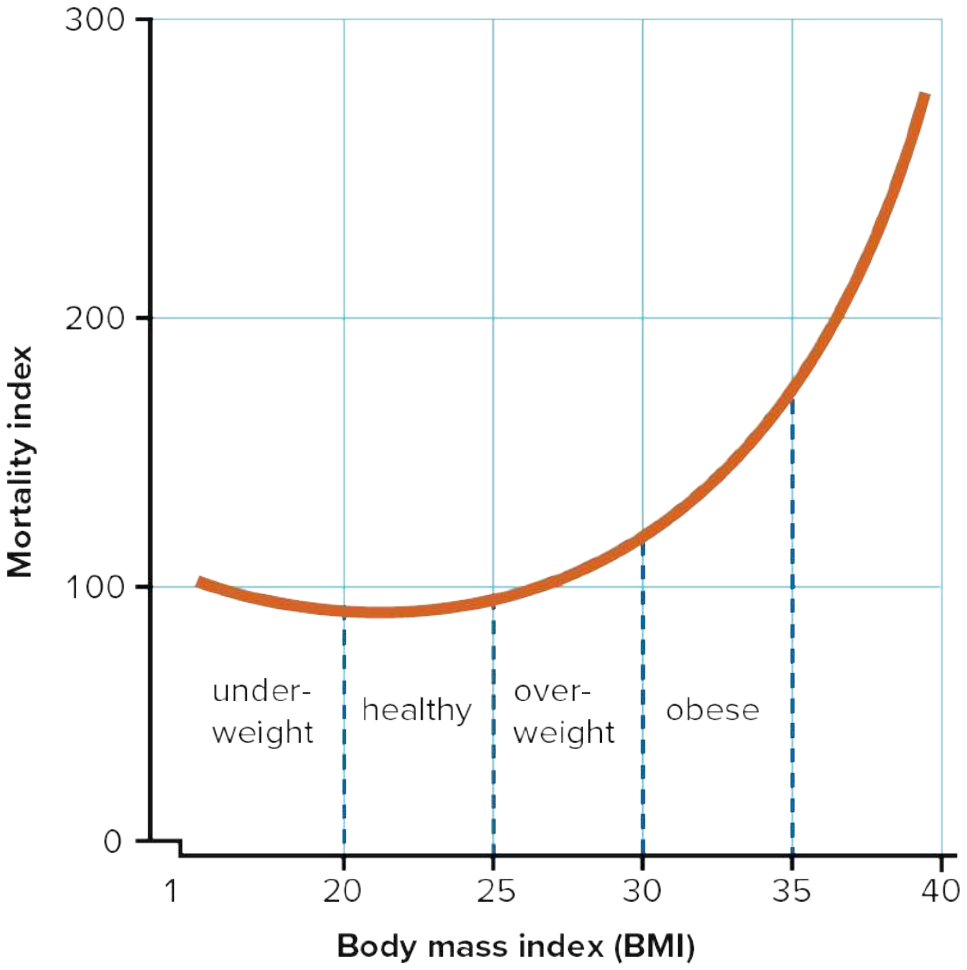

FIGURE 80.1 Mortality vs body mass index (BMI) reference scale. Note the 'J'-shaped curve.

Other anthropomorphic measurements

- Waist–hip circumference ratio (W/H ratio): a slightly better predictor of cardiovascular risk than BMI. Obesity with a high waist–hip ratio (>1.0 in men and >0.9 in women) confers a significantly greater risk of diabetes, stroke, coronary artery disease and early death than a similarly obese BMI with a lower waist–hip ratio. Thus, abdominal fat ('apple' body shape,

central adiposity) is a greater health hazard than fat in the thighs and buttocks (‘pear’ shape) (see FIG. 80.2)

- Single skinfold thickness (>25 mm suggests increased body fat)
- Four skinfold thicknesses (sum of suprailiac, subscapular, triceps and biceps skinfolds)—estimates percentage body fat, but is impractical for most GPs

Note that most of the excess mortality is due to the presence of obesity-related health conditions, rather than to the obesity itself. Obesity on its own, in the absence of other conditions and risk factors, increases mortality only by around 20%.[6]

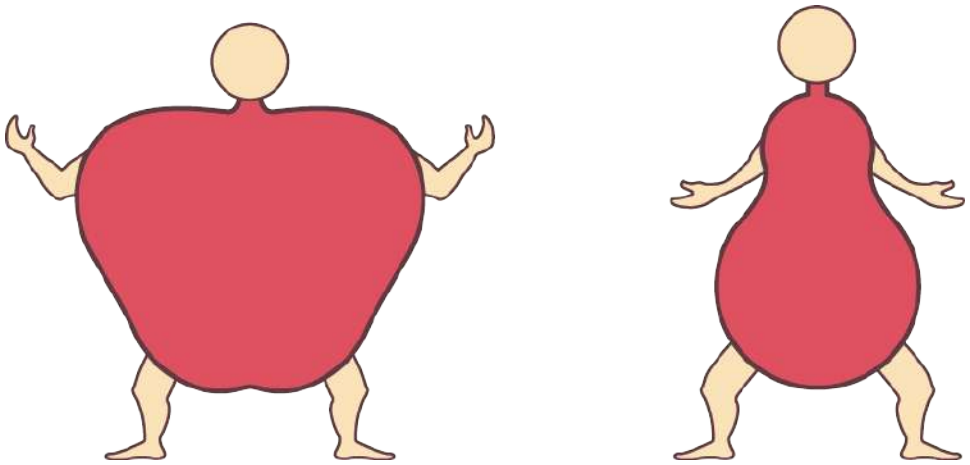

FIGURE 80.2 Comparison of two types of obesity according to distribution of body fat

Causes of obesity

Primary causes of obesity

The NHMRC obesity guidelines point out that:

> Diet and physical activity are central to the energy balance equation, but are directly and indirectly influenced by a wide range of social, environmental, behavioural, genetic and physiological factors.[7]

A complex array of hormones, including ghrelin, leptins, insulin and thyroid hormones, are responsible for moderating appetite, energy intake and energy expenditure over time; they ‘defend’ against straying too far above or below an ideal body weight.

However, when energy intake is consistently larger than energy expenditure over a long period, the body ‘resets’ to maintain a higher body weight. This tendency to reset is influenced by the

individual's genetics, epigenetics (particularly in utero) and early childhood experience. The last two of these are potentially modifiable via antenatal care and support in early childhood, including breastfeeding support.

Many of the sociocultural, political, legal and economic frameworks of developed nations help contribute to an 'obesogenic' environment. Thousands of examples abound; for example, a USA study indicated that a one standard deviation increase in the density of fast-food outlets was associated with a 7% increase in overweight/obesity.[8]

Australian obesity expert Professor Gary Egger notes that:

> Obesity is seen more as 'a canary in a mineshaft' signalling problems in the broader environment, suggesting that population obesity management should be focussed more upstream if chronic diseases are to be better managed.[9]

General practitioners will vary in their enthusiasm for becoming involved in the 'big picture' local environment; advocating for local improvements in food marketing and availability, sport and exercise programs, and the urban built environment.

Secondary causes of obesity

A large number of medical conditions and their treatments can cause obesity. See TABLE 67.1.

- *Modifiable*. Particularly consider iatrogenic causes such as medications. The dose of a steroid, antipsychotic or hypoglycaemic medication may be reduced, ceased or substituted.
- *Non-modifiable* (e.g. congenital). Concentrate on managing obesity with the end goal of improving health and function.
- *Requires diagnosis*. Weight gain, particularly of recent onset, may warrant searching for a secondary cause via history, examination and investigation. Hypothyroidism causes classic obesity, while cardiac failure and nephrotic syndrome cause fluid retention that may be mistaken for adiposity.

See CHAPTER 67 .

Managing obesity

Raising the issue during a consultation

GPs should find appropriate opportunities to discuss weight management as a preventive health measure when:

- the patient raises the issue
- the presenting issue is loosely related (e.g. discussing abnormal liver function or writing

repeats for cardiovascular medications)

- performing a dedicated health check
- an opportunistic chance arises

Asking about weight should be done sensitively, using non-judgmental language and listening carefully to the responses. Be aware that for many, obesity is a sensitive issue that may have an emotional (sometimes traumatic) ‘back story’ entirely unknown to the GP.

Weight stigma is common in society (the media is an exemplar) and unfortunately this also extends into the world of health services and medical professionals. Weight bias may be subconscious: attributing individual responsibility for obesity and subsequent illness in a pejorative way and to an unreasonable extent. It has been shown that people who perceive having experienced weight stigma by a health provider are less likely to partake in preventive activities such as cervical and breast screening, and more likely to have delayed cancer diagnoses.

Sensitive questioning may also uncover eating disorders such as bulimia (can cause either cachexia or obesity) and binge eating. Unless the GP has a special interest in managing eating disorders, strongly encourage a referral to a specialised unit.

Encouraging behaviour change

Successful weight loss requires some change in behaviour. Even with a ‘medicalised’ intervention such as bariatric surgery or weight medication, the patient’s behaviour around diet and physical activity remain the key to a successful outcome.

The general practice consultation is an ideal setting to use motivational interviewing techniques to encourage behaviour change. Sustainable change is far more likely when the motivation to change is shifted from external (‘Dr X told me to lose weight for my blood pressure’) to internal (‘After talking to Dr Y, I realised those truck-stop greasy foods are no good for me’).

Seemingly inflexible eating and exercise behaviours are learned and therefore can ideally be modified.[10] Counselling techniques include: stimulus control (What food is available at home and work? What are the eating triggers?); working on negative internal thoughts and self-sabotage; identifying barriers to change; then problem-solving solutions.[11] Referral to a psychologist is ideal.

Behavioural models: ‘stages of change’

A GP consultation should run entirely differently for someone in the precontemplation stage (e.g. presents with a medical condition related to obesity) compared to the preparation stage (e.g. presents to develop a weight-loss plan). The maintenance stage for someone who has successfully lost weight is crucial for maintaining long-term health benefits, so a good doctor–patient relationship is pivotal. Sustainably maintaining weight loss has been likened to holding a rubber band in outstretched hands and not letting go—it takes constant effort and attention.[11]

Diet

A healthy diet is key, and should be a primary focus of any obesity management plan. The typical Western dietary intake has too few unprocessed whole-foods (particularly vegetables and grains/legumes) and too much sugar, saturated fats, salt and (often) alcohol. CHAPTER 5 outlines the NHMRC dietary guidelines for children and adults and describes the general principles of optimal nutrition and a nutritional assessment.

Many patients will try a specific, named diet. If so, the two crucial aspects are nutritional soundness and long-term sustainability. A multitude of fad diets fail in one or both. Rapid weight loss of 5 kg during the initial enthusiastic phase is readily achievable with all manner of diets, but has limited value if the weight soon returns to baseline.

Diets with good evidence for both nutritional value and sustainability include the Mediterranean diet and the DASH diet (designed for hypertension). Other diets can be successful for weight loss depending on individual capacity to sustain them; these include intermittent fasting diets, some low-carb diets (but be alert for fads) and commercially prepared diet meals, with or without group support programs.

The '5 As' model may also be useful (see TABLE 80.3).

Table 80.3 The 5 As model for managing obesity[11,12]

Ask	Sensitively enquire about the individual's ideas, concerns and expectations around weight loss How is obesity affecting this person? What do they think might realistically work?
Assess	Record BMI, waist circumference, BP, glucose Consider important comorbidities Review lipid profile, liver function, ask about sleep apnoea and depression
Advise	Tailor advice according to the individual's knowledge gaps and motivations Delivering a routine 'spiel' is less effective than nudging the conversation towards a realistic, SMART goal
Assist	Help set up a lifestyle-based weight-loss program What support does the person need? Numerous dietary and exercise options exist—assist with the individual's selection Very low energy diets and pharmacological options require more regular review
Arrange	Review and monitor over time

Support the person's journey
Involve allied healthcare providers
Consider referral to specialist team, including bariatric surgery

Loosely adapted from Grima & Dixon[12] and Sturgiss[11].

It is important for GPs to develop a relationship with one or more trusted Accredited Practising Dietitians (APDs) and refer patients to them wherever appropriate. The *Dietitians Australia* website maintains a contact list of APDs (see: https://dietitiansaustralia.org.au/).

During review consultations (which improve the success of weight loss), be wary of 'cheering the scales' because an individual has considerably more control over what foods they eat than they do over the number that appears at the doctor's weigh-in, which may go down one week and up the next. Instead, a nutrition (and/or exercise) diary can be used as a source of encouragement. A diary may also reveal unhelpful patterns that can be a symptom of bulimia.[11]

Calorie count

1 kilocalorie (often called 1 Calorie with a capital C)	= 4.2 kilojoules (kJ)
Weight maintenance diet (varies with wt, age, gender)	≈ 2000 kcals/day (8700 kJ)
Low calorie diet	<1200 kcals/day (<5000 kJ)
Very low calorie diet (VLCD)	<800 kcals/day (<3400 kJ)

The DiRECT trial

The extent to which dietary support in general practice can be successful is exemplified by the DiRECT trial (2017–ongoing) in the UK for people with type 2 diabetes and obesity attending their usual GP.[13] The intervention group underwent intensive dietary modification (total calorie replacement for 3 months) followed by structured support for weight-loss maintenance. The control group received standard GP care. At 12 months in the intervention group, 24% had lost ≥15 kg (vs 0% control), mean weight loss was 10.0 kg (vs 1.0 kg control) and 46% had diabetes remission off all hypoglycaemic medication (vs 4% control). Most of these gains were maintained at 2-year follow-up, some 21-months after ceasing the total calorie replacement, but still receiving structured general practice support. It can be done!

Exercise

The health benefits of regular exercise (compared to a sedentary lifestyle) are more profound than the majority of other interventions that GPs regularly prescribe to prevent or manage chronic disease. Increased physical activity can alleviate a multitude of symptoms and reduces

the risk of a host of cardiovascular, respiratory, mental health and other disorders. Those benefits sometimes appear lost among the constant supply of information and competitive marketing around drug interventions. Projects such as the Handbook of Non-Drug Interventions (HANDI Guidelines)[14] seek to address this imbalance, and currently list more than 20 evidence-based indications for exercise.

However, exercise alone is unlikely to be effective for weight loss until around 3.0–3.5 hours (around 90 000 steps) is expended per week, which is more than most people can manage, in practice.[10] The flip side of this unfortunate observation is that GPs can reassure patients that their health will improve with increased physical activity long before they 'lose a kilogram' in weight.

Where the aim is weight loss, increased exercise should be accompanied by decreased calorie intake. 'Prescribe' exercise for a minimum of 150 minutes (2.5 hours) per week, choosing an activity the individual will find sustainable. This equates to around 70 000 steps/week, which will burn off around 2500 kcal in an 80 kg person. Evidence suggests that exercise for weight loss maintenance in a post-obese individual is 60–80 mins/day of moderate activity (>100 000 steps/week) combined with a hypocaloric diet.[10]

Physical activity that can be sustained is likely to be:[11]

- something the person enjoys
- affordable for them
- sustainable within their weekly schedule
- based around regular routines, e.g. travelling to work
- (if preferred) an activity with a friend or group. GPs should become familiar with the free group exercise activities in their local area (e.g. Parkrun, Active in Parks, Heart Foundation Walking, programs sponsored by state and local governments)

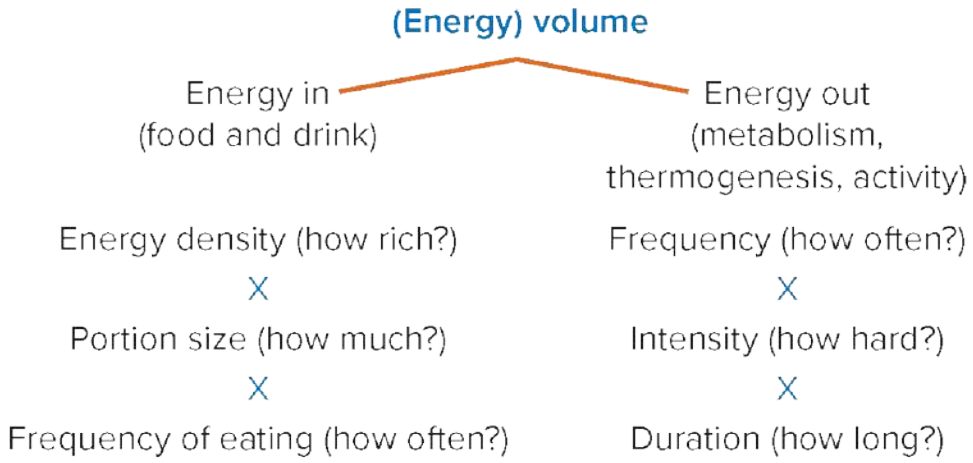

FIGURE 80.3 An energy 'volume' approach to energy balance

Source: Egger, G. Helping patients lose weight: what works? Aust Fam Physician, 2008; 37: 20–3.

Medication

Despite the enormous commercial incentives to develop a safe, well-tolerated medication that results in clinically significant weight loss and improved morbidity and mortality, no such medication exists. Hence, the repeated mantra that GPs should encourage lifestyle changes first and foremost; improvements in diet and physical activity fulfil every one of those criteria.

GPs should resist the pressure to recommend medications, supplements, over-the-counter products or therapeutic devices that are purported to aid weight loss but are not supported by evidence. This category applies to the vast majority of products on the market.

A small number of medications have some limited evidence for weight loss.

Orlistat

NHMRC guidelines state that orlistat is currently the only medication registered for use in treating obesity that has been evaluated for long-term safety.[7] It reduces intestinal fat absorption by inhibiting lipases. Unpleasant gastrointestinal side effects are common, particularly after eating high-fat meals (the avoidance of which is probably partly responsible for its efficacy).

orlistat 120 mg 3 times daily with meals containing fat

Continue beyond 12 weeks only if ≥5 kg weight loss; may be continued indefinitely.

Phentermine[7,11]

Phentermine is now only available in Australia and the USA; other countries have ceased dispensing it. It is only registered for up to 3 months' use. Side effects include hypertension, tachycardia and insomnia. Its long-term safety profile has not been tested.

Medications primarily for other indications

Some medications used for diabetes, depression or epilepsy have been found to also result in modest weight loss. These include metformin, fluoxetine and topiramate.

Of the newer classes of hypoglycaemic medication, the SGLT2 inhibitors (gliflozins) result in a mean weight loss of 2.5 kg per year, and the injectable GLP-1 agonists by around the same amount, but potentially more (4–6 kg per year) for higher-dose liraglutide in people trying to lose weight.[15]

These medications are not subsidised under the PBS for the purpose of weight loss. However, where indicated for diabetes, they have the added benefit of modest weight loss plus reductions in cardiovascular and renal risks.

Bariatric surgery

Bariatric surgery aims to reduce intake by restricting gastric capacity and/or by reducing exposure to the small bowel absorptive area. Three operations are available:

- adjustable gastric band
- sleeve gastrectomy
- roux-en-Y gastric bypass (5% risk of a complication requiring hospitalisation, 1 in 500 mortality rate)

Note: Monitor for malabsorption of iron and B12.[16]

Surgery delivers substantial weight loss: initial 20–30% in those with BMI >35 kg/m^2, and 20% longer term.[7,16] Researched health outcomes:

- Improved physical quality of life (e.g. mobility)
- Improved metabolic risk factors, cardiovascular events and deaths
- No improvement in psychological well-being, perhaps reflecting the complex psychological antecedents of obesity[16]

Bariatric surgery involves a significant up-front cost (whether borne by the patient or a third party) and post-surgical follow-up. However, it compares favourably to the annual costs of many medications for weight loss or for diabetes (particularly insulin and the newer hypoglycaemics).

Consider referral for adults with:

- BMI >40 kg/m^2
- BMI >35 kg/m^2 plus comorbidities that may improve with weight loss[7]

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81 Osteoporosis

Like bones which, broke in sunder, and well set, knit the more strongly . . . but old bones are brittle.

JOHN WEBSTER (1580–1625)

Osteoporosis, which literally means porous bone, is reduced bone mass per unit volume (see FIG. 81.1), thus predisposing the person with it to an increased risk of fracture. It also refers to the increased bone fragility that accompanies ageing and many illnesses. Following menopause, women begin to lose calcium from their bone at a much faster rate than men, presumably in response to low levels of oestrogen. By the age of 65 the rate of fractures in women has increased to 3–5 times that of men.[1] However, a third of all hip fractures in the community occur in men.

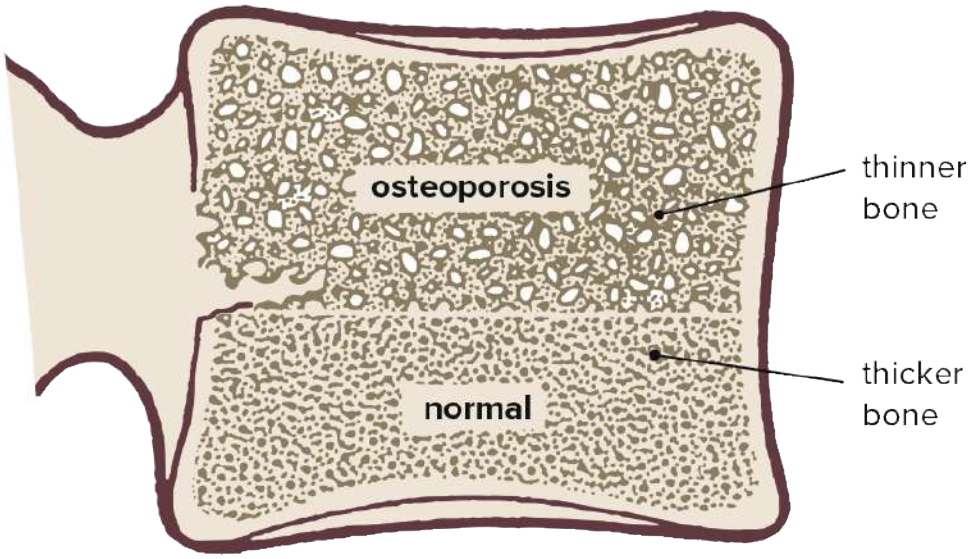

FIGURE 81.1 Osteoporosis is reduced bone mass per unit volume

In recent decades osteoporosis was largely prevented by correction of oestrogen deficiency through the use of hormone replacement therapy but the balance has changed since the controversial association of HRT with breast cancer was reported.

Key facts and checkpoints

- Osteoporosis is silent, common, measurable, treatable and potentially lethal.[2]
- Osteoporosis is commonest in postmenopausal women.
- An estimated 2 in 5 women and 1 in 4 men will develop fragility fractures in their lifetime and 30% of all women reaching 90 years of age will suffer a hip fracture.[1,3]
- Osteoporosis leads to reduced bone strength and susceptibility to fracture, even with minor trauma.
- Osteoporosis usually causes pain when complicated by fracture.
- First presentation is usually a fracture (Colles, femoral neck and vertebra) or height shrinkage.
- Vertebral collapse is the hallmark of osteoporosis.
- For osteoporosis in a vertebra including a pathological fracture, multiple myeloma needs exclusion.
- The first step in prevention is regular exercise, an adequate dietary intake of calcium (1500 mg per day) and maintenance of adequate serum vitamin D levels.

Classification[4]

Primary

Type 1: Postmenopausal (typically vertebral or distal forearm fractures between the ages of 51 and 75). Due to increased osteoclast activity. It is six times more common in women than men.

Type 2: Involutional or senile osteoporosis (typically fracture of proximal femur and other bones). It affects those over 60 years and is twice as common in women as in men.

Idiopathic osteoporosis: Occurs in children and young adults of both sexes with normal gonadal function.

Secondary

Secondary to endocrine disorders, malabsorption and malignancies. Various causes and risk

factors are presented in TABLE 81.1 .

Table 81.1 Osteoporosis: risk factors and/or causes[3]

Constitutional and non-modifiable
Female sex
Ageing: M >60, F >50 (including sarcopenia)
Thin build; low BMI <20; short stature
Race: Asian, Caucasian
Family history (e.g. maternal hip fracture <75 yrs)
Premenopausal oestrogen deficiency (e.g. amenorrhoea)
Late menarche
Early menopause <45 years (natural or surgical)
Modifiable lifestyle factors
Cigarette smoking
High alcohol intake >2 standard drinks per day
Low calcium intake
Lack of vitamin D
Physical inactivity
Medical causes
Eating disorders (e.g. anorexia nervosa)
Malabsorption syndrome (e.g. coeliac disease)
Endocrine disorders:
• Cushing syndrome
• diabetes mellitus
• hyperparathyroidism
• thyrotoxicosis
• amenorrhoea in elite athletes
• hypogonadism/sex hormone deficiency
• acromegaly
Connective tissue disorders (e.g. RA)
Chronic organ failure (kidney, liver, heart, lungs)
Drugs causing bone loss:
• corticosteroids >3 months, ≥7.5 mg/day
• anti-epileptic drugs, especially hepatic enzyme inducers
• proton-pump inhibitors