

CHAPTER 1

What is diabetes?

People with **type 1 diabetes**, can live **healthy and fulfilling lives** with the provision of an **uninterrupted supply** of insulin and blood glucose testing equipment, when combined with a **healthy lifestyle**

Despite being largely **preventable**, **type 2 diabetes** accounts for the vast majority of diabetes cases



Women with **hyperglycaemia during pregnancy** can control their blood glucose levels through a **healthy diet, moderate exercise and blood glucose monitoring**

Type 2 diabetes can be effectively managed by reducing overweight and adopting a **healthy lifestyle** (diet and physical activity), combined with **medication** when required

Women with **GDM** can have high blood pressure and large babies for gestational age, which increases the risk of **pregnancy complications**

What is diabetes?

Diabetes mellitus, more simply called diabetes, is a chronic condition that occurs when there are raised levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively.¹ Insulin is an essential hormone produced in the pancreas gland of the body, and it transports glucose from the bloodstream into the body's cells where the glucose is converted into energy. The lack of insulin or the inability of the cells to respond to insulin leads to high levels of blood glucose, or hyperglycaemia, which is the hallmark of diabetes. Hyperglycaemia, if left unchecked over the long term, can cause damage to various body organs, leading to the development of disabling and life-threatening health complications such as cardiovascular disease, neuropathy, nephropathy and eye disease, leading to retinopathy and blindness. On the other hand, if appropriate management of diabetes is achieved, these serious complications can be delayed or prevented.

The classification and diagnosis of diabetes are complex and have been the subject of much consultation, debate and revision stretching over many decades, but it is now widely accepted that

there are three main types of diabetes, type 1 diabetes, type 2 diabetes and gestational diabetes (GDM).

There are also some less common types of diabetes which include monogenic diabetes and secondary diabetes. Monogenic diabetes is the result of a single genetic mutation in an autosomal dominant gene rather than the contributions of multiple genes and environmental factors as seen in type 1 and type 2 diabetes. Examples of monogenic diabetes include conditions like neonatal diabetes mellitus and maturity-onset diabetes of the young (MODY). Around 1-5% of all diabetes cases are due to monogenic diabetes.^{2,3,4,5,6,7} Secondary diabetes arises as a complication of other diseases such as hormone disturbances (e.g., Cushing's disease or acromegaly), diseases of the pancreas (e.g., pancreatitis) or as a result of drugs (e.g., corticosteroids).

For diagnosing diabetes, diagnostic criteria have been debated and updated over decades but the current criteria from the World Health Organization (WHO) state that diabetes is diagnosed by observing raised levels of glucose in the blood (Figure 1.1).

Figure 1.1 Diabetes diagnostic criteria^{8,9}

DIABETES should be diagnosed if ONE OR MORE of the following criteria are met	IMPAIRED GLUCOSE TOLERANCE (IGT) should be diagnosed if BOTH of the following criteria are met	IMPAIRED FASTING GLUCOSE (IFG) should be diagnosed if ANY of the following criteria are met
Fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dL)	Fasting plasma glucose < 7.0 mmol/L (126 mg/dL)	Fasting plasma glucose 6.1-6.9 mmol/L (110 to 125 mg/dL)
or	and	or
Two-hour plasma glucose ≥ 11.1 mmol/L (200 mg/dL) following a 75g oral glucose load	Two-hour plasma glucose ≥ 7.8 < 11.1 mmol/L (≥ 140 to < 200 mg/dL) following a 75g oral glucose load	Two-hour plasma glucose < 7.8 mmol/L (140 mg/dL) following a 75g oral glucose load
or		
A random glucose > 11.1 mmol/L (200 mg/dL) or HbA1c ≥ 48 mmol/mol (equivalent to 6.5%)		

Type 1 diabetes

Type 1 diabetes is caused by an autoimmune reaction where the body's immune system attacks the insulin-producing beta cells in the islets of the pancreas gland. As a result, the body produces none to very little insulin with a relative or absolute deficiency of insulin. The causes of this destructive process are not fully understood but a combination of genetic susceptibility and environmental triggers such as viral infection, toxins or some dietary factors have been implicated.¹⁰ The disease can develop at any age but type 1 diabetes occurs most frequently in children and adolescents. People with type 1 diabetes need daily insulin injections in order to maintain a glucose level in the proper range and without insulin would not be able to survive.

People with type 1 diabetes, with proper daily insulin treatment, regular blood glucose monitoring and maintenance of a healthy diet and lifestyle can live a healthy life and delay or avoid many of the complications associated with diabetes.

Type 1 diabetes is diagnosed by an elevated blood glucose level (Figure 1.1) in the presence of the symptoms listed in Figure 1.2. However, diagnosing type of diabetes is sometimes difficult to determine and additional testing may be required to distinguish between type 1 or type 2 diabetes or other forms of diabetes.¹¹

The incidence of type 1 diabetes is increasing worldwide, but there is huge variation by country with some regions of the world having much higher incidence than others.¹⁰ The reasons for this are unclear but an interplay between genetic and environmental factors is suspected.¹²

Figure 1.2 The symptoms of type 1 diabetes



Type 2 diabetes

Type 2 diabetes is the most common type of diabetes, accounting for around 90% of all cases of diabetes.¹³⁻¹⁵ In type 2 diabetes, hyperglycaemia is the result of an inadequate production of insulin and inability of the body to respond fully to insulin, defined as insulin resistance. During a state of insulin resistance, insulin is ineffective and therefore initially prompts an increase in insulin production to reduce rising glucose levels but over time a state of relative inadequate production of insulin can develop. Type 2 diabetes is most commonly seen in older adults, but it is increasingly seen in children, adolescents and younger adults due to rising levels of obesity, physical inactivity and poor diet.

The symptoms of type 2 diabetes may be identical to those of type 1 diabetes (Figure 1.1) including in particular, increased thirst, frequent urination, tiredness, slow-healing wounds, recurrent infections and tingling or numbness in hands and feet (Figure 1.3). However, the onset of type 2 diabetes is usually slow and its usual presentation without the acute metabolic disturbance seen in type 1 diabetes means that the true time of onset is difficult to determine.

As a result, there is often a long pre-detection period and as many as one-third to one-half of type 2 diabetes cases in the population may be undiagnosed because they may remain without symptoms for many years. When unrecognized for a prolonged time period, the complications of chronic hyperglycaemia may develop. Some patients with type 2 diabetes are first diagnosed with this condition when they present with a complication due to hyperglycaemia such as a foot ulcer, change in vision, renal failure or infection.

The causes of type 2 diabetes are not completely understood but there is a strong link with overweight and obesity and with increasing age as well as with ethnicity and family history. Some important modifiable risk factors include: excess adiposity (obesity), poor diet and nutrition, physical inactivity, prediabetes or impaired glucose tolerance (IGT), smoking and past history of GDM with exposure of the unborn child to high blood glucose during pregnancy. Among dietary factors, recent evidence has also suggested an association between high consumption of sugar-sweetened beverages and risk of type 2 diabetes.¹⁶⁻¹⁸

Figure 1.3 The symptoms of type 2 diabetes



Other factors include inadequate intake of fruit and vegetables, wholegrains and dietary fibre and high intake of energy as saturated fat. Overall, according to the latest research, emphasis for diet should move away from that on nutrients to consuming whole foods and instead following dietary patterns such as, but not limited to, the Mediterranean-type diet pattern and others.¹⁹⁻²¹

The cornerstone of type 2 diabetes treatment is healthy lifestyle which includes the adoption of a healthy diet, increased physical activity, smoking cessation plan and maintenance of a healthy body weight. If attempts to change lifestyle are not adequate to control blood glucose levels, oral medication is usually initiated for treatment of hyperglycaemia with metformin being the most commonly used initial treatment worldwide. If treatment with a single antidiabetic medication is not adequate, a range of combination therapy options are now available, including; sulphonylureas, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 agonists, and acarbose. When oral hypoglycaemic medications are unable to control hyperglycaemia to recommended targets, insulin injections may be prescribed. Beyond the control of raised glucose levels, it is vital to manage blood pressure and to screen regularly (at least annually) and manage the risk for or development of renal (kidney) complications, retinopathy (eye disease) and foot ulcer. It is important to note that with regular check-ups and good management with lifestyle and medications when needed, it is possible for people with type 2 diabetes to lead long and healthy lives.

Globally, the prevalence of type 2 diabetes has been high and is rising across all world regions. This rise is likely fuelled by an aging population, economic development and increasing urbanisation leading to more sedentary lifestyles and greater consumption of unhealthy foods linked with obesity.²²

Type 2 diabetes is most commonly seen in older adults, but it is increasingly seen in children, adolescents and younger adults due to rising levels of obesity, physical inactivity and poor diet

Hyperglycaemia in Pregnancy

Hyperglycaemia (high blood glucose level) that is first detected during pregnancy is classified as either gestational diabetes mellitus (GDM) or hyperglycaemia in pregnancy. Women with slightly elevated blood glucose levels are classified as having GDM and women with substantially elevated blood glucose levels are classified as women with hyperglycaemia in pregnancy.²³ It has been estimated that most (75–90%) of cases of high blood glucose during pregnancy are gestational diabetes.²⁴

GDM is a type of diabetes that affects pregnant women usually during the second and third trimesters of pregnancy though it can occur at any time during pregnancy. In some women diabetes may be diagnosed in the first trimester of pregnancy but in most such cases diabetes likely existed before pregnancy, but was undiagnosed.

As overt symptoms of hyperglycaemia during pregnancy are rare and may be difficult to distinguish from normal pregnancy symptoms, an oral glucose tolerance test (OGTT) is recommended for screening of GDM between the 24th and 28th week of pregnancy, but for high risk women the screening should be conducted earlier in pregnancy.²⁵ An OGTT is performed by measuring the plasma glucose concentration while fasting and two hours after ingesting a drink containing 75 grams of glucose. For diagnosing gestational diabetes (GDM), the following criteria are recommended (Figure 1.4)

GDM arises because the action of insulin is diminished (insulin resistance) due to hormone production by the placenta.²⁶ Other risk factors for GDM include older age, overweight or obesity, excessive weight gain during pregnancy, a family history of diabetes and a history of stillbirth or giving birth to an infant with a congenital abnormality.

GDM usually exists as a transient disorder during pregnancy and resolves once the pregnancy ends. However, pregnant women with hyperglycaemia

are at higher risk of developing GDM in subsequent pregnancies and about half of women with a history of GDM will develop type 2 diabetes within five to ten years after delivery. Babies born to mothers with GDM also have a higher lifetime risk of obesity and developing type 2 diabetes.²⁷⁻²⁹

Women with hyperglycaemia detected during pregnancy are at greater risk of adverse pregnancy outcomes. These include high blood pressure and a large baby for gestational age, a condition called foetal macrosomia, which can make a normal delivery difficult and risky. Identification of hyperglycaemia in pregnancy combined with good control of blood glucose during pregnancy can reduce these risks. Women of child-bearing age who have known pre-existing diabetes prior to pregnancy should receive pre-conception advice and all women who have hyperglycaemia in pregnancy whether it is GDM, previously undiagnosed diabetes in pregnancy or existing and known diabetes, require optimal antenatal care and appropriate postnatal management. Women with hyperglycaemia during pregnancy can control their blood glucose levels through a healthy diet, gentle exercise and blood glucose monitoring. In some cases, insulin or oral medication may also be prescribed.

Figure 1.4 Diagnostic criteria in studies used for hyperglycaemia in pregnancy²⁴

Criteria	Fasting		1h		2h		3h	
	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L
ADA/NDDG	105	5.8	190	10.5	165	8.6	145	7.8
ADA	95	5.3	180	10	155	8.6	Not measured	
ADIPS	99	5.3	Not measured		144	8		
CDA	95	5.3	191	10.6	160	8.9		
WHO	140	7.8	Not measured		140	7.8		
WHO	126	7			140	7.8		
IADPSG	92	5.2	180	10	153	8.5		

Impaired glucose tolerance and impaired fasting glucose

Raised blood glucose levels above the normal range and below the diabetes diagnostic thresholds meet criteria for impaired glucose tolerance (IGT) based on a two-hour post 75 grams oral glucose load or impaired fasting glucose (IFG). These conditions are also called intermediate hyperglycaemia or prediabetes.

In IGT, the glucose level is higher than normal, but not high enough to make a diagnosis of diabetes (between 7.8 and 11.0 mmol/L (140 to 199 mg/dL)) at two-hours after an OGTT. IFG is present when the fasting glucose level is higher than normal (> 6.1 mmol/L), but not high enough to make a diagnosis of diabetes which is made when the fasting glucose is above 7.0 mmol/L (or > 126 mg/dL). IFG is diagnosed with fasting glucose level between 6.1 to 6.9 mmol/L (110 to 125 mg/dL) (Figure 1.1). Raised levels of HbA1c in the non-diabetic range can also be used to identify persons at risk of developing type 2 diabetes.

People with prediabetes are at high risk of developing type 2 diabetes. Prediabetes is also characterised by decreased insulin sensitivity or increased insulin resistance. The risk factors of prediabetes are the same as for type 2 diabetes: overweight, advanced age, poor diet and excess calories or poor nutrition, lack of physical activity, smoking and family history.^{30,31} However, not everyone with prediabetes goes on to develop type 2 diabetes. High quality evidence exists from randomised controlled trials of primary prevention to support the effectiveness of lifestyle interventions in preventing the progression of prediabetes to diabetes.³²⁻³⁵

In IGT, the glucose level is higher than normal, but not high enough to make a diagnosis of diabetes

IFG is present when the fasting glucose level is higher than normal, but not high enough to make a diagnosis of diabetes

Preventing diabetes

No effective intervention currently exists to prevent type 1 diabetes. Therefore, this section focuses on factors that have been identified for the prevention of type 2 diabetes.

Of the established risk factors for type 2 diabetes, some are potentially amenable to change while others are not. For example, non-modifiable risk factors for type 2 diabetes include ethnicity, genetics and age. Other risk factors such as diet, adiposity, physical activity and environmental exposures are modifiable using a combination of approaches at both population and individual levels.

While there are many factors that influence the development of type 2 diabetes, it is evident that the most influential are the behaviours commonly associated with urbanisation and a modern lifestyle. These include consumption of unhealthy foods and inactive lifestyles with sedentary behaviour. Randomised controlled trials from different parts of the world including Finland, USA, China, India and elsewhere have established the proof of principle that lifestyle modification with physical activity³⁶ and/or healthy diet^{21,37-40} can delay or prevent the onset of type 2 diabetes.

IDF has released nine recommendations for a healthy diet for the general population (Table 1.1). Additionally, dietary recommendations of WHO for the prevention of type 2 diabetes include limiting saturated fatty acid intake to less than 10% of total energy intake (and for high risk groups, less than 7%); and achieving adequate intake of dietary fibre (minimum daily intake of 20 grams) through consumption of wholegrain cereals, legumes, fruits and vegetables.⁴¹ WHO strongly recommends reducing the intake of free sugars to less than 10% of total energy intake.⁴² IDF fully supports these recommendations and in response published the IDF Framework for Action on Sugar.⁴³

Modern lifestyles are characterised by physical inactivity and long sedentary periods. Community-based interventions can reach individuals and families through campaigns, education, social marketing and encourage physical activity both inside and outside school and the workplace.^{44,45} IDF recommends physical activity at least between three to five days a week for a minimum of 30-45 minutes.⁴⁶ WHO has also developed recommendations on physical activity among different age groups.⁴⁷ (Table 1.2)

Taking a life course perspective is essential for preventing type 2 diabetes and its complications. Early in life, when eating and physical activity habits are established and when the long-term regulation of energy balance may be programmed, there is an especially critical window to prevent the development of overweight and mitigate the risk of type 2 diabetes.⁴⁸ Healthy lifestyles can improve health outcomes at later stages of life as well.⁴⁹⁻⁵¹

Population based interventions and policies allow healthy choices through policies in trade, agriculture, transport and urban planning to become more accessible and easy. Healthy choices can be promoted in specific settings (school, workplace and home) and contribute to better health for everyone. They include exercising regularly and eating wisely which will help to maintain normal levels of blood glucose, blood pressure and lipids.^{41,52}

Table 1.1 IDF recommendations for a healthy diet for the general population⁵³

	Choosing water, coffee or tea instead of fruit juice, soda or other sugar sweetened beverages		Choosing lean cuts of white meat, poultry or seafood instead of red or processed meat.
	Eating at least three servings of vegetables every day, including green leafy vegetables.		Choosing peanut butter instead of chocolate spread or jam.
	Eating up to three servings of fresh fruit every day.		Choosing whole-grain bread, brown rice, or whole-grain pasta instead of white bread, rice, or pasta.
	Choosing nuts, a piece of fresh fruit or unsweetened yoghurt for a snack.		Choosing unsaturated fats (olive oil, canola oil, corn oil or sunflower oil) instead of saturated fats (butter, ghee, animal fat, coconut oil or palm oil).
	Limiting alcohol intake to a maximum of two standard drinks per day.		

Table 1.2 WHO recommendations on physical activity for different age groups^{45,51}

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 - Children and youth aged 5–17 years should do at least 60 minutes of moderate- to vigorous- intensity physical activity daily.
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 - Adults aged 18–64 years should do at least 150 minutes of moderate-intensity aerobic physical activity (brisk walking, jogging, gardening) spread throughout the week, or at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week, or an equivalent combination of moderate- and vigorous-intensity activity.
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 - For older adults, the same amount of physical activity is recommended, but should also include balance and muscle strengthening activity tailored to their ability and circumstances.

Management of diabetes

For those diagnosed with diabetes, a series of interventions can improve health outcomes and these can be cost-effective or even cost-saving over time.⁵⁴ Diabetes is a chronic, progressive disease but people who have diabetes can live long, high quality lives with good diabetes management. This includes management of not only glycaemia but also cardiovascular disease risk factors such as hypertension and hypercholesterolemia with a healthy diet, recommended levels of physical activity and correct use of medicines as appropriately prescribed by a physician.⁵⁵⁻⁵⁷

People with diabetes require access to systematic, regular and organized healthcare delivered by a team of skilled providers. Outcomes can be improved at the primary care level with basic interventions such as medication, health and lifestyle counselling, and individual and/or group education with regular and appropriate follow-up. This systematic care should include a periodic review of metabolic control and complications, a continually updated diabetes care plan and access to patient-centred care provided by a multidisciplinary team when indicated.

Such care is especially needed if resources are limited in many parts of the world, where self-care may be more difficult due to lack of education and limited or no availability of monitoring of glycaemia with home devices or programmes to detect diabetes complications.^{46,58} Such limitations may be effectively addressed by local adaptations of comprehensive lifestyle programmes⁵⁴ or new technology innovations such as telemedicine and mobile health tools.

Periodic referral may be needed for specialist care such as comprehensive eye examinations, treatment of eye complications (retinopathy) if needed, measurement of urine albumin and creatinine and estimated glomerular function (eGFR) for kidney health, foot examinations, and assessment and treatment of cardiovascular diseases. In addition, the availability of inpatient

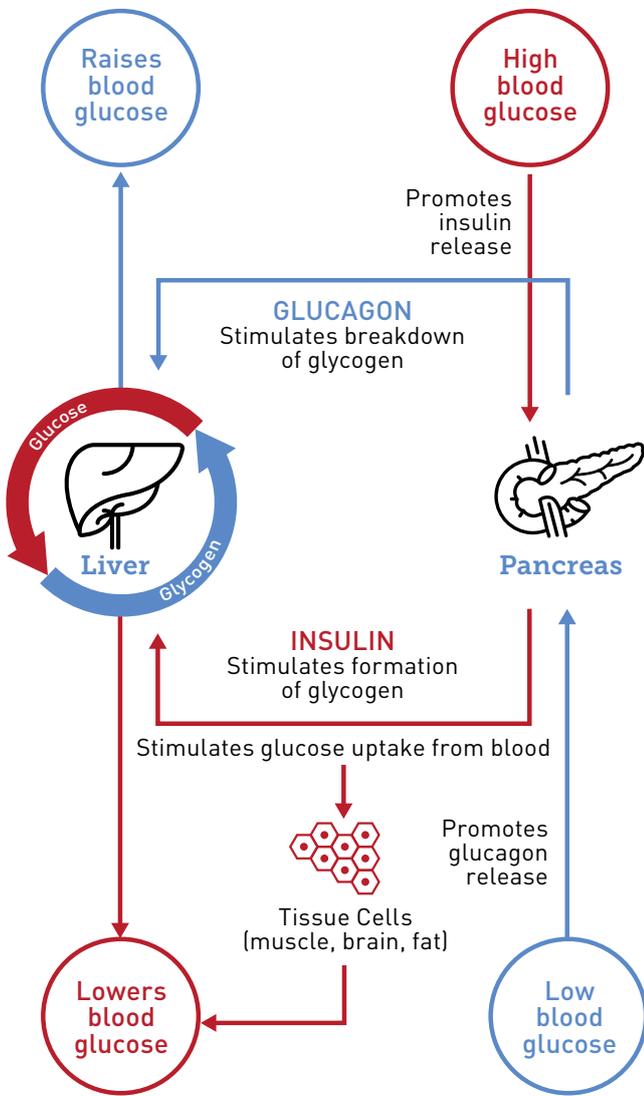
hospitalization is necessary when needed to manage acute and chronic complications such as stroke, myocardial infarction, critical limb ischemia, ketoacidosis, hyperosmolar coma, kidney failure, serious foot infections requiring amputation, treatment of hypoglycaemic episodes or stabilisation of poor control of hyperglycaemia.

Uninterrupted supply of high quality insulin is essential for survival in people with type 1 diabetes (Figure 1.5). Regular short-acting human insulin and long-acting NPH or isophane insulin should be available to everyone in all parts of the world. Versus more recently developed and costly insulin analogs, commonly available in more economically developed countries.⁵⁹ Insulin is also frequently prescribed for treatment of type 2 diabetes and hyperglycaemia in pregnancy if other hypoglycaemic medication and lifestyle intervention don't succeed in reaching glycaemic treatment goals.

The commonly used medications for type 2 diabetes are metformin, sulphonylureas, GLP-1 analogues and DPP4 inhibitors. These treatments both enhance the body's natural response to ingested food, and reduce glucose levels after eating.

Unfortunately, insulin is not readily available in many regions of the world. According to the *IDF Access to Medicines and Supplies* report, no low income country had full government provision (at no or low cost) of essential insulins to children or adults. Even for those who can pay for their insulin, less than half of middle income countries and only one low income country reported that insulin was always available. Additionally, full provision and availability of injection and monitoring equipment is even lower than it is for insulin especially for adults with diabetes. The cost of blood glucose supplies often exceeds the cost of insulin especially in some of the poorest countries.⁵⁹ Through IDF's Life For A Child programme, IDF provides insulin to over 18,000 of the poorest children and adolescents with type 1 diabetes in over 41 countries.⁶⁰

Figure 1.5 Insulin production and action



WHO lists five diabetes-related medicines on its Model List of Essential Medicines including short-acting insulin, intermediate-acting insulin, metformin, gliclazide, and glucagon. These same medicines should be included on the National Essential Medicines List (NEML) of countries although assuring their availability and proper use may require changes in procurement decisions, staff training, reimbursement mechanisms and pharmacy systems. Essential medicines are defined by WHO as “those that satisfy the priority healthcare needs of the population.”⁶¹

The use of medications to treat diabetes does not obviate the importance of other measures to combat this disease. Both healthy nutrition and physical activity have beneficial effects on insulin action, blood glucose control and metabolic abnormalities. Dietary management of diabetes includes a lower calorie intake for overweight patients, replacing saturated fats with unsaturated fats, intake of dietary fibre, and avoiding tobacco use, excessive alcohol use and added sugar.²¹ Physical activity is most effective when it includes a combination of both aerobic exercise and resistance training, as well reduction of sedentary time.⁶²⁻⁶⁵ For refractory obesity resulting in metabolic diseases, bariatric surgery (gastric bypass, gastric banding) has been demonstrated as an effective treatment for severe obesity-related type 2 diabetes, but currently its availability is primarily accessible in wealthier countries.⁶⁶