Case histories

Type 1 diabetes

Writing in 1649, the English herbalist Nicholas Culpeper despaired of his patients with diabetes: their "continual pissinge" was resistant to all treatment, and their deaths were rapid and certain. No longer: type 1 diabetes is a striking example of the transformation of the meaning of a diagnosis by application of clinical research. Its history reflects the trajectory of medicine away from heroic interventions and towards long-term treatment, from cure to care.

In antiquity diabetes was one of a constellation of diseases thought to be related to the retention or loss of life-giving water. In an arresting phrase Aretaeus of Cappadocia, a Greek physician of the 2nd century CE, called the disease "a melting down of the flesh and limbs into urine", a view reflected in its Greek name: "diabetes", meaning "siphon". The Hindi term for diabetes—"madhumeha", honey-urine disease—shows that ancient Indian medicine was aware of one major symptom of the disease. The sweet taste of diabetic urine seems to have escaped the attention of western physicians until 1679, when the English physician Thomas Willis used it to identify two forms of the disease: mellitus, from the Latin for honey, and insipidus, meaning tasteless.

Well into the 19th century diabetes was framed in terms of its symptoms—in the words of the clinician and historian Robert Tattersall, "a fatal disease characterised by polyuria, thirst, progressive weight loss, and debility". The anatomo-localism of Paris medicine, and the emergence of physiology as a discipline rooted in the laboratory, raised the possibility that localised lesions in organs might cause systemic disease. Initially the liver seemed the most likely candidate, as the French physiologist Claude Bernard elucidated its role in carbohydrate metabolism. With the discovery of "internal secretions"—later named hormones—in the late 19th century, researchers turned their attention to the relations between organs. In 1893 Bernard's countryman, the pathologist Gustave-Édouard Laguesse, proposed that small cellular clusters in the pancreas—named after his German contemporary Paul Langerhans, who first described them—were responsible for regulating blood sugar concentration.

If diabetes was a disorder of the pancreas, how could this knowledge be applied in treatment? In 1889 the Mauritian physiologist Charles Édouard Brown-Séquard proposed, controversially, that organ extracts containing internal secretions could be used to treat many diseases, including diabetes. Some diabetics adopted a dispiriting diet of raw pig pancreas, and several researchers tried to identify the distinctive internal secretion of the pancreas. In 1921–22, Canadian physicians Frederick Banting and Charles Best used a series of surgical experiments on dogs to show that a new hormone, insulin, was responsible, and that injections of insulin could treat diabetes in humans.

Insulin, like Salvarsan and later the antibiotics, was seen by the public and medical profession alike as a magic bullet in an age of heroic discoveries. Banting shared the 1923 Nobel Prize in Physiology or Medicine with John Macleod, who had provided laboratory space and technical assistance, rather than Best. Within a few years diabetics could enjoy longer lives, but as type 1 diabetes became a chronic disease researchers, patients, and welfare states began to encounter more intractable long-term complications—retinopathy, neuropathy, cardiovascular disease. This new demand for continuing care was reflected in the foundation of the British Diabetic Association in 1934 and the emergence of diabetology as a clinical specialty.

For the first half-century of insulin therapy diabetics used extracts of pig or cow insulin, derived from industrial meat production. Since the early 1980s this has been replaced with synthetic human insulin—although some diabetics found, paradoxically, that the lack of impurities in synthetic insulin made it harder to recognise the signs of an impending crisis. Recent research has focused on the clinical difficulties of distinguishing type 1 and type 2 diabetes, while immunologists have suggested that type 1 is the result of an autoimmune attack on pancreatic β cells. The development of insulin pumps and continuous blood glucose monitors has improved diabetes care in wealthier nations, but worldwide the quality of care is uneven, mapping on to broader inequalities in access to health care. Diabetes may no longer be a death sentence, but for more and more people in the 21st century it will become a life sentence.

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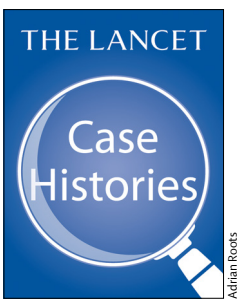

Adrian Roots

For more on **Case histories** see **Comment** *Lancet* 2016; **387:** 211 and **Perspectives** *Lancet* 2017; **390:** 1941

For more on **type 1 diabetes** see http://www.thelancet.com/clinical/diseases/diabetes-type1

Further reading

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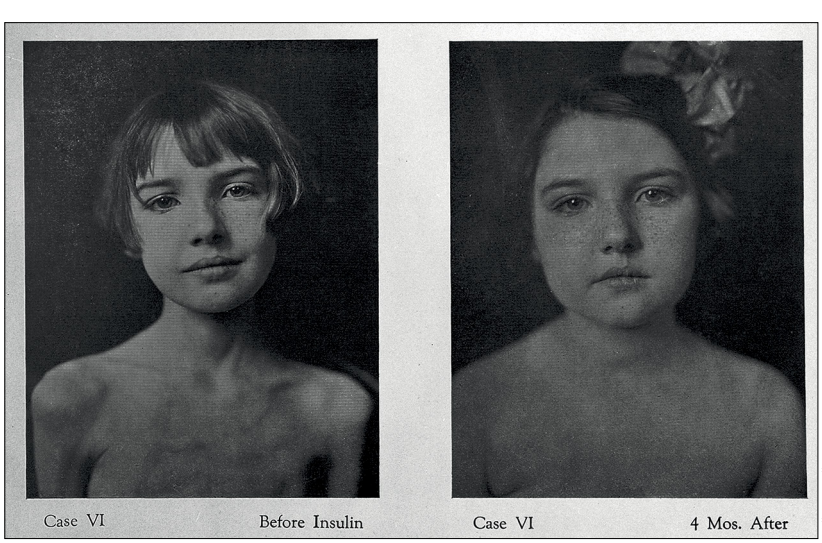

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