



Medicine for Managers

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The History Of Diabetes

Mention the word ‘diabetes’ and for very many people the names of Sir Frederick Banting and Charles Best spring to mind. Nearly a century ago, in 1921, they took the knowledge of diabetes, its cause and its treatment huge steps forward and the modern management of the disease began. However, it had already had a long history in medical writings going back millennia.

There has been an awareness of diabetes for thousands of years. The first known mention occurred in 1552BC when an Egyptian physician identified a mystery disease with frequent urination and loss of weight leading to emaciation, named, rather colourfully, “*the too great emptying of the urine*”.

A century later, physicians in India recognised the same condition and, observing that the urine of sufferers attracted ants, they named it “*honey urine disease*”.

In many cases the deterioration associated with diabetes was quite rapid leading to death and it was untreatable. That may account for why Hippocrates did not write about it.

It was also relatively rare and the Greek physician *Galen*, who lived and worked in Rome in the second century, wrote that he had only seen two cases.

As a junior medical student I learned a hard lesson in the name of diabetes.

The physiology lecturer said that diabetes could be diagnosed by tasting urine.

He took a pot of urine, dipped his finger in it and then tasted it. Ugh! Worse was to follow.

He gave us each a pot and told us to do the same thing, which we dutifully did.

The lecturer then pointed out that this was a lesson in *observation* not diabetes. He demonstrated that he had put his ring finger in the urine but had in fact put his middle finger in his mouth.

We had all dipped our ring fingers in the urine and then put the *same* finger in our mouths. It happened over forty years ago but I remember it well.

The first use of the Greek word meaning diabetes, and translated into “*to pass through*”, was first coined by the Greek physician *Apollonius of Memphis* in 250BC.

Interestingly, over 1,500 years ago, it was identified that there was a difference between *Type 1* (associated with the young) and *Type 2* (associated with the obese and the middle aged or older) diabetes

and their consequences.

In 150AD another Greek physician, **Arateus**, described the disease as “*the melting down of flesh and limbs into urine*”. As the significance of the urinary sweetness and its consequences in terms of the progress of the disease became more apparent, people known as “*water tasters*” diagnosed diabetes by tasting the urine of those suspected of having it.

It was in the early seventeenth century that **Thomas Willis**, the English Physician who discovered the circle of blood vessels in the base of the brain which bears his name, coined the term ‘*mellitus*’, meaning “*from honey*” to distinguish ‘sugar diabetes’ from diabetes insipidus.



This is a condition also associated with passing large volumes of urine and extreme thirst and it is induced by an abnormality of the hormone vasopressin (also known as anti-diuretic hormone) which prevents the kidney retaining water.

During the eighteenth and nineteenth centuries, there was a realisation that the disease, though not curable or effectively treatable, could be managed.

Early treatments consisted of increased exercise, often horse riding, thought to ease the symptoms.

Dietary advice was provided, recommending the fat and meat of animals and avoiding large quantities of sugar. The French physician, **Bouchardat**, observed that, during the Franco-Prussian war of

July 1870 to January 1871, which France lost, diabetic patients’ symptoms improved as a result of the *food rationing*.

He developed individual diets for his diabetic patients. The results included the appearance of fad diets in the early twentieth century including ‘*potato therapy*’ and ‘*oat-cure*’.

In 1910-20, **Joslin**, a scientist in Boston, established himself as a diabetic expert with his book *The Treatment of Diabetes Mellitus* and showed reduced death rates with controlled diets, fasting and exercise, principles still used today to manage lifestyle changes with the disease.

Another milestone in the understanding of the disease was reached when, in 1857, **Claude Bernard** identified the role of the liver in *glycogenesis* (the formation of glycogen from sugar) and *storage* and that diabetes was due to excess glucose production.

Perhaps, some might argue, the greatest milestone in diabetic understanding occurred in Strasbourg in 1889 when researchers **Oskar Minkowski** and **Joseph von Mering** showed that removal of the pancreas in a dog resulted in diabetes.

The German physician, **Georg Zuelzer**, developed the concept when, in 1906, he injected Acomatrol, an extract of pancreas, into a dying comatose diabetic patient. The patient improved but developed side effects and died when the Acomatrol supply ran out.

Modern diabetic care became a reality with **Banting and Best**. Their work was predicated on the research of the

anatomist **Paul Langerhans** who, in 1869, had discovered the eponymous Islets of Langerhans and he had identified key cells which produce a substance which controlled glucose levels.

In 1910 **Sir Edward Sharpey-Shafer** identified the chemical deficient in diabetics and produced in the pancreas. He called it ***insulin*** (from the Latin *insula* meaning an island) in recognition of Langerhans' Islets.

In 1921, Sir Frederick Banting and Charles Best demonstrated that they could reverse diabetes in dogs by giving extract of pancreatic islets harvested from healthy dogs.

They went on with the chemist **James Collip** at the University of Toronto, under the directorship of **John Macleod**, to purify insulin from bovine pancreases and the first diabetic patient, a fourteen-year-old boy, was treated with injections of insulin in 1922.

Its use rapidly developed. The Pharmaceutical company, Eli Lilly, started mass production of insulin in 1923. Banting and Macleod were awarded the **Nobel Prize for Physiology and Medicine** in 1923 although, surprisingly, Best and Collip were not recognised. Banting and Best released their patents without charge and insulin production rapidly spread throughout the world.

As with most diseases and disorders, developments and discoveries have come rapidly since the 1920s.

Oral preparations have been identified to manage Type 2 diabetics.

- Metformin 1922
- Sulphonylurea 1942
- Biguanides 1958

The first long-acting form of insulin was introduced by Novo-Nordisk in 1946

In terms of the development of the knowledge of the disease itself, key milestones included:

- The amino acid sequencing of insulin by Sir Frederick Sanger for which he was awarded the Nobel Prize in 1958.

- The radioimmunoassay of insulin, discovered by Solomon Berson and Rosalyn Yalow. Rosalyn Yalow was awarded the Nobel Prize in Physiology and Medicine in 1977 (since Berson had already died and Nobel Prizes are only awarded to the living)
- The three-dimensional structure of insulin was elucidated in 1972.

Huge research continues apace as the ever increasing number of diabetic patients need to be managed. There may soon be developments in pancreatic implants, the development of new pancreatic tissue,



preventative vaccines and new classes of drugs.

The gradual acquisition of knowledge about diabetes has been happening over three-and-a-half thousand years.

There have been many brilliant observers, physicians and chemists who have driven the work forward.

For me, my vote goes to the poetic physician who described diabetes as “the too great emptying of the urine”.

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