- Mitral stenosis
- Pulmonary stenosis
- Rosacea
- SLE
- Mesenteric adenitis

Spider naevi

- Pregnancy
- Liver disease
- Vitamin B deficiency in normal people

Enlarged tongue

- Acromegaly
- Hypothyroidism
- Amyloidosis
- Down syndrome

Cataracts: risk factors

- Ageing
- Senility
- Corticosteroid therapy
- Diabetes
- Hypoparathyroidism
- Dystrophia myotonia
- Trauma (may be delayed)
- Ocular disease (e.g. glaucoma)
- Smoking

Telangiectasia

- Systemic sclerosis
- CREST syndrome
- Liver disease (e.g. alcoholism)

Cyanosis

Cyanosis is a bluish discolouration of the skin and mucous membranes due to deoxygenated haemoglobin concentrated in the superficial blood vessels. The arterial oxygen saturation is 80–85% before it is clinically apparent. It is classified as central or peripheral.

Central

Cyanosis is present in parts of the body with good circulation, such as the lips and tongue. The areas feel warm. The main causes are pulmonary disease, pulmonary oedema, cyanotic congenital heart disease (right to left shunt), respiratory depression and polycythaemia (see FIG. 8.4).

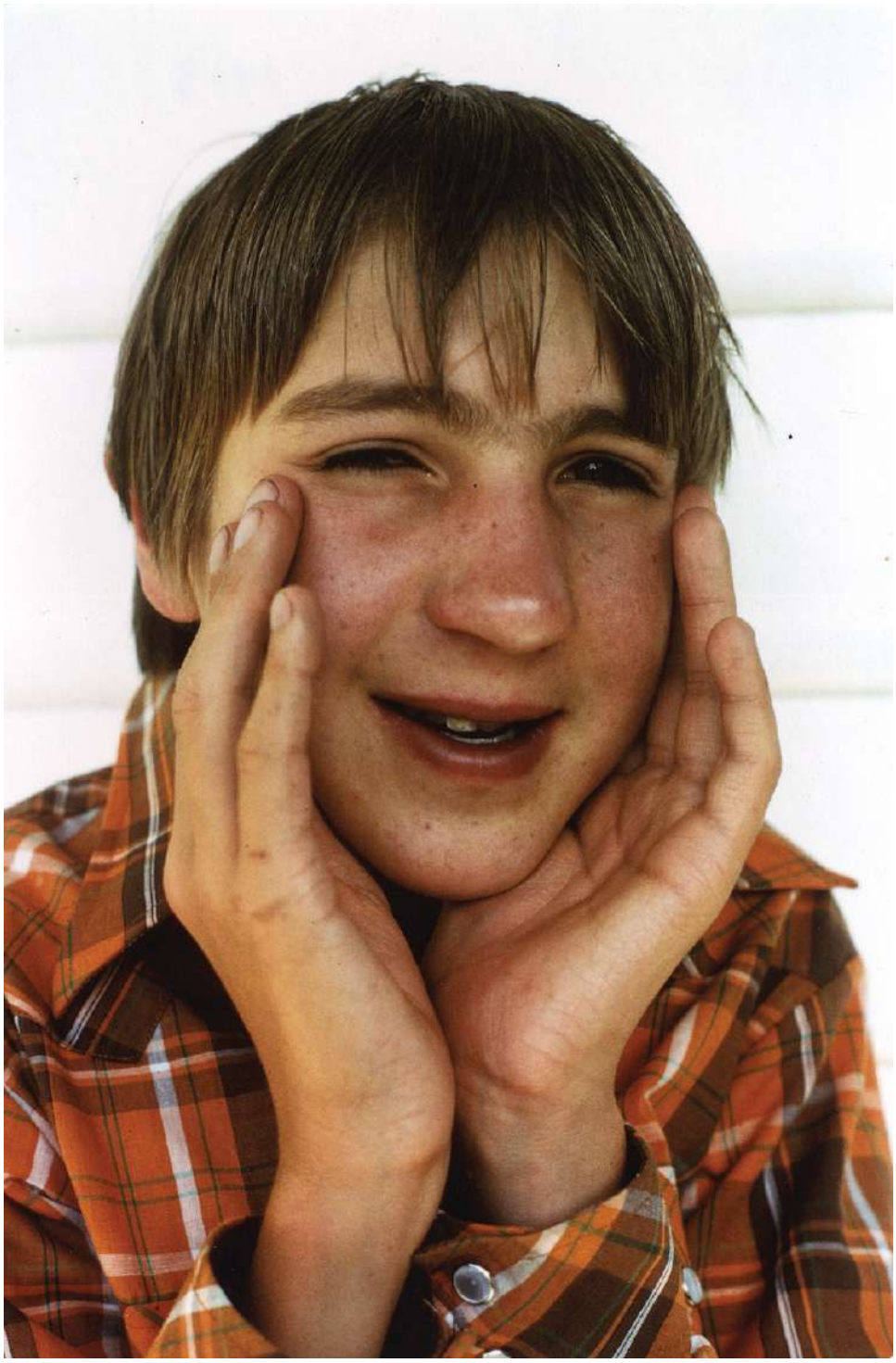

FIGURE 8.4 Adolescent patient with central cyanotic heart disease and associated clubbing of the fingers

Peripheral

Cyanosis is in the extremities, such as the outer surface of the lips, finger tips, nose and ears. The areas feel cold. The main causes are peripheral vascular disease, cardiac failure, ‘shock’, exposure to cold, left ventricular failure and all causes of central cyanosis.

Clubbing of fingers

Features

- Loss of usual angle between base of nail and nail fold
- Curvature in two planes
- Increased sponginess in base of nail
- Increased convexity of nail
- Mainly caused by respiratory disease

Causes

1. Lung disease:
   - carcinoma
   - bronchiectasis
   - cystic fibrosis
   - abscess/empyema
   - pulmonary fibrosis
2. Heart disease:
   - infective endocarditis
   - cyanotic congenital heart disease (see FIG. 8.4)
3. Liver disease:
   - cirrhosis
4. Gastrointestinal disease:
   - ulcerative colitis
   - Crohn disease

- coeliac disease

5. Congenital

Increased general pigmentation

Increased pigmentation is not common but if obvious in areas exposed to the sun, look for ‘hidden’ areas, such as the inner aspect of the forearms. Causes include those listed below.

Increased melanocyte-stimulating hormone (MSH)

- Addison disease (see CHAPTER 14)
- Cushing syndrome
- Ectopic ACTH syndrome
- AIDS

Metabolic

- Hyperthyroidism
- Haemochromatosis (see FIG. 8.5)
- Cirrhosis of the liver
- Porphyria cutanea tarda
- Chronic kidney failure
- Malnutrition/malabsorption
- Pregnancy

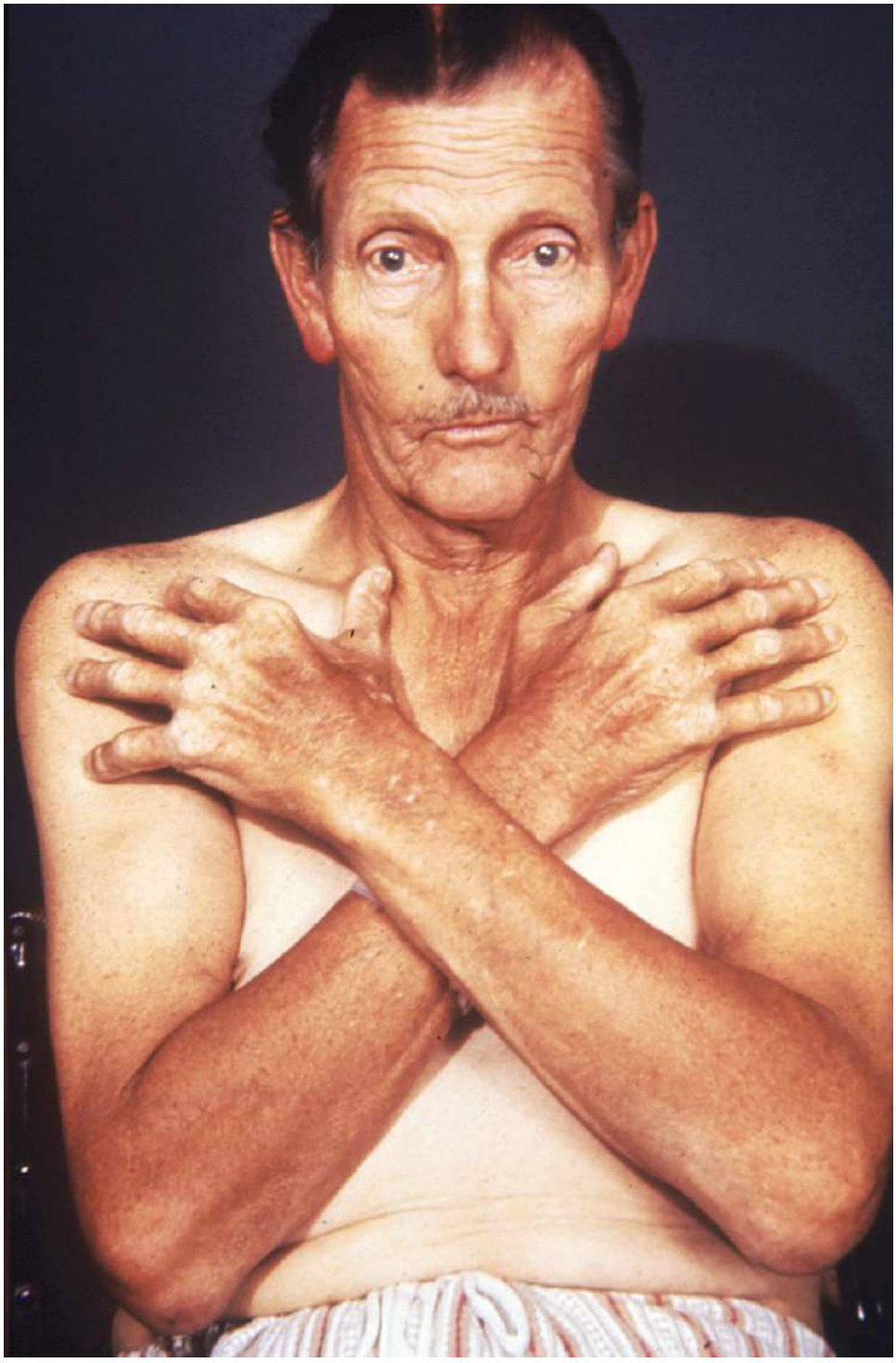

FIGURE 8.5 Patient showing pigmentation of primary haemochromatosis and associated arthritis of fingers

Drugs

- Amiodarone
- Antibiotics (busulphan, bleomycin, minocycline)
- Antimalarials (chloroquine/hydroxychloroquine)
- Arsenic, gold, silver
- Chemotherapy
- Dapsone
- Oral contraceptive pill (OCP)
- Phenothiazines
- Photochemotherapy (PUVA)
- Psoralens
- Thiazides

Tumours

- Lymphomas
- Acanthosis nigricans
- Metastatic melanoma

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Part 2 Diagnostic perspective in general practice

9 A safe diagnostic model

For most diagnoses all that is needed is an ounce of knowledge, an ounce of intelligence, and a pound of thoroughness.

ANON (1951), *LANCET*

The discipline of general practice is probably the most difficult, complex and challenging of all the healing arts. Our field of endeavour is at the very front line of medicine and as practitioners we shoulder the responsibility of the early diagnosis of very serious, perhaps life-threatening, illness in addition to the recognition of anxiety traits in our patients.

The teaching of our craft is also an exciting challenge and presupposes that we have a profound comprehension of our discipline.

Our area is characterised by a wide kaleidoscope of presenting problems, often foreign to the classic textbook presentation and sometimes embellished by a ‘shopping list’ of seemingly unconnected problems or vague symptoms—the so-called undifferentiated illness syndrome.[1] Common undifferentiated symptoms include tiredness or fatigue, sleeping problems, anxiety and stress, dizziness, headache, indigestion, anorexia and nausea, sexual dysfunction, weight loss, loss of interest, flatulence, abdominal discomfort and chest discomfort.[2] It is important, especially in a busy practice, to adopt a fail-safe strategy to analyse such presenting problems. Such an approach is even more important in a world of increasing medical litigation and specialisation.

To help bring order to the jungle of general practice problems, the principal author has developed a simple model to facilitate diagnosis and reduce the margin of error.

The concept of diagnostic triads

A most useful guide to learning or memorising diagnoses, especially of elusive and uncommon conditions, is to remember three key points to the condition. The cognitive process of learning these so-called ‘triads’ and even ‘tetrads’ provides a useful template for the diagnostic

methodology required in general practice. Some simple examples are shown in the following box.

Examples such as these are interspersed throughout the text, especially in this chapter, and are prefixed by the symbol DxT.

Examples of diagnostic triads

DxT angina + dyspnoea + blackouts → aortic stenosis

DxT menstrual dysfunction + obesity + hirsutism → polycystic ovarian syndrome

DxT malaise + night sweats + pruritus → Hodgkin lymphoma

DxT abdominal pain + diarrhoea + fever → Crohn disease

DxT vertigo + vomiting + tinnitus → Ménière syndrome

DxT dizziness + hearing loss + tinnitus → acoustic neuroma

DxT fatigue + muscle weakness + cramps → hypokalaemia

The basic model

The use of the diagnostic model requires a disciplined approach to the problem with the medical practitioner quickly answering five self-posed questions. The questions are shown in TABLE 9.1 .

Table 9.1 The diagnostic model for a presenting problem

1	What is the probability diagnosis?
2	What serious disorders must not be missed?
3	What conditions are often missed (the pitfalls)?
4	Could this patient have one of the ‘masquerades’ in medical practice?
5	Is this patient trying to tell me something else?

This approach, which is based on considerable experience, requires the learning of a predetermined plan which, naturally, would vary in different parts of the world but would have a

certain universal application in the so-called developed world.

Each of the above five questions will be expanded.

An excellent acronym on this theme, ‘PROMPT’, was devised by a reader, Dr Kelly Teagle:

P **P**robability
R **R**ed flag
O **O**ften missed
M **M**asquerades
P **P**atient wants to
T **T**ell me something

Another contribution is by Flinders University medical student, Judah:

Things are not always ‘cut and dried’:

C **C**onnective tissue disorders
U **U**TIs, particularly in very old and very young
T **T**hyroid disease
and
D **D**epression
R remember to **R**ule out serious and **R**are causes
I **I**atrogenic causes
E **E**motional needs
D **D**iabetes

1 The probability diagnosis

The probability diagnosis is based on the doctor’s perspective and experience with regard to prevalence, incidence and the natural history of disease. GPs acquire first-hand epidemiological knowledge about the patterns of illness apparent in individuals and in the community, which enables them to view illness from a perspective that is not available to doctors in any other disciplines. Thus, during the medical interview, the doctor not only is gathering information, allocating priorities and making hypotheses, but also is developing a probability diagnosis based on acquired epidemiological knowledge.

2 What serious disorders must not be missed?

While epidemiological knowledge is a great asset to the GP, it can be a disadvantage in that he or she is so familiar with what is common that the all-important rare cause of a presenting symptom may be overlooked. On the other hand, the doctor in the specialist clinic, where a different spectrum of disease is encountered, is more likely to focus on the rare at the expense of the

common cause. However, it is vital, especially working in the modern framework of a litigation-conscious society, not to miss serious, life-threatening disorders.

To achieve early recognition of serious illness, the GP needs to develop a ‘high index of suspicion’. This is generally regarded as largely intuitive, but this is probably not the case, and it would be more accurate to say that it comes with experience.

The serious disorders that should always be considered ‘until proven otherwise’ include malignant disease, acquired immunodeficiency syndrome (AIDS), coronary disease and life-threatening infections such as meningitis, meningococcal infection (see FIG. 9.1), *Haemophilus influenzae* b infections, septicaemia and infective endocarditis (see TABLE 9.2).

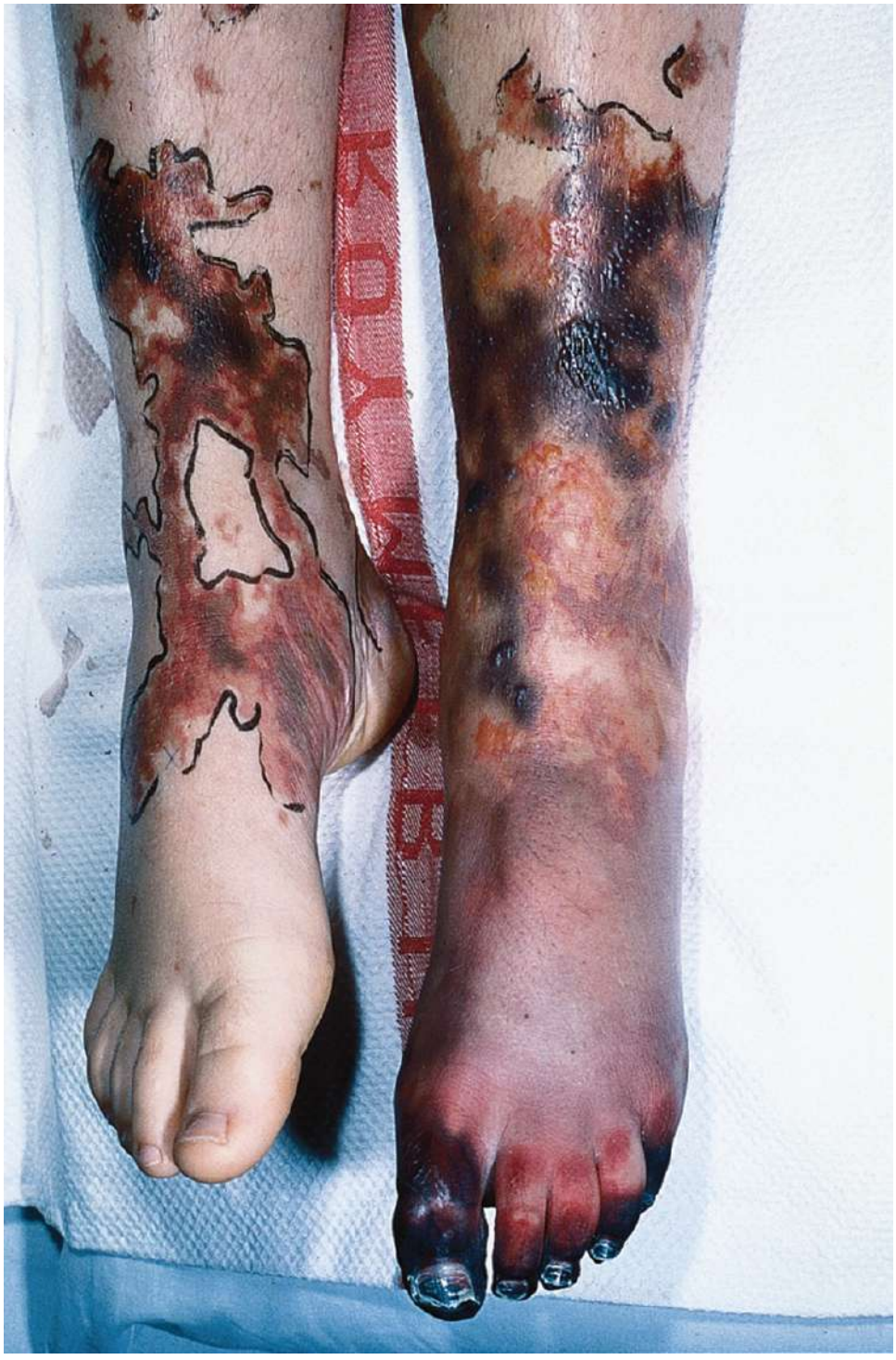

FIGURE 9.1 Meningococcal infection: complications of infarction (DIC) including gangrene from meningococcaemia

Table 9.2 Serious ‘not to be missed’ conditions

Neoplasia, especially malignancy

HIV infection/AIDS

Asthma/anaphylaxis

Severe infections, especially:

- meningoencephalitis
- septicaemia
- meningococcal infection (see FIG. 9.1)
- epiglottitis
- infective endocarditis
- pneumonia/influenza/SARS
- clostridia infections, e.g. tetanus, botulism, gas gangrene

Coronary artery disease:

- myocardial infarction
- unstable angina
- arrhythmias

Imminent or potential suicide

Intracerebral lesions (e.g. subarachnoid haemorrhage)

Ectopic pregnancy

Myocardial infarction or ischaemia is extremely important to consider because it is so potentially lethal and at times can be overlooked by the busy practitioner. It does not always manifest as the classic presentation of crushing central pain but can present as pain of varying severity and quality in a wide variety of sites. These sites include the jaw, neck, ear, arm, epigastrium and interscapular region. Coronary artery disease may manifest as life-threatening arrhythmias that may present as palpitations and/or dizziness. A high index of suspicion is necessary to diagnose arrhythmias.

Diagnostic triads for life-threatening conditions (examples)

DxT fever + rigors + hypotension → septicaemia

DxT fever + vomiting + headache → meningitis

DxT fatigue + dizziness ± syncope → cardiac arrhythmia

DxT fever + drooling + stridor (child) → epiglottitis

DxT headache + vomiting + altered consciousness → subarachnoid haemorrhage (SAH)

DxT abdominal pain + amenorrhoea + abnormal vaginal bleeding → ectopic pregnancy

DxT fatigue + dyspnoea on exertion + dizziness → cardiomyopathy

Consider M^2I^2

A traditional way of classifying serious diseases is the pathology aide-mémoire:

- Malignancy
- Metabolic
- Infarction
- Infection

Danger: think VIC

V = **V**ascular

I = **I**nfection (severe)

C = **C**ancer

Red flags

Red flags (alarm bells) are symptoms or signs that alert us to the likelihood of significant harm. Such underlying disease *must not be missed* and demands careful investigation. Examples include weight loss, vomiting, altered cognition, fever >38°C, dizziness, and/or syncope at the toilet and pallor. Red flags will be outlined under presenting symptoms throughout the text.

3 What conditions are often missed?

This question refers to the common ‘pitfalls’ so often encountered in general practice. This area is definitely related to the experience factor and includes rather simple, non-life-threatening problems that can be so easily overlooked unless doctors are prepared to include them in their diagnostic framework.

Classic examples include smoking or dental caries as a cause of abdominal pain, allergies to a whole variety of unsuspected everyday contacts, foreign bodies, occupational or environmental hazards as a cause of headache, respiratory discomfort or malaise, and faecal impaction as a cause of diarrhoea. We have all experienced the ‘red face syndrome’ from a urinary tract

infection, whether it is the cause of fever in a child, lumbar pain in a pregnant woman or malaise in an older person. The dermatomal pain pattern caused by herpes zoster prior to the eruption of the rash (or if only a few sparse vesicles erupt) is a common trap.

A typical pitfall is Addison disease, where some patients can wait up to 15 years before being diagnosed. The absence of subdued classic pigmentation (see FIG. 9.2) can mask the early diagnosis.

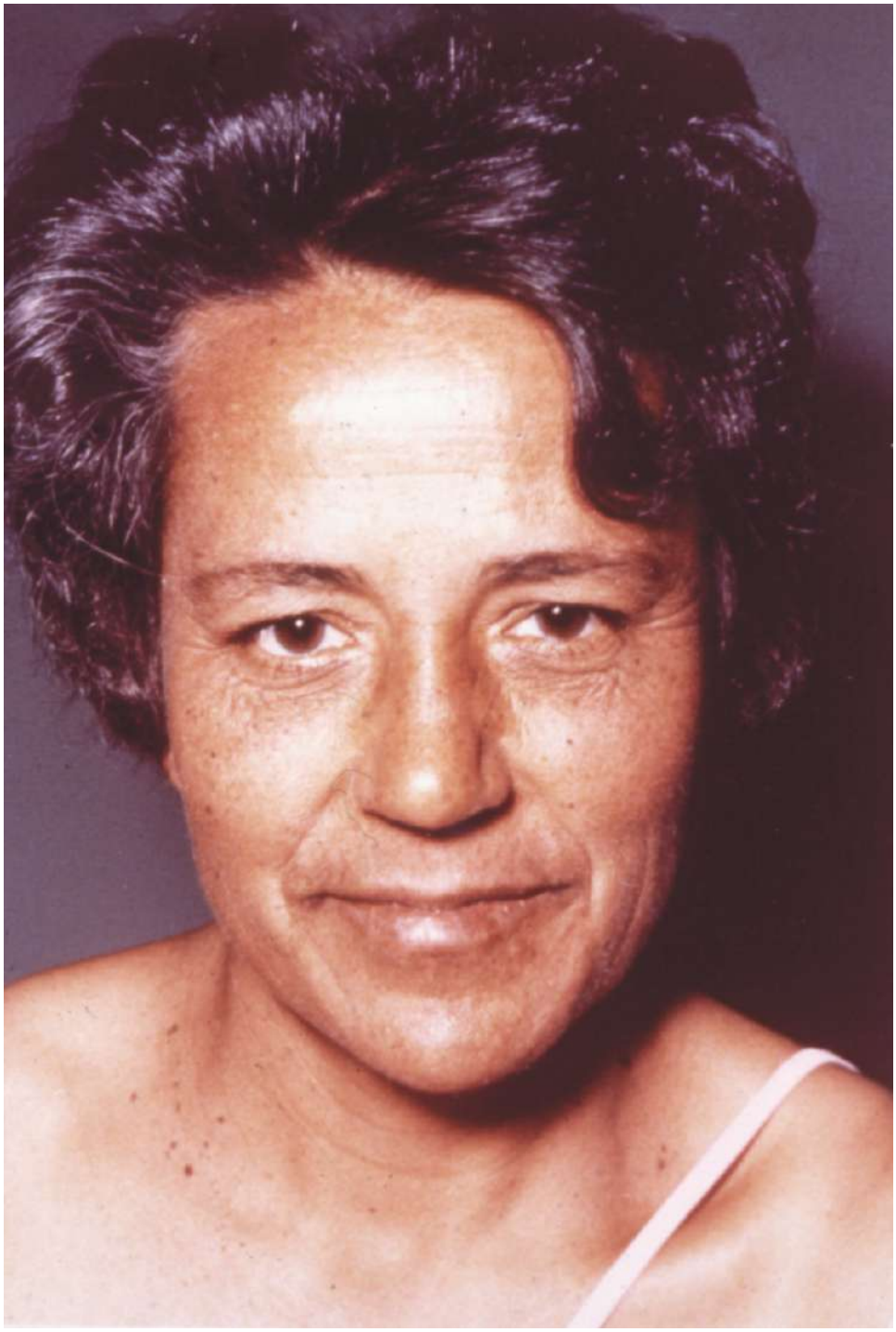

FIGURE 9.2 Woman with Addison disease showing facial pigmentation

Haemochromatosis can be a surprise diagnosis, often discovered by serendipity following a screening blood test for unexplained fatigue. Coeliac disease is a classic master of disguise in both children and adults. It now ranks as one of the most common, widespread and undiagnosed illnesses affecting humans. In Australia, 1.5% of the population are affected but 80% remain

undiagnosed.[3] Research by dermatologists[4] has highlighted that it can present in a number of ways that can affect the skin and hair. Apart from typical gastrointestinal symptoms, such as chronic diarrhoea, steatorrhoea, weight loss, anorexia and abdominal distension, the following atypical symptoms have been described:

- nutritional presentations, including folate, zinc or iron (in particular) deficiency
- grouped blisters around the knees, elbows and buttocks (dermatitis herpetiformis)
- hair loss and mouth ulcers

Menopausal symptoms can also be overlooked as we focus on a particular symptom. Some important pitfalls are given in TABLE 9.3 .

Table 9.3 Classic pitfalls

Abscess (hidden)
Addison disease
Allergies
Candida infection
Chronic fatigue syndrome
Coeliac disease
Domestic abuse, including child abuse
Drugs (see TABLE 9.4)
Endometriosis
Faecal impaction
Foreign bodies
Giardiasis
Haemochromatosis
Herpes zoster
Lead poisoning
Malnutrition (unsuspected)
Menopause syndrome
Migraine (atypical variants)
Paget disease
Pregnancy (early)
Sarcoidosis
Seizure disorders
Tourette syndrome
Urinary infection

Diagnostic triads for some ‘pitfalls’

DxT fatigue + weight loss + diarrhoea → coeliac disease

DxT anorexia/nausea + faecal leaking + abdominal bloating → faecal impaction

DxT abdominal cramps + flatulence + profuse diarrhoea → giardiasis

DxT lethargy + tiredness + arthralgia → haemochromatosis

DxT lethargy + abdominal pains + irritability (in child) → lead poisoning

DxT aching bones + waddling gait + deafness → Paget disease

DxT malaise + cough + fever (± erythema nodosum) → sarcoidosis

DxT (male child) snorting, blinking + oral noises (e.g. grunts) ± loud expletives → Tourette syndrome

4 The masquerades (‘chameleons’)

It is important to utilise a type of fail-safe mechanism to avoid missing the diagnosis of these disorders. Some practitioners refer to consultations that make their ‘head spin’ in confusion and bewilderment, with patients presenting with a ‘shopping list’ of problems. It is in these patients that a checklist is useful. Consider the apparently neurotic patient who presents with headache, lethargy, tiredness, constipation, anorexia, indigestion, shortness of breath on exertion, pruritus, flatulence, sore tongue and backache. In such a patient we must consider a diagnosis that links all these symptoms, especially if the physical examination is inconclusive; this includes iron deficiency anaemia, depression, diabetes mellitus, hypothyroidism (see FIG. 9.3) and drug abuse.

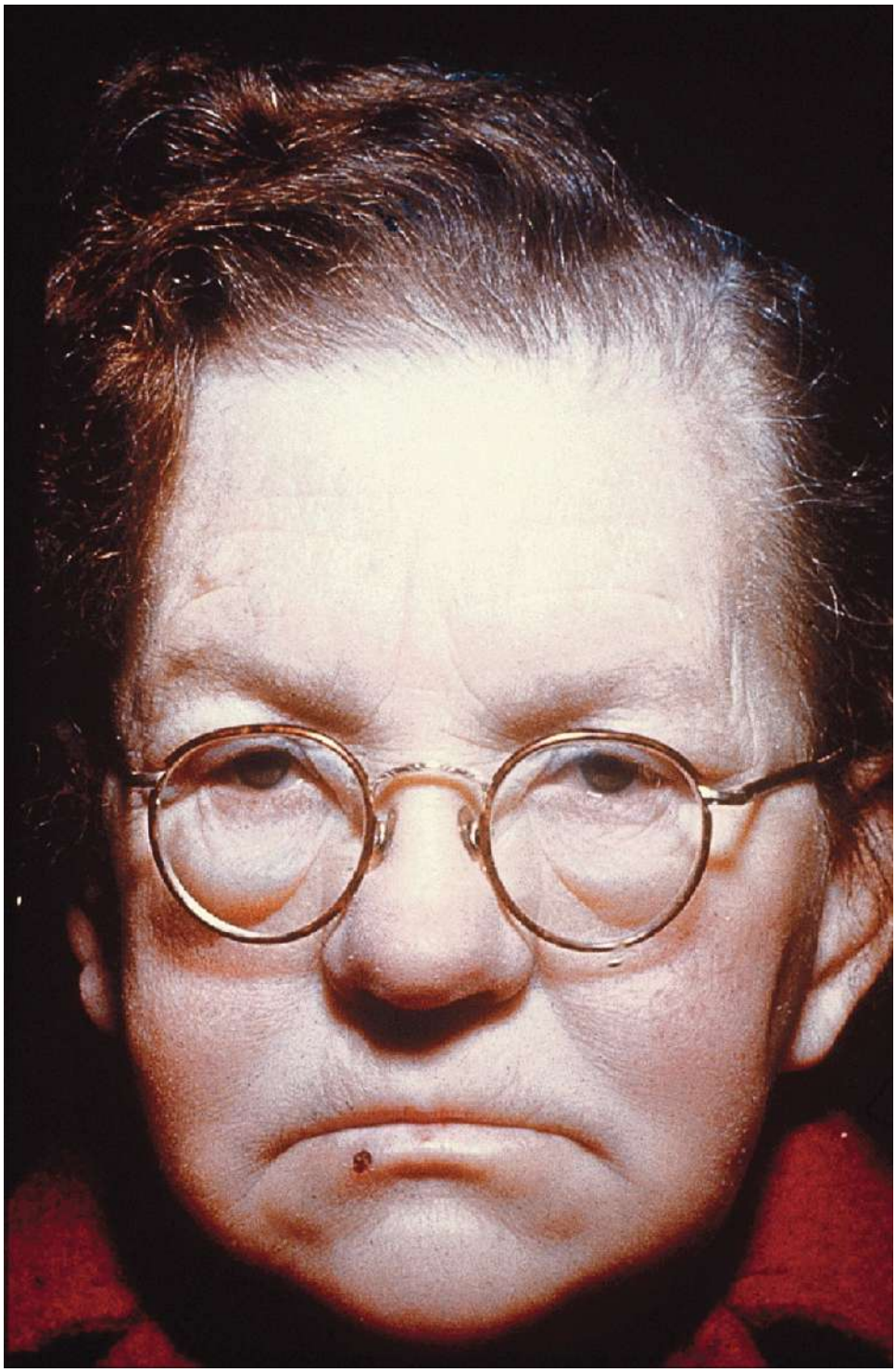

FIGURE 9.3 Hypothyroidism in a 60-year-old woman, a classic masquerade, with a slow subtle onset of facial changes

A century ago it was important to consider diseases such as syphilis and tuberculosis as

the great common masquerades, but these infections have been replaced by iatrogenesis, malignant disease, alcoholism, endocrine disorders and the various manifestations of atherosclerosis, particularly coronary insufficiency and cerebrovascular insufficiency.

If the patient has pain anywhere it is possible that it could originate from the spine, so the possibility of spinal pain (radicular or referred) should be considered as the cause for various pain syndromes, such as headache, arm pain, leg pain, chest pain, pelvic pain and even abdominal pain. The author's experience is that spondylogenic pain is one of the most underdiagnosed problems in general practice.

A checklist that has been divided into two groups of seven disorders is presented in TABLES 9.4 and 9.5 . The first list, 'the seven primary masquerades', represents the more common disorders encountered in general practice; the second list includes less common masquerades—although some, such as Epstein–Barr mononucleosis, can be very common masquerades in general practice.

Table 9.4 The seven primary masquerades

1. Depression
2. Diabetes mellitus
3. Drugs
   - iatrogenic
   - self-abuse
     - alcohol
     - narcotics
     - nicotine
     - others
4. Anaemia
5. Thyroid and other endocrine or metabolic disorders
   - hyperthyroidism
   - hypothyroidism
   - Addison disease
6. Spinal dysfunction
7. Urinary tract infection (UTI)

Table 9.5 The seven other masquerades

1. Chronic kidney failure
2. Malignant disease
   - lymphomas
   - lung
   - caecum/colon
   - kidney
   - multiple myeloma
   - ovary
   - pancreas
   - metastasis
3. HIV infection/AIDS
4. Baffling bacterial infections
   - syphilis
   - tuberculosis
   - infective endocarditis
   - the zoonoses
   - *Chlamydia* infections
   - atypical pneumonias (e.g. Legionnaire disease)
   - others
5. Baffling viral (and protozoal) infections
   - Epstein–Barr mononucleosis
   - TORCH organisms (e.g. cytomegalovirus)
   - hepatitis A, B, C, D, E
   - mosquito-borne infections
     - malaria
     - Ross River fever
     - dengue fever
     - others
6. Neurological dilemmas
   - Parkinson disease
   - Guillain–Barré syndrome
   - seizure disorders
   - multiple sclerosis
   - myasthenia gravis
   - space-occupying lesion of skull
   - migraine and its variants
   - others

7 Connective tissue disorders and the vasculitides

- connective tissue disorders
  - systemic lupus erythematosus (SLE)
  - systemic sclerosis
  - dermatomyositis
  - overlap syndrome
- vasculitides
  - polyarteritis nodosa
  - giant cell arteritis/polymyalgia rheumatica
  - granulomatous disorders

Neoplasia, especially malignancy of the so-called ‘silent areas’, can be an elusive diagnostic problem. Typical examples are carcinoma of the nasopharynx and sinuses, ovary, caecum, kidney and lymphopoietic tissue. Sarcoidosis is another disease that can be a real masquerade (see CHAPTER 38).

Systemic lupus erythematosus (SLE) has been described as ‘the great pretender’.[5] The two most common symptoms are joint pain and fatigue but it is a multisystem disease that may present with involvement of any of these organ systems and may not initially be recognised as such.

As a practical diagnostic ploy, the author has both lists strategically placed on the surgery wall immediately behind the patient. The lists are rapidly perused for inspiration should the diagnosis for a particular patient prove elusive.

5 Is the patient trying to tell me something?

The doctor has to consider, especially in the case of undifferentiated illness, whether the patient has a ‘hidden agenda’ for the presentation.[6] Of course, the patient may be depressed (overt or masked) or may have a true anxiety state. However, a presenting symptom such as tiredness may represent a ‘ticket of entry’ to the consulting room.[7] It may represent a plea for help in a stressed or anxious patient. We should be sensitive to patients’ needs and feelings and, as listening, caring, empathetic practitioners, provide the right opportunity for the patient to communicate freely.

Deep sexual anxieties and problems, poor self-esteem, and fear of malignancy or some other medical catastrophe are just some of the reasons patients present to doctors.

The patient with a self-induced bruising (see FIG. 9.4) was a health professional who was deeply attracted to an inpatient haematologist (Munchausen syndrome).

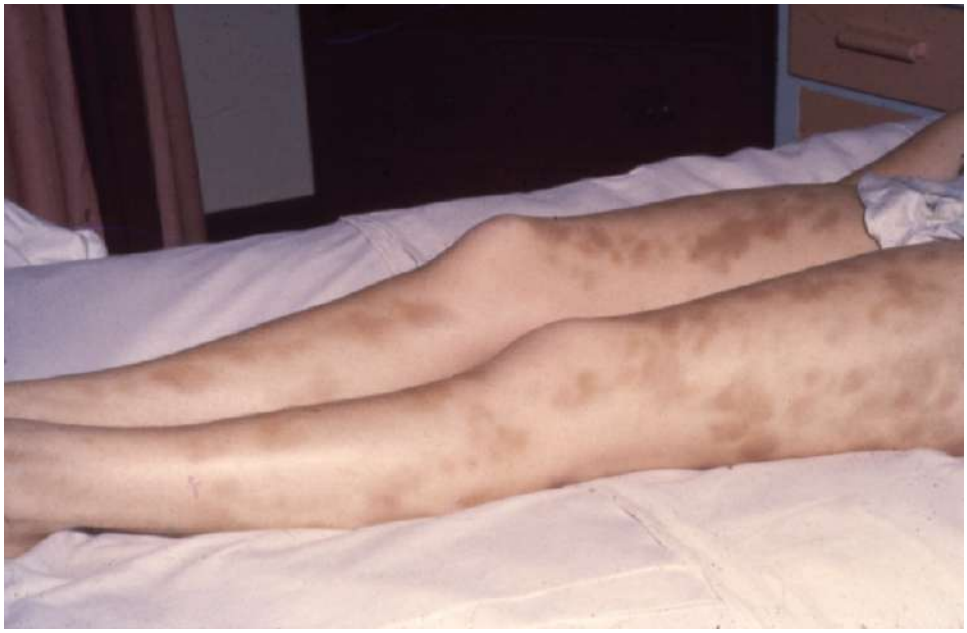

FIGURE 9.4 Artefactual purpura showing an unusually symmetrical distribution in sites that can be reached by the patient (a 'ticket of entry')—Munchausen syndrome

The author has another checklist (see TABLE 9.6) to help identify the psychosocial reasons for a patient's malaise.

Table 9.6 Underlying fears or image problems that cause stress and anxiety

1	Interpersonal conflict in the family
2	Identification with sick or deceased friends
3	Fear of malignancy
4	STIs, especially AIDS
5	Impending 'coronary' or 'stroke'
6	Sexual problem
7	Drug-related problem
8	Crippling arthritis
9	Financial woes
10	Other abnormal stresses

In the author's experience of counselling patients and families, the number of problems caused by interpersonal conflict is quite amazing and makes it worthwhile to specifically explore the quality of close relationships, such as those of husband–wife, mother–daughter and father–son.

Diagnostic triads for some 'masquerades'

DxT malaise + fever + cough (± erythema nodosa) → TB *or* sarcoidosis

DxT fever + sore throat + cervical lymphadenopathy → EB mononucleosis

DxT fatigue + a/n/v + sallow skin → chronic kidney failure

DxT polyuria + polydipsia + skin/orifice infections → diabetes mellitus

DxT FUO + cardiac murmur + embolic phenomena → infective endocarditis

DxT fatigue + polyarthritis + fever or skin lesions → SLE

DxT loin pain + haematuria + palpable loin mass → kidney carcinoma

DxT malaise + weight loss + cough → lung carcinoma

DxT fever + myalgia/headache + non-productive cough → atypical pneumonia

DxT malaise + night sweats + painless lymphadenopathy → non-Hodgkin lymphoma

DxT arthralgia + Raynaud phenomenon + GORD (± skin changes) → systemic sclerosis

DxT fatigue + headache + jaw claudication → temporal arteritis

DxT weakness + back pain + weight loss → multiple myeloma

DxT lethargy + physical/mental slowing + constipation → hypothyroidism

Note: Diagnostic triads for neurological dilemmas are included in CHAPTER 22 .

Another common yet overlooked stressor is bullying,[8] whether it is in the workplace, school, university, home, internet or elsewhere. It is a significant public health issue. The current

fashion for tough, dynamic, ‘macho’ management styles has created a culture in which bullying can thrive. As GPs, we should be more aware of the possibility that workplace bullying may be contributing to the stresses with which many patients present. A simple, direct, routine question such as ‘How are things at work?’ can create an opportunity to raise the issue.

Identification and transference of illness, symptoms and death, in particular, are important areas of anxiety to consider. Patients often identify their problems with relatives, friends or public personalities who have malignant disease. Other somatoform disorders and the factitious disorders, including the fascinating Munchausen syndrome, may be obvious or extremely complex and difficult to recognise. Consider also ‘Munchausen by proxy’ where carers intentionally produce or feign symptoms in the person (child or elderly patient) in their care. These subtle psychosocial issues are usually termed ‘yellow flags’.

Yellow flags[7]

Yellow flags are signs or behaviours that flag or indicate a psychosocial barrier to recovery. They have been described originally within the framework of chronic pain and disability, especially chronic back pain, and require a shift in our focus of care. Conditions to consider are anxiety, depression, adjustment disorder and personality disorder. Typical yellow flags are presented in TABLE 9.7 .

Table 9.7 Yellow flags: examples

Abnormal illness behaviour
Devious behaviour
Cancelling appointments
Treatment non-compliance/refusal
Somatisation
Absenteeism from work
Poor work performance
Personal neglect
Relationship breakdown
Law and order incidents

A survey by researchers at Melbourne’s Centre for Behavioural Research[9] revealed that the three most feared diseases are cancer (81%), heart disease (32%) and HIV/AIDS (21%).

The bottom line is that patients are often desperately searching for security and we have an important role to play in helping them.

Some examples of application of the model

Hiccough

1	**Probability diagnosis**
	Food and alcohol excess Psychogenic/functional Postoperative • gastric distension • phrenic nerve irritation
2	**Serious disorders not to be missed**
	Neoplasia • CNS • neck • oesophagus • lung Subphrenic abscess Myocardial infarction/pericarditis CNS disorders (e.g. CVA infection) Chronic kidney failure
3	**Pitfalls**
	Alcohol excess Smoking Aerophagy Gastrointestinal disorders • oesophagitis • peptic ulcer • hiatus hernia • cholecystitis • hepatomegaly *Rarities:* • sudden temperature change • neck cysts and vascular abnormalities
4	**Seven masquerades checklist**
	Drugs

5 **Is the patient trying to tell me something?**

Emotional causes always to be considered

Halitosis

(see CHAPTER 61)[10]

1 **Probability diagnosis**

Dietary habits—odour-causing foods, e.g. garlic
Poor oral hygiene
Orodental disease, e.g. gingivitis, dental abscess
Dry mouth (e.g. on waking)
Smoking/alcohol

2 **Serious disorders not to be missed**

Malignancy: lung, oropharynx, larynx, stomach, nose, leukaemia
Pulmonary tuberculosis
Quinsy
Oral candidiasis
Lung abscess
Blood dyscrasias/leukaemia
Uraemia
Hepatic failure

3 **Pitfalls**

Nasal and sinus infection
Systemic infection
Appendicitis
Bronchiectasis
Hiatus hernia
Starvation
Rarities
Pharyngeal and oesophageal diverticula
Sjögren syndrome
Scurvy

4 **Seven masquerades checklist**

Depression
Diabetes: acidosis (acetone)

	Drugs
5	**Is the patient trying to tell me something?** Possible manifestation of psychogenic disorder Halitophobia

Practice tips

- Follow the ‘baseball rule’ for a delayed or puzzling diagnosis: ‘Three strikes and you’re out’.
- Infarction—think fast!

  acute coronary events: 60–90 minutes

  stroke: 3–4 hours

  femoral artery: 4 hours

  torsion of testis: 4–6 hours

Patient education resources

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

- Bullying of children
- Bullying in the workplace

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10 Depression

I am ignorant and impotent and yet, somehow or other, here I am, unhappy, no doubt, profoundly dissatisfied... In spite of everything I survive.

ALDOUS HUXLEY (1894–1964)

Depressive illness, which is probably the greatest masquerade in general practice, is one of the commonest illnesses in medicine and often confused with other illness. Untreated, depression can result in disability and death.[1] The most feared outcome is suicide. It is present in at least 17% of patients who present to GPs[2] and has a 12-month prevalence of 5% and a lifetime risk of 15%.[3] It is often unrecognised,[1] yet moderate to severe depression is as disabling as congestive heart failure[1] and with a morbidity comparable to coronary heart disease. Further, depression is the *leading* cause of disability for all conditions among both sexes, both in Australia and worldwide.[4,5] The lifetime risk of suicide in patients diagnosed with depression is 6% and treatment halves this risk.[1]

Despite being treatable, 60% of sufferers have not used any form of health service in the previous months.[4] Lack of awareness, stigma and shame on behalf of the patient contribute to this. Of those receiving treatment, three-quarters will be managed in general practice.[5,6] As Whiteford[4] notes:

> It is clear that the main focus of activity aimed at reducing the burden of common mental health disorders in Australia is in primary care. Specialist mental health services play a supporting, but not central, role.

Depression is a chronic relapsing organic brain disease. Its mean onset is at 27 years of age. However, 40% of sufferers present by 20 years of age.[7] The average duration of episodes is 3–4 months and 40% of patients will relapse within a 12-month period.[7]

The cause of depression is multifactorial, having biological, psychological and social factors. Mood disorders in general have a strong familial tendency, and the risk of developing a depressive disorder can be thought of in terms of a ‘stress-vulnerability model’. That is, an individual may have a genetically determined vulnerability and if enough stress is endured a mood disorder may result. Those who are more genetically vulnerable require less stress, but if enough stress is applied, any individual can develop a mood disorder. A significant characteristic is that it impairs thinking, leading to pessimism with negativity and a loss of drive and productivity.

There are six clusters of depressive symptoms:

- mood, e.g. sadness, anhedonia, irritability
- vegetative, e.g. sleep, appetite, sexual drive
- cognitive, e.g. attention, memory, self-worth
- impulse control, e.g. suicide, anger, homicide
- behavioural, e.g. motivation, interests, tiredness
- physical, e.g. headaches, constipation

A useful working rule is to consider depression as an illness that dampens the five basic innate activities of humans:

- energy for activity
- sex
- sleep
- appetite and thirst
- elimination of waste

Classification

- The DSM-5 classification divides depressive disorders into major depressive disorder (MDD), disruptive mood dysregulation disorder, persistent depressive disorder (PDD) and premenstrual dysphoric disorder. Other ‘specified’ and ‘unspecified’ disorder categories allow for diagnosis of those patients who fall short of the various diagnostic criteria.
- MDD includes those disorders with one or more major depressive episodes. Excluding criteria include any previous mania or hypomania, and the episode not being attributable to a psychotic disorder, or a substance or medical condition.

  MDD is subclassified with coded course and severity specifiers. These include mild, moderate and severe (see TABLE 68.1),[8] with psychotic features, in partial remission and in full remission.

- A significant subtype of depression is dysthymia, which is a chronic mild depression lasting at least 2 years but not fulfilling the criteria for MDD. For other subtypes, refer to CHAPTER 68 .

The diagnostic approach

The diagnosis is based on the history and the mini mental state examination.

The two key criteria for major depressive disorder (MDD) in the DSM-5 are a pervasive depressed mood and marked loss of interest or pleasure (otherwise referred to as anhedonia) persisting for at least 2 weeks. Other criteria (listed below) include sleep issues, fatigue, lack of energy, poor concentration and feelings of worthlessness.

In a general practice setting, having a checklist of these symptoms to work through with a patient can be a useful part of the assessment of the depressed patient.

Questions to assess level of depression

- What do you think is the matter with you?
- Do you think that your feelings are possibly caused by nerves, anxiety or depression?
- Can you think of any reason why you feel this way?
- Do you feel down in the dumps?
- Do you feel that you are coping well?
- Do you have any good times?
- Has anything changed in your life?
- How do you sleep? Do you wake early?
- What time of the day do you feel at your worst?
- Where would you put yourself between 0% and 100% (a visual analogue scale is useful here)?
- Have you felt hopeless?
- Do you brood about the past?
- What is your energy like?
- What is your appetite like?
- Are you as interested in sex as before?
- Do you feel guilty about anything?
- Do you feel that life is worthwhile?
- Has the thought of ending your life occurred to you?
- Do you cry when no one is around (especially useful for children)?

Two particularly good questions are:

- In the past month, have you been bothered by the fact that you feel down, depressed or hopeless?
- In the past month, have you often been bothered by the fact that you have little interest or pleasure in doing things?

Rule out other mental disorders

Enquire about substance use and abuse, anxiety, psychosis, manic/hypermanic episodes, intimate partner violence, bereavement and postpartum depression.

Important differentiated diagnoses (organic disease)

Important differential diagnoses (organic disease) to consider are malignancy (especially of lung, brain, pancreas and blood/lymphatics), early dementia, CCF, endocrine disorders (e.g. thyroid disease), menopause, liver and renal failure, infections (e.g. mononucleosis), neurological (e.g. MS, Parkinson), adverse effects of medication, anaemia, SLE and cerebrovascular disease.

Diagnostic guidelines for major depressive disorder[9]

At least 5 of the following 9 symptoms with anhedonia and/or depressed mood for ≥ 2 weeks:

- Depressed mood
- Anhedonia (decreased interest/pleasure)
- Sleep change: increased/decreased
- Guilt/worthlessness
- Decreased energy
- Impaired/increased concentration
- Changer of appetite and weight
- Psychomotor retardation or agitation
- Suicidal ideation

Screening investigations to consider

FBE; TFTs; U&Es; vitamins B, D, folate; blood glucose; urine toxicology; CT or MRI.

Depression scales

Depression scales are useful both to detect potential mood disorders (i.e. screening) and to monitor an individual patient over time. Scales commonly used include K10 (a distress score), DASS 21 or 42 (for depression and anxiety symptoms) and PHQ 2.

Somatisation

Another issue with depression in the primary care setting is recognising somatising patients who present without obvious psychological symptoms. Non-specific symptoms such as insomnia, prolonged fatigue, headache, nausea and musculoskeletal pain are common presentations in people with depression.[10] Studies suggest GPs find it challenging to identify these patients, and that using self-reporting patient-screening tools can help with identification.[3]

Key facts and checkpoints

- Depression is common, serious and treatable.
- Depression is a chronic relapsing organic brain disease.
- It may coexist with anxiety disorders, stress (physical and mental) and substance abuse disorders.
- 1 million Australians live with depression (compared with anxiety, which is 2 million) and 8 lives are taken every day, of which 6 are men.[11]
- The cause of depression is multifactorial, and can be thought of in terms of a ‘stress-vulnerability model’.
- Somatising patients without obvious psychopathology are common and difficult to recognise and manage.
- It is strongly associated with an increased risk of suicide, a fact that demands risk assessment.

Depression in the elderly

The rate of antidepressant prescribing for Australians over 80 years of age is higher than for any other age group.[12] Despite this, depression in the elderly is underdiagnosed.[13] Depression can have bizarre features in the elderly and may be misdiagnosed as dementia or psychosis. Agitated

depression is the most frequent type of depression in the aged. Features may include histrionic behaviour, delusions and disordered thinking.

Depression is often missed in the elderly because it is atypical and less expressive, and patients tend to be ashamed and reluctant to admit it.

A useful clue can be a change in sleep pattern. Medical illness is also an important precipitant of depression in the elderly.

Older patients may have more side effects from medications (especially nausea, dizziness, falls and hyponatraemia).[13] They also tend to have only a modest response to antidepressants, and, if medication is used, a low initial dose and slow increase is recommended.[1] Psychological therapies can be useful, but tend to be underused.[13]

Depression in children and adolescents

Sadness is common in children, but depression, although not as common, does occur and is characterised by feelings of helplessness, worthlessness and despair. Parents and doctors both tend to be unaware of depression in children.[14]

Major depression in children and adolescents may be diagnosed using the same criteria as for adults, namely loss of interest in usual activities and the presence of a sad or irritable mood, persisting for 2 weeks or more. In children, irritability may be more prominent than sadness.[15] The other constellation of depressive symptoms, including somatic complaints, may be present. Examples include difficulty in getting to sleep, not enjoying meals, poor concentration and low self-esteem. Poor motor skills and family instability are an association. Depression can present as antisocial behaviour or as a separation anxiety (e.g. school refusal). Although suicidal thoughts are common, suicide is rare before adolescence.

Depressed adolescents are a difficult challenge for the general practitioner. Effective engagement and establishing rapport in a ‘youth-friendly’ environment is critical.[16]

See CHAPTER 90 for the evaluation and treatment of depression in adolescents.

Perinatal depression

This term refers to depression occurring either in the antenatal period or in the 12 months after delivery. It affects 9% of women during pregnancy and 16% after the birth[17] and affects the well-being of the woman, the baby and significant others. Anxiety is likely to be as or more common.[17] Women at risk of perinatal depression include those with previous mental health problems, those who do not have support and those who have been through difficult times (e.g. family problems, abuse or loss) or who feel isolated either by distance or culture or both.

Because it is so prevalent, routine screening is recommended by the Beyond Blue guidelines. This involves implementing the use of the Edinburgh Postnatal Depression Scale (EPNDS), a

validated screening tool, at least once, preferably twice, both antenatally and postnatally. Asking permission and explaining the process before implementing the screening is helpful. Women at higher risk will require more intense screening and monitoring.

If perinatal depression is identified, the GP should take into account the individual woman's context, her family and cultural setting, and use a family-centred approach. Because of the intense emotions involved in having a baby, establishing a strong therapeutic relationship, using an open collaborative approach and active listening techniques, will help to develop trust, confidence, mutual respect and empowerment. Psycho-education should be provided and appropriate follow-up and continuity of care, with (if appropriate) a coordinated team approach.

If a woman or a baby is at risk, urgent referral is recommended. Pharmacological therapies can be used in pregnancy, but the benefits need to be balanced against the risks to both mother and fetus. Psychosis in perinatal depression is fortunately rare but does occur, and requires urgent psychiatric assessment. Refer to CHAPTER 101 .

Management of depression

Important considerations from the outset are:

- Is the patient a suicide risk?
- Does the patient require inpatient assessment?
- Is referral to a specialist psychiatrist indicated?

Suicide assessment

Data from the Australian Bureau of Statistics illustrate the levels of suicide in Australia over the 10 years to 2019:[18]

- Intentional self-harm (suicide) is the 13th leading cause of death in Australia, but the 10th leading cause in males
- 75% of all suicide deaths in Australia were males
- The national rate is 12.9 suicides per 100 000 people
- The rate of suicide in men has risen over this period from 17.5 per 100 000 to 19.8, and in women, from 5.0 to 6.3
- The median age of people who suicide is in their early to mid-40s

If the symptoms are major and the patient appears in poor health or is a suicide risk, referral is appropriate.

The importance of putting these safety issues at the beginning of the management process is reflected in the SET A PACE[7] model of treatment, proposed by Mahli et al.

To clarify the risk of suicide and appropriate response, ask about:[16]

- suicidal thoughts
- plan
- lethality
- means
- past history
- suicide of family member or peer

Low risk (fleeting thoughts of self-harm or suicide but no current plan or means):

- Discuss availability of support and treatment options.
- Arrange follow-up consultation (timing of this will be based on clinical judgment).
- Identify relevant community resources and provide contact details.

Medium risk (suicidal thoughts and intent but no current plan or immediate means):

- Discuss availability of support and treatment options.
- Organise reassessment within 1 week.
- Have contingency plan in place for rapid reassessment if distress or symptoms escalate.
- Develop a safety plan (a prioritised written list of coping strategies and sources of support to use when experiencing suicidal thinking).

High risk (continual/specific suicidal thoughts, intent, plan and means):

- Ensure that the person is in an appropriately safe and secure environment.
- Organise reassessment within 24 hours and monitoring for this period.
- Follow-up outcome of assessment.

A useful suicide risk assessment is the SAD PERSONS (mnemonic) index (see TABLE 10.1). A score greater than 7 represents a very high risk that demands careful attention, including referral to an acute psychiatric service. The suicide rates in Australia, which demonstrate two peaks in males, are illustrated in FIGURE 10.1 .

Table 10.1 SAD PERSONS index: suicide risk assessment

Risk factor	Criteria	Score
Sex	Male	1
Age	<20 years; >45 years	1
Depression	Major (e.g. depressed mood)	2
Psychiatric history	Previous attempts	1
Excessive drug use	Ethanol or other drug use	1
Rationality loss	Psychosis, severe depression	2
Separated	Loss of spouse or other single	1
Organised plan	Determined suicide plan	2
No supports	No community back-up; generally isolated	1
Sickness	Chronic illness	1

Score >7 = high suicide risk

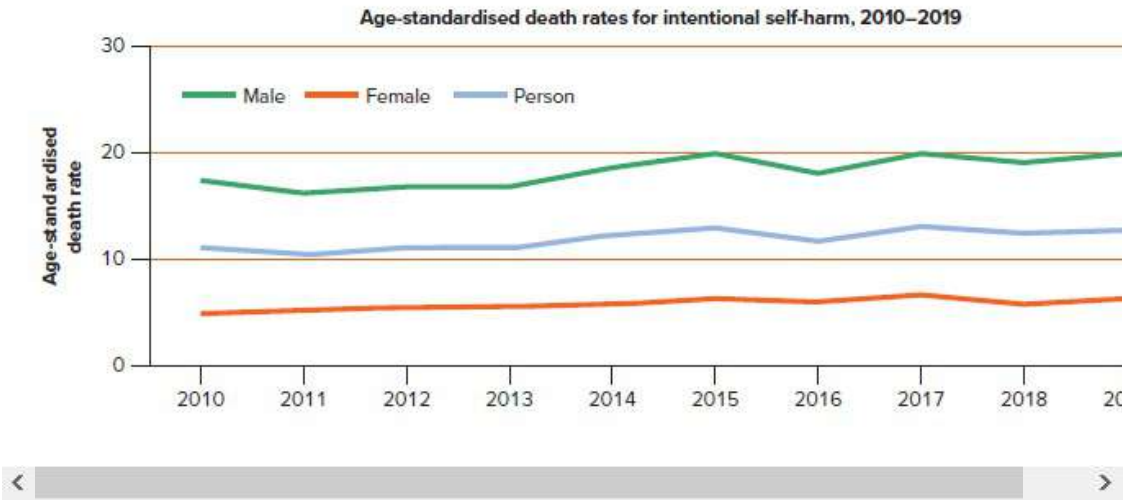


FIGURE 10.1 Death from intentional self-harm (suicides) in Australia, 2010–2019, as a whole and by sex

Source: Australian Bureau of Statistics[17]

Notes: Age-standardised death rate. Death rate per 100 000 estimated resident population as at 30 June (mid year). See the Data quality section of the methodology for further information on specific issues related to interpreting time-series and 2019 data. Care needs to be taken when interpreting data derived from Victorian coroner-referred deaths including suicide. Changes in coding processes have been applied to 2019 data.

If there is concern about suicide risk and treatment is supervised outside hospital,

provide closer supervision and considerable support, and prescribe drugs that are less toxic in overdosage (e.g. mianserin or fluoxetine). If tricyclics are prescribed, useful guidelines are that dangerous medical complications occur with an equivalent dosage of 1000 mg (40 tablets) or imipramine and a high risk of death with 2000 mg (80 tablets).[15]

After safety is established (and this will need to be continually reassessed at each consultation), the two other aspects that need to be developed early in the process (and also continue on through the long-term management of the patient) are **educating** the patient about his or her condition and individual situation, and establishing a **therapeutic relationship.**

Assessment includes:

- **characterising** the symptom profile
- **calibrating** the severity and chronicity—rating scales can be employed here
- **corroborating** (if possible and appropriate) medical and psychiatric comorbidities and context. Significant psychiatric, physical and social comorbidities of depression are common. These include 49% suffering an anxiety disorder, 40% reporting child sexual abuse, 57% child physical abuse, 42% having been at some stage afraid of their partner and 72% reporting a chronic physical condition.[20] Putting the patient's condition into his or her individual psychosocial and medical context will improve the assessment
- **considering** coping styles, and the social, financial and occupational consequences of the patient's condition and situation

This assessment is often spread over multiple consultations.

Treatment

The basic treatments are outlined by the acronym **PACE** (which purposefully places priority on the psychological treatments—see FIG. 10.2). These are:

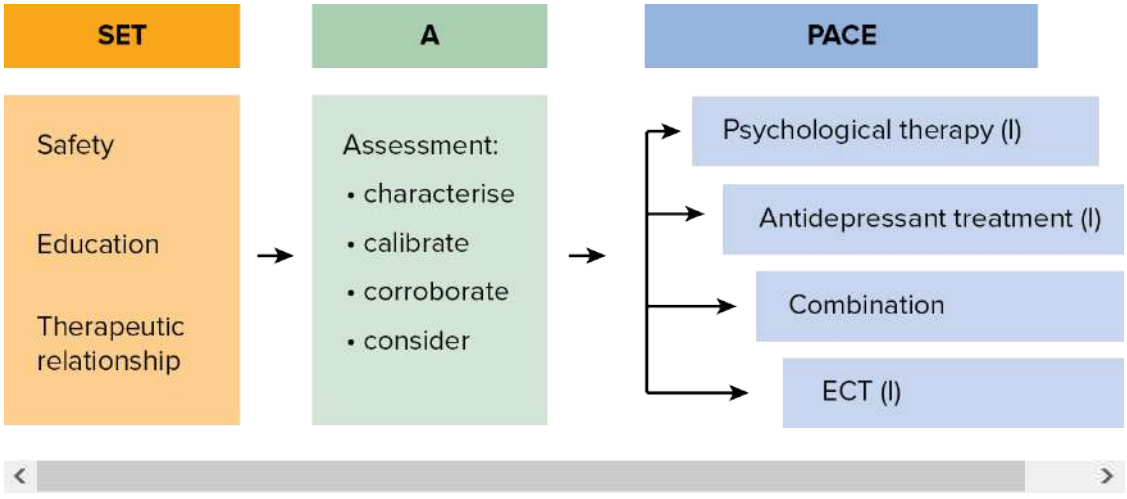
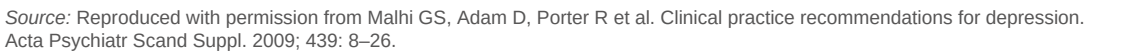


FIGURE 10.2 The SET A PACE model of treatment of depression



Source: Reproduced with permission from Malhi GS, Adam D, Porter R et al. Clinical practice recommendations for depression. Acta Psychiatr Scand Suppl. 2009; 439: 8–26.

- **Psychological**, including basic psychological treatments, such as advice on lifestyle changes, problem solving, guided self-help, structured supervised exercise and supportive counselling.[1,6] All patients with depression should be offered these types of support.[1,16] More sophisticated techniques, such as cognitive behaviour therapy (CBT) or interpersonal therapy (IPT), may be used for selected patients[7] and should be undertaken only by appropriately trained doctors or therapists.[6] Another option that some patients may prefer is computer-based cognitive behaviour therapy (CBT) programs.[13] CBT involves teaching patients new ways of positive thinking, which have to be relevant and achievable for the patient (see CHAPTER 4). Patients need to be able to recognise their own negative cognitions, including their anxieties and worries.

- **Antidepressants:** antidepressant medication is useful in moderate to severe depression (see TABLE 10.2), or when depression has an anxiety disorder codiagnosis.[13] Antidepressant therapy should be avoided if bipolar disorder is suspected, and screening should be actively conducted for symptoms of past or previous mania.[13]

In terms of which drug to use, there is no single drug that is preferred. Most antidepressant agents are approximately equal in efficacy, although individual patient response may vary considerably.[21] However, selective serotonin reuptake inhibitors (SSRIs) are considered to have the most favourable balance of benefit to harm in moderate to severe depression.[13] Sexual dysfunction and gastrointestinal side effects are common.[7] The most toxic agents are the tricyclic antidepressants (TCAs) and the monoamine oxidase inhibitors (MAOIs). Other suitable first-line agents are reboxetine (common side effects include hypersomnia, fatigue and nausea) and mirtazapine (which can cause weight gain and drowsiness).[7] SSRIs have a relatively flat dose–response curve, but dose increase within the recommended range is reasonable if there is a partial response at a lower dose and no troublesome side effects.

Combining different antidepressants or augmentation with lithium or antipsychotics should be done with psychiatrist supervision.[7]

Serotonin and noradrenaline reuptake inhibitors (SNRIs) appear to be more effective in treating severe depression symptoms (and may be a suitable first-line option here) but otherwise adverse effects may limit them to second-line treatment.[7] TCAs and MAOIs are considered second-line because of their side effect profiles.[14]

Table 10.2 First-line pharmacological treatment options for depression[15]

Drug	Usual initial dose	Maximum dose

SSRIs		
citalopram	20 mg (10 mg >65 years)	40 mg (20 mg >65 years)
escitalopram	10 mg	20 mg
fluoxetine	20 mg	80 mg
fluvoxamine	50 mg (at night), then 100 mg after 5–7 days	300 mg
paroxetine	20 mg	60 mg
sertraline	50 mg, then 100 mg after 5–7 days	200 mg
SNRIs		
desvenlafaxine (controlled-release)	50 mg	200 mg
duloxetine	60 mg	120 mg
venlafaxine (controlled-release)	75 mg	375 mg
Other		
mirtazapine	15–30 mg (at night)	60 mg
agometaline	25 mg (at night)	50 mg
reboxetine	2–4 mg (bd)	10 mg

The benefit of medication in moderate depression is equivalent to psychological therapies such as CBT/IPT and both of them are around 20% more likely to achieve remission than placebo.[1] In severe depression, medication is more effective than psychological therapies (see FIG. 10.3), though the latter in addition may help reduce relapse rates once remission is achieved by medication.[1,6]

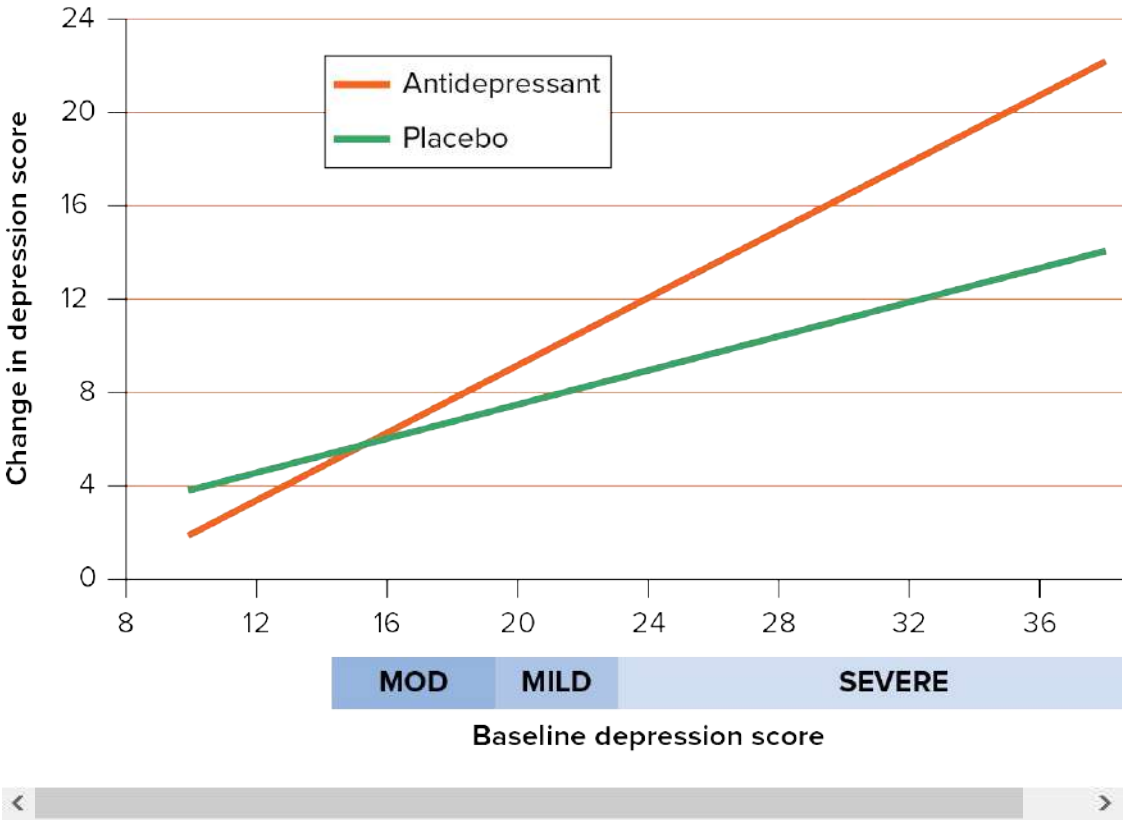


FIGURE 10.3 Antidepressant vs placebo drug effect on depression[19]

The aim of treatment of depression is to achieve and maintain remission.[1] Remission is defined as having minimal or no symptoms of depression,[7] and a good way of asking patients about this is to ask 'Do you think you are back to your normal self?'.

When using antidepressants, if a response is not evident in the first 2 weeks or there is an inadequate response in 6 weeks, then it is unlikely that this medication will work for this patient, and a treatment change is recommended.[7] A washout period will be required before a second medication is tried. Patients need close monitoring early on in the course of treatment, and weekly monitoring may be helpful.[13] If remission is not achieved in 3 months, then consider a second opinion and continue active treatment.[7]

- **A combination** of antidepressants and psychological therapy can be considered if there is an inadequate response to either therapy alone. Combining medication with psychological therapy is more effective than either therapy alone in moderate or severe depression.[7]

- **ECT (electroconvulsive therapy)** is a relatively safe and effective therapy for severe or resistant depression. There is some risk of transient short-term cognitive impairment and long-term memory impairment, and this therapy is reserved for severe depression when pharmacotherapy has failed;[7] it is administered under the supervision of a psychiatrist.

  Possible indications include:

psychotic depression (e.g. delusions, hallucinations)

melancholic depression unresponsive to antidepressants

severe postnatal depression and psychosis

substantial suicide risk

ineffective antidepressant medication and/or previous response to ECT

severe psychomotor depression: refusal to eat or drink, depressive stupor, severe personal neglect

Immediate referral for hospital admission is necessary in most of these circumstances. The course, which is highly variable and individually tailored, is about 8–12 sessions given at 1–3 sessions a week. The most common initial ECT method is unilateral therapy.[1]

Transcranial direct current electro-magnetic stimulation, where no anaesthetic is required, is a procedure being explored as a less invasive alternative to ECT.[22]

Useful management guidelines

- **Mild depression:** psychological therapy
- **Moderate depression:** psychological therapy and/or antidepressants
- **Severe depression:** antidepressants, and consider addition of psychological therapy to maintain remission. Consider psychiatric review, ECT.

When to refer

- Uncertainty about diagnosis
- Inpatient care obviously necessary
- Severe depression
- Inability to cope at home
- Psychotically depressed (with delusions or hallucinations)
- Substantial suicide risk
- Failure of response to routine antidepressant therapy

- Associated psychiatric or physical disorders
- Depression in the elderly can be a difficult problem—where diagnosis including dementia is doubtful
- Children with apparent major depression

Choice of treatment

The choice of treatment should be determined together by doctor and patient, and the best outcomes are likely when a good therapeutic alliance is formed[6] and patient preferences are taken into account.[13] To quote the RANZCP guidelines: 'Of greatest benefit is the therapeutic relationship, which enables agreement on treatment selection and continuation.'[1] A strong determining factor on patient preference may be the patient's own previous experience of treatments, or his or her perceptions of treatment results in other people they know or potential adverse effects of the proposed treatment.[13]

Whatever treatment is chosen by the doctor and patient working together, the choice is less important than persisting with treatment. As the Beyond Blue guidelines state, it is 'not so much what you do but that you keep doing it'.[6] This is why consistent follow-up and monitoring is so beneficial.

Complementary and alternative therapies

Complementary and alternative therapies are widely used for depression. It is estimated that only 50% of Australians who are depressed receive an evidence-based professional intervention.[23] A large driver for this is the public's belief in complementary and alternative therapies. One study[24] showed 57% regarded vitamins, minerals, tonics or herbal medicines as likely to be helpful for treating depression, compared with 29% who regarded antidepressants as likely to be helpful.

Despite this, none of these therapies is supported by evidence, though some warrant further evaluation.[25] Because of their common usage (nearly half of Australians have used a complementary medicine in the previous 12 months),[25] actively enquiring about use of any complementary and alternative therapies in patients with depression is advised.

One of the more commonly used and extensively researched alternative therapies is St John's wort (*Hypericum perforatum*), which has had mixed results in the research on its effectiveness. One review of the literature suggests it is effective in mild to moderate depression,[26] though two others suggest it is not.[27,28]

Regardless of its effectiveness (or not), it has a lot of medication interactions. These include HIV medicines, warfarin, digoxin, anticonvulsants, oral contraceptives and triptans.[21] Because of this, care needs to be taken with using St John's wort, including when switching between different preparations that may contain different amounts of active compound.[19]

Serotonin syndrome

- While rare, serotonin syndrome is a serious adverse reaction to the use of SSRIs and other serotonergic medications, including St John's wort.
- Symptoms must coincide with the introduction or dose increase of a serotonergic agent. Drugs to be considered here include antidepressants, opioids (especially tramadol), stimulant drugs, illicit drugs, anti-emetics, lithium and selegiline.
- Other causes, such as infection, substance abuse or withdrawal, must be excluded.
- At least three of the symptoms or signs attributed to the syndrome must be present, e.g.:

  mental status/behaviour changes (e.g. agitation, confusion, hypomania, seizures)

  altered muscle tone (e.g. tremor, shivering, myoclonus, hyper-reflexia)

  autonomic instability (e.g. hypertension or hypotension, tachycardia, fever, diarrhoea)

The offending agents should be withdrawn immediately and supportive therapy initiated; refer to an emergency department.

Continuing treatment

If antidepressant medication is used and remission achieved, it is recommended that it be continued for a minimum of 12 months for an initial episode, and for 2–3 years in subsequent episodes or in those at high risk of relapse.[1,13] Risk factors for relapse include:[7,13]

- residual depressive symptoms
- 2 or more prior episodes in the past 5 years
- 3 or more prior episodes
- history of severe or prolonged depression (especially with psychosis or attempted suicide)
- comorbid medical problems
- life stressors

When remission is achieved, and the treatment is in the maintenance phase, ongoing monitoring of treatment effectiveness, tolerability and adherence is recommended.[7] Encouragement to persist with the treatment will improve compliance.[1] When ceasing medication, withdrawal reactions are common, so a gradual withdrawal by halving the dose each week may help reduce these.[1]

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11 Diabetes mellitus

Those labouring with this Disease, piss a great deal more than they drink. Authors who affirm the drink to be little or nothing changed are very far from the truth, because the urine very much differed both from the drink taken in and also in being wonderfully sweet as if it were imbued with honey or sugar.

THOMAS WILLIS (1621–1675), *THE PISSING EVIL*

Diabetes comes from a Greek word meaning 'to pass or flow through' (i.e. excessive urination) and *mellitus* means 'sweet'. It is a disease caused by a relative or absolute deficiency of insulin.

There are two main types of diabetes (see TABLE 11.1).

Table 11.1 Clinical differentiation between type 1 and type 2 diabetes

	Type 1	Type 2
Relative frequency (approx.)	10%	85–90%
Peak age incidence	10–30 years	>40 years
Age of onset	Usually young <20	Usually middle-aged >40
Onset	Rapid	Insidious/slow
Presentation	Polyuria, polydipsia weight loss	Milder symptoms, often asymptomatic
Weight at onset	Low (thin)	High (obese)
Ketoacidosis	Yes	Rare
Familial	Weak	Strong
Insulin status	Deficient	Resistant

Note: These are generalisations and the clinical features may vary (e.g. patients with type 2 diabetes may be thin and have a rapid onset, or present at an earlier age).

- Type 1 is also known as juvenile onset diabetes or insulin dependent diabetes mellitus (IDDM).
- Type 2 is also known as maturity onset diabetes or non-insulin dependent diabetes mellitus (NIDDM).

Type 1 has an autoimmune causation which is also responsible for a late-onset form known as late onset autoimmune diabetes in adults (LADA).

Diabetes: a real masquerade

The onset of type 2 diabetes can be subtle and by stealth. In 2014–15, around 1.2 million (5%) Australians had diagnosed type 2 diabetes[1] and another 500 000 (2.1%) were estimated to have type 2 diabetes but were not yet diagnosed.[2] A further 2 million (8.4%) had impaired fasting glucose or impaired glucose tolerance. Around half of those with type 2 diabetes have complications (when microalbuminuria is included), many of whom already have a complication at the time of diagnosis. The challenge for GPs is to be on constant lookout for these individuals, especially those at risk. Type 2 diabetes is becoming more prevalent in industrial countries—due to the ageing population, broadened diagnostic definitions and because our lifestyle encourages us to 'eat more and walk less'.[3] Furthermore, roughly 60% of our population are overweight or obese.

Complications occur in both type 1 and type 2 diabetes.

- Several causes of secondary diabetes are uncommon (pancreatic disease; approx. 2.5%) or very uncommon (see TABLE 11.2).
- Asymptomatic people at high risk of undiagnosed diabetes should be screened by blood glucose or HbA1c measurement.

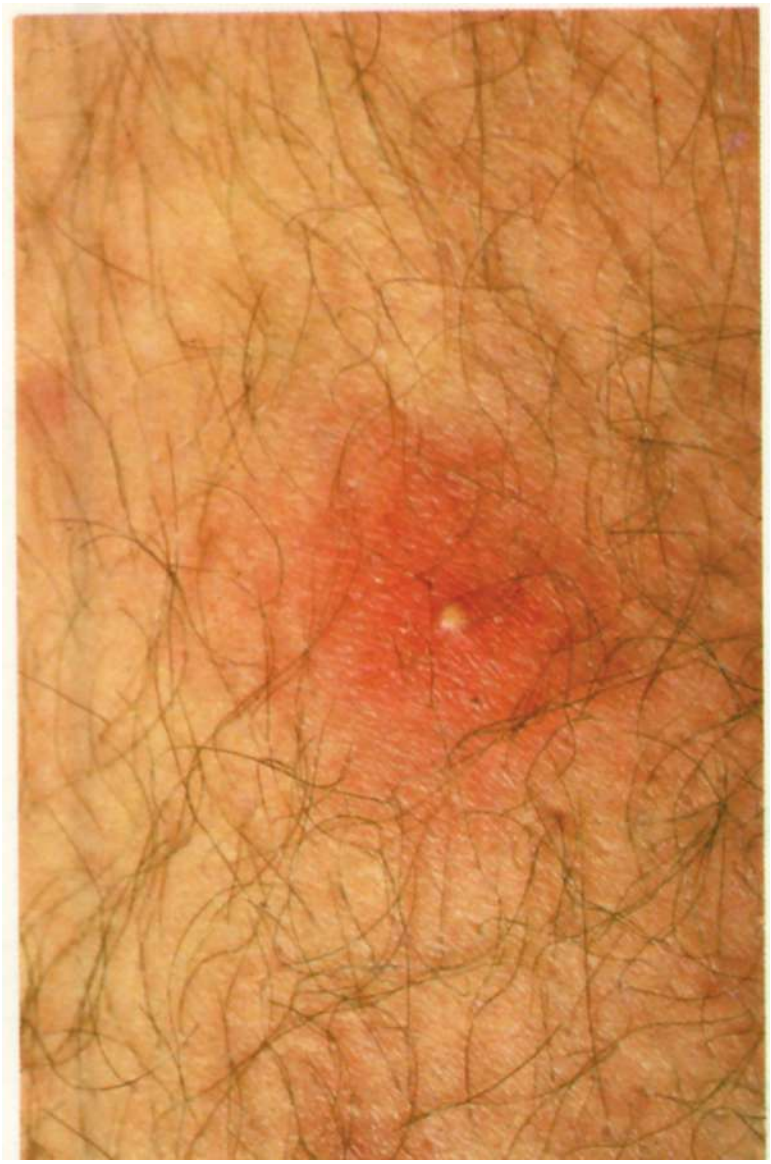
Table 11.2 Causes of secondary diabetes

Pancreatic disorders (sometimes called 'Type 3c diabetes')
Chronic pancreatitis
Endocrine disorders
Cushing syndrome
Acromegaly
Phaeochromocytoma
Polycystic ovarian syndrome
Haemochromatosis
Drug-induced diabetes (transient)
Thiazide diuretics

Oestrogen therapy (high dose—not with low-dose HRT)
Corticosteroids
Other transient causes
Gestational diabetes
Medical or surgical stress

Key facts and checkpoints

- In Australians older than 25 years the prevalence of diabetes is 7.5%, with another 10.6% having impaired glucose tolerance.[1]
- About 30% of those with impaired glucose tolerance will develop clinical diabetes within 10 years.[3]
- Many people with type 2 diabetes are asymptomatic.
- Diabetes can exist for years before detection and complications may be evident.
- Blood glucose may be temporarily elevated during acute illness, after trauma or surgery.



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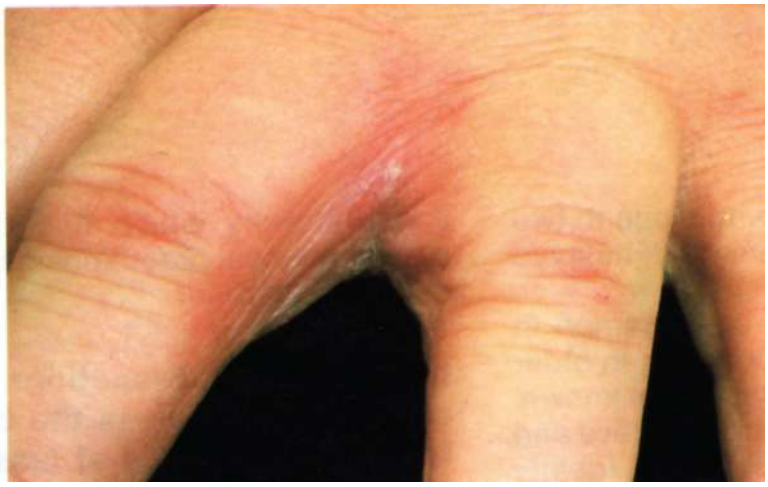

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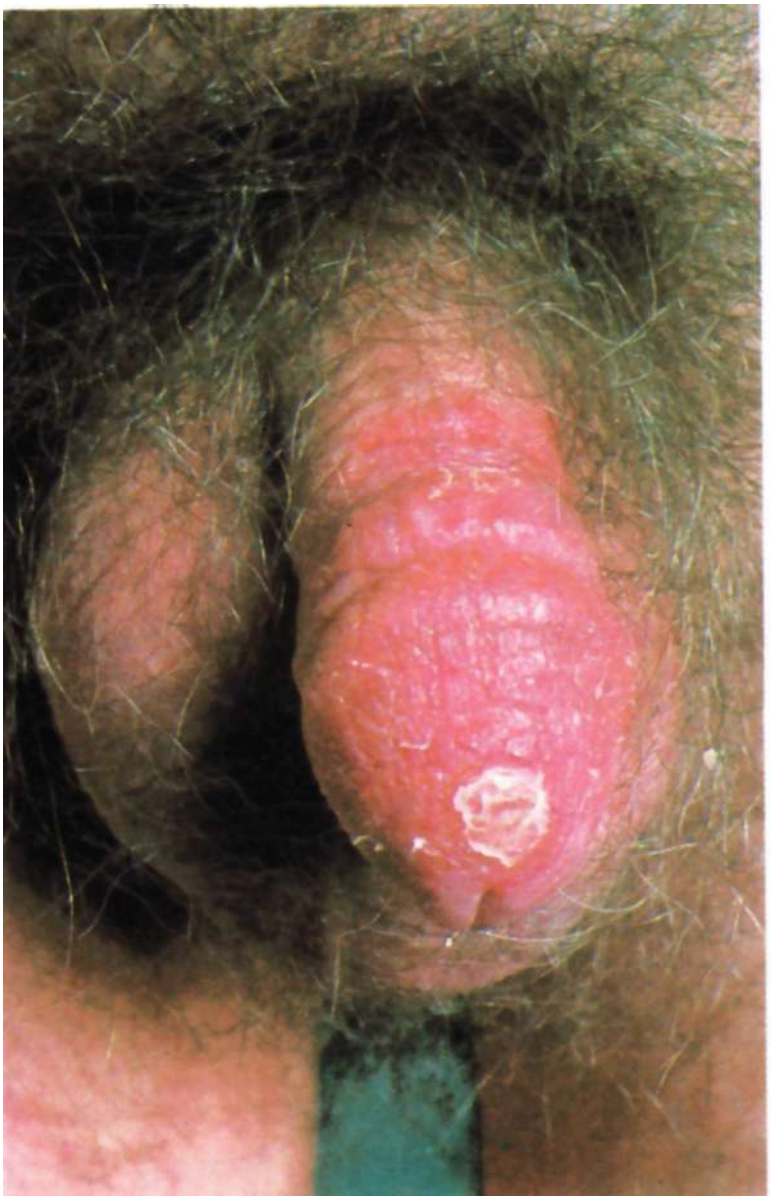

(c)

FIGURE 11.1 Skin signs of diabetes: **(a)** Recurrent staphylococcus folliculitis, **(b)** *Candida albicans* erosio interdigitalis, **(c)** *Candida albicans* balanitis

Clinical features

The classic symptoms of uncontrolled diabetes are:

- polyuria

- polydipsia
- loss of weight (type 1)
- tiredness and fatigue
- propensity for infections, especially of the skin and genitals (vaginal thrush)

The young person with type 1 diabetes typically presents with a brief 2–10 week history of the classic triad of symptoms:

DxT thirst + polyuria + weight loss → type 1 diabetes

The first presentation of type 1 diabetes (typically an unwell child with a high finger-prick blood glucose) is a medical emergency, requiring hospital assessment. Other possible symptoms are:

- vulvovaginitis
- pruritus vulvae
- balanitis

} due to *Candida albicans*

- nocturnal enuresis (type 1)
- blurred vision/visual changes

Symptoms of complications (may be presenting feature) include:

- staphylococcal skin infections
- polyneuropathy: tingling or numbness in feet, pain (can be severe if present)
- impotence

- arterial disease: myocardial ischaemia, peripheral vascular disease

History

The history from a person with suspected or known diabetes should cover the following features, including assessment of cardiovascular risks and end-organ damage.

- Specific symptoms:

  polyuria

  polydipsia

  loss of weight

polyphagia

tiredness/malaise/fatigue

nocturia

- Related general symptom review:

  cardiovascular (e.g. chest pain, dyspnoea)

  urinary function

  sexual function

  neurological (e.g. tingling in feet/hands)

  vision (e.g. blurred)

  infection tendency (e.g. skin, urine, genital)

  genital itching

- General:

  family history

  medication

  smoking and alcohol

  obstetric history (where applicable)

  physical activity

  nutrition/eating habits

Examination

The physical examination should ideally follow the protocol for annual review.

Initial screening for suspected diabetes should include:

- general inspection, including skin
- BMI (weight/height)
- waist circumference
- visual acuity

- blood pressure—lying and standing
- test for peripheral neuropathy: tendon reflexes, sensation (e.g. cotton wool, 10 g monofilament, Neurotips)
- urinalysis: glucose, albumin, ketones, nitrites

Investigations

- Initial: fasting or random blood sugar, follow-up oral glucose tolerance test (OGTT) or glycated haemoglobin (HbA1c) if indicated
- Other tests according to clinical assessment (e.g. lipids, kidney function, urine albumin–creatinine ratio (ACR), ECG)

Risk factors

- Age >40 years
- Family history
- Overweight/obesity
- Sedentary lifestyle
- History of gestational diabetes, pancreatitis
- Women with polycystic ovarian syndrome (PCOS)
- Hypertension/ischaemic heart disease
- Medication causing hyperglycaemia
- Ethnic/cultural groups: Aboriginal and Torres Strait Islanders, Pacific Islanders, people from Indian subcontinent, Chinese, Afro-Caribbeans

Screening (type 2)[4]

- People with known impaired fasting glucose/glucose tolerance (‘prediabetes’)
- Age >40 years, or younger age (e.g. >30 years) with: family history (first-degree relative with T2D), obesity (BMI >30), high-prevalence ethnic groups
- Age >18 years in Aboriginal and Torres Strait Islander people
- Previous gestational diabetes
- People on long-term steroids or antipsychotics

- Polycystic ovarian syndrome, especially if overweight
- Previous cardiovascular event

The optimal frequency is every 3 years from age 40 years using AUSDRISK (www.diabetesaustralia.com.au/are-you-at-risk-type-2). If score ≥12, do fasting blood glucose or HbA1c. Screen annually in very high-risk groups, including Aboriginal and Torres Strait Islander people and those with 'prediabetes'.[5]

Diagnosis

Diabetes is diagnosed as follows:[3,4]

1. If symptomatic (at least two of polydipsia, polyuria, frequent skin infections or frequent genital thrush):
   - fasting venous blood glucose (VBG) ≥7.0 mmol/L

     or

   - random VBG (at least 2 hours after last eating) ≥11.1 mmol/L

     or

   - HbAIc >6.5% (>48 mmol/mol)
2. If asymptomatic:
   - at least two separate elevated values, either fasting, 2 or more hours postprandial, or the two values from an oral glucose tolerance test (OGTT)

Note: If random or fasting VBG lies in an uncertain range (5.5–11.0 mmol/L) in either a symptomatic patient or a patient with risk factors (over 50 years, overweight, first-degree relative with T2D), perform an OGTT. The cut-off point for further testing is 5.5 mmol/L.[4,6]

The 2-hour blood sugar on an OGTT is still the gold standard for the diagnosis of uncertain diabetes, i.e. >11.1 mmol/L.

The OGTT should be reserved for true borderline cases and for diagnosing gestational diabetes, where a 75 mg OGTT is recommended at 24–28 weeks' gestation.[7]

Prediabetes

This is the condition where the VPG is elevated above the normal range (i.e. 6.1–6.9) but does not satisfy the type 2 diagnostic criteria. It includes two states:

- impaired fasting glucose (IFG)

- impaired glucose tolerance (IGT)

A diagnosis of prediabetes is not a call to start medication, but it increases the urgency of promoting lifestyle changes such as weight reduction and increased physical activity.

Urinalysis is unreliable in diagnosis since glycosuria occurs at different plasma glucose values in patients with different kidney thresholds.

For a summary of diagnosis of diabetic states, refer to FIGURE 11.2 .

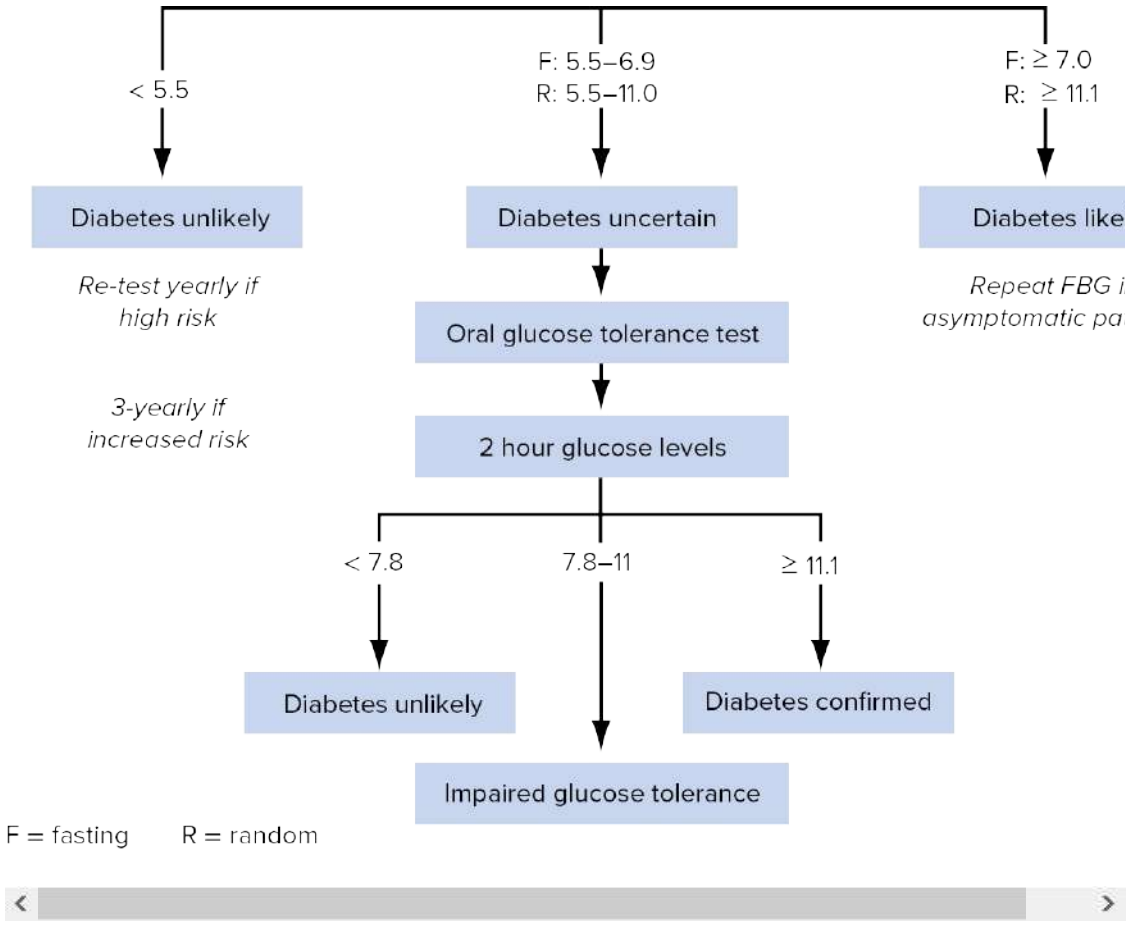

FIGURE 11.2 Blood glucose levels: venous plasma (mmol/L)

Source: Reproduced with permission from RACGP. General Practice Management of Type 2 Diabetes: 2016–18. East Melbourne, 2016 (book available from: http://www.diabetesaustralia.com.au or http://www.racgp.org.au).

Table 11.3 Interpreting diagnostic tests for diabetes[8]

Test	Normal	Intermediate hyperglycaemia	Diabetes

Venous blood glucose concentration	fasting	up to 6 mmol/L	6.1–6.9 mmol/L	≥7 mmol/L
	random	up to 6 mmol/L		≥11.1 mmol/L
Oral glucose tolerance test	2-hour venous blood glucose concentration	up to 7.7 mmol/L	7.8–11 mmol/L	≥11.1 mmol/L
HbA1c				≥48 mmol/mol

Diabetes in children

A study by Sinah and colleagues detected impaired glucose tolerance in 25% of 55 obese children (4 to 10 years of age) and 21% of 112 obese adolescents (11 to 18 years of age).[9] Type 2 diabetes was identified in 4% of obese adolescents. However, over 30% of newly diagnosed diabetes in children and adolescents is upon presentation with diabetic ketoacidosis. Children with type 1 diabetes usually exhibit the classic features of polyuria, polydipsia, weight loss and lethargy. Be aware of unusual presentations such as urinary disorders including enuresis or daytime wetting accidents when a misdiagnosis of urinary infection or some other condition is sometimes forthcoming. The diagnosis can be made by an elevated random or fasting blood sugar. Oral glucose tolerance tests are inappropriate in the very young. Upon diagnosis it is appropriate to refer the child or adolescent to a multidisciplinary diabetes team. The sick child with a high blood glucose is an emergency presentation of type 1 diabetes until proven otherwise.

Gestational diabetes

Gestational diabetes is the new onset of abnormal glucose tolerance during pregnancy. Pregnancy is diabetogenic for those with a genetic predisposition. All pregnant women should be screened at 24–28 weeks with a 75 g oral glucose tolerance test (OGTT). The definition of gestational diabetes mellitus (GDM) by the Australasian Diabetes in Pregnancy Society has widened considerably in the past two decades, and far more women are captured by the lower thresholds.[10] The 2014 consensus definition of gestational diabetes is a fasting plasma glucose of ≥5.1 mmol/L, or a post-75 g oral glucose load at 1 hour ≥10.0, or at 2 hours 8.5–11.0. Refer to CHAPTER 100 .

Diabetes in the elderly

The incidence of diabetes rises with age. The elderly have increased mortality and morbidity from the disease, but also are at increased risk from aggressive treatment regimens. Careful monitoring is required, especially with adverse drug effects aggravated by polypharmacy and comorbidities. Special issues include diet, foot care and postural hypotension.

Complications of diabetes

Complications may occur in patients with both type 1 and type 2 diabetes, even despite early diagnosis and treatment (see FIG. 11.3).

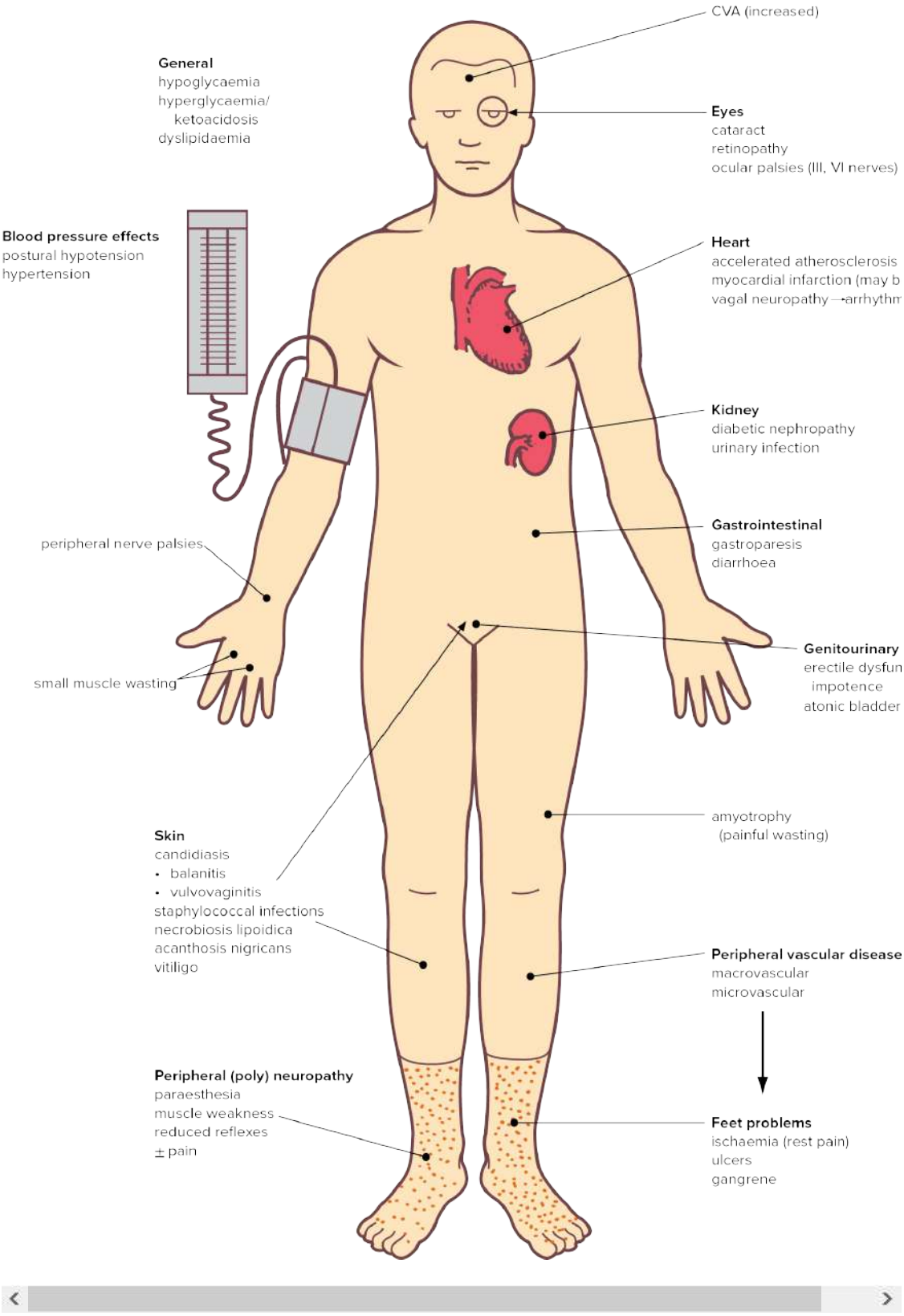

FIGURE 11.3 The complications of diabetes

People with type 1 diabetes still have a significantly reduced life expectancy. The main causes of death are diabetic nephropathy and vascular disease (myocardial infarction and stroke).

Diabetes causes both macrovascular and microvascular complications but microvascular disease is specific to diabetes. Special attention should be paid to the association of type 2 diabetes with obesity, hypertension and dyslipidaemia—the ‘deadly quartet’.[6,11]

Macrovascular complications include:

- ischaemic/coronary heart disease
- cerebrovascular disease
- peripheral vascular disease

An analysis of type 2 diabetes in the HOPE study[12,13] showed a benefit of ramipril to reduce the risk of:

- death (24%)
- myocardial infarction (22%)
- stroke (33%)
- cardiovascular death (37%)
- overt nephropathy (24%)

Consider organs/problems affected by diabetes under the mnemonic ‘KNIVES’:

- **K**idney
- **N**erves
- **I**nfection
- **V**essels
- **E**yes
- **S**kin

Microvascular disease

The small vessels most affected from a clinical viewpoint are the retina, nerve sheath and kidney glomerulus. In younger people it takes about 10 to 20 years after diagnosis for the problems of diabetic retinopathy, neuropathy and nephropathy to manifest.

Nephropathy

Prevention of diabetic nephropathy is an essential goal of treatment. Early detection of the yardstick, which is microalbuminuria, is important as the process can be reversed with optimal control, particularly of blood pressure. The dipstick method is unreliable and the preferred hospital method of 24-hour urine collection is considered impractical in general practice. Screening is done simply by a first morning urine sample to determine the albumin–creatinine ratio (see CHAPTER 79).

ACE inhibitors (or angiotensin II receptor blockers if a cough develops) should be used for evidence of hypertension.

Retinopathy and maculopathy

Retinopathy develops as a consequence of microvascular disease of the retina. Its prevalence is related to the duration of illness but up to 20% of people with type 2 diabetes have diabetic retinopathy at the time of diagnosis. The European multicentre study[14,15] showed that diabetes is the single most common cause of blindness in European adults in the 16–64 years age groups. Assessment of the fundus by an expert is recommended every 1–2 years, via direct ophthalmoscopy (with dilated pupils), retinal photography or, if necessary, fluorescein angiography. Early diagnosis of serious retinopathy is vital since the early use of laser photocoagulation may delay and prevent visual loss.

Neuropathy

The following types of neuropathy may occur:

- radiculopathy (diabetic lumbosacral radiculoplexopathy)
- sensory polyneuropathy
- isolated or multiple mononeuropathy

    isolated peripheral nerve lesions (e.g. median nerve)

    cranial nerve palsies (e.g. III, VI)

    amyotrophy
- autonomic neuropathy, which may lead to:

    erectile dysfunction

    postural hypotension and syncope

    impaired gastric emptying (gastroparesis)

diarrhoea

delayed or incomplete bladder emptying

loss of cardiac pain → ‘silent’ ischaemia

hypoglycaemic ‘unawareness’

sudden arrest, especially under anaesthetic

Infections

People with poorly controlled diabetes are prone to infections, especially:

- skin: mucocutaneous candidiasis (e.g. balanitis, vulvovaginitis), staphylococcal infections (e.g. folliculitis)
- urinary tract: cystitis (women), pyelonephritis and perinephric abscess
- lungs: pneumonia (staphylococcal, streptococcal pneumonia), tuberculosis

Diabetic metabolic complications

- Hypoglycaemia
- Diabetic ketoacidosis
- Hyperosmolar hyperglycaemia
- Lactic acidosis

Other complications

- Cataracts
- Refractive errors of eye
- Sleep apnoea
- Depression
- Musculoskeletal: neuropathic joint damage (Charcot-type arthropathy), tendon rupture
- Foot ulcers (related to neuropathy)

Prevention of diabetes

Several large studies have demonstrated it is possible to prevent or delay the onset of type 2 diabetes in those at risk.[14,15] This involves intensive lifestyle intervention in individuals who are overweight with impaired glucose tolerance or raised fasting blood glucose. The ongoing DiRECT trial demonstrates that even once type 2 diabetes has been present for a few years, remission of diabetes is a realistic aim in general practice, using intense dietary measures for 3 months followed by structured support for weight loss management.[16]

The primary strategy is to follow the SNAP guidelines (Smoking, Nutrition, Alcohol, Physical activity), particularly with a view to weight loss.[17] The essentials are healthy eating, weight loss and physical activity. This represents an important approach that GPs can recommend to their patients at risk. The enormous health gains that can be made in this prediabetic population by concentrating on SNAP outweigh any later health gains from diabetes medication (see CHAPTER 80).

Management of diabetes

The main objectives for the GP are to prevent the development of cardiovascular disease and other complications. Aim to achieve:[4]

1. reduction of 'lifestyle' risks—weight, smoking, low physical activity
2. strict glycaemic control as measured by HbA1c (target varies with circumstance, but usually ≤7%)
3. blood pressure control (≤140/90 mmHg, lower if tolerated)[18]
4. control of blood lipid levels

Note: Refer to the estimations of cardiovascular risk (see FIGS. 75.1 and 75.2 in CHAPTER 75).

Management principles

- Provide detailed and comprehensive patient education, support and reassurance.
- Achieve control of presenting symptoms.
- Achieve blood pressure control (huge impact on mortality risk).
- Develop a diabetes care plan.
- Emphasise the importance of the diet: good nutrition, adequate protein, complex carbohydrates (low carb diets are an option), restrict fats and sugars.
- Promptly diagnose and treat urinary tract infection.

- Treat and prevent life-threatening complications of ketoacidosis or hyperosmolar coma.
- Treat and prevent hypoglycaemia in those taking insulin and oral hypoglycaemic agents.
- Organise self-testing of blood glucose for those on insulin.
- Detect and treat complications of diabetes—neuropathy, nephropathy, retinopathy, vascular disease.
- Ensure immunisation schedule, including influenza and pneumococcus, is updated.

Monitoring techniques

- Blood glucose estimation (mainly useful if on insulin; fasting and postprandial)
- Urine glucose (of limited usefulness)
- Urine or blood ketones (for type 1 diabetes)
- Glycated haemoglobin (HbA1c) (3-monthly)
- Microalbuminuria (usually urine ACR, regarded as an early and reversible indicator of nephropathy)
- Blood pressure
- Serum lipid levels
- Kidney function (serum urea/creatinine eGFR)
- ECG

Control guidelines are summarised in FIGURE 11.4 and TABLE 11.4 .

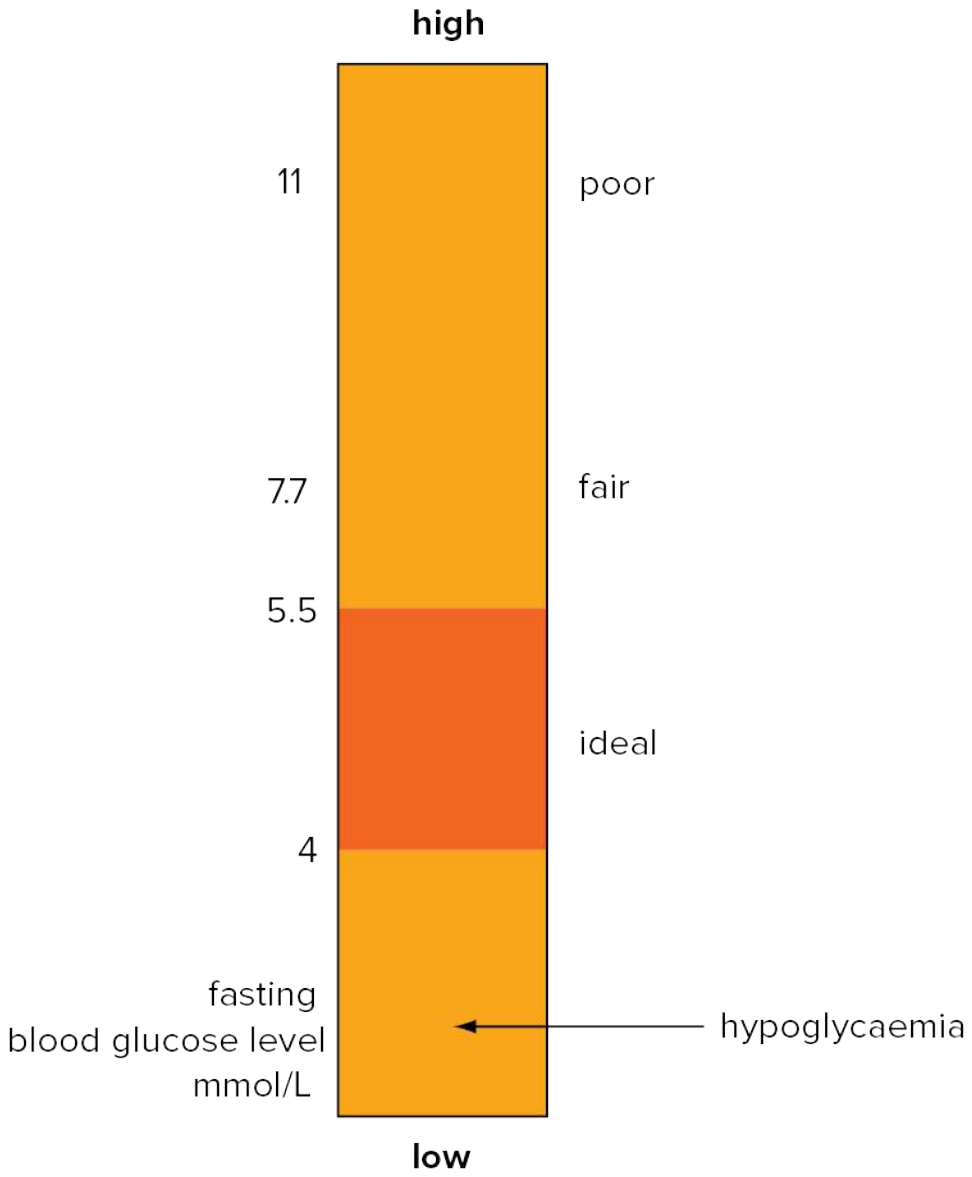

FIGURE 11.4 Blood glucose control guidelines for diabetes management

Table 11.4 Suggested guidelines for glycaemic control (blood glucose mmol/L)[4,5,19]

	Ideal	Suboptimal or unacceptable
Before meals (fasting)	<5.5	>7.7
After meals (2 hours postprandial)	<7	>11
HbA1c %*	≤7	>8

*HbA1c is an index reflecting the mean plasma glucose levels over the preceding 2–3 months (assume a reference range of 4.5–8%).

Blood glucose monitoring at home

This is done using a glucose meter (glucometer). A wide variety of meters and smart phone apps are available: patients will require advice about what suits them.

How often and when?

- Type 1 diabetes:

  four times a day (before meals and before bedtime) at first and for problems

  twice a day (at least once)

  may settle for 1–2 times a week (if good control)

- Type 2 diabetes:

  important for those on insulin, not routinely recommended for oral medication (monitor with HbA1c instead, in most circumstances)

  more useful for pregnant women, frail elderly, heavy machinery operators or symptomatic hypoglycaemia

Goals of management[4,5]

All people with diabetes should be encouraged to maintain the following goals for optimum management:

- Blood glucose (fasting) — ideal 4–6 mmol/L NHMRC 6–8 mmol/L
- Blood glucose (postprandial) — 8–10 mmol/L
- HbA1c — ≤7% (53 mmol/mol)
- Total cholesterol — <4.0 mmol/L
- LDL cholesterol — <2.0 mmol/L
- HDL cholesterol — ≥1.0 mmol/L
- Non-HDL-C — <2.5 mmol/L
- Triglycerides — <2.0 mmol/L
- Blood pressure

	<140/90 mmHg, lower if tolerated, esp. stroke risk ≤125/80 mmHg with proteinuria (1 g/day)
• BMI	18–25 where practicable
• Urinary albumin excretion	<20 mcg/min timed overnight collection <20 mg/L spot collection
• Albumin–creatinine ratio	<2.5 mg/mmol—men <3.5 mg/mmol—women
• Cigarette consumption	zero
• Alcohol intake	≤2 standard drinks, 20 g/day (men and women)
• Exercise	at least 30 minutes walking (or equivalent) 5 or more days/week (total 150 minutes/week)

Note:

- Capillary blood glucose is approximately 7% higher than venous blood.
- Glucometer error is usually ±5%.

Glycated haemoglobin

HbA1c, which normally comprises 4–6% of the total haemoglobin, is abnormally abundant in those with persistent hyperglycaemia, reflecting suboptimal metabolic control. Glycohaemoglobins have a long half-life and their measure reflects the mean plasma glucose levels over the past 2–3 months and hence provides a good method of assessing overall diabetes management. HbA1c should be checked every 3–6 months.

Type 1 diabetes

The three main objectives of the treatment of type 1 diabetes are:

- maintain good health, free from the problems of hyperglycaemia and hypoglycaemia
- achieve proper growth and maturation for children and protect the fetus and mother in a mother with type 1 diabetes

- prevent, arrest or delay long-term macrovascular and microvascular complications

Insulin regimens for type 1 diabetes[4,20]

The most commonly used insulin injection preparations are the 'artificial' human insulins. Insulins are classified according to their time course of action:

- rapid-acting and short duration (ultra-short)—insulin lispro, insulin aspart
- short-acting—neutral (regular, soluble)
- intermediate-acting—isophane (NPH) or lente
- long-acting—ultralente, insulin detemir, insulin glargine
- pre-mixed short/intermediate—biphasic (neutral + isophane)

Also: continuous subcutaneous insulin infusion.

Starting insulin[20]

For less experienced GPs, shared care with an endocrinologist is recommended.

It is important to use the simplest regimen for the individual and to provide optimal education about its administration and monitoring. Full replacement of insulin is achieved by using 2, 3 or 4 injections per day. However, automated glucose monitoring linked to 'smart' insulin pumps can make an injection decision every five minutes. See TABLE 11.5 for available insulins.

Table 11.5 Available insulins[4,20]

Type	Brand name
Ultra-short-acting (peak 1 hour, duration 3.5–4.5 hours)	
Insulin lispro	Humalog*
Insulin aspart	NovoRapid**
Insulin glulisine	Apidra*
Short-acting (peak 2–5 hours, duration 6–8 hours)	
Neutral (regular)	Actrapid**
	Humulin R*
	Hypurin Neutral*
Intermediate-acting (duration 12–24 hours)	

Isophane (NPH)	Humulin NPH*
	Protaphane**
	Hypurin Isophane
Long-acting (analogues)	
Insulin glargine (duration 24–36 hours)	Optisulin (Lantus)
Insulin detemir (duration up to 24 hours)	Levemir
Pre-mixed (short- and intermediate- or long-acting)	
Lispro 25%/Protamine 75%	Humalog Mix 25*
Lispro 50%/Protamine 50%	Humalog Mix 50*
Insulin aspart 30%/Protamine 70%	NovoMix 30**
Neutral 30%/Isophane 70%	Humulin 30/70*
	Mixtard 30/70**
Neutral 50%/Isophane 50%	Mixtard 50/50**

*Available in cartridges for use in pen injectors
**Available in cartridges for use in pen injectors or in disposable insulin pens

1. *The pre-mixed 2 injection (biphasic) system*
   Give twice daily, 30 minutes before breakfast and before evening meal (e.g. Mixtard 30/70, Humulin 30/70—the most common)

   - Typical starting dose: 0.3 IU/kg/day—for a 70 kg person use 10 units bd

2. *3 injections per day*

   - Short-acting insulin before breakfast and lunch
   - Intermediate- or long-acting insulin before evening meal

3. *4 injections (basal-bolus) system*

   - Short-acting insulin before breakfast, lunch and dinner (bolus)
   - Intermediate- or long-acting insulin at bedtime (basal)

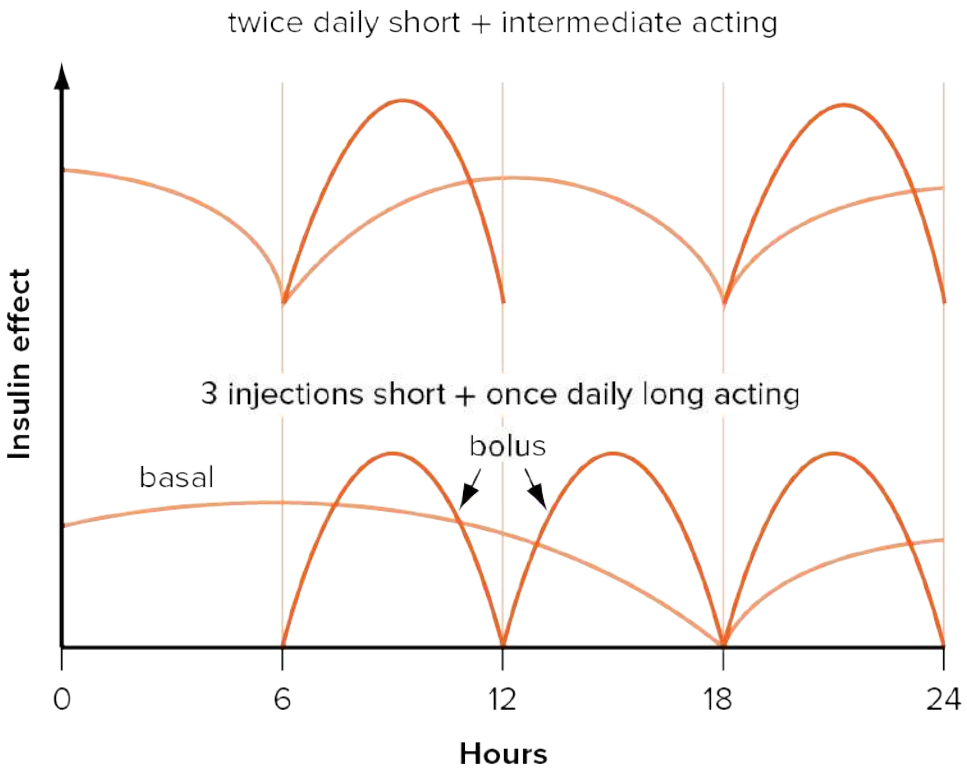

FIGURE 11.5 Illustration of time course of insulin injection regimens

Insulin requirements often vary significantly even in the same individual under different lifestyle conditions. The rapid-acting analogues can be taken with meals.

Methods of giving insulin injections

When

Suggest the patient develops a set routine, such as eating meals on time and giving the injection about 30 minutes before the meal.

Where

Into subcutaneous tissue—the best place is the abdomen. The leg is also acceptable. It is advisable to keep to one area (usually abdomen) and avoid injections into the arms, near joints and the groin. The injection should be given at a different place each time, at least 3 cm from the previous injection. This reduces the risk of the development of lipodystrophy. The means of delivery is the insulin syringe or the insulin delivery pen.

How

Pinch a large area of skin on the abdomen between the thumb and fingers and insert the needle

straight in. After withdrawing the needle, press down firmly (do not rub or massage) over the injection site for 30 seconds. Alcohol swabs are unnecessary.

Guidelines for the patient[4]

- Take your insulin every day, even if you feel ill.
- Do not change your dose unless instructed by your doctor or you are competent to do so yourself.

Problems

Injection sites should be inspected regularly because lipohypertrophy or lipoatrophy can occur.

Sick days

Have a prearranged action plan.

Never omit the insulin dose even if the illness is accompanied by nausea, vomiting or marked anorexia. More top-up insulin is usually required (rapid/fast acting).

Maintain glucose. Keep regular blood glucose checks (a concern if >15 mmol/L).

Seek support and help.

Sport

Encourage sporting activities. Careful planning (use expert help) and monitoring of blood sugar is required. Insulin doses may need to be adjusted before activities.

Additional carbohydrate may be needed.

Glycaemic targets for adults with type 1 diabetes

- HbA1c: 7% (53 mmol/mol)
- Blood glucose: fasting preprandial 4–7 mmol/L; postprandial 5–10 mmol/L

Type 2 diabetes[8,19]

First-line treatment (especially if obese):

- diet therapy
- exercise program
- weight loss

Most symptoms improve within 1–4 weeks on diet and exercise.[3] Prescribe and ask about exercise at every visit. Aim for an average of 20–30 minutes a day. Suggest variations such as social-type exercises. The secret to success is patient adherence through good education and supervision. The role of a diabetic education service, especially with a dietitian, can be invaluable. If unsatisfactory control persists after 3–6 months, consider adding an oral hypoglycaemic agent (see TABLE 11.6). The usual first-line agent is metformin, which reduces insulin resistance. If glycaemic targets are not achieved on monotherapy, usual practice is to add in a secretagogue, such as a sulfonylurea, which increases insulin production. However, the newer agents SGLT2 inhibitors (the gliflozins) and GLP-1 receptor agonists (injected) should be considered for their cardioprotective and renoprotective effects. DPP-4 inhibitors (oral gliptins) and thiazolidinediones (glitazones) are other options.

Table 11.6 Commonly prescribed non-insulin hypoglycaemic agents[8,20] (with examples)

Drug	Duration of action (hours)	Daily dose range	Notes including main generic adverse effects
Metformin (a biguanide)	12 (also slow-release daily dosage)	0.5–3 g	Side effects: • GIT disturbances (e.g. diarrhoea, a/n/v) • avoid in cardiac, hepatic and kidney disease (eGFR <30) • lactic acidosis, a rare but serious complication
Sulfonylureas			
Gliclazide	18–24	40–320 mg	Hypoglycaemia most common side effect

			Others: weight gain (common), rash and GIT (rare) Shorter acting sulfonylurea is preferred in elderly
Glipizide	16–24	2.5–40 mg	Longer acting potent ones cause troublesome hypoglycaemia in elderly
Glibenclamide	18–24	2.5–20 mg	
Glimepiride	>24	1–4 mg	
α-glucosidase inhibitors			
Acarbose	3	150–600 mg	Flatulence, skin rashes, diarrhoea, liver effects
Thiazolidinediones (glitazones)			Dubious mortality benefit. Caution with heart failure.
Pioglitazone	24	15–45 mg	Oedema, weight gain, heart failure
Rosiglitazone	24	4–8 mg	Hepatic effects, fracture risks
DPP-4 inhibitors (gliptins)			Slight pancreatitis risk
Sitagliptin	>24	25–100 mg	Rhinorrhoea, headache hypersensitivity, e.g. urticaria
Linagliptin	>24	5 mg	
Saxagliptin	24	5 mg	
Vildagliptin	>24	50–100 mg	Dizziness, fatigue
Alogliptin	>24	25 mg	
$SGLT_2$ inhibitors			Modest short-term efficacy
Empagliflozin	24	10–25 mg	

Dapagliflozin	24	5–10 mg	• genitourinary infections • dehydration, dizziness, hypoglycaemia
Ertugliflozin	24	5–15 mg	
GLP-1 agonists			Nausea, pancreatitis
Dulaglutide	1 week	1.5 mg	
Exenatide	12 hours 1 week (MR)	5 mcg bd 2 mg weekly	
Liraglutide	24 hours	0.6–1.8 mg daily	

Consider metformin as the first-line agent for all patients with type 2 diabetes, irrespective of their weight, unless contraindicated. The usual starting dose is 500 mg once or twice daily. It has proven benefits over the sulphonylureas, especially in those that are overweight. Other benefits include no significant weight gain, no hypoglycaemia and an improved lipid profile. If monotherapy does not provide adequate glycaemic control, a combination of metformin with another agent (see FIG. 11.6) is recommended.[20]

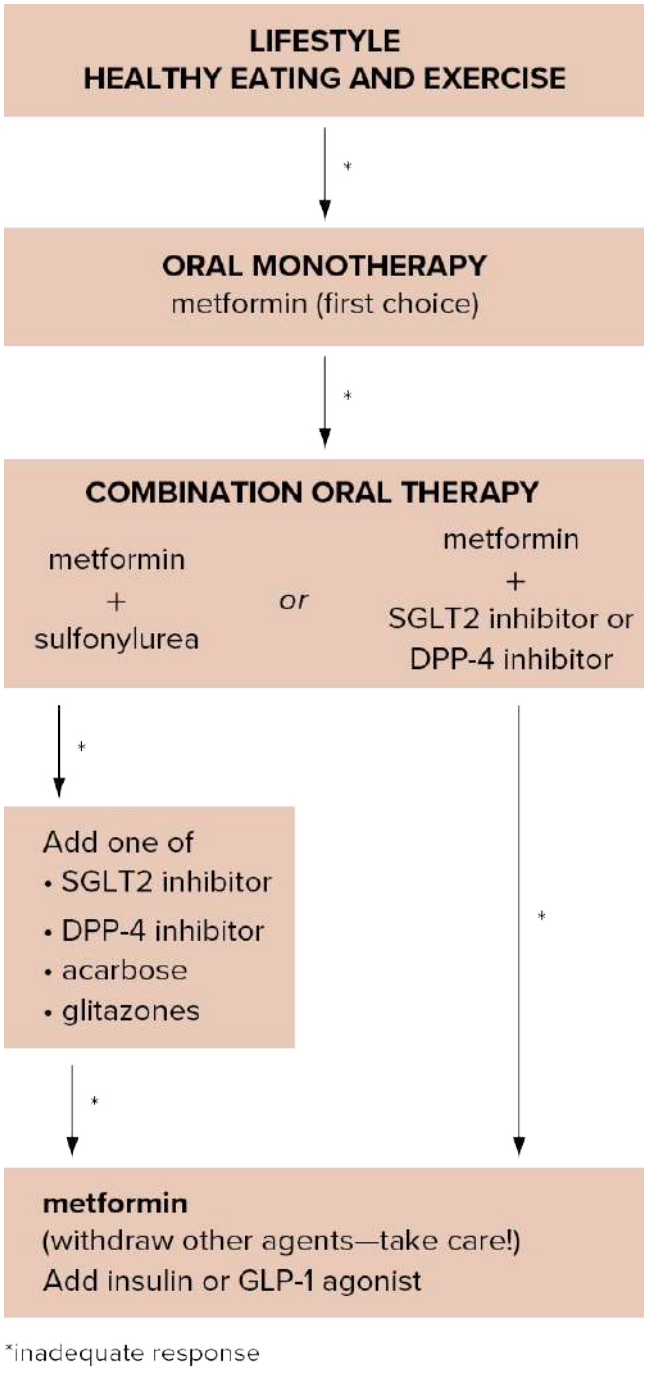

FIGURE 11.6 Step-up approach to management of type 2 diabetes[20]

When the first oral hypoglycaemics fail (secondary failure), a second agent can be added (usually sulfonylurea, DPP-4 inhibitor, SGLT2 inhibitor). Alternatives include GLP-1 receptor antagonists or insulin, and less commonly acarbose or a glitazone. The newer treatment options in type 2 diabetes include:[20]

- dipeptidyl peptidase-IV (DDP-4) inhibitors (gliptins, e.g. sitagliptin)
- sodium glucose cotransporter 2 (SGLT2) inhibitors taken orally, e.g. dapagliflozin, empagliflozin
- glucagon-like peptide-1 receptor (GLP-1) agonists (e.g. exenatide modified release—weekly dosing, liraglutide—daily dosing) given by SC injection. These improve satiety and are associated with weight loss. Nausea is fairly common, but tends to settle. Pancreatitis is a rare but important side effect.

Approximately 30% of those with type 2 diabetes eventually require insulin, although that figure may decrease with the availability of newer agents. An algorithm for the management of type 2 diabetes is presented in FIGURE 11.6 .

Remember that insulin is not a substitute for healthy eating and activity.

Starting insulin in type 2 diabetes[14,21]

Before commencing insulin one should be assured that the patient's lifestyle activities are being adequately addressed and that oral medication (at recommended maximum dose) is appropriate. There is no clear-cut rule about when to start insulin for those with HbA1c >7%, but this can be as early as when drug therapy does not provide adequate control. Two golden rules are 'don't delay initiating basal insulin' and then 'start low and go slow'.[21]

When commencing insulin, reassure the person that the injections are not as uncomfortable as finger pricks and that they will feel much improved with more energy.

It is appropriate to refer to your diabetic team for shared care at this point—when starting insulin.

Suggested stepwise approach[14,19]

Step 1

- Continue oral agents: metformin + sulfonylurea ± glitazone or acarbose or DPP-4 inhibitor (limited to 3).
- Add 10 units isophane insulin at bedtime.

Step 2

- Titrate insulin therapy according to fasting blood glucose (6 mmol/L).
- Increase insulin in about 4–5 U increments every 3–4 days (or more gradually).

Step 3

If larger or multiple daily doses of insulin are required (NPH or mixed regimen),

continue metformin but usually withdraw sulfonylureas, DPP-4s and thiazolidinediones.

Note: The combination of a glitazone and insulin has been shown to improve control of diabetes sometimes to the extent of being able to reduce insulin dosage. Consider using a glitazone, GLP1 agonist or SGLT2 inhibitor to reduce the insulin dose requirement. However, check PBS requirements for triple therapies.

The importance of diet and nutrition

Nutrition management is based on controlling weight, having a healthy eating plan and supplementing it with exercise. It is recommended to eat a wide variety from all food groups:

- protein 10–20%, fat 20–40%, carbohydrate 35–60%
- reduce fat, especially saturated fats, sugar and alcohol

People with type 1 diabetes often require three meals and sometimes regular snacks each day. People with type 2 usually require less food intake and restriction of total food intake.

Principles of dietary management

- Keep to a regular nutritious diet.
- Achieve ideal body weight.
- Reduce calories (kilojoules), particularly:
    - added sugar
    - dietary fat
- Follow the glycaemic index values (see: www.glycaemicindex.com).
- Increase proportions of vegetables, fresh fruit and cereal foods.
- Special diabetic foods are not necessary.
- ‘Whole foods’ are preferred to supplements.
- Qualitative diets are often more sustainable than quantitative diets (such as ‘exchanges’ or ‘portions’).

The importance of exercise[4,19]

Exercise is fundamental to good management. Exercise is any physical activity that keeps you fit. Good examples are brisk walking (e.g. 2 km per day), jogging, tennis, skiing and aerobics. Aim for at least 30 minutes three times a week, but daily exercise is ideal. Go slow when you

start and increase your pace gradually.

Psychosocial considerations

The psychological and social factors involving the patient are very influential on outcome. Considerable support and counselling may be necessary to help both patient and family cope with the ‘distress’ of the diagnosis and the discipline required for optimal control of their blood glucose. Reasons for poor dietary compliance and insulin administration must be determined and mobilisation of a supportive multidisciplinary network (where practical) is most helpful. The GP should be the pivot of the team. Encourage joining a self-support group where available.

Foot care

Foot problems are one of the commonest complications that need special attention; prevention is the appropriate approach. By international standards, Australia has an unenviably high rate of amputations in people with diabetes. Pressure sores can develop on the soles of the feet from corns, calluses, ill-fitting footwear, and stones and nails. Minor injuries such as cuts can become a major problem through poor healing. Infection of wounds is a major problem. Check the footwear.

Control of hypertension

Studies have highlighted the importance of blood pressure control to reduce macrovascular and microvascular complications in diabetes patients.[22] In fact, blood pressure control has more mortality benefits than blood glucose control. Try non-pharmacological measures first.

Preferred pharmacological agents are ACE inhibitors or ARBs and calcium-channel blockers.[5,19]

Getting to target blood pressure (<140/90 mmHg, lower if tolerated)*

Step 1: Diet, exercise, weight control

Step 2: ACEI or ARB

Step 3: ACEI/ARB and diuretic or calcium channel blocker

Step 4: Beta blocker

ARB = angiotensin II receptor blocker

*<125/80 mmHg if proteinuria >1 g/day (ACR >70) present

Current target recommendations vary according to guideline, but aim for blood pressure below 140/90 mmHg, and lower if tolerated, particularly in those with proteinuria or at high risk of stroke. Monitor for treatment-related adverse effects such as hypotension, syncope, electrolyte abnormalities and acute kidney injury, and review medication if any adverse events occur.[18]

The target may need to be relaxed for those at risk of postural hypotension, particularly the elderly.

Control of dyslipidaemia[4,19]

Mixed hyperlipidaemia is a common finding in patients with diabetes. Dyslipidaemia (especially hypercholesterolaemia) is an independent risk factor for the macrovascular complications of diabetes, and proper control is important. Non-pharmacological measures should be tried first. The preferred agents are HMG-CoA reductase inhibitors and resins for hypercholesterolaemia, and fibrates and resins for mixed hyperlipidaemia.

Targets should be:

- total cholesterol: <4 mmol/L
- triglycerides: <1.5 mmol/L
- HDL cholesterol: ≥1 mmol/L
- LDL cholesterol: <2.0 mmol/L

Management in summary[22]

The ABC of diabetic care is summarised in TABLE 11.7 . A key to ongoing control of diabetes is to maintain the HbA1c at or below 7%, and recognising that it is cardiovascular disease that causes most of the complications and excess mortality in type 2 diabetes. In patient review, the National Health and Medical Research Council (NHMRC) guidelines emphasise lifestyle review as step one.[19] A useful lifestyle evaluation mnemonic is NEAT:

- **N**utrition—eat less, reach ideal weight, healthy low fat/complex carbohydrate diet
- **E**xercise—including ‘walk more’, interesting physical activities
- **A**voidance of toxins—alcohol, tobacco, salt, sugar, illicit drugs
- **T**ranquillity—rest, recreation and stress reduction

Table 11.7 The ABC of diabetes care[3]

Risk factor	Target
Hb**A**1c	<7%
BP	<140/90*
Cholesterol	<4 mmol/L**
Smoking	Quit

*lower if tolerated
**corresponding to LDL cholesterol <2.0 mmol/L

Antihypertensives and statins have an important role in management. A meta-analysis of the use of low-dose aspirin (acetylsalicylic acid 75–150 mg/day) showed secondary risk reduction in people with diabetes and a history of a cardiovascular event (AMI or CVA).[23] However, aspirin is not indicated in people with diabetes who have not had a cardiovascular event.

Metabolic complications of diabetes

Hypoglycaemia

Hypoglycaemia is theoretically defined as blood glucose falling below 4.0 mmol/L, although symptoms usually start at <3.5 and become serious at <3.0.[24] It is most common with insulin use (especially type 1 diabetes but also type 2) and can occur on oral hypoglycaemic drugs, notably sulfonylureas (metformin hardly ever causes hypoglycaemia). It is appropriate to ask often about symptoms of hypoglycaemia: ‘recurrent hypoglycaemia begets hypoglycaemic unawareness’.

Clinical variations

1. Classic warning symptoms: sweating, tremor, palpitations, hunger, peri-oral paraesthesia
2. Rapid loss of consciousness, usually without warning
3. Coma: stuporose, comatose or ‘strange’ behaviour

- In alert patients able to swallow, give refined carbohydrate orally (15 grams, e.g. 7 jelly beans, 3 teaspoons sugar or honey, half glass soft drink or juice)
- Repeat BGL every 15 minutes. If <4, repeat above. If >4, give complex carbohydrate snack or meal (minimum 15 g, e.g. tub of yoghurt, slice of bread, piece of fruit)

Treatment (reduced conscious state or unconscious)[24]

Treatment of choice (after DRABC—call ambulance if unconscious)

30 mL 50% glucose slow IV push (instil rectally using the nozzle of the syringe if IV access

difficult). Usually 10 mL in children.

or

1 mL (= 1 ampoule) glucagon IM or SC (0.5 mL in child <25 kg)

When fully conscious, follow up with snack or meal. Admit to hospital if concerned. Ascertain cause of the hypoglycaemia and instruct the person how to avoid a similar situation in the future.

Diabetic ketoacidosis[24]

This life-threatening emergency requires intensive management. It usually occurs during an illness (e.g. gastroenteritis) when insulin is omitted. It can also occur in type 2 diabetes.

Clinical features

- Develops over a few days, but may occur in a few hours in ‘brittle’ diabetics
- Hyperglycaemia (often >20 mmol/L, lower or normal if on SGLT2 inhibitor)
- Preceded by polyuria, polydipsia, drowsiness
- Vomiting and abdominal pain, dehydration
- Hyperventilation—severe acidosis (acidotic breathing): ↓BP, ↑pulse, ↑resp. rate
- Ketosis (blood and urine)

Management

- Arrange urgent hospital admission
- Early IV fluids—normal saline fast first litre, then caution
- IV insulin—slow, e.g. 10 U in first hour
- ECG—arrhythmia in electrolyte disturbances

Tip: Diabetic ketoacidosis with coma requires fluid, sodium (eventually 3 L N saline), potassium (KCl) and insulin.

Hyperosmolar hyperglycaemia[4]

People with this problem may present with an altered conscious state varying from stupor to coma and with marked dehydration. The onset may be insidious over a period of weeks, with fatigue, polyuria and polydipsia. The key features are marked hyperglycaemia and dehydration

without ketoacidosis. It occurs typically in uncontrolled type 2 diabetes, especially in elderly patients. Sometimes they have previously undiagnosed diabetes. There may be evidence of an underlying disorder such as pneumonia or a urinary infection. The essential findings are extreme hyperglycaemia and high plasma osmolarity. The condition has a high mortality—even higher than ketoacidosis.

Treatment

- IV fluids, e.g. normal to ½ normal saline, given slowly
- Insulin—relatively lower doses than acidosis

Lactic acidosis[4,8]

Patients with lactic acidosis present with marked hyperventilation ‘air hunger’ and confusion. It has a high mortality rate and must be considered in the very ill person taking metformin, especially if kidney function is impaired. The risk of lactic acidosis is low if the therapeutic dose of metformin is not exceeded. Investigations reveal blood acidosis (low pH), low bicarbonate, high serum lactate, absent serum ketones and a large anion gap. Treatment is based on removal of the cause, rehydration and alkalinisation with IV sodium bicarbonate.

Other issues in diabetes

Erectile dysfunction[20]

The prevalence of erectile dysfunction in men with type 2 diabetes over 40 years may be as high as 50%. It may be caused by macrovascular disease, pelvic autonomic neuropathy or psychological causes. Those with organic-based ED may benefit from appropriate counselling and (if not taking nitrates) one of the phosphodiesterase inhibitors, starting with a low dose. The risk of cardiovascular disease needs to be evaluated.

Female sexual dysfunction

Autonomic dysfunction may result in reduced vaginal lubrication with arousal in women, but not the degree of sexual dysfunction that affects men. Appropriate education, reassurance and the use of lubricants should be helpful.

Postural hypotension[20]

Autonomic neuropathy-related postural hypotension may be compounded by medication, including antihypertensives and anti-angina agents. The usual strict blood pressure targets may need to be relaxed, particularly in the elderly. Persistent problems may be helped by graduated compression stockings to decrease venous pooling. If it continues to be a severe problem, the use of oral fludrocortisone may be helpful.

Gastroparesis

Symptoms of gastroparesis (due to autonomic neuropathy) with decreased gastric emptying include a sensation of fullness, dysphagia, reflux or recurrent nausea and vomiting, especially after meals. Treatment options include medication with domperidone, cisapride or erythromycin. Injections of botulinum toxin type A into the pylorus via gastroscopy may facilitate gastric emptying.

Diabetes and driving[4]

Diabetes may impair driving via hypoglycaemia (due to medication) or complications (particularly visual impairment). *Assessing Fitness to Drive 2016* (amended 2017) outlines the specific legal obligations of medical practitioners for assessing drivers of private and commercial vehicles. Drivers are obligated to provide details to the driver licensing authority and to their vehicle insurance company. In general terms, people controlled by diet alone have no restrictions for driving whereas those on insulin may obtain a conditional licence subject to annual or 2-yearly review. The main specific risk is hypoglycaemic episodes. Further details can be found at: www.austroads.com.au/drivers-and-vehicles/assessing-fitness-to-drive.

Contraception

Long-acting reversible contraceptives (e.g. Implanon, Mirena) or the combined oral contraceptive pill are appropriate options for birth control in women not interested in permanent sterilisation. Bear in mind the possibility of polycystic ovarian syndrome.

The future[4,20]

- Use of immunosuppressants and immunomodulators for type 1 diabetes
- Increased availability of glucagon-like and amylin-like peptides for type 2 diabetes
- Continuous implantable venous glucose monitoring
- Closed-loop sensor-and-insulin-delivery devices (‘the artificial pancreas’)
- Combination ‘type 2 polypill’
- Inhaled insulin
- Transplantation:

    combined kidney/pancreas

    islet cells

Treatment errors and pitfalls[19]

- Avoid prescribing oral hypoglycaemic agents prematurely. Allow a reasonable trial of diet and exercise for type 2 patients, especially if they are overweight.
- Review the need for continued oral therapy after 3 months of treatment.
- Glucose tolerance tests should be avoided if the diagnosis can be made on the basis of symptoms and fasting, or random blood sugar or HbA1c (a glucose load carries a small risk of hyperosmolar coma).
- Keep an eye on the development of ketones in type 1 diabetes by checking urinary ketones and, if present, watch carefully because diabetic ketoacidosis is a life-threatening emergency.

When to refer[20]

- Type 1 diabetes requires specialist evaluation and then 1- to 2-yearly review
- Type 2 diabetes: depends on the GP's comfort level and experience. Particularly consider referral for:

  young people

  those requiring insulin

  those with complications
- For ophthalmological screening: every 2 years to inspect retina (or use retinal photography)
- Those with treatable complications, including:

  retinopathy

  nephropathy

  neuropathy: test annually

Shared care

The management of the person with diabetes provides an ideal opportunity for shared care between a cooperative team comprising the patient, the GP and the specialist diabetic team. The objective is to encourage patients to attend their own doctor for primary care and be less reliant on hospital outpatient services or the diabetic clinics. A well-coordinated arrangement with good communication strategies provides optimal opportunities for the ongoing education of the patient, the GP and the specialist diabetic team.

Practice tips

- Many cases of type 2 diabetes remain undiagnosed, so vigilance is important.
- Follow-up programs should keep to a prepared format. Example formats are presented in TABLES 11.8 and 11.9 .
- Hyperglycaemia is a common cause of tiredness. If elderly people with type 2 diabetes are very tired, think of hyperglycaemia and consider giving insulin to improve their symptoms.
- The management of the person with diabetes is a team effort involving family members, a nurse education centre, podiatrists, domiciliary nursing service, GP and consultant.
- If a person with diabetes (particularly type 1) is very drowsy and looks sick, consider first the diagnosis of ketoacidosis.
- Foot care is vital: always examine the feet when the person comes in for review.
- Treat associated hypertension with ACE inhibitors or a calcium-channel blocker (also good in combination).
- Use a team approach and encourage joining special support groups (e.g. Diabetes Australia).
- 'Never let the sun go down on pus in a diabetic foot'—admit to hospital.[20]
- If a foot ulcer hasn't healed in 6 weeks, exclude osteomyelitis. Arrange for an MRI and investigate the vasculature.
- Prevention/detection of coronary heart disease should be an integral part of all consultations.

Table 11.8 Diabetes control: 3-monthly review

Discourage smoking and alcohol
Review symptoms
Review nutrition
Check weight (BMI), BP, urine
Review self-monitoring

Review exercise and physical activity
Review HbA1c (test at least every 6 months)
Review lipid levels (test every 12 months)

Table 11.9 Diabetes control: an annual review program[4]

1 History

Smoking and alcohol use
Symptoms of hypoglycaemia, hyperglycaemia
Check symptoms relating to eyes, circulation, feet*
Immunisation

2 Examinations

Weight, height, BMI
Blood pressure—standing and lying
Examine heart*
Carotid and peripheral pulses*
Eyes:

- visual acuity (Snellen chart)
- ?cataracts
- optic fundi (or ophthalmologist referral)*
- ?diabetic retinal photography

Tendon reflexes and sensation for peripheral neuropathy*
Skin (general)
Foot examination including footwear*
Check injection sites
Urine examination: albumin, ketones, glucose

3 Review biochemical levels

*These items comprise a program for detection of long-term complications. They should be conducted annually, commencing 5 years after diagnosis.

Patient education resources

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

- Diabetes

- Diabetes: blood glucose monitoring at home
- Diabetes: foot care for diabetics
- Diabetes: healthy diet for diabetes
- Diabetes: insulin injections
- Diabetes: type 1
- Diabetes: type 2

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12 Drug and alcohol problems

A custome loathsome to the eye, hateful to the nose, harmeful to the braine, dangerous to the lungs and the blacke stinking fume thereof, neerest resembling the horrible Stigian smoke of the bottomless pit.

JAMES I (1566–1625), *ON SMOKING*

Ecstasy: a drug so strong it makes white people think that they can dance.

LENNY HENRY (1958–)

If you want to keep a dead man, put him in whisky; if you want to kill a live man put whisky in him.

THOMAS GUTHRIE (1803–1873)

Drug-related problems are true masquerades in family practice. This includes prescribed drugs, over-the-counter drugs and social or illegal street drugs. It is important therefore that all prescribing doctors maintain a high index of suspicion that any clinical problem may be associated with their treatment of the patient.

Adverse drug reactions

An adverse drug effect is defined as ‘any unwanted effect of treatment from the medical use of drugs that occurs at a usual therapeutic dose’. Almost every drug can cause an adverse reaction, which must be elicited in the history. Any substance that produces beneficial therapeutic effects may also produce unwanted, adverse or toxic effects. The severity of the reaction may range from a mild skin rash or nausea to sudden death from anaphylaxis. A study has shown that the incidence of adverse reactions increases from about 3% in patients 10–20 years of age to about 20% in patients 80–89 years of age.[1]

Reactions can be classified in several ways—side effects, overdosage, intolerance, hypersensitivity and idiosyncrasy. However, a useful classification of unwanted effects is divided into type A and type B.

Type A reactions are the most common and involve *augmented pharmacology;* that is, they are caused by unwanted, albeit predictable, effects of the drug. Examples include:

- constipation due to verapamil
- blurred vision and urinary outflow problems due to tricyclic antidepressants
- hyperuricaemia due to thiazide diuretics

Type A reactions are dose-dependent.

Type B reactions are idiosyncratic. The reactions are unpredictable from known properties of the drug. Examples include hepatotoxicity and blood dyscrasias.

Golden rules for prevention of adverse effects

Before prescribing any drug the prescriber should consider the following rules:

1. Is the drug really necessary?
2. What will happen if it is not used?
3. What good do I hope to achieve?
4. What harm may result from this treatment?

Common adverse effects

There is an extensive list of clinical problems caused by drugs as side effects or interactions that are highlighted throughout this book. Common side effects include:

- CNS—malaise, drowsiness, fatigue/tiredness, headache, dizziness
- CVS—palpitations, peripheral oedema, hypotension
- GIT—nausea, vomiting, dyspepsia, change in bowel habit (diarrhoea, constipation)
- skin—rash, pruritus, flushing
- psychiatric/emotional—insomnia, irritability, anxiety, depression, agitation

Drugs that commonly produce adverse effects

- Antidepressants (number 1 cause): tricyclics, MAOIs, SSRIs
- Antimicrobials: penicillin/cephalosporins, sulfonamides, tetracyclines, streptomycin, ketoconazole

- Anticonvulsants: carbamazepine, phenobarbitone, phenytoin, sodium valproate
- Anti-inflammatories and analgesics: aspirin/salicylates, opioids (e.g. codeine, morphine), NSAIDs, gold salts, DMARDs, bDMARDs

- Antihypertensive agents: several
- Cardiac agents: digoxin, quinidine, amiodarone, other antiarrhythmics
- Diuretics: thiazides, frusemide
- Tranquillisers: phenothiazines, benzodiazepines, barbiturates, chlordiazepoxide
- Other drugs: cytotoxics, hormones, allopurinol, warfarin

Tobacco use

'Smoking is good for you', according to an old Arab proverb. 'The dogs will not bite you because you smell so bad; thieves will not rob you at night because you cough in your sleep and you will not suffer the indignities of old age because you will die when you are relatively young.'

Tobacco smoking is the largest single, preventable cause of death and disease in Australia. It has been estimated to have caused approximately 15 000 deaths in 2004–2005, over six times the number of deaths from road accidents.[2] Diseases attributed to smoking are summarised in FIGURE 12.1 . Signs of major dependence are smoking within 30 minutes of waking and ≥20 cigarettes a day.

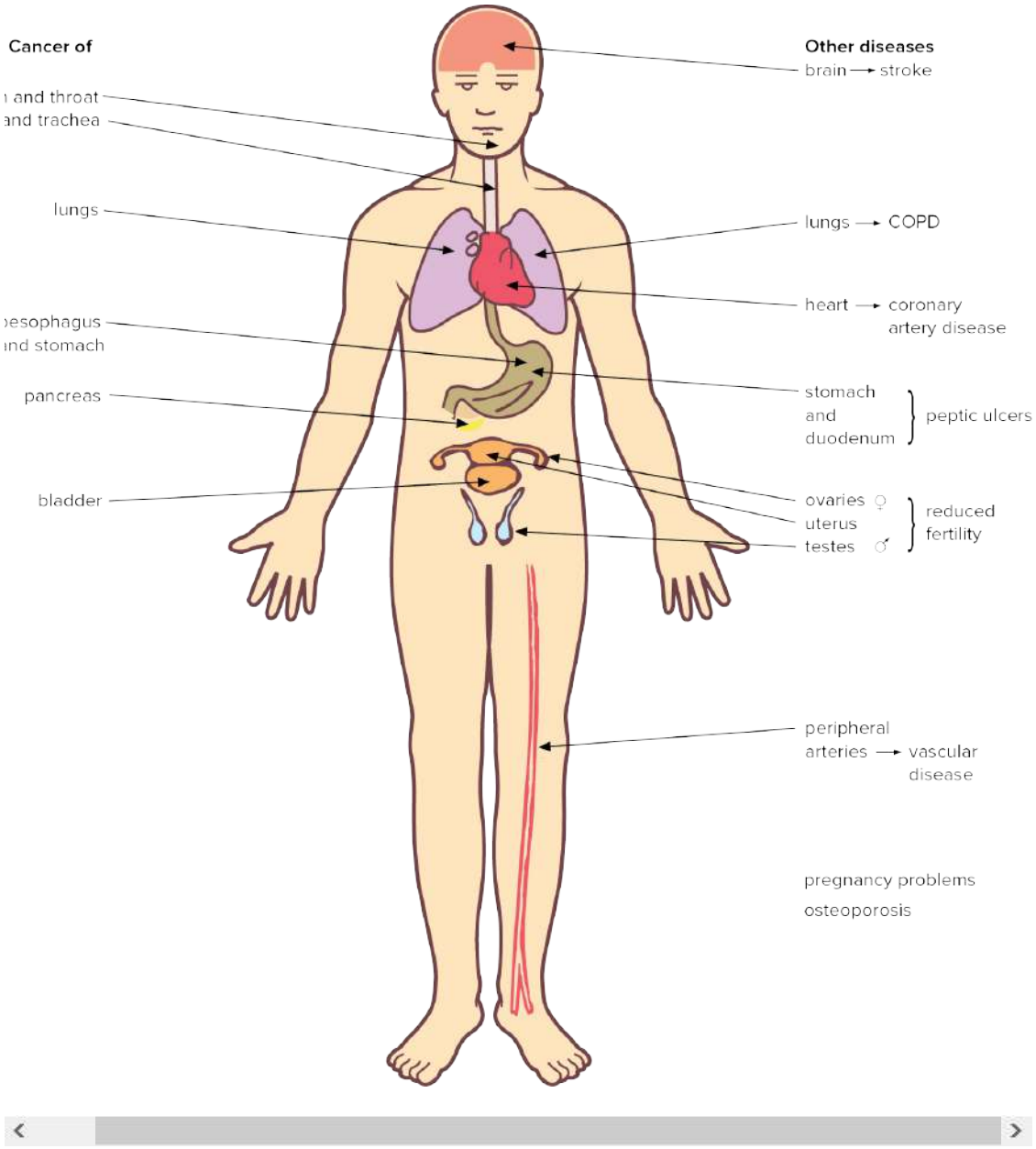

FIGURE 12.1 Possible serious adverse effects of nicotine smoking

Advice to patients (quitting)

Several studies have highlighted the value of opportunistic intervention by the family doctor. It is important not only to encourage people to quit but also to organise a quitting program and follow-up. In Australia, 80% of smokers (representing about 30% of the adult population) have indicated that they wish to stop smoking. Point out that it is not easy and requires strong will power. As Mark Twain said, ‘Quitting is easy—I’ve done it a thousand times.’

- Educate patients about the risks to their health and the many advantages of quitting smoking,

and emphasise the improvement in *health*, *longevity*, *money savings*, *looks* and *sexuality*.

- Point out the following advantages to quitting:

  food tastes better

  sense of smell improves

  exercise tolerance is better

  sexual pleasure is improved

  bad breath improves

  risk of lung cancer drops: after 10–15 years of quitting it is as low as someone who has never smoked

  early COPD can be reversed

  decreases URTIs and bronchitis

  chance of premature skin wrinkling and stained teeth is less

  removes effects of passive smoking on family and friends

  removes problem of effects on pregnancy

- The extent of nicotine dependence can be assessed using a questionnaire (based on the Fagerström test) and scoring system.[3] As a baseline, ask about the number of cigarettes smoked per day, how soon after waking to smoking the first cigarette of the day and any difficulties with coping with antismoking venues (e.g. cinemas, plane travel).

Intervention: the 5A framework[3]

- *Ask* about and document tobacco use at every opportunity.
- *Assess* motivation and confidence to quit: 'Are you interested in quitting?'
- *Advise* all smokers to quit (in a diplomatic way).
- *Assist* the smoker to stop with counselling and pharmacotherapy.
- *Arrange* follow-up to maintain quit advice or non-smoking.

- Ask them to keep a smoker's diary.

- If they say no to quitting, give them motivational literature and ask them to reconsider.
- If they say yes, make a contract (example below).

A contract to quit

'I ..... agree to stop smoking on ..... I understand that stopping smoking is the single best thing I can do for my health and that my doctor has strongly encouraged me to quit.'

..... (Patient's signature)

..... (Doctor's signature)

- These motivated patients will require educational and behavioural strategies to help them cope with quitting. Ongoing support by their GP is very important.
- Organise joining a support group.
- Contact your local Quitline (or similar service) for information about and support for quitting, especially if smoking ≥20 cigarettes a day.
- Arrange follow-up (very important), at least monthly, especially during first 3 months.

- Going 'cold turkey' (stopping completely) is preferable but before making the final break it can be made easier by changing to a lighter brand, inhaling less, stubbing out earlier and reducing the number. Changing to cigars or pipes is best avoided.

Withdrawal effects[3]

The initial symptoms are restlessness, cravings, hunger, irritability, poor concentration, headache and frustration (refer to TABLE 12.1). After about 10 days most of these effects subside but it takes about three months for a smoker to feel relatively comfortable with not smoking any more. Nicotine replacement therapy certainly helps patients cope.

Table 12.1 Nicotine withdrawal symptoms (DSM-5)

1. Irritability, frustration or anger
2. Anxiety
3. Difficulty concentrating
4. Increased appetite

5. Restlessness
6. Depressed mood
7. Insomnia

Treatment

Pharmacological[3]

Nicotine replacement therapy (NRT), which should be used in conjunction with an educational support program, has been proved to be effective and is available as chewing gum, inhaler, oral spray, lozenges, sublingual tablets or transdermal patches (the preferred method). Ideally the nicotine should not be used longer than 3 months. Eight weeks of patch therapy is as effective as longer courses.

NRT should be directed at smokers with a moderate to high nicotine dependency who are motivated to quit. There is little evidence that drug treatment will benefit individuals with low levels of nicotine dependence who smoke fewer than 10 cigarettes a day.[4]

All forms of NRT are effective: a pooled analysis of all NRT trials showed an absolute increase in cessation at 1 year of 7% compared to placebo.[4]

NRT should start at the quit date, not while still smoking.

The RACGP Expert Advisory Group for Supporting Smoking Cessation strongly recommend the use of NRT varenicline and bupropion with high certainty, and nortriptyline with moderate certainty.[5]

Nicotine gum[3]

This is available as 2 mg and 4 mg.

- Low dependence (less than 10 cigarettes per day): use non-pharmacological methods rather than replacement
- Moderate dependence (10–20 cigarettes per day): 2 mg every 1–2 hours, chew max. 8–12 pieces daily
- High dependence (>20 per day, waking at night to smoke or first thing after waking): 4 mg initially, 6–10 pieces chewed daily changing to 2 mg after 4–8 weeks (max. 12 pieces/24 hours)

  Useful points:

- Chew each piece slowly for about 30 minutes.

- Ensure all the nicotine is utilised.
- Chew at least 6 pieces per day, replacing at regular intervals (not more than 1 piece per hour).
- Use for 3 months, weaning off before the end of this period.

Transdermal nicotine[3]

This is available as 16-hour or 24-hour nicotine patches in three different strengths. The patients should stop smoking immediately on use.

Recommendations:

- low to moderate dependence (10–20 cigarettes/day): 15 mg/24 hour or 10 mg/16 hour patch, daily; aim to cease within 12 weeks
- high dependence (>20/day): 21 mg/24 hour or 15 mg/16 hour patch; change to 15 mg or 10 mg patch after 4–6 weeks; aim to cease within 12 weeks; use lower dose if patient is <45 kg or has CVS disease

Apply to non-hairy, clean, dry section of skin on upper outer arm or upper chest and leave in place for 24 hours. Rotate sites with a 7-day gap for reuse of a specific site.

Nicotine inhaler

Uses cartridges (15 mg) in a mouthpiece resembling smoking.

- 6/day for 12 weeks then taper

Nicotine oral spray

- 1 mg/spray: 1–2 sprays into mouth orally (max. 64 sprays/24 hours)

Nicotine lozenges and sublingual tablets

These are available in 2 mg and 4 mg strengths, the strength used according to the level of dependence, e.g. high dependence: suck 4 mg lozenges (max. 15/24 hours), or 4 mg SL every 1–2 hours (max. 80 mg/24 hours).

Combination therapy

Controlled trials have shown enhanced outcomes when nicotine patches are combined with gum or inhaler. Consider it for highly addicted smokers.

Other agents for smoking cessation[6]

Bupropion (Zyban)

This oral agent has a similar effectiveness to NRT.

Adverse effects include insomnia and dry mouth (both common), with serious effects, such as allergic reactions and increased seizure risk.[7] It is contraindicated in persons with a history of epilepsy.

Recommended dose: 150 mg (o) daily for 3 days then bd for 12 weeks.

Varenicline tartrate (Champix)[3,6]

- Commence with 0.5 mg (o) daily with food for 3 days titrating slowing to 1 mg bd by day 7 until the end of the 12-week course

It is an effective agent but there are several adverse side effects, especially nausea with a concern about neuropsychiatric effects.[7] Avoid in end-stage kidney disease and take care with diabetics.

Nortriptyline

- Start with 25 mg (o), increasing gradually to 75 mg (o) daily, starting 14 days before quit date then continue for 12 weeks

Note: Regular follow-up for all methods is essential for outcome.

Vaping

This involves inhaling and exhaling the vapour from ‘electronic’ e-cigarettes. Its use is controversial, especially since the addition of nicotine e-liquids ± other substances have led to serious adverse effects including death. Currently, nicotine e-cigarettes are allowed to be imported and purchased under a doctor prescription.[8] The RACGP Expert Group concludes ‘conditional recommendation for intervention—low certainty’.[5]

Excessive and harmful drinking

Excessive drinking of alcohol is one of the most common and socially destructive problems in the world. One survey found that 5% of Australian men and 1% of women were alcohol-dependent. It also showed that 86% of men and 79% of women drink alcohol, with 8.3% of the population drinking alcohol every day.[7]

- Alcohol is estimated to have a harmful effect on about 1 in 10 people.
- At least 20–40% of acute general and psychiatric hospital admissions have an alcohol-related illness.
- About 20%-plus of fatal traffic accidents involve alcohol.