Chapter 1

Diagnosing and Classifying Diabetes

Cancer, diabetes, and heart disease are no longer diseases of the wealthy. Today they hamper the people and economies of the poorest populations…this represents a health emergency in slow motion.

(Ban Ki Moon, Secretary General of the United Nations)

Key points

- Diabetes is the modern pandemic. It represents a considerable global economic and social burden for the person with diabetes and for health services.
- The prevalence of the metabolic syndrome, Type 1, Type 2 and gestational diabetes is increasing.
- The greatest increase in diabetes prevalence is occurring in Africa, the Middle East and South East Asia.
- The overlapping mechanisms by which obesity leads to the metabolic syndrome and Type 2 diabetes are complex and not yet fully understood.
- Not everybody who is obese has insulin resistance or diabetes
- Central obesity plays a key role in the progression to insulin resistance and Type 2 diabetes.
- Lean people may be at higher risk of morbidity and mortality than obese people.
- Primary prevention and early detection are essential to reduce the personal and community burden associated with the metabolic syndrome and diabetes and their complications.
- Type 2 diabetes is a progressive disease and complications are often present at diagnosis. Thus, insulin will eventually be necessary in most people with Type 2 diabetes.
- The prevalence of obesity, the metabolic syndrome and Type 2 diabetes is increasing in children.

Care of People with Diabetes: A Manual of Nursing Practice, Fourth Edition. Trisha Dunning.

What is diabetes mellitus?

Diabetes mellitus is a metabolic disorder in which the body's capacity to utilise glucose, fat and protein is disturbed due to insulin deficiency or insulin resistance. Both states lead to hyperglycaemia and glycosuria.

The body is unable to utilise glucose in the absence of insulin and draws on fats and proteins in an effort to supply fuel for energy. Insulin is necessary for the complete metabolism of fats, however, and when carbohydrate metabolism is disordered fat metabolism is incomplete and intermediate products (ketone bodies) can accumulate in the blood leading to ketosis, especially in Type 1 diabetes. Protein breakdown also occurs and leads to weight loss and weakness and contributes to the development of hyperglycaemia and lethargy.

The different types of diabetes have different underlying causal mechanisms and clinical presentation: in general, young people are insulin-deficient (Type 1 diabetes), while older people usually secrete sufficient insulin in the early stages but demonstrate resistance to insulin action (Type 2 diabetes). In the early stages of Type 2 hyperinsulinaemia might be present. Type 2 is a progressive disease with slow destruction of the insulin-producing beta cells and, consequently, insulin deficiency.

However, ~10% of older people with presumed Type 2 diabetes have markers of islet autoimmunity and become insulin dependent early in the course of the disease (Turner *et al*. 1997) (see latent autoimmune diabetes (LADA) later in this chapter); Type 2 is becoming increasingly prevalent in children and adolescents as a result of the global obesity epidemic (Barr *et al*. 2005; Zimmet *et al*. 2007). Type 2 diabetes is the most common, accounting for ~85% of diagnosed cases; Type 1 accounts for ~15% of diagnosed cases.

Prevalence of diabetes

Diabetes is a global health problem affecting ~371 million people worldwide (International Diabetes Federation (IDF) 2012) and more than 187 million are unaware they have diabetes. The prevalence is expected to increase to 552 million by 2030 unless the epidemic can be halted. In lower income families, 3 out of 4 people have diabetes. The number of deaths attributed to diabetes in 2012 was ~4.8 million, and global diabetes-related spending was estimated to be >471 billion US dollars (IDF 2012). The three countries with the highest diabetes prevalence are China (92.3 million), India (63 million) and USA (24.1 million).

In Australia, AusDiab data show 100 000 people develop diabetes annually (Cameron *et al*. 2003) and the prevalence continues to increase: 7.5% of people over 25 years and 16.8% of people over 65 have diabetes and a further 16.1% >65 have impaired glucose tolerance (IGT). In addition, >200 000 progress from being overweight to obese, 3% of adults develop hypertension, and 1% develop renal impairment annually, and the average waist circumference increases by 2.1 cm, particularly in women. The prevalence increases annually by 0.8% (Australian Diabetes Society (ADS) 2012). Thus, a significant proportion of the population develops features of the metabolic syndrome with the associated increased risk of Type 2 diabetes and other associated conditions and leads to high health costs (Colagiuri *et al*. 2003; Australian Institute of Health and Welfare (AIHW) 2005).

In the UK, an estimated 2.3 million people have diabetes and up to another 750 000 people have undiagnosed diabetes (SIGN 2010). In Scotland, approximately 228 000 people were registered as having diabetes in 2009; an increase of 3.6% from 2008 (SIGN 2010). The reason for the increased prevalence of Type 2 diabetes is due to many inter-related factors including genetic predisposition, environmental factors and the ageing population. Type 2 is the most common type, accounting for 80–90% of cases.

There is wide variation in the incidence rates of newly diagnosed Type 1 diabetes in children in different populations. However, Type 1 in children and adolescents is increasing, particularly in developed countries (EURODIAB 2000; The DIAMOND Project Group 2006; Soltesz *et al*. 2006). The incidence of Type 1 diabetes in children <15 years on the Western Australian Children's Database has increased gradually over the past 25 years but occurs in peaks and troughs rather than in a linear progression (Haynes *et al*. 2012). For example peak years were 1992, 1997 and 2003 in Australia. The incidence of type 1 appears to fluctuate in five-year cycles and might be influenced by circulating viruses, especially enterovirus infections or other environmental factors (Haynes *et al*. 2012).

The association between ingestion of cow's milk in infancy and pathogenesis of Type 1 diabetes is discussed in Chapter 13. Recently, the role of IRE1∂ in inducing thioredoxin-interacting protein to activate the NLRP3inflammasome and promote programmed pancreatic cell death (Lerner *et al*. 2012). The researchers stated that the findings suggest dietary modification could extend the honeymoon period in Type 1 diabetes or possibly prevent diabetes.

Thus, the economic burden of diabetes and health care costs are high. Over 9% of people admitted to hospital in Australia have diabetes and rates of 11–25% are reported in other countries. The proportion of people with diabetes admitted to hospital is increasing, and they mostly have longer lengths of stay (ADS 2012). Some people, not known to have diabetes, develop hyperglycaemia in hospital. Hyperglycaemia is associated with increased morbidity and mortality, independently of diabetes (Chapter 7). It is not clear whether hyperglycaemia in people without a diabetes diagnosis is due to undiagnosed diabetes/IGT or whether it is an indicator of underlying critical illness. However, because in-hospital hyperglycaemia in non-diabetics may represent undiagnosed diabetes or risk of future diabetes, these people should receive education and be followed up.

Classification of diabetes

Diabetes is broadly classified into Type 1 and Type 2 diabetes and other types.

- Type 1 diabetes has two forms:
  - Immune-mediated diabetes mellitus, which results from autoimmune destruction of the pancreatic beta cells leading to absolute insulin deficiency.
  - Idiopathic diabetes mellitus refers to diabetes forms that have no known aetiologies.

Type 2 diabetes mellitus refers to diseases associated with relative insulin deficiency as a result of progressive beta cell failure and insulin resistance.

- Impaired glucose homeostasis is an intermediate metabolic stage between normal glucose homeostasis and diabetes. It is a significant risk factor for cardiovascular disease and Type 2 diabetes. Thus early detection and management are important. There are two forms:
  (1) Impaired fasting glucose (IFG) where the fasting plasma glucose is higher than normal but lower than the diagnostic criteria.
  (2) Impaired glucose tolerance (IGT) where the plasma glucose is higher than normal and lower than the diagnostic criteria after a 75 g glucose tolerance test. IFG and FPG often occur together and are associated with the metabolic syndrome.
- Gestational diabetes mellitus, which occurs during pregnancy.

- Other specific types, which include diabetes caused by other identifiable disease processes and other factors:
  - Genetic defects of beta cell function such as Maturity Onset Diabetes of the Young (MODY).
  - Genetic defects of insulin action.
  - Diseases of the exocrine pancreas such as cancer and pancreatitis.
  - Endocrine disorders such as Cushing's disease and acromegaly.
  - Medicines, such as glucocorticoids and atypical antipsychotics have been associated with weight gain but the newest second-generation antipsychotic medications such as aripiprazole are weight neutral (Citrome *et al*. 2005). Possible causes of weight gain associated with medicines include food cravings and eating more, changed resting metabolic rate, changes in neurotransmitters and neuropeptides such as leptin, which regulate appetite, and weight loss before medicines are commenced (Zimmermann & Himmerich 2003). Individuals with schizophrenia are generally more overweight than those without.
- Chemical-induced diabetes.

Overview of normal glucose homeostasis

Blood glucose regulation (glucose homeostasis) relies on a delicate balance between the fed and fasting states and is dependent on several simultaneously operating variables including hormones, nutritional status, especially liver and muscle glucose stores, exercise, tissue sensitivity to insulin, and the type of food consumed. Figure 1.1 shows the key features of the fed and fasting states. Insulin release occurs in two phases. The first phase is important to controlling the postprandial blood glucose rise and is lost early in the progression to Type 2 diabetes. Postprandial glucose >7.8 mmol/L is associated with cardiovascular events and plays a role in the development of other co-morbidities (IDF 2011). Insulin action is mediated via two protein pathways: Protein 13-kinase through insulin receptors and influences glucose uptake into the cells; and MAP-kinase, which stimulates growth and mitogenesis.

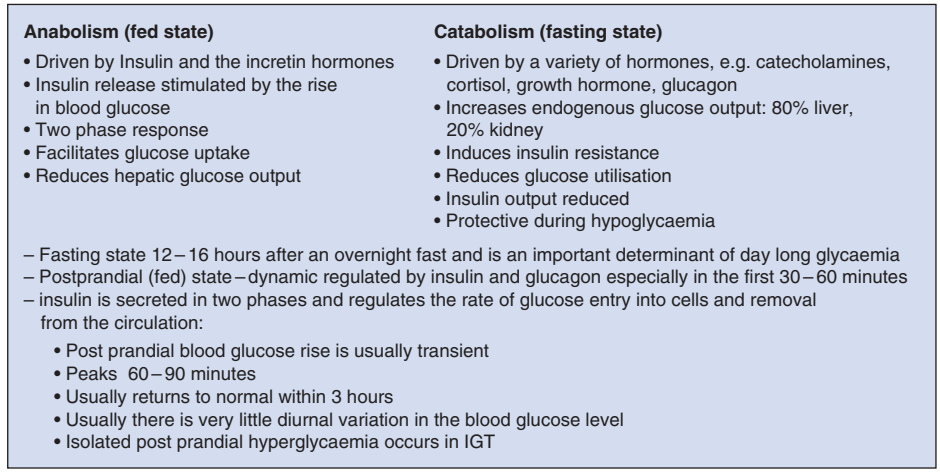

Figure 1.1 Overview of glucose homeostasis showing the key factors operating during the fed and fasting states. Usually the blood glucose is maintained within the normal range by the interplay of the anabolic and catabolic hormones, which are in turn influenced by other hormones and a number of factors such as nutritional status and intake.

Recently researchers identified the interaction of insulin with its primary binding site on the insulin receptor; revealing a conformational switch in insulin once it engages with the receptor (Menting *et al*. 2012). Conformational switching is unusual in the tyrosine receptor kinases. The clinical significance of the finding is not yet clear but it could influence the development of future insulin analogues.

The metabolic syndrome

The metabolic syndrome consists of a cluster of risk factors for cardiovascular disease and Type 2 diabetes. Several researchers have explored the factors that predict diabetes risk including the World Health Organization (WHO), IDF, Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria in Europe (DECODE 2008), Epidemiology Study on the Insulin Resistance Syndrome (DESIR), US National Cholesterol Education Programme Adult Treatment Panel (NCEP ATP 111), and the European Group for the Study of Insulin Resistance: Relationship Between Insulin Sensitivity and Cardiovascular Disease Risk (EGIR-RISC).

Key features of the metabolic syndrome

- The metabolic syndrome appears to be a result of genetic predisposition and environmental factors, which include high saturated fat diets, inactivity, smoking, hormone imbalances contributing to metabolic stress, maternal obesity, age and some medicines (Bruce & Byrne 2009). These factors represent a cumulative risk and are largely modifiable.
- Central obesity, waist circumference: Europoids >94 cm in men and >80 cm in women; South Asian and Southeast Asian men >90 cm, women >80 cm: (Zimmet, *et al*. 2005); childhood/adolescent Body Mass Index (BMI) 25–29 overweight, >30 obese. Interestingly, Carnethon *et al*. (2012) reported overweight people diagnosed with diabetes live longer than leaner people with diabetes in a prospective study to identify cardiovascular risk factors (n = ~ 2600). The death rate was 1.5 in overweight people compared to 2.8 in lean people after accounting for cardiovascular risk factors such as age, hypertension, hypercholesterolaemia and smoking. The authors acknowledged the limitations of the study. They also noted Asian people are more likely to be normal weight at diagnosis and stressed the need for extra vigilance in leaner people. Significantly, not all obese people develop the metabolic syndrome. See also Chapter 4.
- Raised serum triglycerides >1.7 mmol/L.
- Low serum HDL-c: <1.03 mmol/L males, <1.29 mmol/L women.
- Hypertension: systolic > 130 mmHg or diastolic >85 mmHg in women.
- IFG: >5.6 mmol/L or previously diagnosed diabetes (e.g. gestational diabetes (GDM). IFG is associated with a 20–30% chance of developing Type 2 diabetes within 5–10 years. The chance increases if FPG is also present.

Other key features include:

- Increasing age.
- Insulin resistance. High serum levels of sugar metabolites, amino acids and chlorine-containing phospholipids are associated with reduced insulin sensitivity and insulin secretion and higher risk of Type 2 diabetes (Floegel *et al*. 2012). A small study suggests people who sleep for <4 hours are 30% more insulin resistant than those who sleep longer (Cappuccio & Miller 2012). However, the sample size was a small one and only one participant was female which could be important because men and women respond to sleep deprivation differently. Thus, further research is needed.

- Genetic predisposition and the Developmental Origins of Adult Health and Disease (DOHaD) hypothesis (Barker *et al*. 1990). Maternal obesity at conception alters gestational metabolism and affects placental, embryonic and foetal growth and development (King 2006) and increases the susceptibility of the child to components of the metabolic syndrome (Taylor & Poston 2007; Bruce & Byrne 2009; Armitage *et al*. 2008; Nakamura & Omaya 2012). Epigenetic changes occur during early foetal development when mothers suffer malnutrition during pregnancy. Their children are more likely to develop metabolic syndrome, diabetes, obesity and cardiovascular disease. In addition, the grandchildren of malnourished mothers are more likely to be low weight at birth, regardless of the nutritional status of their mothers, (see www.themedicalbiochemistrypage.org 1996–2012). In addition, under-nutrition increases susceptibility to infection and obesity, or over-nutrition leads to immunoactivation and susceptibility to inflammatory diseases such as diabetes (Dandona *et al*. 2010). Likewise, *Helicobacter pylori* may predispose individuals to diabetes (Haan *et al*. 2012). Haan *et al*. followed 800 Latino non-diabetic adults over age 60 for 10 years; 144 developed diabetes. People who tested positive for *Helicobacter pylori* were 2.7 more likely to develop diabetes compared to other infections.
- Hyperinsulinaemia, which occurs in the presence of insulin resistance and exaggerates the proliferative effects of the MAP-kinase pathway.
- Procoagulent state: elevated plasma fibrinogen and plasminogen activator inhibitor-1 (PAI-1).
- Vascular abnormalities: increased urinary albumin excretion and endothelial dysfunction, which affect vascular permeability and tone.
- Inflammation: both over nutrition and infection induce inflammation. Dietary fats and sugars can induce inflammation by activating an innate immune receptor, Toll-like receptor 4 (TLR4) (Omaye 2012). Recent research suggests 'good' intestinal bacteria have a preventative role and pre- and probiotics help maintain healthy gut and immune systems (www.themedicalbiochemistrypage.org 1996–2012; Nakamura & Omaya 2012). Inflammatory markers such as cytokines, Interleukin, adhesion molecules and TNF-alpha alter endothelial function. C-reactive protein is a significant predictor of cardiovascular disease and possibly depression, and there is an association among diabetes, cardiovascular diseases and depression. In fact some experts suggest depression could be an independent risk factor for Type 2 diabetes (Loyd *et al*. 1997) and accelerates the progression of coronary artery disease (Rubin 2002). Depression is associated with behaviours such as smoking, unhealthy eating, lack of exercise and high alcohol intake, which predisposes the individual to obesity and Type 2 diabetes. Peripheral cytokines induce cytokine production in the brain, which activates the hypothalamic-pituitary-adrenal axis and the stress response, which inhibits serotonin and leads to depression. Inflammation appears to be the common mediator among diabetes, cardiovascular disease and depression (Lesperance & Frasure-Smith 2007; Bruce & Byrne 2009).
- Hyperuricaemia: More recently, liver enzymes such as sustained elevations of alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT), which are associated with non-alcoholc fatty liver disease and low adiponectin, have been associated with diabetes and cardiovascular disease. Therefore, the relationship is complex. Conversely, normal testosterone levels appear to be protective against diabetes in men, and low testosterone levels in men with diabetes are associated with a significantly increased risk of death (Jones *et al*. 2011). In women high testosterone indicates greater risk of developing diabetes: high oestradiol levels confer increased diabetes risk in both men and women (American Diabetes Association 2007).

Consequences of the metabolic syndrome include:

- A five-fold increased risk of Type 2 diabetes.
- A two- to three-fold increased risk of cardiovascular disease (myocardial events, stroke and peripheral vascular disease).
- Increased mortality, which is greater in men but women with Type 2 diabetes have a greater risk than non-diabetic women.
- Increased susceptibility to conditions such as:
  - Gestational diabetes (GDM)
  - Foetal malnutrition
  - Polycystic ovarian syndrome
  - Fatty liver
  - Gallstones
  - Asthma
  - Sleep problems
  - Some forms of cancer.

The risk of developing cardiovascular disease and Type 2 diabetes increases significantly if three or more risk factors are present (Eckel *et al*. 2005).

The metabolic syndrome in children and adolescents

The prevalence of metabolic syndrome in children and adolescents is usually extrapolated from adult definitions and may not be accurate. However, it is vital that children and adolescents at risk of developing the metabolic syndrome be identified early. Future risk appears to be influenced *in utero* and early childhood by factors such as GDM, low birth weight, feeding habits in childhood, genetic predisposition and socio-economic factors (Burke *et al*. 2005; Nakamura & Omaya 2012).

The IDF proposed that the metabolic syndrome should not be diagnosed before age 10 but children at risk should be closely monitored especially if there is a family history of metabolic syndrome, diabetes, dyslipidaemia, cardiovascular disease, hypertension and obesity, and preventative strategies should be implemented (Weiss & Caprio. 2005; Zimmet *et al*. 2007).

In the 10–16-year-old age range diagnostic features are waist circumference >90th percentile, triglycerides >1.7 mmol/L, HDL-c >1.03 mmol/L, glucose >5.6 mmol/L (OGGT recommended), systolic blood pressure >130 mm Hg and diastolic >85 mm Hg. Adult criteria are recommended for adolescents over 16 years. The long-term impact on morbidity and mortality will emerge as young people with the metabolic syndrome become adults. However, heart disease may be apparent in children as young as 10 (Sinaiko 2006) and early onset of Type 2 diabetes in adolescents is associated with more rapid progression of complications than occurs in Type 1.

Management of the metabolic syndrome in children and adults consists of primary prevention through population-based strategies aimed at early detection, regular follow-up of at-risk individuals and personalised education. Secondary prevention concentrates on preventing the progression to diabetes and cardiovascular disease. Lasting effects demonstrating reduced cardiovascular and Type 2 diabetes risk has been demonstrated in studies such as the Diabetes Prevention Program (DPP), the Finnish Diabetes Prevention Study and the Da Quing IGT and Diabetes Study. These studies showed the importance of multidisciplinary team care, modifying lifestyle factors that contribute to obesity by improving diet and activity levels to reduce weight (10% body weight in the long term), and stopping smoking. Some programmes

include health coaching but the cost–benefit has not been demonstrated (Twigg *et al*. 2007). The Transformational Model of Change is frequently used to implement preventative strategies.

Medicines might be required for secondary prevention, for example to control blood glucose and lower lipids, antihypertensives such as statins, and weight management medicines in addition to lifestyle modification. Several medicines have been shown to reduce the incidence of diabetes in people with the metabolic syndrome. These include Metformin 850 mg BD, which showed a 31% risk reduction in the DPP; 100 mg of Acarbose TDS by 25% after three years (STOP-NIDDM); and women with a history of GDM in the TRIPOD trial were less likely to develop diabetes when they were treated with Troglitazone. Troglitazone was withdrawn from the market because of the tendency to cause liver disease. Other thiazolidinediones such as pioglitazone and rosiglitazone do not have the same adverse effects on the liver. Rosiglitazone reduced the risk of prediabetes progressing to diabetes by 60% over three years in the DREAM study but has since been associated with increased risk of MI and Poiglitizone might increase the risk of bladder cancer; the risk appears to be higher with long duration of use (NPS 2012) (see Chapter 5). Orlistat, an intestinal lipase inhibitor taken TDS, reduced the risk of progression to diabetes in obese adults with metabolic syndrome by 37% over four years (XENDOS study). However, compliance with Orlistat is low due to the side effects, see Chapter 5.

The macrovascular risk factors need to be managed proactively and screening programmes are imperative so abnormalities are treated early, see Chapter 8. A 75 g OGGT may be performed initially to diagnose the metabolic syndrome and repeated after 12 months to determine whether glucose tolerance changed, then the test interval can be increased to every two to three years (WHO 1999). However, if an individual demonstrates significant changes in weight gain, OGGT may be performed earlier.

The Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes (American Diabetes Association *et al*. 2004) recommended monitoring people on antipsychotic medicines including:

- BMI at baseline and every visit for 6 months then quarterly and treat if weight increases by one BMI unit;
- Blood glucose and lipids at baseline and if weight increases by 7% and then annually;
- HbA_{1c} 4 months after starting antipsychotic medicines and then annually in people with metabolic syndrome or diabetes risk factors.

Type 1 and Type 2 diabetes

Type 1 diabetes

Type 1 diabetes is a disease of absolute insulin deficiency that usually affects children and young adults but can occur in older people where it usually manifests as latent autoimmune diabetes (LADA), see the following section. Recent research has indicated that insulin resistance is also a feature in lean people with uncomplicated Type 1 diabetes (Donga *et al*. 2012). However, Donga *et al*.'s sample was small, eight people using insulin pumps and eight healthy controls matched for age, gender and BMI, thus, the clinical relevance of the finding is not clear.

The symptoms usually occur over a short space of time (two to three weeks) following a subclinical prodromal period of varying duration where the beta cells are destroyed. The precipitating event may have occurred many years prior to the

development of the symptoms. Type 1 diabetes can be due to an autoimmune or idiopathic process. Various researchers have demonstrated that exogenous factors play a role in the development of Type 1 diabetes on the basis that <10% of susceptible people develop diabetes and <40% of monozygotic twins both develop diabetes, the >10-fold increase in the incidence of Type 1 diabetes in European Caucasians in the last 50 years, and migration studies that show the incidence of Type 1 has risen in people who migrated from low to high incidence regions (Knip *et al*. 2005). This is known as the trigger-bolster hypothesis. Seasonal variations in incidence of new diagnosis occur.

The EURODIAB sub-study 2 study group researchers (EUROBIAB 1999) suggested low plasma 25-hydroxyvitamin D may be implicated in the development of Type 1 diabetes (1999). Later, Stene & Jones (2003) suggested there was no link between vitamin D supplementation and lower rates of Type 1 diabetes. A systematic review and meta-analysis of observational studies and a meta-analysis of cohort studies undertaken in 2008 suggest vitamin D supplementation in early childhood might reduce the risk of Type 1 diabetes by 30% (Zipitis & Akoberng 2008). A recent prospective study in Spain identified a significant inverse association between vitamin D and risk of Type 2 diabetes (Gonzalez-Molero *et al*. 2012). However, randomised controlled trials are required to clarify whether there is a causal link and the optimal vitamin D dose, duration of treatment, and the best time to begin using vitamin D supplements.

As indicated earlier in this chapter, and in Chapter 13, a range of other environmental triggers has been implicated in the development of Type 1 such as potatoes, cow's milk, and various viruses. Thus, the cause of Type 1 diabetes appears to be multifactorial due to a combination of genetic predisposition and a diabetogenic trigger that induces an immune response, which selectively destroys pancreatic beta cells. Islet cell antibodies (ICA), glutamic acid carboxylase (GAD), or tyrosine phosphatase (IA-2A) antibodies are present in 85% of cases.

Type 1 diabetes in children usually presents with the so-called classic symptoms of diabetes mellitus:

- Polyuria
- Polydipsia
- Lethargy
- Weight loss
- Hyperglycaemia
- Glycosuria
- Blood and urinary ketones.

In severe cases the person presents with diabetic ketoacidosis (DKA) (see Chapter 7). Bed-wetting may be a consequence of hyperglycaemia in children (and older people). Classically, insulin secretion does not improve after treatment but tissue sensitivity to insulin usually does.

Figure 1.2 is a schematic representation of the progression of Type 1 diabetes. It shows the progressive relentless destruction of the beta cells from the time of the initial triggering event. Five to ten per cent of first-degree relatives of people with Type 1 diabetes have beta cell antibodies, usually with normal glucose tolerance, and some progress to diabetes.

Recent studies suggest early infant feeding is associated with the development of Type 1 diabetes-related autoantibodies such as GAD, 1A-2A with a male preponderance and is more common in children of mothers with Type 2 diabetes or coeliac disease and with short term breast feeding (Zeigler *et al*. 2003; Wahlberg *et al*. 2006) (Chapter 13).

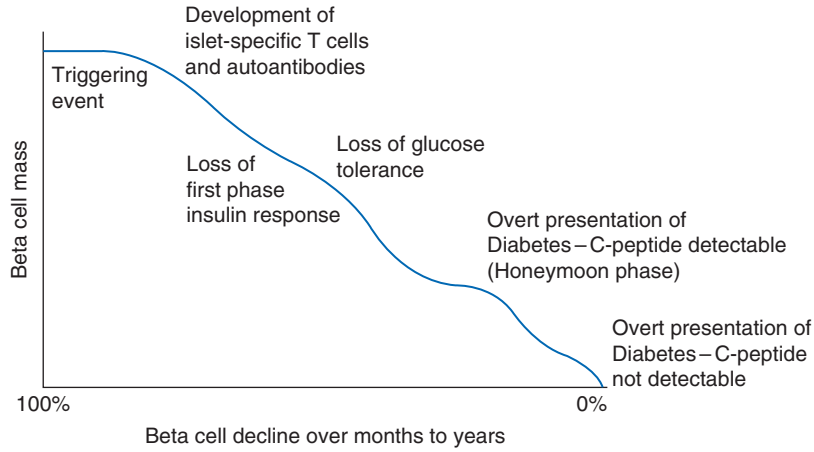

Figure 1.2 Schematic representation of the slow progressive loss of beta cell mass following the initial trigger event in Type 1 diabetes.

Latent autoimmune diabetes (LADA)

LADA is a genetically linked autoimmune disorder that occurs in ~10% of people who are often initially diagnosed with Type 2 diabetes. LADA prevalence varies among ethnic groups (www.actionlada.org). LADA has some features of both Types 1 and 2 diabetes. The UKPDS (1998) identified that one in 10 adults aged between 25 and 65 presumed to have Type 2 diabetes were GADAb positive, and these findings have been evident in other studies (Zinman *et al.* 2004). LADA often presents as Type 2 but has many of the genetic and immune features of Type 1 (see the previous section and Table 1.2).

People with LADA had a different clinical course from Type 2 diabetes: in a 6-year follow up in the UKPDS 84% of people with GADA required insulin compared to 14% of antibody negative people. LADA is primarily an insulin deficiency state, where Type 2 has a long progression to insulin and is characterized by insulin resistance. The clinical features also resemble Type 1 in that people with LADA are not usually obese, are often symptomatic, and do not have a family history of Type 2 diabetes.

However, GADA appears to have a bimodal distribution in LADA identifying two LADA subgroups with different, distinct clinical, autoimmune and genetic features. People with high GADA titers are younger, leaner, insulin deficient, have lower C-peptide and high HbA1c, higher prevalence of other diabetes-specific autoantibodies or other autoimmune diseases such as thyroid disease and lower prevalence of metabolic syndrome than people with LADA and low GADA titers (Buzzetti *et al.* 2007).

There are no current guidelines for managing LADA (Cermea *et al.* 2009) although an expert panel convened by the ADA suggested C-peptide response is an appropriate measure of beta cell function and response to treatment. Management depends on the GADA titers and clinical presentation and should be individualised. Management considerations include:

- Testing lean people presenting with Type 2 diabetes for autoantibodies, especially GADA and C-peptide to correctly diagnose LADA, treat it appropriately with insulin and prevent episodes of ketoacidosis (Niskanen *et al.* 1995; Cermea *et al.* 2009).
- Introducing insulin early to support insulin secretion and protect the remaining beta cells (Cernea *et al.* 2009). Sulphonylureas appear to achieve similar or worse glycaemic control than insulin alone and lead to the early need for insulin, thus Sulphonylureas are not recommended as first line treatment (Cremea *et al.* 2009).

- Thiazolidediones may have a beta cell protective/augmentative effect but their benefit in LADA has not been demonstrated and the contraindications need to be considered.
- Metformin may be contraindicated because insulin resistance is not always a feature of LADA and because of the potential risk of lactic acidosis in susceptible people (Chapter 5).
- Diet and exercise relevant to the individual and the treatment mode.
- Stress management and regular complication screening and mental health assessment (as per Types 1 and 2 diabetes).
- Appropriate education and support.

Type 2 diabetes

Type 2 diabetes is not 'just a touch of sugar' or 'mild diabetes'. It is a *serious*, insidious progressive disease that is often diagnosed late when complications are present. Therefore, population screening and preventative education programs are essential. Type 2 diabetes often presents with an established long-term complication of diabetes such as neuropathy, cardiovascular disease, or retinopathy. Alternatively, diabetes may be diagnosed during another illness or on routine screening. The classic symptoms associated with Type 1 diabetes are often less obvious in Type 2 diabetes, however, once diabetes is diagnosed and treatment instituted, people often state they have more energy and are less thirsty. Other subtle signs of Type 2 diabetes, especially in older people, include recurrent candida and urinary tract infections, incontinence, constipation, symptoms of dehydration and cognitive changes, particularly in information processing speed, and executive function (Spauwen *et al*. 2012). As indicated, insulin resistance often precedes Type 2 diabetes.

Insulin resistance is the term given to an impaired biological response to both endogenous and exogenous insulin that can be improved with weight loss and exercise. Insulin resistance is a stage in the development of impaired glucose tolerance. When insulin resistance is present, insulin production is increased (hyperinsulinaemia) to sustain normal glucose tolerance; however, the hepatic glucose output is not suppressed and fasting hyperglycaemia and decreased postprandial glucose utilisation results in postprandial hyperglycaemia.

Insulin resistance is a result of a primary genetic defect and secondary environmental factors (Turner & Clapham 1998). When intracellular glucose is high, free fatty acids (FFAs) are stored. When it is low FFAs enter the circulation as substrates for glucose production. Insulin normally promotes tryglyceride synthesis and inhibits postprandial lipolysis. Glucose uptake into adipocytes is impaired in the metabolic syndrome and Type 2 diabetes and circulating FFAs as well as hyperglycaemia have a harmful effect on hepatic glucose production and insulin sensitivity. Eventually the beta cells do not respond to glucose (glucose toxicity). Loss of beta cell function is present in over 50% of people with Type 2 diabetes at diagnosis (United Kingdom Prospective Study (UKPDS) 1998) (Figure 1.2). Figure 1.3 depicts the consequences of insulin resistance.

Insulin is secreted in two phases: an effective first phase is essential to limit the postprandial rise in blood glucose. The first phase is diminished or lost in Type 2 diabetes leading to elevated postprandial blood glucose levels (Dornhorst 2001; IDF 2011). Postprandial hyperglycaemia, >7.8 mmol/L two hours after a meal, contributes to the development of atherosclerosis, hypertriglyceridaemia and coagulant activity, endothelial dysfunction, and hypertension, and is a strong predictor of cardiovascular disease and contributes to the development of other diabetes complications (Ceriello 2003; IDF 2011).

Interestingly, the beta cells do respond to other secretagogues, in particular sulphonylurea medicines.

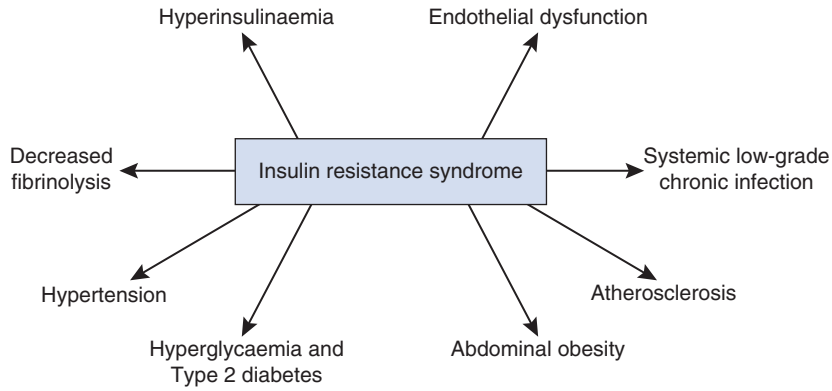

Figure 1.3 Some consequences of the insulin resistance syndrome. These factors lead to increased morbility and mortality unless diabetes is diagnosed early treatment commenced.

The net effect of these abnormalities is sustained hyperglycaemia as a result of:

- impaired glucose utilisation (IGT);
- reduced glucose storage as glycogen;
- impaired suppression of glucose-mediated hepatic glucose production;
- high fasting glucose (FPG);
- reduced postprandial glucose utilisation leading to postprandial hyperglycemia.

Various tools and risk calculators are used to detect Type 2 diabetes. They encompass some or all of the following risk factors (AUSDRISK Tool; Abassi *et al*. 2012):

- have the metabolic syndrome;
- are overweight: abdominal obesity, increased body mass index (BMI), and high waist-hip ratio (>1.0 in men and >0.7 in women). The limitations of the waist circumference in some ethnic groups are outlined later in the chapter. Elevated FFAs inhibit insulin signalling and glucose transport (see Figure 1.4) and are a source of metabolic fuel for the heart and liver. Binge eating precedes Type 2 diabetes in many people and could be one of the causes of obesity; however, the prevalence of eating disorders is similar in Type 1 and Type 2 diabetes (Herpertz *et al*. 1998);
- are over 40 years of age, but note the increasing prevalence in younger people (see also Chapter 13);
- are closely related to people with diabetes;
- are women who had gestational diabetes or who had large babies in previous pregnancies;
- the children of a woman who had gestational diabetes, maternal obesity or maternal malnutrition;
- are inactive; high levels of sedentary time is associated with 117% increase in the relative risk of Type 2 diabetes and 147% increase in the risk of cardiovascular disease and 49% increased risk of all-cause mortality (Wilmot *et al*. 2012). Occupational sitting time also represents increased risk of Type 2 diabetes (van Ufelen *et al*. 2010).

Other metabolic syndrome-associated risk factors for Type 2 diabetes have already been described. In addition, active and former smoking and acanthosis nigricans are associated with hyperinsulinaemia (Kong *et al*. 2007). Baseline and hypertension progression are independent predictors of Type 2 diabetes (Conen *et al*. 2007). Recent research suggests insulin lack might be partly due to the enzyme PK Cepsilon (PKCe),

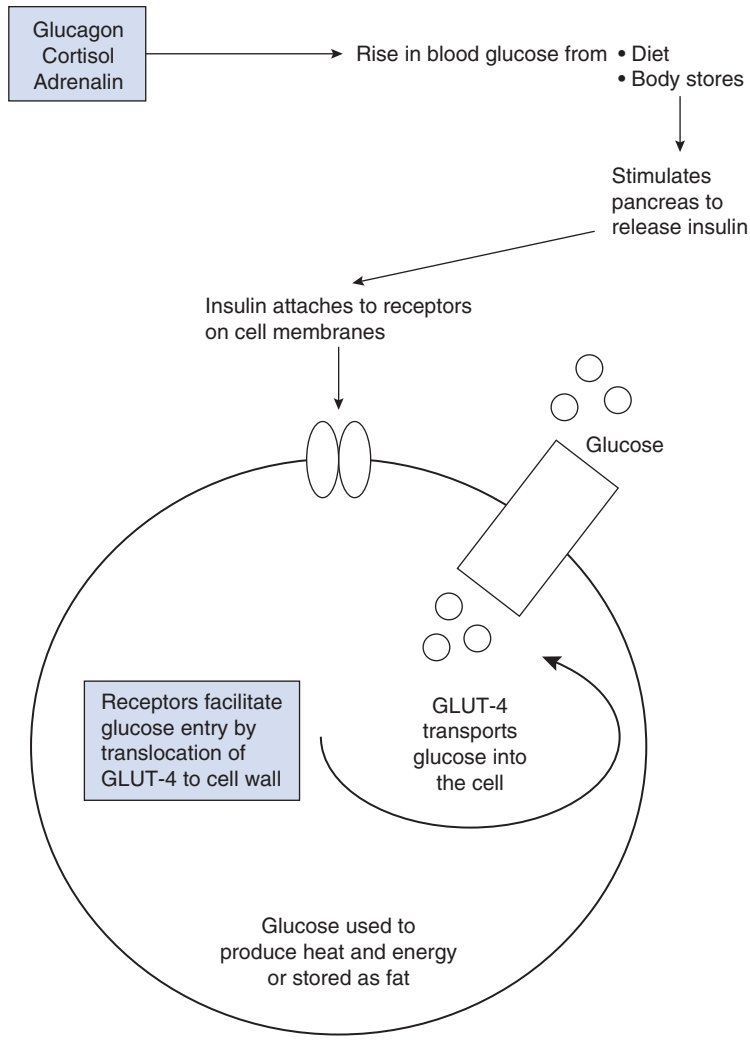

Figure 1.4 Diagrammatic representation of insulin binding, insulin signalling, translocation of GLUT-4 and glucose entry into the cell. GLUT-4 is a glucose transporter contained in vesicles in the cell cytoplasm. Once insulin binds to an insulin receptor GLUT-4 moves to the cell membrane and transports glucose into the cell. During fasting GLUT-4 is low and increases in response to the increase in insulin. Failure of GLUT-4 translocation could explain some of the insulin resistance associated with Type 2 diabetes. The effects of insulin are mediated by two protein pathways: P13-kinase through the insulin receptors (glucose uptake) and MAP-kinase, which stimulates growth and mitogenesis.

which is activated by fat and reduces insulin production. Future medicines may target this deficiency and restore normal insulin function (Biden 2007).

In addition, Swedish researchers Mahdi *et al*. (2012) demonstrated that people with high serum Secreted Frizzled-Related protein 4 (SFRP4) have a 5-fold increased risk of developing diabetes in the following five years. SFR4 plays a role in the inflammatory process and its release from islet cells is stimulated by interleukin-1β. High serum SFRP4 reduces glucose tolerance. SFRP4 is elevated several years before Type 2 diabetes is diagnosed indicating it could be a useful risk marker for Type 2 diabetes independently of other risk factors

Table 1.1 Generally agreed characteristics of Type 1 and Type 2 diabetes mellitus.

	Type 1	*Type 2*
Age at onset	Usually <30 years[a]	Usually >40 years. But increasing prevalence in children and adolescents
Speed of onset	Usually rapid	Usually gradual and insidious
Body weight	Normal or underweight; often recent weight loss	80% are overweight
Heredity	Associated with specific human leukocyte antigen (HLA-DR3 or 4)[b]	No HLA association Genetic predisposition, which is complex and only beginning to be understood
	Autoimmune disease and environmental triggers	Environmental and lifestyle factors contribute
Insulin	Early insulin secretion Impaired later; may be totally absent	Often preceded by the metabolic syndrome (see section on 'The metabolic syndrome'). Insulin resistance is reversible if appropriate diet and exercise regimens are instituted. Type 2 is associated with slow, progressive loss of beta cell function
Ketosis	Common	Rare
Symptoms	Usually present	Often absent, especially in the early stages. Acanthosis nigricans is common in some ethnic peoples
Frequency	~15% of diagnosed cases	~85% of diagnosed cases
Complications	Common but not usually present at diagnosis	Common, often present at diagnosis
Treatment	Insulin, diet, exercise, stress management, regular health and complication assessment	Diet, GLM, exercise, insulin, stress management, regular health and complication assessment

[a] Increasing incidence of the metabolic syndrome and Type 2 diabetes in children and adolescents.
[b] Occurs in older people; see LADA.

Vitamin D deficiency may also be a risk factor for diabetes independently of other risk factors in longititudinal studies such as the Australian Obesity and Lifestyle (AusDiab) study (Gagnon *et al*. 2011). Given the increasing information about the complexity of Type 2 diabetes pathophysiology, it is unlikely any single intervention will prevent or treat the disease effectively; thus, it is not clear whether vitamin D supplementation is likely to modify diabetes risk. Vitamin D deficiency is very common and is also a marker of general health status and may be indicated to manage other concomitant conditions such as osteoporosis.

The characteristics of Type 1 and Type 2 diabetes are shown in Table 1.1.

Management is discussed in Chapter 2. The majority of people with Type 2 diabetes require multiple therapies to target the multiple underlying metabolic abnormalities and achieve and maintain acceptable blood glucose and lipid targets over the first nine years after diagnosis (UKPDS 1998). Between 50% and 70% eventually require insulin, which is often used in combination with other glucose lowering medicines (GLM), which means diabetes management becomes progressively more complicated for people with Type 2 diabetes, often coinciding with increasing age when their ability to manage may be compromised, which increases the likelihood of non-adherence and the costs of managing the disease for the patient and the health system.

Type 2 diabetes in Indigenous children and adolescents

Type 2 diabetes in children and adolescents is discussed in Chapter 13 but it is a significant problem in Indigenous children and adolescents. Indigenous Australians, like other Indigenous peoples, are at high risk of Type 2 diabetes, especially when they live in remote communities, and it develops at a younger age (Minges *et al*. 2011). Onset is often in early adolescence and frequently asymptomatic. Indigenous children and adolescents with diabetes usually have a family history of Type 2 diabetes, are overweight and have signs of hyperinsulinaemia and acanthosis nigricans. There is a high prevalence of misrovascular and macrovascular complications and the associated morbidity and mortality (Azzopardi *et al*. 2012).

A number of causative factors are implicated including intrauterine exposure to risk during maternal pregnancy, obesity, physical inactivity, genetic predisposition and socioeconomic and environmental factors. Consequently, experts recommend screening Aboriginal and Torres Strait Islander children over age 10 for metabolic syndrome and diabetes. The IDF (2011) criteria for diagnosing Type 2 diabetes in Indigenous children and adolescents are:

- Random laboratory venous blood glucose (BG) >100 mmol/L and polyuria and polydipsia especially when the symptoms occur at night. OR
- Fasting laboratory venous BG > 7 mmol/L performed after fasting for at least 8 hours. OR
- Random laboratory plasma BG .11.1 mmol/L on at least two separate occasions.

Oral glucose tolerance tests (OGTT) are not practical in many remote Indigenous communities. Point-of-care HbA1c might be an alternative but no clear diagnostic recommendations are available for children. Ketones should be checked in newly diagnosed Indigenous children to ensure treatment is appropriate. Management should be individualised taking into account the psychosocial factors that influence adherence.

Gestational diabetes

Diabetes occurring during pregnancy is referred to as gestational diabetes (GDM). GDM occurs in ~5% of all pregnancies (Rice *et al*. 2012). The incidence of GDM is increasing with the global obesity epidemic. GDM refers to carbohydrate intolerance of varying degrees that first occurs or is first recognised during pregnancy. Several factors have been implicated in the development of GDM including diet and lifestyle, smoking, some medicines, older age, genetic background, ethnicity, number of previous pregnancies and recently, short stature (Langer 2006).

People at risk of GDM should be screened for diabetes using standard diagnostic criteria at the first prenatal visit. High risk women have impaired fasting glucose (5.6–6.9 mmol/L) and/or, impaired glucose tolerance (2-hour OGTT 7.8–11.0 mmol/L). Women with HbA1c 5.7%–6.4% are also at increased risk (Rice *et al*. 2102). For more information about GDM refer to Chapter 14.

Maturity onset diabetes of the young (MODY)

Maturity onset diabetes of the young (MODY) is a rare heterogeneous group of disorders that result in beta cell dysfunction. MODY can develop at any age up to 55. It has a genetic basis and at least nine different genes that result in the MODY phenotype, which

Table 1.2 Classification of single gene mutations resulting in MODY (Data from Rice *et al.* [2012]).

Genetic variety	*Prevalence: % of overall MODY gene mutations depending on the populations studied*	*Features*
HNFIA	30–50%	Common mutation Progressive beta cell failure > 5 mmol/L BG rise at 2 hours on OGTT (75 gram) Sensitive to sulphonylureas
GCK	30–50%	Common mutation Elevated fasting BG with small, <3 mmol/L, rise at 2 hours on OGTT (75 gram) Mild hyperglycaemia and may not require treatment
HNF-4A	5%	Similar presentation to HNF1A Associated with higher birth weight Transient neonatal hyperglycaemia Progressive beta cell failure Sensitive to sulphonylureas
HNF1B	5%	Associated with renal disease Urogenital tract abnormalities in girls
* INS	< 1%	Varied clinical presentation Usually present with neonatal diabetes but can present in childhood and early adulthood
* IPF1	< 1%	Average age at diagnosis 35 years
* NUEROD1	< 1%	Vary rare Similar to type 2 diabetes Onset mid 20s Development of beta cell failure and reduced insulin production May be overweight
* CEL	< 1%	Very rare Due to exocrine pancreatic dysfunction but pathophysiology is unknown Adult onset ~ age 36
* PAX4	< 1%	Vary rare

*fewer than five families reported with the genes.

suggests MODY is a single entity. MODY accounts for 1%–2% of people diagnosed with diabetes, but the prevalence could be underestimated because population-based screening programmes have not been performed (Gardner & Tai 2012). The different genetic aetiologies vary in age at onset, hyperglycaemia pattern, response to treatment and extra-pancreatic manifestations. The varieties of MODY are shown in Table 1.2.

People with MODY often have a strong family history of diabetes, insulin independence, no insulin autoantibodies and evidence of endogenous insulin production, low insulin requirement and generally do not become ketotic (McDonald *et al.* 2011). However, there are distinct phenotypes which might present differently. Treatment depends on the MODY type but generally includes GLMs, diet and exercise, although insulin may eventually be required. HNFIA individuals are very sensitive to sulphonylureas.

MODY can be difficult to recognise and the diagnosis missed or delayed (Appleton & Hattersley 1996). This can have implications for the individual and their family in commencing appropriate treatment for the specific type of MODY. Genetic counselling is also advisable.

Practice points

(1) MODY is a different disease process from Type 2 diabetes that occurs in young people and has a different genetic and inheritance pattern from Type 2.
(2) The prevalence of Type 2 diabetes in children is increasing and is associated with obesity and insulin resistance (Sinha *et al*. 2002).
(3) MODY has been misdiagnosed as Type 1 diabetes and insulin commenced unnecessarily.
(4) MODY has also been diagnosed instead of Type 1 diabetes in the UK (Health Service Ombudsman 2000).
(5) Type 2 diabetes is a serious, insidious life-threatening disease.

These points demonstrate the importance of taking a careful clinical history and undertaking appropriate diagnostic investigations.

Diagnosing diabetes

Urine glucose tests should not be used to diagnose diabetes; if glycosuria is detected, the blood glucose should be tested. When symptoms of diabetes are present, an elevated blood glucose alone is often sufficient to confirm the diagnosis. See Table 1.3 for diagnostic criteria.

If the person is asymptomatic, abnormal fasting blood glucose values of >7 mmol/L should be demonstrated on at least two occasions before the diagnosis is made (note that some guidelines suggest >6.5 mmol/L). Random plasma glucose >11.1 mmol/L and symptoms are diagnostic of Type 2 diabetes. An oral glucose tolerance test (OGTT) using a 75 g glucose load may be indicated to determine the presence of glucose intolerance if results are borderline. The criteria for diagnosing diabetes according to the World Health Organization are shown in Table 1.3. A protocol for preparing the patient and performing an OGTT are outlined later in the chapter. However, some experts suggest 75 g may be too high a load for some ethnic groups such as Vietnamese.

Abnormal plasma glucose identifies a subgroup of people at risk of diabetes-related complications. The risk data for these complications is based on the 2-hour OGTT

Table 1.3 Diagnostic criteria for non-pregnant adults with diabetes based on the World Health Organization and the American Diabetes Association Guidelines.

Stage	*Fasting plasma glucose*	*Random plasma glucose*	*Oral glucose tolerance test (OGTT)*
Normal	<6.1 mmol/L		2 hour plasma glucose <7.8 mmol/L
Impaired glucose tolerance	Impaired fasting glucose – fasting glucose ≥6.1 and <7.0 mmol/L		Impaired glucose tolerance – 2 hours plasma glucose ≥7.8 and <11.1 mmol/L
Diabetes	≥7.0 mmol/L	≥11.1 mmol/L and symptoms	2 hour plasma glucose >11.1 mmol/L

Note: In this table venous plasma glucose values are shown. Glucose in capillary blood is about 10–15% higher than venous blood. HbA1c can be used to make the diagnosis instead of or as well as venous blood glucose; >6.5% in a laboratory using certified assay method standardised to DCCT criteria.

Practice point

Hyperglycaemia often occurs as a stress response to serious intercurrent illness such as cardiovascular disease and it may be difficult to diagnose diabetes in such circumstances. However, controlling the blood glucose during the illness is important and leads to better outcomes including in non-diabetics (Chapters 7 and 9).

plasma glucose level. However, the fasting glucose of >7.8 mmol/L does not equate with the 2-hour level used to diagnose diabetes. Recently, the ADA and the WHO lowered the fasting level to 7.0 mmol/L to more closely align it to the 2-hour level.

The WHO continues to advocate routine OGTT screening in at-risk individuals to identify people at risk of complications early, in order for early treatment to be instituted. The ADA does not advocate routine OGTT use because it believes that the revised fasting level is sensitive enough to detect most people at risk. Therefore, there could be differences internationally about the routine use of the OGTT. The ADA and the WHO do agree on how the test should be performed. Australia supports the continued use of the OGTT when the diagnosis is equivocal and to detect GDM (Hilton *et al*. 2002; Twigg *et al*. 2007). However, OGTT may not always be practical in remote communities (Azzopardi *et al*. 2012).

A recent study suggested untrained people could perform self-administered OGTT in the community setting using a specific device (n = 18 people without diabetes and 12 with Type 2) OGTT were performed unaided in the home twice, unaided but observed in the clinic and one OGGT/participant was perfumed by a nurse. The results were verified with simultaneous laboratory values of the 0 and 120-minute samples (Bethel *et al*. 2013). A data recorder attached to the test device recorded information about the test. Device failures meant 0 and 120 minutes BG was only available for 141/180 OGTTs independent of the test setting. Self-performed and laboratory values were similar and reproducible. The clinical implications are unclear at this time.

Other prevention measures include providing the public with information about screening and health maintenance programmes, and self-risk assessment lists, for example checklists from the Agency for Healthcare Research and Quality (AHRQ). Checklists can be downloaded from the Internet (http://www.ahrq.gov/ppip/healthywom.htm or http://www.ahrq.gov/ppip/helthymen.htm). The information is based on the US Preventative Services Task Force recommendations.

HbA1c has an accepted place in monitoring metabolic control in people with diabetes. In addition, the WHO, IDF, and the American Diabetes Association (ADA) recommend using HbA1c as screening test for Type 2 diabetes. The Australian Diabetes Society (ADS), Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists released a position statement in 2102 that recommended HbA1c be used to diagnose diabetes if the analysis is performed in a laboratory that meets external quality assurance standards and recommended HbA1c >6.5% (48 mmol/mol) as the diagnostic cut point. Point-of-care HbA1c tests are useful clinical decision-making tools but they are not recommended for diagnosing diabetes. The ADS noted HbA1c <6.5% (48 mmol/mol) does not exclude a diagnosis of diabetes based on existing fasting BG or OGTT criteria. The latter remain the diagnostic tests of choice for GDM, Type 1 diabetes and when people have conditions that affect the HbA1c result (d'smden *et al*. 2012). In November 2012 a Medicare Consultation paper was released in Australia proposing a rebate of

$16.90 when HbA1c was performed as a diagnostic test, but the rebate would be limited to one test per year per person; an additional confirmatory test would be covered if the result was ≥6.5% (48 mmol/mol). The rate of screening in primary care might increase if the rebate is introduced.

Advantages of HbA1c as a diagnostic test are people do not need to fast before blood is collected and the test can be performed at any time of the day. HbA1c measures chronic glycaemia and HbA1c levels are strongly associated with retinopathy, macrovascular outcomes and mortality (d'Emden *et al*. 2012). HbA1c assays are standardised and generally reliable in most countries. However, errors associated with non-glycaemic factors such as haemoglobinopathies and anaemia that affect HbA1c need to be considered when interpreting the findings (Saudek *et al*. 2008).

Other markers of hyperglycaemia and diabetes risk include Fructosamine, glycated albumin and 1,5 anhydroglucitol (1,5-AG), which are associated with the development of diabetes independently of baseline HbA1c and fasting glucose (Juraschek *et al*. 2012). It is not clear what place these markers have in diagnosing or monitoring diabetes as yet, but they could be useful when HbA1c is not reliable such as haemoglobinopathies. In fact, fructosamine is recommended in the latter situation.

Other experts suggests the combination of HbA1c 5.7%–6.4% (39–46 mmol/mol) and fasting plasma glucose 5.6–6.9 mmol/L are likely to reduce the likelihood of missing a diagnosis of diabetes and be more likely to identify people with prediabetes (fasting plasma glucose 6.1–6.9 and HbA1c 6.0%–6.4% (42–46 mmol/mol) who are likely to progress to diabetes (Heianza *et al*. 2012). Abikshyeet *et al*. 2012) suggested salivary glucose could be a useful non-invasive diagnostic and monitoring test for diabetes but acknowledged more research is needed before salivary glucose testing is adopted.

Most prediction models for the risk of developing Type 2 diabetes appear to identify individuals at high and low risk of developing diabetes but extended models that include conventional biomarkers perform better. Some models overestimate risk (Abbassi *et al*. 2012). Thus, it could be important to ensure the screening parameters such as BMI and glycaemic targets are relevant to the target population.

Oral glucose tolerance test (OGTT)

An OGTT is used to diagnose diabetes:

- When fasting and random blood glucose results are equivocal.
- When there is a strong family history of diabetes, especially during pregnancy.
- If the suspicion of diabetes is high but blood glucose tests are normal/equivocal.

An OGTT should not be performed when the person:

- Is febrile;
- Is acutely ill, for example postoperatively, or uraemic;
- Has been immobilised for more than 48 hours;
- Has symptoms of diabetes or an elevated blood glucose before commencing the test.

Rationale for OGTT

Early diagnosis and treatment of diabetes reduces the morbidity and mortality associated with the hyperglycaemia.

Preparing the patient for an OGTT

(1) Give specific oral and written instructions to the patient. A sample is given in Example Instruction Sheet 1 below.
(2) Ensure the diet contains at least 200 g/day carbohydrate for at least 3–5 days before the test.
(3) If possible stop medicines that can influence the blood glucose levels 3 days before the test: some of these will need to be reduced gradually, for example corticosteroids (Chapter 10). People should be informed about the consequences of stopping their medicines and when to resume taking them after the test:
   - thiazide diuretics
   - antihypertensive medicines
   - analgesic and anti-inflammatory medicines
   - antineoplastic medicines
   - steroids.
(4) Fast from 12 midnight, the night before the test.
(5) Avoid physical/psychological stress for 1 hour prior to, and during, the test.
(6) Avoid smoking for at least 1 hour prior to the test.
(7) Allow the patient to relax for 30 minutes before beginning the test.

Example Information Sheet: Preparation for an oral glucose tolerance test

PATIENT INSTRUCTIONS FOR ORAL GLUCOSE TOLERANCE TEST

Date of test: **Name**:

Time: **I.D. label**

Location where test will take place:

(1) Please ensure that you eat high carbohydrate meals each day for 3 days before the test. Carbohydrate foods are: breads, cereals, spaghetti, noodles, rice, dried beans and pulses, vegetables, fruit. These foods should constitute the major part of your diet for the 3 days.
(2) Have nothing to eat or drink after 12 midnight on the night prior to the test day, except water.
(3) Specific information about managing medicines: .....
(4) Bring a list of all the tablets you are taking with you when you come for the test.
(5) Do not smoke for at least one hour before the test.

The test

The test is performed in the morning. You are required to rest during the test, which will take approximately 3 hours to complete. A small needle will be inserted into an arm vein for blood sampling. The needle will stay in place until the test is completed. You will be given 300 mL of glucose to drink. This is very sweet but it is important to drink it all over the 5 minutes, so that the results of the test can be interpreted correctly. Water is permitted.
You will be given a drink and something to eat when the test is finished. The doctor will discuss the results with you.

Test protocol

(1) The person should rest during the test to avoid dislodging the cannula.
(2) Insert a cannula into a suitable vein for blood sampling e.g. the cubical fossa.

(3) The blood glucose should be tested before commencing the test. If elevated, clarify with the doctor ordering the test before proceeding. Collect two milliliters of blood in fluoride oxalate tubes for laboratory analysis at each test time point.
(4) Flush the cannula with normal saline between samples to prevent clots forming in the cannula. One to two milliliters of blood should be withdrawn and discarded before collecting each sample to avoid contaminating the sample with saline left in the tubing.
(5) Collect blood samples at the following times. However, sometimes only a baseline (0) and a two-hour sample are collected:
minutes: –10
0
⇒ 75 g glucose, consumed over 5 minutes. Water can be given after the glucose is all consumed. It is very sweet and some people find it difficult to drink.
+30
+60
+120
The glucose used for an OGTT is prepacked in 300 mL bottles containing exactly 75 g of glucose.
(6) Ensure the person has a follow-up appointment with the referring doctor whose responsibility it is to explain the test results and commence or arrange for appropriate management and education.

Screening for diabetes

Because of the insidious nature and increasing incidence and prevalence of Type 2 diabetes, many countries have instituted population-based education and screening and/or case detection programmes in at-risk populations. Fingerprick blood glucose tests are not generally used to diagnose diabetes: see Table 1.3 for the diagnostic criteria. Many programmes also involve checking for obesity and cardiovascular risk factors. At-risk groups include:

- age >55 years;
- high-risk ethnic groups such as indigenous people, Southeast Asians, Indians from the subcontinent;
- women with Polycystic Ovarian Syndrome (PCOS)
- previous GDM;
- family history of diabetes;
- people with symptoms, but symptoms are often absent in Type 2 diabetes;
- older people >65 years;
- People with known diabetes complications such as cardiovascular, erectile dysfunction, and renal disease;
- active smokers (Willi *et al*. 2007).

Screening for Type 1 diabetes is not usually necessary because it presents differently and has a more rapid onset and symptoms are usually present. First-degree relatives of people with Type 1 diabetes can be tested for risk markers (autoantibodies) for diabetes but the preventative strategies applicable to Type 2 diabetes do not apply.

An example of one screening and preventative model of care is shown in Figure 1.5.

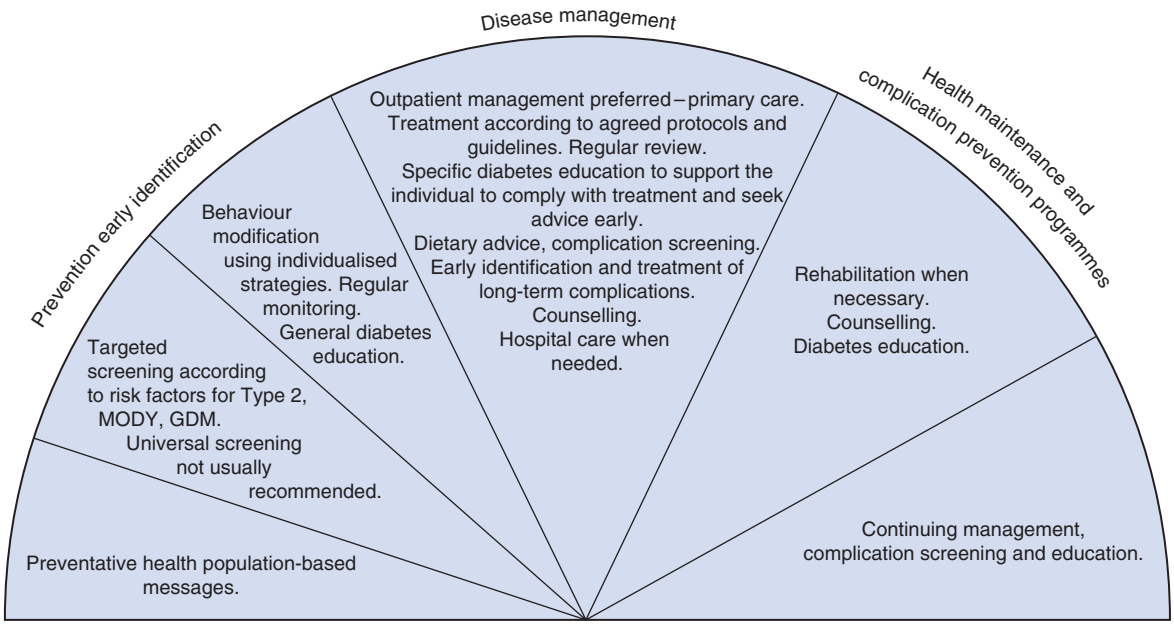

Figure 1.5 Example of a screening and preventative model of health care.

Preventing Type 2 diabetes

A number of clinical trials have demonstrated that it is possible to prevent Type 2 diabetes and may in turn prevent the associated morbidity from long-term complications. Most prevention trials were conducted among people with IGT because it is a strong predictor of Type 2 diabetes. These programmes include the Da Qing Study (Pan 1997), the Oslo Diet and Exercise Program, the Diabetes Prevention Program (DPP) (2002), and the Finnish Diabetes Prevention Study (DPS) (2003), which showed a 58% reduction in the progression to diabetes in people who followed a healthy lifestyle and the effects were still present at the four-year follow up. (Tuomilehto *et al*. 2001). The DPS was stopped early because the intervention was so successful but the researchers continued to follow people who did not develop diabetes for up to 10 years. The intervention group achieved a reduction of ~40% compared to controls.

Elements of these programmes have been adapted and implemented in many countries since the findings were first published, especially the DPP, for example *Go For Your Life* and the Life Programme in Australia. However, a Cochrane review (Nield *et al*. 2008) stated 'There is no high quality data on the efficacy of dietary intervention for the prevention of Type 2 diabetes.' Since causes of the metabolic syndrome and Type 2 diabetes are complex and multifactorial, it is not surprising that dietary interventions in isolation are ineffective.

Key features of the DPS are weight reduction (~5%), reducing fat intake to <30%, with <10% coming from saturated fats, fibre intake of >15 g per 1000 calories and >30 minutes of moderate exercise per day. In the DPS, weight loss and exercise appeared to be more important than dietary goals in preventing diabetes. Achieving weight loss and making dietary changes is difficult and only 2% of participants in

the DPS achieved four or five targets but no participant who did so developed diabetes compared to 50% of the control group. Weight management strategies are discussed in Chapter 4.

Studies concentrating on increasing fibre and magnesium to prevent Type 2 diabetes show inconsistent results despite current guidelines to increase the total fibre intake. The type of fibre consumed may be important in that soluble fibre may enhance gastric emptying and reduce the postprandial glucose rise. A meta-analysis revealed lower diabetes risk with increased intake of cereal fibre but no significant association with fruit and vegetable fibre. Thus, including whole grain foods is important in diabetes prevention diets (Krishnan *et al*. 2007) and, as indicated, pre- and probiotics are emerging as important considerations for gut health and preventing immune- and inflammatory-related diseases such as diabetes. An example of a screening and prevention model is shown in Figure 1.5.

Vegetarians appear to have reduced risk of metabolic syndrome and reduced risk of Type 2 diabetes. (Nash 2012). Likewise Mediterranean diets, while not strictly vegetarian, are generally high in fibre, prebiotics and whole grains and are associated with reduced risk of Type 2 diabetes. Avoiding liquid calories such as those in sugar sweetened beverages, fruit juice and alcohol appears to be important. These liquids also lead to dental caries. Rice is the staple food in many countries such as China where white rice is consumed at 3–4 times per day. The Glycaemic Index of white rice is higher than other whole grains and Basmati type rice. Studies suggest the relative risk of developing diabetes is 1.11 for every serving of white rice consumed per day (Hu *et al*. 2012).

Many existing public health screening and prevention models fall into four main categories (Lang & Rayner 2012):

- Sanitary-environmental model.
- Biomedical model that can be individual or population focused.
- Social behavioural model, which rivals the biomedical model. It might not take account of who has the strongest influence on behavior, which may be companies like Coca Cola.
- Techno-economic model, which views health as depending on economic growth and knowledge development.
- Ecological model, which focuses on interactions among factors that impact on health, including climate change, and integrates elements of the other four models. Climate change impacts on factors such as food security/availability, extreme weather events, which displace people and affect their lifestyle and social circumstances (IDF 2012).

The relative merits of these models have not been tested but current policies do not appear to be halting the exponential rise in the prevalence of the metabolic syndrome and diabetes. In fact Simmons *et al*. (2012) suggested screening for diabetes does not reduce deaths. The researchers followed a cohort of nearly 12 000 people at high risk of diabetes for 10 years and found they were no more likely to have died than 4000 people who were not screened, and there were no significant differences between the two groups for deaths specifically attributable to diabetes. Interestingly, benefits for microvascular disease were not analysed. It is unlikely that screening alone *would* reduce risk unless relevant prevention strategies were used and early diagnosis and management incorporated into the model. Likewise, population-wide prevention may not reduce healthcare spending because it does not reduce the risk of serious illness or premature death, because of the number of people who need to receive a particular

preventive treatment to prevent a single illness (Reuters Health Information 2013). Targeted prevention programmes that incorporate environmental and social factors and collaborating with local government and religious institutions and other key stakeholders need to be part of prevention programmes.

Two European projects DE-PLAN and IMAGE are addressing implementation processes for diabetes prevention programs and developing a toolkit to help people develop and implement programmes for preventing Type 2 diabetes. The kit includes a practical guideline that targets everybody who could have a role in prevention such as health professionals, teachers, traditional healers, and politicians, it explains key aspects of financial management, how to identify people at risk, as well as educating and training key personnel, and monitoring and quality assurance processes that need to be addressed. It will be interesting to determine whether the toolkit makes a difference in actual practice, since many prevention programmes already encompass all the elements in the tool kit including education.

One important factor that might lead to changes is the Global Monitoring Framework (GMF) for non-communicable disease, which was agreed in November 2012 between the WHO and national governments. The GMF is ambitious and has been dubbed '25 by 25' in recognition of the first target, which is to reduce NCD-related deaths by 25% by 2025. Other targets include reducing the:

- increase in diabetes and obesity;
- prevalence of inactivity by 10%;
- harmful use of alcohol by 10%;
- consumption of salt by 30%;
- prevalence of tobacco use by 30%;
- prevalence of hypertension by 25%.

Signatory countries to the agreement will be required to report their performance against the agreed targets in 2013. The targets reflect metabolic syndrome risk factors such as hypertension, inactivity and smoking. Importantly, one target is to halt the increasing prevalence of diabetes and premature mortality from non-communicable diabetes. Important proposed strategies to help meet the Global Framework is to ensure essential medicines and self-management preventative education are available (IDF 2012).

Meanwhile, research is underway to understand the genetics that predispose people to insulin resistance and Type 2 diabetes and help predict the risk for diabetes to better target prevention and management strategies. Significant progress has been made in identifying the variations in DNA sequence involved in the development of diabetes as part of the Genome-wide study (GWAS). Sixty-five regions of the human genome associated with diabetes have been identified (Morris 2012), however the effects of the variants are too subtle to be used as risk predictors at present.

Research to determine how beta cells and insulin-responsive tissues normally develop and function are also progressing, for example discovering the relationship between the FTP gene and obesity. Animal studies are underway to determine the mechanisms that affect appetite and metabolism and predispose to obesity. Genetic studies are increasing our understanding of the relationship between SHBG levels and diabetes risk. SHBG is a binding protein produced in the liver that transports testosterone, and to oestrogen to some extent, to target tissues. SHBG levels are often low in people with Type 2 diabetes. Previously, researchers assumed that insulin resistance lowered SHBG, however genetic studies suggest low SHBG may have a causal role in Type 2 diabetes (Ding *et al.* 2009).

Preventing Type 1 diabetes

Research for the elusive cure for Type 1 diabetes continues. Approaches include:

- Immune intervention using monoclonal antibodies to prevent the immune system destroying beta cells. People diagnosed early enough to still have some functioning beta cells receive a combination of medicine such as Teplizumab and Otelixizumab. The medicines protect the remaining beta cells and people may need less insulin. The results of clinical trials vary among countries. For example, in Europe and America young, slim people appear to benefit from the medicines; however, people from Asia derive less benefit. Genetic differences, age and BMI might account for the different responses.
- Stem cells: blood stem cells have been used in a similar way to treatment for leukemia in Brazil. Radiation is used to destroy the immune system and fresh blood stem cells are infused to calm the immune system so it no longer destroys beta cells. Early clinical studies show 'promise.' The following is more specifically treatment but it is relevant to stem cell research. In Australia, researchers have isolated stem cells in the adult pancreas and developed a technique to transform the stem cells into insulin-producing beta cells that release insulin in response to glucose. The hope is people with Type 1 diabetes may be able to regenerate their own beta cells if the immune attack that initially caused diabetes can be prevented.
- Reprogrammed liver cells are being researched in animal studies in Israel (Jaekel 2012).

Managing diabetes mellitus

Key points

- The person with diabetes undertakes >90% of their diabetes management, thus they are experts in *their* diabetes and their lives.
- Visits to health professionals occur at regular intervals and mostly concern assessing physical, psychological and metabolic status and making treatment recommendations.
- Diabetes education is the cornerstone of management. The phrase generally refers to people with diabetes BUT it applies equally, if not more so to the health professionals who provide education and care for people with diabetes.
- It is essential to individualise care plans and develop them with the individual concerned.

Management strategies for specific aspects of care are discussed in almost every chapter of the book. This section deals with general management information.

Many 'diabetes care models' have been developed as the framework within which to provide diabetes care. These include the Chronic Disease Model and its derivations such as the Flinders Model used in some Australian states. Research suggests effective diabetes care models need to enable early diagnosis and coordinate diagnosis, treatment and ongoing management, and educate people with diabetes and their health professionals (Renders *et al*. 2012). Effective components of management programs appear to be high frequency of contact with people with diabetes and ability for the people managing the disease (primarily the person with diabetes) to adjust their medicines and are

more effective for people with inadequate glycaemic control (HbA1c >8% at baseline) (Pimouguet *et al*. 2010).

Diabetes education is an essential component of diabetes management and the benefit seems to apply equally to groups and individual education and combinations of both (Pimouguet *et al*. 2010) (Chapter 16).

Currently, the Australian Government is evaluating a new care model: the Diabetes Care Project (DCP) in a large randomised control trial involving general practices, nurses and allied health professionals in Queensland, Victoria and South Australia. The DCP consists of two models of coordinated care. General practices that enroll will be randomised to either usual care (control) or intervention 1 or 2. Intervention 1 will test an electronic tool that creates individualised care plans and enables health professionals and the individual to access the care plan and health record and update information, and automated follow-up and review processes. Patient progress will be monitored against their care plan. Health professional compliance with Medicare will also be monitored.

Intervention 2 uses the same electronic tool and a new funding model and encompasses a new team member, the care facilitator. The new funding model is risk adjusted and enables patients to access diabetes educators and allied health professionals. It will be interesting to track progress of this innovative model. The model appears to comply with Pimouguet *et al*. (2010) and Renders *et al*. (2012) criteria for effective models.

The diabetes team

Effective diabetes management depends on having a collaborative multidisciplinary health care team. The person with diabetes is the central player in the team. Good communication among team members is vital and information the patient receives must be consistent between, and within, hospital departments, health services and health professionals to ensure smooth transition among services and avoid confusing the patient with inconsistent information. The team usually consists of some or all of the following:

- Diabetologist;
- Diabetes nurse specialist/diabetes educator and/or diabetes nurse practitioner;
- Dietitian;
- Podiatrist;
- Social worker;
- Psychologist;
- General practitioner.

Other professionals who contribute regularly to the diabetes management:

- Opthalmologist
- Optometrist
- Pharmacist
- Specialists such as vascular and orthopaedic surgeons, neurologists, and urologists, audiologists;
- Cultural/traditional health workers, for example, Aboriginal health workers in Australia and traditional healers in Africa;
- Exercise physiologists;
- Hospital physiotherapists.

The ward staff who care for the patient in hospital and the community also become team members during presentations to hospital and emergency departments and care in home settings including:

- Doctors
- Nurses
- Dietitians
- Community physiotherapists
- Occupational therapists.

It is easy to understand why people with diabetes can be confused about health professional roles and responsibilities and about their own role and responsibilities in diabetes care if they receive conflicting information from health professionals.

Managing diabetes consists of dietary modification, regular exercise/activity and in some cases insulin or GLMs. Diabetes education and regularly assessing metabolic control and complication status is essential. In addition, general health care is very important and includes dental checks, mammograms, prostate checks and preventative vaccinations, for example, fluvax and pneumovax. As indicated many times in this book, it is essential to personalize the care plan and individualise management targets to suit the person's risk status, social situation and capabilities. (Repetition is one important education strategy. Politicians and marketers also use it! Helping people manage their diabetes requires health professionals to be effective marketers, politicians and communicators.)

Aims of management

Diabetes management should be determined within the Quality Use of Medicine framework, see Chapter 4. Management aims for Australia are defined in the National Diabetes Strategy and a number of other specific guidelines such as those described in the Australian Diabetes Society Position Statements, and Clinical Management Guidelines for Diabetes in General Practice. A range of other guidelines produced by various countries and diabetes associations such as the UK, Scotland, the USA and the IDF, some of which are listed in this and other chapters in the book.

The aim of diabetes management is to maintain quality of life and keep the person free from the symptoms of diabetes, and the blood glucose and blood lipids within in an acceptable range. The blood glucose range needs to be determined on an individual basis, usually between 4.0 and 6.0 mmol/L for 90% of tests, especially during acute illness and surgery, young people and during pregnancy and HbA1c <7% (Diabetes Australia (DA 2011/12) and Royal Australian College of General Practitioners (RACGP) 2011/12), Table 1.4. However, higher targets might be more appropriate for people at risk of hypoglycaemia (Chapter 6), older people (Chapter 12) and children (Chapter 13). The aim is to obtain results as near as possible to the target blood glucose range but there must be a balance between the food plan, medication (insulin/GLMs) and exercise/activity. Maintaining emotional well-being is essential (Chapter 1). General management goals (targets) are shown in Table 1.4.

The regimen should affect the person's lifestyle as little as possible, although some modification is usually necessary. People with Type 1 require insulin in order to survive. Obese people with Type 2 can sometimes be treated effectively with a combination of diet and exercise, but research suggests that people managed with diet are not as rigorously monitored and have more hyperglycaemia and hypertension than those on medicines (Hippisley-Cox & Pringle 2004). Many people with Type 2 diabetes require GLMs and usually eventually insulin due to the progressive loss of beta cell function

In the current person-centred empowerment model of diabetes care, the person with diabetes is the pivotal person in the management team. Forming a therapeutic

Table 1.4 Diabetes management targets; but note most current guidelines recommend targets be individualised according to specific microvascular, macrovascular and hypoglycaemia risk (ADS 2012, ADA 2013, DA/RACPG 2011/12, SIGN 2010, NICE 2008).

Glucose: Fasting blood glucose 4–6 mmol/L; HbA_{1c} <7% (53 mmol/mol)
Lipids: LDL-c <2.5 mmol/L; triglycerides <1.5 mmol/L; HDL-c >1.0 mmol/L, total cholesterol <4.0 mmol/L
Blood pressure: 130/80 mmHg; 125/75 mmHg if proteinuiria exceeds 1 g/day: 140/90 if over 65 years.
BMI <25 kg/m^2 (ideal); waist circumference women <80 cm, men <94 cm.
Renal function: Urine albumin excretion 20 mm/min in timed overnight collection; <20 mm/min spot collection; albumin–creatinine ratio <3.5 mg/mmol in women, <2.5 mg/mmol men eGFR.
Alcohol intake: Women, 1 standard drink/day, men, 2 standard drinks/day.
No smoking
Exercise/activity: >150 minutes/week; at least 30 minutes brisk walking or equivalent/day or on at least five days/week

partnership with the individual and accepting their choices is essential to achieving optimal outcomes. Putting the person at the centre of care means respecting their choices, even when the individual elects not to follow advice after receiving adequate information (informed decision-making). Not following advice should not be labeled 'non-compliant or non-adherent.' Accepting the person's decision does not mean the health professional does not continue to provide information and advice. It does mean *they* might need to change the way they do things and try new strategies.

Clinical observation

Diabetes is a balancing act. The individual's physical, psychological, spiritual and social and relationship needs must be balanced to enable people to undertake the necessary self-management to achieve management targets (optimal physical health). In fact, the emphasis should be on balance rather than control. Spirituality, resilience and positive thinking, in particular, are important but neglected aspects of current diabetes management strategies and are key to being able to manage life changes (turning/tipping points), self-empowerment and self-determination (Parsian & Dunning 2008).

Management involves educating the person with diabetes and other family members and carers in order to help them:

- Understand diabetes, be involved in deciding their care plan and adopt relevant self-care strategies necessary to maintain optimal health and meet glycaemic targets.
- Manage the impact of diabetes on their physical, psychological and spiritual functioning to maintain an acceptable quality of life.
- Achieve and maintain an acceptable weight.
- Achieve acceptable blood glucose levels and HbA1c.
- Achieve a normal blood lipid profile.
- Relieve symptoms of diabetes (polyuria, polydipsia and lethargy). This involves helping the person recognise and manage relevant signs and symptoms associated with diabetes and any concomitant condition/s.
- Prevent and/or manage hypolycaemia.
- Manage intercurrent illnesses (sick days).
- Prevent complications of diabetes and of treatment.

Table 1.5 Guidelines for assessing the patient's blood glucose testing pattern. The results should be considered as part of the overall situation not as isolated pieces of data. The target HbA_{1c} is <7% (<6.5% in some countries).

% Haemoglobin A1c	*Glucose (mmol/L)*		*Control*
	Fasting	*Two hours after food*	
4.0–6.0 (~ 31–48 mmol/mol)	4	<7	Excellent or 'too good' high risk of hypoglycaemia[a]
6.0–7.4 (48–58 mmol/mol)	7	9	Upper limit of target range
7.5–9.4 (58–75 mmol/mol)	10	14.5	Increased short- and long-term complication risk.
>9.5 (> 75 mmol/mol)	14	20	Increased short- and long-term complication risk

[a]If fasting glucose is high postprandial glucose is often also high. Postprandial glucose is affected by first phase insulin response, glucagons secretion, muscle and live glucose stores, fat tissue sensitivity to insulin, food intake and digestion and absorption of food from the gut.Both affect the HbA1c level. Fasting and postprandial have the same effect on HbA1c when the HbA1c is 7.3%–8.4%. Fasting glucose has a greater effect when the HbA1c is >8.5%. The higher the HbA1c the greater the effect fasting glucose has on HbA1c.
Note the HbA1c mmol/mol values are the closest approximations to the HbA1c percentage values. The general target is < 53 mmol/mol.

- Maintain a healthy, independent lifestyle where the person is able to manage the necessary self-care tasks to achieve acceptable glycaemic control and have a good quality of life.
- Understand social and legal responsibilities and entitlements such as driving, insurance, National Diabetes Supply Scheme (in Australia).
- Plan for life transitions including stopping driving, moving to supported or aged care facilities and end of life care.

Table 1.4 described the management targets. Table 1.5 provides some glycaemic information to consider when assessing metabolic control. ***HbA1c is only part of the overall picture and should NOT be considered in isolation.***

A suggested model for managing diabetes is shown in Figure 1.6. The model is divided into phases and indicates that management, education and counselling are required for life.

Exercise/activity

Exercise plays a key role in the management of Type 1, Type 2 diabetes, and GDM as well as people without diabetes (including health professionals). It increases tissue sensitivity to insulin aiding in the uptake and utilisation of glucose during exercise and for several hours afterwards. The energy sources during exercise are depicted in Figure 1.7.

In addition, regular exercise may have beneficial effects on the risk factors that contribute to the development of diabetes complications especially cardiovascular disease (Boule *et al*. 2001). Exercise:

- Increases cardiovascular efficiency;
- Reduces blood pressure;
- Reduces stress;
- Aids in weight reduction and appetite control;
- Promotes a sense of wellbeing;
- Aids in blood glucose control;
- Improves strength and reduces the risk of falls in older people, which helps them remain independent (anaerobic exercise).

All of these factors also reduce the risk of developing the long-term complications of diabetes. People are advised to have a thorough physical check-up before commencing

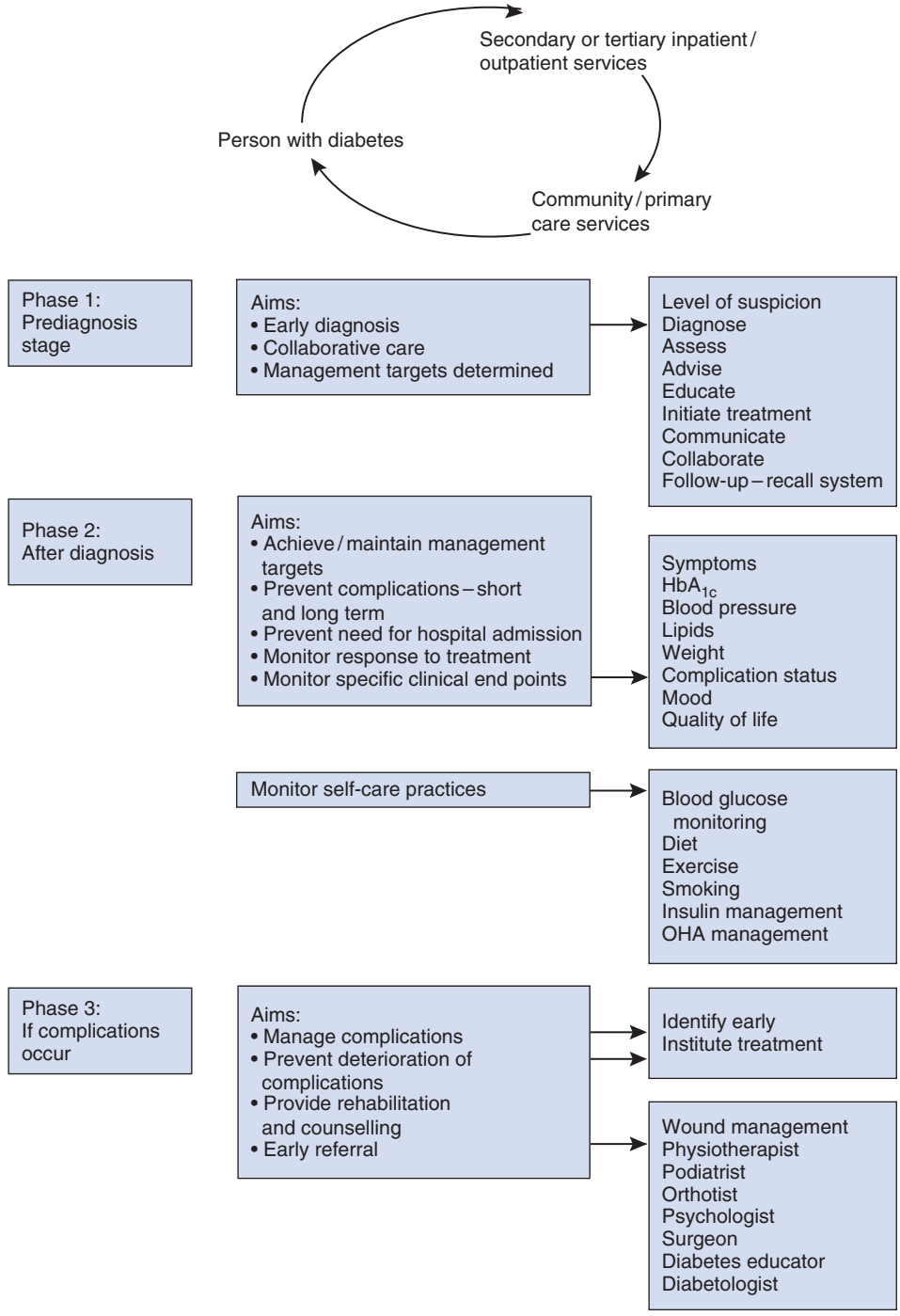

Figure 1.6 Suggested diabetes management model. Most diabetes management occurs in primary care settings in collaboration with secondary and tertiary care services.

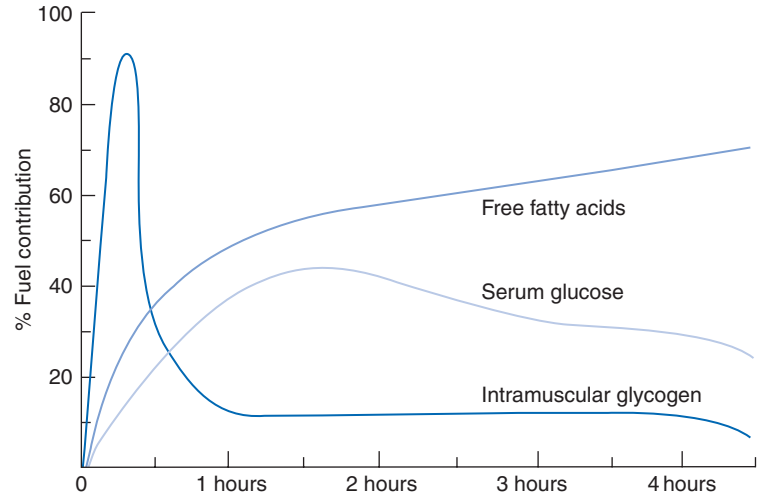

Figure 1.7 Normal energy sources during exercise. *Note*: At rest free fatty acids are the major energy source. As exercise begins muscle glycogen is utilised as the predominant energy source. As exercise continues the blood glucose is utilised, reverting to free fatty acids as the major energy source if exercise is prolonged. Blood glucose is maintained by hormonal regulation of hepatic glucose output and lipolysis.

an exercise programme; in particular, the cardiovascular system, eyes, nerves and feet should be examined. Food, fluid and clothing should be suitable for the type of exercise and the weather.

Insulin/GLM doses might need to be adjusted. Where the duration of the exercise is <30 minutes adjustments are generally not required. Adjustments are often necessary where the duration of the exercise exceeds 30 minutes (Perlstein *et al*. 1997). Exercise should be decided in consultation with the individual and suited to their preferences and physical capabilities. It is advisable that the person tests their blood glucose before and after exercising and to have some carbohydrate available during exercise in case of hypoglycaemia. Infrequent exercise is not advisable; the aim should be to begin with 10–15 minutes exercise and progress to 30–60 minutes of moderate intensity three to five times per week, daily if possible.

Footwear and clothing should be appropriate to the type of exercise and the feet inspected after exercising. Exercise is not recommended in extremes of temperatures, or at periods of hyperglycaemia, especially if ketones are present in the urine or blood. People should discuss their exercise plans with the diabetes team and/or exercise physiologist in order to plan an appropriate routine, adequate carbohydrate intake, and appropriate medication doses. Ensure adequate fluid intake to replace water loss especially in hot weather.

In general, anaerobic exercise (e.g. weight lifting) does not significantly enhance glucose utilisation. It does build muscle mass and improve strength but does not improve

Practice point

Hypoglycaemia can occur several hours after vigorous or prolonged aerobic exercise due to continuing glucose uptake by muscles. People need to be informed about adequate carbohydrate intake and medication dose adjustment as well as recognising and treating hypoglycaemia before and after exercise, see Chapter 5.

cardiovascular fitness and may reduce falls risk in older people. Anaerobic exercise is unlikely to cause an increase in blood glucose. Aerobic exercise (e.g. running, cycling, swimming) uses glucose as the major fuel source and hypoglycaemia can occur. It also confers cardiovascular benefits. Chapter 12 discusses exercise in older people. Falls risks need to be considered in older people.

Specific advice about medications and food intake needs to be tailored to the individual. The relationship between hypoglycaemia and exercise is generally well recognised. Hyperglycaemia can also occur if insulin levels are low when exercising. In this situation the counter-regulatory hormones predominate and increase the blood glucose and extra medicine doses might be needed. Insulin is easier to titrate in such circumstances.

Exercise for the person in hospital

(1) Encourage as much mobility/activity as the person's condition allows.
(2) Increase movement and activity gradually after a period of being confined to bed.
(3) Consider postural hypotension and differentiate it from hypoglycaemia to ensure correct management is instituted.
(4) Consult the physiotherapy department for assistance with mobility, chair or hydrotherapy exercises.
(5) Consider having the occupational therapist undertake a home assessment to ensure safety at home, for example, following a stroke.

Practice point

Be aware that resuming normal activity after a period of prolonged inactivity, for example in rehabilitation settings, constitutes unaccustomed exercise and can result in hypoglycaemia, especially if the person is on insulin/GLM and is not eating well or is malnourished. Exercise/activity increases the basal energy requirement by ~20%.

Diabetes education

Diabetes education is an integral part of diabetes management. Regular support and contact with the diabetes care team assists people to self-manage their diabetes by providing advice and support when necessary. For more details see Chapter 16.

Practice points

(1) People with Type 2 diabetes do not become Type 1 when insulin is needed to control blood glucose. The current accepted term is insulin-treated or insulin-requiring diabetes. The basic underlying pathophysiology does not change and usually enough endogenous insulin is produced to prevent ketosis occurring except during severe intercurrent illness.
(2) Type 2 diabetes is characterised by progressive beta cell destruction and insulin is eventually required by >50% of people (UKPDS 1998).
(3) People with LADA often require insulin soon after diagnosis, because they are insulin deficient not insulin resistant.

Complications of diabetes

Many people with diabetes are admitted to hospital because they have an active diabetes complication. The presence of a diabetic complication can affect the duration of the admission and the patient's ability to care for him or herself. Hence diabetic complications contribute to the overall cost of health care for these patients. In addition, they represent significant physical and mental lifestyle costs to the person with diabetes and their family.

Complications can be classified as acute or long term. Acute complications can occur during temporary excursions in blood glucose levels. Long-term complications occur with long duration of diabetes and persistent hyperglycaemia, especially in the presence of other risk factors. In Type 2 diabetes long-term complications are frequently present at diagnosis. Often there are few symptoms and both the diagnosis of diabetes and the coexisting complication/s can be overlooked (Chapter 8).

Acute complications

(1) Hypoglycaemia (refer to Chapter 6).
(2) Hyperglycaemia:
   - diabetic ketoacidosis (refer to Chapter 7)
   - hyperosmolar states (refer to Chapter 7).
(3) Infections can occur if blood glucose control is not optimal. Common infections include dental disease, candidiasis and urinary tract infections.
(4) Fat atrophy/hypertrophy and insulin allergy occur very rarely with modern highly purified insulins and correct injection site rotation.

Long-term complications

Two important studies, the DCCT in 1993 and the UKPDS in 1998 (DCCT 1993; UKPDS 1998) demonstrated the relationship between the development and progression of the long-term complications of Type 1 and Type 2 diabetes, respectively. In addition, the UKPDS demonstrated the importance of controlling blood pressure to reduce the risk of cardiovascular disease. Diabetes management guidelines and metabolic targets are regularly revised as new evidence emerges.

Current management targets are shown in Table 1.4.

(1) Macrovascular disease or disease of the major blood vessels, for example:
   - myocardial infarction
   - cerebrovascular accident
   - intermittent claudication.
(2) Microvascular disease or disease of the small blood vessels associated with thickening of the basement membranes of the small blood vessels, for example:
   - retinopathy
   - nephropathy.
(3) Neuropathy: diabetes can also cause damage to the central and peripheral nerves:
   - *peripheral*: decreased sensation in hands and particularly the feet, which can lead to ulcers, Charcot's arthropathy and amputation.
   - *autonomic*: erectile dysfunction, atonic bladder, gastroparesis, mononeuropathies.
(4) Complications of pregnancy: diabetes during pregnancy carries risks for both mother and baby:
   - *mother*: toxaemia, polyhydramnous intrauterine death, and Caesarian section
   - *baby*: congenital malformations, prematurity, respiratory distress, hypoglycaemia at birth.

A number of other factors might play a role in the development of diabetic complications. For example, studies are under way to determine the role of free radicals or reactive oxygen species (ROS), advanced glycated end products (AGE), changes in cellular signalling and endothelial humoral components that determine coagulation status and the tendency to form microthrombi. Long term complications are discussed in Chapter 8.

It is the responsibility of all health professionals involved in providing care to comprehensively assess the patient including the presence of complications to determine their self-care potential and devise an appropriate achievable management plan in consultation with the individual, and to be involved in preventative teaching about reducing risk factors for the development of diabetic complications. Health professionals need to be proactive about identifying opportunities for health screening and education.

Practice points

(1) Hyperglycaemia and insulin resistance commonly occur in critically ill patients, even those who do not have diabetes (van den Berghe *et al*. 2001; ADS 2012).
(2) It is important to control these states in people with diabetes during illness because of the extra stress of the illness and/or surgery, and their compromised insulin response. Elevated blood glucose in these situations in people without diabetes will require decisions to be made about the diagnosis of diabetes after the acute episode resolves.

Aim and objectives of nursing care of people with diabetes

In hospital

Being hospitalised is more common for people with diabetes than those without, and they are more likely to stay longer (ADS 2012). Current diabetes management guidelines are heavily weighted towards screening and primary care management but recently the ADS (2012) and other diabetes professional associations released guidelines for managing people with diabetes in hospital and these guidelines should be used to guide care. Specific nursing care is described in most other chapters of the book.

Factors that complicate diabetes management during illness

- Age.
- Gender.
- Type and duration of diabetes.
- Presence of diabetes complications.
- Nutritional status.
- Potentially erratic insulin absorption, especially in Type 1.
- Haemodynamic changes in blood flow.
- Counter-regulatory stress response to illness, hospitalisation, treatment, pain, psychological stress and fear.
- Timing of meals and snacks as well as during TPN, fasting and renal dialysis and especially in relation to medicine administration.

- Duration of time between insulin administration and meals.
- Effect of medications on the gut, especially narcotics for pain relief. Glucose requirements may need to be increased to compensate for slow transit times, to supply sufficient energy and prevent hypoglycaemia.
- Increased white cell count and impaired leukocyte function as a result of hyperglycaemia might not indicate the presence of infection.
- Presence of 'silent' disease such as MI, UTI and few classic symptoms of Type 2 diabetes, hypoglycaemia or hyperglycaemia.
- Delayed wound healing and strength of healing tissue.
- Increased risk of thrombosis.
- Development of ketoacidosis and/or hyperosmolar states if hyperglycaemia is not reversed.
- Impaired cognitive function and lowered mood can make problem-solving, self-care, and learning difficult.
- Depression.

People's stories

(1) People with diabetes worry that hospital staff will make mistakes, especially with their medication doses and administration times and managing hypoglycaemia.
(2) They dislike being made to feel incompetent and not trusted by staff who 'take over' the self-care tasks they usually perform for themselves, and who do not believe what they say.
(3) Conversely, some people prefer the nurses to take on diabetes slef-care tasks because it is an opportunity to 'let go of' the responsibility for a short time.
(4) They find judgmental attitudes about eating sweet things demeaning, especially when they are accused of dietary indiscretions when their blood glucose is high.
(5) They dislike being labelled non-compliant, or uncooperative, if they have difficulty learning and remembering information.

Aims and objectives of nursing care

Aims

To formulate an individual nursing management plan so that the person recovers by primary intention, maintains their independence and quality of life as far as possible and does not develop any complications of treatment and, in some cases, helping them prepare for a peaceful death.

Recognise the importance of support from the family and other key individuals to the individual's well-being, self-care capacity and ability to take responsibility for their disease.

Rationale

Early diagnosis of diabetes and monitoring for short- and long-term complications enables early treatment and improved outcomes. The nurse's understanding of the pathophysiology and classification of diabetes and its complications will improve the care they provide.

Objectives

(1) Establish a therapeutic relationship based on respect, equality and trust. The therapeutic relationship is essential to healing.
(2) To assess the person's:
    - usual care plan;
    - physical, mental and social status;
    - usual glycaemic control;
    - ability to care for themselves;
    - knowledge about diabetes and its management;
    - the presence of any diabetes-related complications including lowered mood and depression;
    - acceptance of the diagnosis of diabetes;
    - presence of concomitant disease processes;
    - medicine regimen including complementary medicines.
(3) To encourage independence as far as the physical condition allows in hospital (test own blood glucose, administer own insulin, select own meals).
(4) To obtain and maintain an acceptable blood glucose range that minimises hypoglycaemia or hyperglycaemia and keeps the person free from distressing symptoms and fluctuating blood glucose levels.
(5) To prevent complications occurring as a result of hospitalisation (e.g. falls associated with hypo- and hyperglycaemia and a range of other factors).
(6) To observe an appropriate management plan in order to achieve these objectives.
(7) To inform appropriate health professionals promptly of the patient's admission, for example, diabetes nurse specialist/diabetes educator, dietitian, or podiatrist.
(8) To ensure the patient has the opportunity to learn about diabetes and its management, particularly self-management and particularly when their usual care changes and new medicines are commenced.
(9) To plan appropriately for discharge including managing medicines and undertaking or referring the person for a home medicine review if they meet the criteria and ensuring they have the equipment necessary to manage their diabetes (medicines, blood glucose meter, insulin devices).
(10) To prevent further hospitalisations as a result of diabetes.

Technology and diabetes management

Technology increasingly supports diabetes management and self-care and health professional learning. Electronic media such as the Internet enables users to retrieve and store information, exchange information by participating in virtual communities and networks of practice and communicate with the people they care for (Harno 2013). For example, health information services, peer communities, practice guidelines, risk assessment tools, self-management tools, research publications and counselling are available online. Telephone general health care advice services often manned by specially trained nurses and diabetes-specific call centres.

In addition electronic media enable people with diabetes to be monitored remotely via teleconferences/telemedicine and by exchanging information such as blood glucose data between the individual and the health professional via email or mobile phone. Electronic patient registers and medical records are a reality in some countries. Research suggests a nurse-led multidisciplinary team can manage a group of people with diabetes in online disease management programmes (Tang *et al*. 2012) and patients are generally satisfied with electronic monitoring (Mehrotra *et al*. 2013), but it is possible to misdi-

agnose the condition and some doctors are not prepared to make a diagnosis without examining the patient.

Some doctors use smart phones to photograph health issues such as wounds to track wound healing, and eye health and for teaching purposes.

Some specific diabetes management technology includes:

- A range of increasingly sophisticated blood glucose meters, some with connectivity to other electronic systems such as mobile phones and insulin pumps and some with inbuilt management algorithms.
- Insulin delivery systems such as pumps.
- Automated support algorithms for adjusting medicine doses and carbohydrate intake.
- Non-invasive devices to detect nocturnal hypoglycaemia.
- Automated, portable system to control blood glucose overnight in people with Type 1 diabetes.
- Online HbA1c converter tool that converts HbA1c percentages to mmol/mol/.
- Health behaviour tracking systems such as stairs climbed, kilojules burned, some of which link to smart phones, which become like a personal trainer.
- Many mobile phone apps such as symptom checkers and risk calculators that help people in a range of ways.
- Electronic decision-support tools for people with diabetes and health professionals including computer-generated reminders. Interestingly, the latter appear to be more effective if they are delivered on paper and if there is space on the reminder for the clinician to document the reminder content or advice (Ariditi Rege-Walther *et al*. 2012).

There is no doubt there will be more the exciting technological advances that will enhance the care of, for, and by people with diabetes. However, like most health care options there are risks and benefits that need to be considered. Some risks to consider include:

- Not all information on the Internet is accurate or appropriate. People with diabetes need help to identify reliable sites such as the websites of diabetes organisations like Diabetes UK, Diabetes Australia, the American Diabetes Association and service providers such as Government websites, Mayo Clinic and sites that display the Hon Code symbol.
- Internet information may improve knowledge but it may not change behaviours (Chapter 16) or health professional practice because social, cultural and behavioural context are not part of the learning process (Kinson 2012) although socialisation might be a feature of online group activities and support groups.
- A combination of education about how to use management guidelines, decision support tools and patient registers can lead to improved outcomes for people with Type 2 diabetes in general practice settings (Barlow 2013).
- Adequate back up and data management systems need to be in place so important data are not lost or accessible to people not involved in the individual's care. That is, stringent, monitored security systems must be in place wherever confidential information is stored, including on mobile phones.
- Medicolegal issues such as breeches of privacy and confidentiality for example storing personal patient information, including research data, on smart phones. There are very significant implications for individuals whose data are not protected and the health professional concerned if the smart phone is lost or stolen.
- Using/communicating patient information without consent including in tele/video health professional management conferences, case discussions, publications and presentations.

A sobering final comment

OPTIMISE, the Optimal Type 2 Diabetes Management Including Benchmarking and Standard Treatment Trial (Hermann *et al*. 2012) compared physician's individual performance with a peer group to determine whether benchmarking and assessing change in three quality indicators of vascular risk: HbA1c, LDL-C and systolic blood pressure improved the quality of Type 2 diabetes care in primary care settings (n = 3980). The findings show HbA1c targets were only met in 52.2%; 34.9% for LDL-C and 27.3% for systolic blood pressure. Other studies show older physicians are less likely to follow guidelines or use new medicines (Tung 2011) and nurses have inadequate diabetes knowledge (Livingstone & Dunning 2010) including about medicines and in aged care settings (Dunning *et al*. 2012).

These findings are very concerning, even allowing for the many confounding variables that affect the ability of people with diabetes to meet targets. As suggested in Chapter 16, patient-related targets may not be the best measure of health professional performance and more appropriate measures should be considered. If they are the best measure of health professional performance, health professionals must examine their care practices, behaviours and attitudes and the care systems in which they operate, to determine whether/how these factors affect their performance. For example, general practitioners identified treatment costs to the patient and reluctance to commence insulin as barriers to their ability to achieve optimal management targets in a cluster randomised trial in Asia-Pacific that involved educating doctors about how to use diabetes guidelines (Reutens *et al*. 2011).

A great deal of time and money is spent on health professional education; if health professionals are ineffective more than 50% of the time, we need to determine whether education programmes adequately train health professionals to deliver diabetes education and care, and/or are delivered in a manner suitable to health professionals' learning needs. Another consideration is inherent weaknesses in the literature and varying interpretations of the same literature base. For example, most guidelines are developed using the same literature but recommendations often differ. In addition, the exclusive nature of randomised trials means the findings might not be relevant in all clinical practice settings.

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