Diabesity – a historical perspective: Part II

David Haslam

Part I of this article, published in the previous issue of *Diabesity in Practice*, documented facts and opinions around what has been described as diabesity, tracing its origins back half a million years, and how the way in which diabetes is viewed has changed over time. Here, part II examines European medical perspectives of diabesity and completes the evolutionary journey from the 16th century to the present day. The article looks at the development of our understanding of the pathogenesis of diabetes, the use of the terms diabetes mellitus and diabetes insipidus, and – more recently – metabolic syndrome, and how diet and obesity came to be viewed as associated with type 2 diabetes.

The 16th century Swiss physician known as Paracelsus reported that urine of people with diabetes contained an abnormal substance that remained as a white powder after evaporation. He concluded that this substance was salt and that diabetes was due to the deposition of salt in the kidneys causing thirst and polyuria (Ali et al, 2006). Paracelsus believed that diabetes was a "generalised disorder" involving the blood; however, he also believed in nymphs, gnomes, giants, dwarves, incubi and succubae, so may not have been totally reliable. Up until the 18th century, diabetes was still generally assumed to be a disease of the kidneys; logic suggested that they were at fault for leaking what was then known to be sugar, hence the sweet taste of the urine, although the Portuguese physicians Amatus Lusitanus and Abraham Zacutus believed that excess food was the cause of the condition, Zacutus even suggesting that the stomach was disordered, a view shared by Thomas Sydenham (Savona-Ventura and Mogenson, 2009). The Swiss anatomist Johann von Brunner (1653–1727) came close to identifying the pancreas as the root of diabetes. He was the first to perform experiments on the internal secretions of the pancreas, which he published in 1709 (von Brunner, 1709). In one of the experiments, he removed the pancreas of a dog, noting that on the fourth day "he was thirsty and drank exceedingly from a brook flowing past the town". However, despite the symptoms of polydipsia and polyuria, Brunner didn't associate them with diabetes (Dukan and Milne, 2002). William Cullen was said to be the first, in 1769 (Sanders, 2002), to distinguish diabetes mellitus from diabetes insipidus ("limpid but not sweet urine"), although different commentators vary in their opinions on who first made this distinction. It wasn't until 1788 that diabetes was first linked with the pancreas. Thomas Cawley hypothesised that it may follow pancreatic damage, such as through calculus formation, based on a post-mortem examination of a patient with diabetes (Cawley, 1788). Thomas Willis, famous for discovering and naming the circle of Willis in the brain, recognised the sweet taste of urine in the illness he called "pissing evil". He wrote a chapter on diabetes in *Pharmaceutice rationalis: sive diatriba de medicamentorum operationibus in humano corpore* describing that "the urine is wonderfully sweet, as if it were imbued with honey or sugar," but didn't realise that the urine actually contained sugar: "it seems more hard to demonstrate, why the Piss of such as are sick of this Distemper, is so wonderfully sweet, or should taste like Honey… why it should be so wonderfully sweet, like Sugar or Honey, is a knot not easie to untie" (Dukan and Milne, 2002). Nevertheless he, amongst others, has been credited with coining the term "mellitus" to distinguish the condition from other causes of excess urination such as diabetes insipidus. He had noticed that diabetes was linked with drinking wine and good fellowship, but didn't make an association with weight. He claimed that diabetes was primarily a disease of the blood and not the kidneys, proposing but not proving that the

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Article points

1. Part I of this two-part article examined the origins of diabetes and obesity back to prehistoric times.
2. Part II examines European history of understanding of diabetes and obesity from the 16th century onwards.
3. Important findings in the 1700s included first linking the pancreas with diabetes, and the distinction between diabetes mellitus and diabetes insipidus.
4. The link between diabetes, diet and obesity was noted by physicians in the late 1700s and early 1800s.
5. In 1863, William Banting wrote the first diet book. In 1921, his great nephew Frederick Banting was instrumental in saving the life of a comatose boy by purifying insulin and using it for the first time to treat diabetes successfully in humans.

Key words

- Diabetes
- History
- Obesity

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Page points

1. Thomas Willis claimed that diabetes was primarily a disease of the blood and not the kidneys, proposing that the sweetness first appeared in blood before later being found in urine and was one of many physicians who treated the condition by replacing the sugar lost in the urine with high levels of dietary sugar.
2. In the late 1700s, the physician Matthew Dobson made crucial observations, including assessing the sweetness of the serum as well as urine, describing the serum as . "sweetish, but I thought, not so sweet as the urine" – the discovery of hyperglycaemia.

sweetness first appeared in blood before later being found in urine. He was one of many physicians who treated the condition by replacing the sugar lost in the urine with high levels of dietary sugar. Clearly, given today's knowledge, this approach is deeply flawed, but arguably no more so than the modern eatwell plates and common national dietary guidelines, with their reliance on refined carbohydrate intake as a nutritional foundation. Matthew Dobson is a crucial figure in the evolution of knowledge in diabetes. Born in Yorkshire around 1735, he was appointed physician to the Liverpool Infirmary in 1770 (Williams, 1912). In *Medical Observations and Inquiries* (Dobson, 1776), his paper begins by discussing the views of his predecessors on the nature of diabetes: "Some authors, especially the English, have remarked that the urine in the diabetes is sweet. Others on the contrary, deny the existence of this quality and consequently exclude it from being a characteristic of the disease. So far as my own experience has extended, and I have met nine persons who were afflicted with the diabetes, the urine has always been sweet in a greater or less degree". He discusses the case of Peter Dickonson, admitted to the infirmary in 1772, passing 28 pints of urine in 24 hours. Amongst the crucial observations Dobson made was the fact that after evaporation of the urine, a granulated white cake, indistinguishable from sugar, was produced. Although this had been known centuries earlier in different cultures, this rediscovery was vital to the subsequent evolution of our modern understanding of diabetes. Even more significantly, Dobson also assessed the sweetness of the serum, which was "sweetish, but I thought, not so sweet as the urine" – the discovery of hyperglycaemia. He concluded that "this saccharine matter was not formed in the secretory organ [kidney], but previously existed in the serum of the blood". Just how much of a major discovery this was can be assessed by his statement "if it is a disease of the system in general, if it is to be considered as a species of imperfect digestion and assimilation, the obvious indication of cure are, to strengthen the digestive powers", which started repositioning the understanding of diabetes from being centred on the kidney. In 1790 Cruickshank confirmed the pathological appearance of the kidneys in diabetes: "the arteries of the kidneys are preternaturally enlarged, particularly those of the crypts or minute glands which secrete the urine, and it is infinitely more probable that the fluid of the diabetes arises from some remarkable change in the vessels usually secreting the urine" (Cruickshank, 1790). In 1797, diabetes was correctly identified as a disease not of the kidneys, but of the gastro-intestinal tract. Physician to the Artillery, the Scot John Rollo studied one of his officers, Captain Meredith, a corpulent man with type 2 diabetes, by boiling down his 24-hour urine output to sugar, and assessing the amount of sugar along with the amount of refined carbohydrate starch in his diet, documenting the correlation between dietary starch and glycosuria. Rollo therefore treated Meredith successfully by restricting dietary carbohydrate, becoming the first proponent of low-carbohydrate, high-protein diets in diabetes and obesity. "The cure of the disease is accomplished by regimen and medicines preventing the formation of sugar… an entire abstinence from every species of vegetable matter or a diet solely of animal food, with emetics hepatized ammonia, and narcotics" (Rollo, 1798).

In 1811 the Physician Robert Thomas (Thomas, 1813) noted not just the existence of fat in individuals with diabetes, but also its location: "The fat within the thorax, abdomen, and pelvis, in some instances has seemed entirely converted into a gelatinous-like matter somewhat of an amber colour… The subcutaneous fat is found in general much diminished". However his comments on the other organs shed no light on the pathogenesis of diabetes: "the kidneys… have been found in a loose flabby state, much enlarged in size… The liver, pancreas, spleen and stomach are in general perceived to be in a natural state; when they are not so, the occurrence is to be considered accidental."

Erasmus Darwin believed in drunken diabetes on "idle ingurgitation of too much vinous spirit", and the existence of a separate passage from the intestines to the bladder besides the blood of the sanguiferous system affected by the retrograde motions of the urinary branch of the lymphatic system (Darwin, 1794). William Cullen believed diabetes to be a condition of the nervous system. The argument raged for decades; some physicians believed that the kidneys secreted the white substance "under a peculiar action similar to the breasts of women" (Thomas, 1813).

The Study of Medicine by John Mason Good in 1823 sums up the dilemma as to the pathophysiology in diabetes, which he refers to as Diabetes Anglicus: "The pathology of this disease is still involved in a considerable degree of obscurity: for although

anatomy has pointed out a few morbid changes that exist more or less extensively in the urinary or digestive organs, and chemistry has sufficiently explained to us the morbid character of the discharge, they have thrown less light upon its origin than could be wished for, and have hitherto led to no satisfactory opinion on the subject… Even the seat of the disorder is, to the present hour, a point of controversy." Good goes on to describe diabetes as often "a sequel to a life of intemperance" (Good, 1823).

In 1863, William Banting wrote the first diet book: his letter to the public on corpulence. In 1921, his great nephew Frederick Banting was instrumental in saving the life of a comatose 14-year-old boy, Leonard Thompson, by purifying insulin and using it for the first time to treat diabetes successfully in humans. William Banting's obesity-related comorbidity was deafness, due to a build up of fatty tissue around the airways. Fortunately the specialist he chose – William Harvey – had recently attended a lecture by Claude Bernard in Paris, and was au-fait with theories on low-carbohydrate diets. Harvey wrote: "Knowing too that a saccharine and farinaceous diet is used to fatten certain animals and that in diabetes the whole of the fat of the body rapidly disappears, it occurred to me that excessive obesity might be allied to diabetes as to its cause… and that if a purely animal diet were useful in the latter disease, a combination of animal food with such vegetable diet as contained neither sugar nor starch, might serve to arrest the undue formation of fat" (Harvey, 1872).

Claude Bernard, in 1857, had isolated a starch-like substance – "glycogen" – that was the precursor of glucose, "the internal secretion" of the liver. This observation established the liver's role as a vital organ in diabetes, and led to Harvey's effective treatment of Banting. Bernard also realised that the brain was instrumental in glucose homeostasis (Bernard, 1854), an area which is still confused and uncertain today. So pleased was Banting with the success of Harvey's regime, that he published his book (exactly 150 years ago), basing his advice on the proven low-carbohydrate regime (plus seven units of alcohol per day; Banting, 1864).

The Parisian physician Jean-François Dançel (Dançel, 1864) summed up what is now sometimes called the metabolic syndrome, way ahead of his time, explaining how all the bodily systems coordinate and are interdependent, and insisting on the treatment of obesity as part of the management of chronic disease: "The fashion at the present day is, that a physician should know how to treat the diseases of one particular organ, and rarely of two; that he should be, in fact, a specialist. But are not the principal organs of the body, for the most part, mutually dependent on each other, and all of them subject to a general consensus?… Permanent cure becomes impossible, unless assisted by a reduction of fat."

In 1869, Paul Langerhans discovered the eponymous islets in the pancreas, without knowing their function, and later Oscar Minkowski proved the endocrine function of the pancreas in relation to diabetes, which eventually led to the purification for use in humans of insulin (Langerhans, 1869).

The organic chemist Apollinaire Bouchardat applied John Rollo's low-carbohydrate regime successfully, adding vigorous physical activity to successfully improve glucose control (Chast, 2000). In the late 19th century, Bouchardat and Étienne Lançereaux independently recognised a severe type of diabetes affecting the young – "diabète" – and a separate form affecting more elderly and obese individuals, which Lançereaux termed "diabète gros" (Lancereaux, 1880).

In the early 20th century, obesity levels were rising, accompanied by an increasing incidence of diabetes. Elliott Joslin was the first US doctor to specialise in diabetes, and founder of the Joslin Diabetes Center and *The Joslin Guide to Diabetes*. In 1924, Joslin noted: "Diabetes is 15 times as common among adults and 20 times as common among the fat" (Joslin, 1924). As the prevalence increased, it became clear that diabetes affected different ethnic groups in different ways. Joslin speculated: "The reason that [a Jewish person] has more diabetes is not that he is a Jew, but that he is […] fat. There is a tendency among Jews to obesity." Harold Bowcock noted increased levels of obesity and diabetes in black Americans, observing that many gained employment as domestic workers or food handlers who "may have presented opportunities for overeating, with the subsequent development of obesity" (Bowcock, 1928).

Harold Himsworth, a medical researcher at University College Hospital, chose carbohydrate metabolism as a "hot topic" (Himsworth, 2011) and in 1936 wrote a paper in the *Lancet*, comparing and contrasting the two distinct forms of diabetes by their physiology: "two different types of disease

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can be distinguished as causing the symptom-complex of diabetes mellitus. One, the insulin-sensitive type, appears to be caused by deficiency of insulin; the other, the insulin-insensitive type, is apparently due not to lack of insulin, but to lack of an unknown factor which sensitises the body to insulin" (Himsworth, 1936). Furthermore, in 1939 he elucidated his concept: "On the whole the sensitive diabetics tend to be younger and thin and to have a normal blood pressure and normal arteries, and as a rule their disease is of sudden and severe onset. The insensitive diabetics, on the other hand, tend to be elderly and obese and to have hypertension and arteriosclerosis, and in these patients the onset is insidious" (Himsworth, 1939). Himsworth thus defined the common element in "diabesity" and what Gerald Reaven would describe in 1988 as "Syndrome X", now better known as metabolic syndrome. Now, according to new International Diabetes Federation criteria for the metabolic syndrome, abdominal obesity is the one single characteristic a person must have to qualify for the diagnosis. Other authors such as Kylin, Vague and Avogaro could realistically have taken credit for describing the syndrome. (Vague, 1947; Alberti, 2005). When Reaven was interviewed about Syndrome X (Reaven, 2000), he was clear and lucid about insulin resistance and the physiological sequelae, describing organs such as the kidneys and ovaries as "innocent bystanders" of the hyperinsulinaemic state. However his statements concerning the name of the condition reflect the multitude of arguments and counter arguments which also apply to diabesity: "The term 'metabolic syndrome' is less preferable because many of the manifestations of insulin resistance are not 'metabolic'. For example, insulin resistance and compensatory hyperinsulinemia are associated with an increase in plasminogen activator inhibitor-1, a factor that regulates the process of fibrinolysis. Would you consider this a 'metabolic phenomenon'? The word metabolic tends to take the focus away from the non-metabolic manifestations. Another name, "insulin resistance syndrome", implies we know that the basic defect is muscle and adipose tissue insulin resistance. I believe it is[;] however, others have suggested alternative first causes of the whole cluster of events. What the term 'Syndrome X' does is leave us thinking about the fundamental defect without making any definitive decision. The phrase, 'deadly quartet', implies that obesity is an essential component. That is just not the case. Obesity modifies how insulin resistant an individual is, but there are many very obese individuals who are quite insulin sensitive, who have nothing resembling Syndrome X."

The fact that his "less preferable" term has remained in use, and that he suggested that obesity was not a central aspect of the syndrome, means that today's metabolic syndrome is a long way from Reaven's vision, and is still developing alongside modern science. As Elliot Joslin (Joslin, 1941) said: "There is always something new going on in diabetes." ■

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