DIABETES
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DIABETES

The Biography

Robert Tattersall
I have long had an interest in medical history, and this increased when I spent three months at the Wellcome Institute for the History of Medicine in 1993. Its library (free to anyone) has been invaluable in my research, as have the porters at the Greenfield Library of Nottingham University Medical School, who have cheerfully descended into the bowels of the earth to retrieve dusty journals for me.

When I retired from clinical practice in 1998, my intention was (and still is) to write a definitive, exhaustively referenced, history of diabetes, which would be of interest primarily to doctors. However, I jumped at the suggestion of the editors of this series at Oxford University Press that I should write a biography of diabetes that would be about a tenth of the length of a full history with a minimum of references, for a wide general readership.

During the 1980s the British Diabetic Association (now Diabetes UK) decided to ban the use of diabetic as a noun. In this book I often talk about diabetics for two reasons: first, because it becomes tedious to keep reading about ‘persons with diabetes’ or ‘diabetic people’. The other reason is that for most of the period I am writing about it was normal to use ‘diabetic’ as a noun.

Many of my friends in the world of diabetes have helped with my historical research, but I am particularly grateful to Edwin Gale, Harry Keen, Carl-Erik Mogensen, David McCulloch, and the late Michael Berger.
I also thank Bill and Helen Bynum, who have made many helpful suggestions and have constantly reminded me that I am not writing an article for the *Lancet*.

My wife, Bridget, has been a constant support and has made many valuable suggestions.

ROBERT TATTERSALL
Nottingham, 2009.
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PROLOGUE

When people are asked to rank diseases in order of seriousness, diabetes is usually at the mild end of the spectrum. A journalist whose 16-year-old son had just been diagnosed wrote that he had always thought of it as ‘something manageable and unprofound, a disease where not much happens’. By contrast, a patient of mine who had had it for many years compared it to living with a tiger, since, as he said: ‘If you look after it, and never turn your back on it, you can live with a tiger. If you neglect it, it will pounce on you and rip you to shreds.’ The seriousness of the disease was officially recognized in 2006, when the General Assembly of the United Nations described diabetes as ‘a chronic, debilitating and costly disease associated with severe complications, which poses severe risks for families, states and the entire world’.2

Diabetes, or, to give it its scientific name, diabetes mellitus, is a disease in which the defining abnormality is an excessively high level of glucose (often just called sugar) in the blood. The cardinal symptoms in the young are an increased volume of urine (polyuria), thirst (polydipsia), and weight loss. There may also be excessive appetite (polyphagia), so that American doctors
talk about patients having ‘the polys’—polydipsia, polyuria, and polyphagia. Those who develop diabetes in middle or old age have less dramatic or no symptoms and may be diagnosed on a routine blood or urine test.

The simplicity of the diagnostic tests conceals the fact that diabetes is a complicated biochemical disorder that affects the metabolism of all components of our diet. Meals are broken down in the intestine into their component parts of fats (lipids), proteins (amino acids), and carbohydrates (which include sugars such as glucose) by enzymes produced in the pancreas, which lies behind the stomach and is known to butchers as sweetbread. The pancreas is a double organ. The exocrine (externally secreting) part, which forms 99 per cent of its bulk, produces enzymes, which are discharged into the duodenum. The endocrine (internally secreting) part of the pancreas consists of clusters of cells (the islets of Langerhans), which are scattered throughout the organ like islands in a sea. What determines whether glucose is burned immediately or stored in the liver or muscles is the hormone insulin, which is produced in the islets of Langerhans. Absence of insulin or resistance to its action causes diabetes.

Diabetes is not a single disease but a syndrome with at least fifty possible causes. However, there are two main types. In one, most common in children and young people, the insulin-producing cells of the islets (beta cells) are destroyed by antibodies made in the body (autoimmunity), and this eventually results in a complete absence of insulin. This condition used to be called juvenile or insulin-dependent diabetes, but is now called type 1.

The other form mainly affects people over the age of 40 and used to be called adult-onset, maturity-onset, or non-insulin-dependent diabetes. It is now called type 2 and is by far the most
common type. In type 2, the beta cells are intact and, at least in the first few years, produce more insulin than normal because the target tissues (liver and fat) are resistant to its action.

In the healthy body the normal level of glucose in the blood is tightly maintained between 3.5 and 8 mmol/l (63–144 mg/dl). Exposure to persistently high levels of glucose for many years damages small blood vessels, causing the long-term diabetic complications affecting the eyes (retinopathy), nerves (neuropathy), and kidneys (nephropathy). It is important to realize that diabetes is not just a glucose disease. There are also abnormalities of fat metabolism, which contribute to hardening of large arteries (atherosclerosis), causing heart attacks, strokes, and gangrene of the feet.

I have spent most of my working life looking after patients with, and researching, diabetes. It has been an absorbing journey. As the Birmingham physician John Malins wrote in his 1968 textbook:

The more diabetic patients one sees the more difficult it becomes to present the simple picture that so many readers like. Diabetes is a disorder of such infinite variety that it becomes impossible to say that this always occurs or that never happens . . . today a diabetic clinic provides the widest clinical range of any speciality in medicine with metabolic, vascular, neurological and psychiatric problems outstanding. In addition there is a chance to enjoy some of the pleasures of general practice which arise from long acquaintance with many of the patients. The chance, all too frequent, to ease the last years of those whose health is slowly failing calls for all the resources of the general physician.

The effects of diabetes are indeed highly variable, as the following examples show.
Identical twins with type 1 diabetes

In 1971, while doing research on diabetes in identical twins, I met Jane and Sandra, who were born in 1938. At age 5, when Jane developed diabetes, they were as alike as ‘two peas in a pod’. Sandra has remained unaffected, a not uncommon situation for type 1 diabetes in identical twins, indicating that it is not purely a genetic disease. Being a child with diabetes is often lonely and stigmatizing (Fig. 1). Jane’s glucose control was always poor and she had frequent hospital admissions as a teenager. This chronic ill health affected her development, so that her adult height was 2½ inches shorter than Sandra’s and she started her periods four years later—healthy identical twins are the same height and start their periods in the same week or month. In her late teens Jane had anorexia nervosa and told me that she

1. A child’s drawing showing the loneliness of having diabetes.
deliberately underdosed herself with insulin to lose weight. She married in her 20s and, after three miscarriages, she had a still-born child. The first signs of diabetic eye damage were noted when she was 26, and by the age of 35 she was blind. Protein in her urine, the earliest sign of kidney damage, appeared when she was 24, and she was about to start dialysis when she died of a heart attack aged 37.

Before the first clinical use of insulin in 1922–3 Jane would have died within six months of diagnosis. What insulin did was to transform her illness from an acute rapidly fatal condition into a chronic one with what were eventually fatal complications. They are by no means inevitable, as shown by the next case.

**Uncomplicated type 1 diabetes**

In January 1931, Herbert, the 12-year-old son of a butcher in a small town near Nottingham, began to be increasingly thirsty. Things came to a head when he had to leave his confirmation service abruptly to ‘have a wee’. After diabetes was diagnosed by his general practitioner (GP), he was admitted to hospital and discharged two weeks later on 5 units of insulin twice daily and a diet of only 35 grams of carbohydrate per day (equivalent to a small slice of bread). So little aftercare was provided that when the insulin he had been given was running low, his elder brother had to write to the local newspaper to ask where to get more. While in hospital he had to buy a syringe and urine testing kit. Later, when he broke his syringe (a regular occurrence as a result of daily boiling), he had to buy a new one for 5 shillings, ‘a hell of a lot of money for me in those days’ (£1.11 today). As a growing boy he could not manage on so little carbohydrate and, in
his late teens, broke the diet regularly and ate sweets. He had not been told that he could increase the dose of insulin and in 1939, after developing blurred vision, he went to the Eye Hospital, where he was told ‘your eyes will never get better unless you take more care of your diabetes’. He was referred to a physician, who admitted him to hospital for seven weeks, after which he was discharged on a diet of 280 grams of carbohydrate and three doses of insulin a day. Surprisingly, after his next appointment in 1939, he was told not to come again, because ‘you know how to take care of yourself.’ He didn’t really, but in 1941 he got married, and his wife Elsie bought a patient handbook, *The Diabetic ABC* by Dr R. D. Lawrence, which they used in lieu of a doctor for the next forty years. Herbert and Elsie lived above the butcher’s shop, which Herbert took over from his father. Meals were always rigidly on time and Elsie tested his urine before every meal and weighed his food. The only alarms were that once or twice a year Herbert would become unconscious from low blood sugar during the night and Elsie would have to revive him. In 1981 the couple were surprised to be told by their GP, whom they had hardly ever seen, except for the childhood ailments of their children, that Herbert had to attend the hospital to be changed to a new strength of insulin. It was then that I met Herbert and was delighted to discover that, after fifty years, he had no diabetic complications. When I congratulated him, he said, ‘That’s the wife’s doing. I wouldn’t have managed without her.’

**Type 2 or ‘mild’ diabetes**

I took over the diabetic clinic in Nottingham in 1975 and three years later met Lilian, an overweight 60-year-old woman who was on tablets for diabetes. She had had sugar in her urine during
her last pregnancy in 1957 but was well until 1963, when genital itching (pruritus vulvae) led to a diagnosis of diabetes. She attended the clinic for two years but was then sent back to her GP with a letter that read: ‘I am discharging this lady with mild maturity onset diabetes back to your care.’ She continued to collect her tablets but had no other supervision. When I met her after she had had diabetes for eighteen years she was blind, had had a heart attack, and had had one leg amputated below the knee. The reason for the referral to me was an ulcer on her remaining foot, which would not heal. Although complications in type 2 diabetes can be as serious or even worse than in type 1, it was often referred to as mild diabetes, probably the only example of a disease where the seriousness is determined by the perceived unpleasantness of the treatment—injections versus tablets.

Someone whose course is not dissimilar to that of Lilian is Sue Townsend (b. 1946), author of the Adrian Mole books. She developed diabetes at the age of 38 and after only fifteen years was blind from retinopathy and wheelchair bound because of a Charcot foot, a condition in which the ankle disintegrates as a result of nerve damage. Neuropathy has also destroyed the nerve endings in her fingers, so that, like most other blind diabetics, she cannot read Braille. She blames her complications on the fact that she cavalierly disregarded the disease and kept her blood sugars high to avoid the inconvenience of hypoglycaemic (low-blood-sugar) attacks.

**A new kind of diabetes: MODY**

As John Malins pointed out, diabetes is so variable that one can never say that ‘this always occurs or that never happens’. When I was a medical student, it was axiomatic that normal-weight
young people with diabetes needed insulin. Jennifer, whom I met in 1971, disproved that. She developed diabetes in 1943 at the age of 12, presenting with thirst and increased urination. She was put on insulin, but discontinued it on her own initiative between 1948 and 1951. When she returned to the clinic in 1951, she was relatively well but had a high blood sugar. She was given a stern telling-off and restarted on injections. In 1970 she insisted on being tried on anti-diabetic tablets, and, to the surprise of the doctors, they worked. I asked why she had been so certain she could manage without insulin; her answer was that her aunt and cousin had both developed diabetes in their teens and been put on insulin, but had been able to stop it after thirty years. I found two other patients in the clinic at King’s College Hospital with very similar histories. They also had family members with the same unusual form of diabetes. I described them in a paper entitled ‘Mild familial diabetes with dominant inheritance’ and in 1975, while working with Professor Fajans in Ann Arbor, Michigan, changed this to Maturity Onset Type Diabetes or MODY, a name that has stuck. In the 1990s it was found that diabetes in these families was caused by single gene mutations, and it is now clear that MODY (of which there are five separate types) accounts for 1–2 per cent of all diabetes.

A plague of diabetes

In the first two decades of the twentieth century what we now call type 1 diabetes was a tragic but rare condition. It remained uncommon until the second half of the century, when in several Western countries the number of new cases per year doubled or trebled over a twenty-year period before apparently reaching a plateau. This sort of change suggests an environmental
factor, although exactly what this factor might be has remained elusive.

Type 2 diabetes is predominantly a disease of older and fatter people and has become increasingly common as a result of increased life expectancy, urbanization, lifestyle changes, and population growth. In the year 2000 it was estimated that approximately 171 million people worldwide, or about 4.6 per cent of people in the age range 20–79, were affected. This figure conceals tremendous variations between countries and within the same ethnic group. For example, in the 1990s about 3 per cent of rural Chinese in mainland China had diabetes compared to 13 per cent of Chinese in Mauritius, where living standards were much higher. At the same time, a similar picture was seen among Asian Indians, where about 4 per cent of those in rural India were diabetic compared to 23 per cent of Indians living in Fiji or Leicester, England. An observer in 1900 would have been amazed by the magnitude of these figures but not by the concept that diabetes was a product of wealth, dietary change, and urbanization. A Victorian physician had even described diabetes as ‘one of the penalties of advanced civilization’.