

Fast Facts



Fast Facts: Diabetes Mellitus

Ian N Scobie and Katherine Samaras
Third edition



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Declaration of Independence

This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome: feedback@fastfacts.com



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Glossary of abbreviations

ACE: angiotensin-converting enzyme [inhibitor]

ADA: American Diabetes Association

AR2B: angiotensin-II receptor antagonist ['blocker']

CSII: continuous subcutaneous insulin infusion

DAFNE: Dose Adjustment for Normal Eating [program]

DCCT: Diabetes Control and Complications Trial

DKA: diabetic ketoacidosis

DPP-4: dipeptidylpeptidase-4

GAD: glutamic acid decarboxylase

GADA: glutamic acid decarboxylase autoantibodies

GDM: gestational diabetes mellitus

GI: glycemic index

GLP-1: glucagon-like peptide-1

HbA_{1c}: glycated (or glycosylated) hemoglobin [1c component]

HDL(-C): high-density lipoprotein (-cholesterol)

HLA: human leukocyte antigen

HONK: hyperosmolar non-ketoacidotic coma

IA-2: insulinoma-associated autoantigen-2

IAA: insulin autoantibodies

ICA: islet cell antibodies

IDF: International Diabetes Federation

IFN: interferon

IRMA: intraretinal microvascular abnormality

LADA: latent autoimmune diabetes in adults

MHC: major histocompatibility complex

MODY: maturity-onset diabetes of youth

NAFLD: non-alcoholic fatty liver disease

OGTT: oral glucose tolerance test

PTA: pancreas transplant alone

SPK: simultaneous pancreas–kidney [transplant]

Th1: T helper 1 cells

Th2: T helper 2 cells

VEGF: vascular endothelial growth factor

Introduction

It is estimated that 8% of the US population has diabetes mellitus. In the UK, it is estimated that more than 3% of the population has diabetes, with about another 2% having undiagnosed diabetes. The number of people with diabetes worldwide projected for 2025 is more than 300 million. Although the incidence of new cases of type 1 diabetes is increasing in many countries, these statistics reflect a burgeoning near-epidemic of new cases of type 2 diabetes. Societal factors would seem to account for the massive increase in developed and developing countries. Such factors include the adoption of a westernized diet and lifestyle, a decline in physical activity and ever-rising rates of obesity.

Cardiovascular disease is a significant cause of death in both type 1 and type 2 diabetes. Preventive approaches should be adopted in order to minimize the risks. But this should not be at the expense of aiming for good control of hyperglycemia, as this closely correlates with the development of those specific microvascular complications of diabetes that so clearly define this ubiquitous condition.

Fortunately, in parallel with the increase in diabetes prevalence, diabetes research has flourished; from basic science through to clinical trials, there has been a rapid expansion of output in the attempt to determine the pathogenesis of diabetes and its complications and to understand how best to treat them. One particular feature has been the recent advent of new pharmaceutical products to treat type 2 diabetes.

The aim of this third edition of *Fast Facts: Diabetes Mellitus* is to provide readers with an up-to-date picture of our understanding of diabetes mellitus and its various causes, its clinical manifestations and the treatment strategies that can be used to reduce the burden of its metabolic consequences.

The global picture

The prevalence of diabetes around the world is increasing rapidly. The International Diabetes Federation (IDF) estimated that, in the seven regions it monitors around the world, diabetes affected 194 million adults in 2003. By 2007, the number of people affected had increased to 246 million: 7.3% of adults aged 20–79 years. The highest prevalence rates are found in the North American region (9.2%), followed by the European region (8.4%). IDF estimates of prevalence for 2007 are shown in Figure 1.1. Currently, about 7 million people are developing diabetes each year.

Diabetes and its sequelae accounted directly for about 3.8 million deaths in 2007, approximately 6% of the total world mortality. Even more died from cardiovascular diseases, the risk of which is increased by diabetes-related comorbidities such as hyperlipidemia, hypertension and renal disease. Data for deaths attributable to diabetes according to world regions are shown in Figure 1.2.

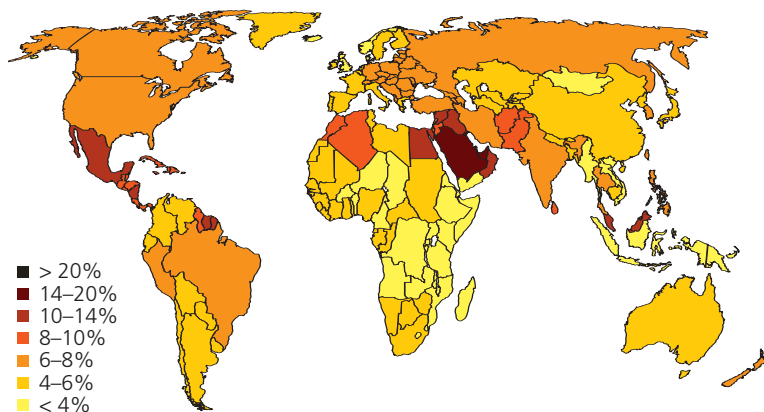


Figure 1.1 Estimated prevalence of diabetes for 2007. From International Diabetes Federation, 2006.

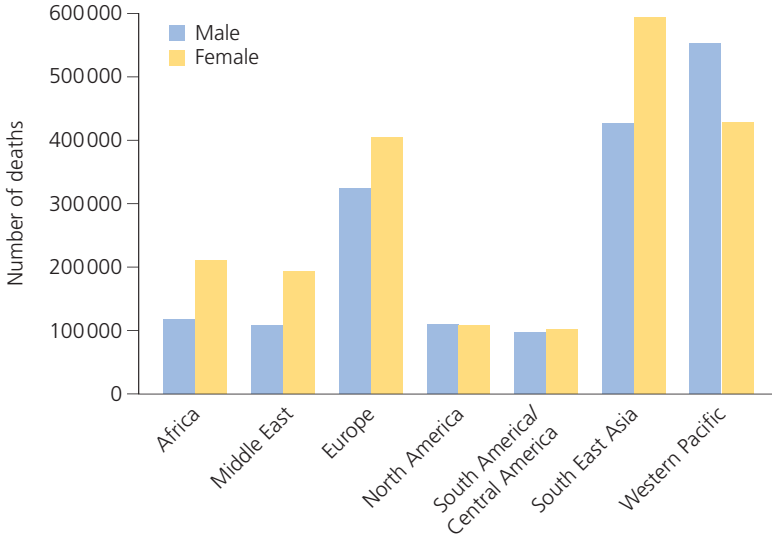


Figure 1.2 Worldwide deaths in adults aged 20–79 years attributable to diabetes, estimated for 2007. From International Diabetes Federation, 2006.

Globally, about half of all people with diabetes are in the age range 40–59 years, where productivity at work and contribution to family life is still anticipated. Illness, disability and premature death in this age group profoundly affect personal and family life, communities and national productivity. The IDF data show that preventable complications of diabetes account for an additional 23 million years of life lost due to disability and reduced quality of life.

Data extrapolations suggest the prevalence will continue to rise steeply and that by 2025, more than 300 million people will be affected. The IDF has identified several reasons for this increase in diabetes prevalence: an increase in the proportion of overweight and obese individuals, unhealthy eating, sedentary lifestyles, urbanization and an aging population.

It is clear that some nations have substantially higher rates of diabetes. Data from 2003, presented in the IDF’s *Diabetes Atlas* (2006), show the highest prevalence of diabetes in adults from Nauru, an island in the South Pacific (around 30%), the United Arab Emirates (20%), and other Middle Eastern and Asian nations (Table 1.1).

A diagnosis of type 1 diabetes changes the lives of patients for ever. Many face the prospect of having to self-inject with insulin for the rest of their lives with considerable dread. However, through time, virtually all patients accommodate to this prospect with a degree of fortitude and it is the minority who live their lives in complete resentment of their condition.

The purpose of insulin treatment of type 1 diabetes is to lower blood glucose levels to as near to the normal (non-diabetic) range as possible (Figure 6.1) without causing significant hypoglycemia. The objectives of this strategy are to:

- maintain bodyweight
- avoid hyperglycemic symptoms

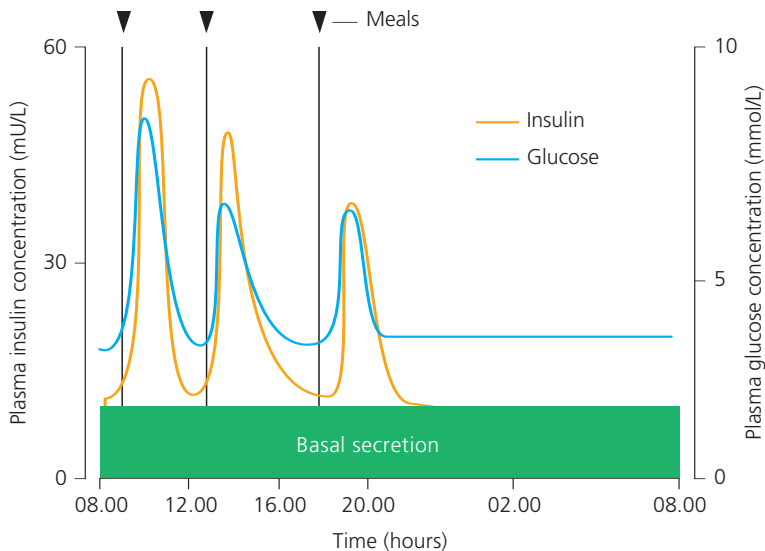


Figure 6.1 Physiological plasma insulin and glucose profiles in the fed and fasted states.

- delay or prevent the onset of complications of diabetes
- save patients from developing diabetic ketoacidosis.

Evidence to support such a strategy emerged in 1993 following the publication of the landmark Diabetes Control and Complications Trial (DCCT), which established beyond reasonable doubt that intensive insulin therapy delays the onset and slows the progression of specific diabetic microvascular complications. However, in practice, achieving normal blood glucose levels is not possible even with multiple-injection therapy, and even achieving near-normal blood glucose values in a 24-hour period poses a formidable challenge to all but a small minority of patients. The *raison d'être* of the diabetes team is to help patients reach this goal while providing appropriate support and guidance along the way.

Insulin regimens

Although porcine and bovine insulins are still used by a very small minority of patients with a long duration of diabetes, nowadays most patients with type 1 diabetes are treated with human insulin preparations or, increasingly, recombinant insulin analogs. Many patients using animal insulins maintain that using human insulin produced either by enzymatic modification or recombinant-DNA technology is associated with lack of awareness of hypoglycemia. This phenomenon has not been reported in the USA and the hypothesis has largely been patient driven. There is no scientific evidence to support this contention, but current practice is to allow patients the choice of continuing on animal insulin as no material harm will ensue. The number of patients taking animal insulin is very small and likely to decline further in future years. Some animal insulin preparations are being phased out by manufacturers.

Rapidly acting insulins such as the analog insulin Humalog have an onset of action of 5–10 minutes and a duration of action of 3–4 hours. Intermediate-acting insulins such as the isophane insulins act within 30–60 minutes and continue to act for 9–12 hours. Insulin glargine (Lantus), a more truly basal insulin, has an onset of action after 5 hours and will act for more than 24 hours in most cases, while insulin detemir (Levemir) acts after 60 minutes and lasts for 24 hours. The biphasic