INSULIN, A MORE THAN 100-YEAR JOURNEY OF DISCOVERY. PART 1

Johan Diesveld

Foreword

In 2021 we celebrated the 100th anniversary of the discovery of insulin (Fig 1). It is an important hormone (chemical messenger) in the human body. Produced in the pancreas, it affects the blood glucose levels, and high levels of glycose can be one of the main causes of diabetes.

In the following story, I will say little about the relationship between the hormone insulin and diabetes and what can be done about it. My main focus will be on the search for the molecule insulin and its chemical structure.

Introduction

Diabetes is not a 'modern' disease. The ancient Egyptians described diabetes as early as 3000 BC (Fig 2). The Greek Aretaeus of Cappadocia (130-200) also described diabetes quite accurately (Fig 3).

In the Middle Ages, people relied on all sorts of more or less 'experts' for their health. One of these was uroscopy, the so-called water-gazing. Observations included: quantity, viscosity, colour, odour, transparency, precipitation/flocculation and foaming. There was a clue for some diseases in the bottle of your personal fluid. There was also further ongoing research, uhm ... tasting. As a doctor, you do everything for your patients, but this is going a bit too far for me. Okay, tasting; urine from diabetics tastes sweet. So the water-gazer (Fig 4) pitched his tent in the market place, people queued up and one by one they were given a consultation. In public, no problem!

Taking things to the next step was the Frenchman Claude Bernard (1813-1878) (Fig.5). He was able to show that the pancreas had a decisive influence on digestion. The pancreas produces all kinds of digestive enzymes that are secreted into the duodenum to begin their work of digesting food. These are called exocrine (external) secretions. The pancreas also has endocrine (internal) secretions, including insulin, which is released directly into the blood.

In 1869, the German pathologist Paul Langerhans (1847-1888) (Fig 6) identified separate cells in the pancreas. Of these, beta-cells were found to produce insulin; these cells are known as the islets of Langerhans.

The next step was taken by the German-Lithuanian doctor Oskar Minkowski (1858-1931) (Fig 7) and the German doctor Josef von Mering (1849-1908). They removed the pancreas of a dog in 1889 and the dog promptly developed diabetes.

Discovery of insulin

The turn of the century saw a major advance in diabetes research. During the first years of the First World War, the Romanian N. Paulescu (1869-1931) worked on it. By feeding a diabetic dog an aqueous extract of the pancreas (in which insulin had been dissolved = pancreatin), he was able to observe a beneficial effect on blood sugar levels (Fig 8). He

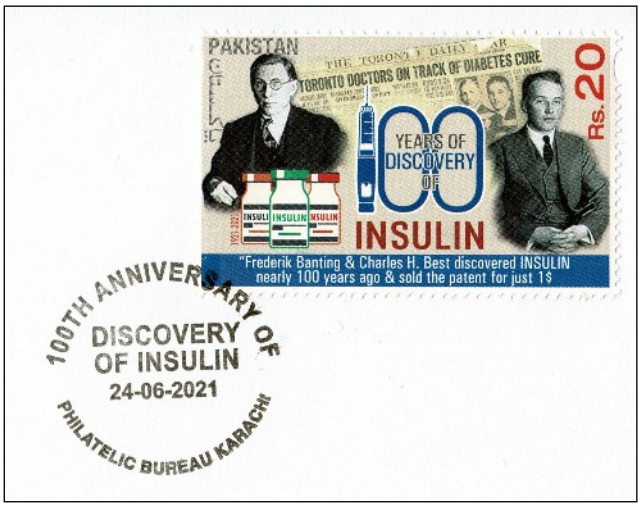

Fig 1:Centenary of discovery of insulin. Pakistan 2021

Fig 2: Ebers Papyrus from around 1550 BC describing insulin. UAR 1971

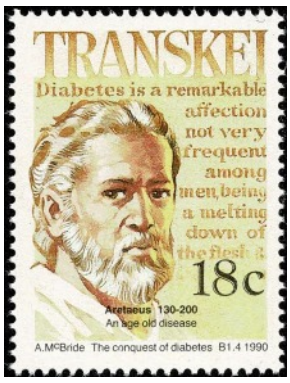

Fig 3: Aretaeus. Transkei 1990

Fig 4: Tasting urine. Urology Conference. Austria 1982.

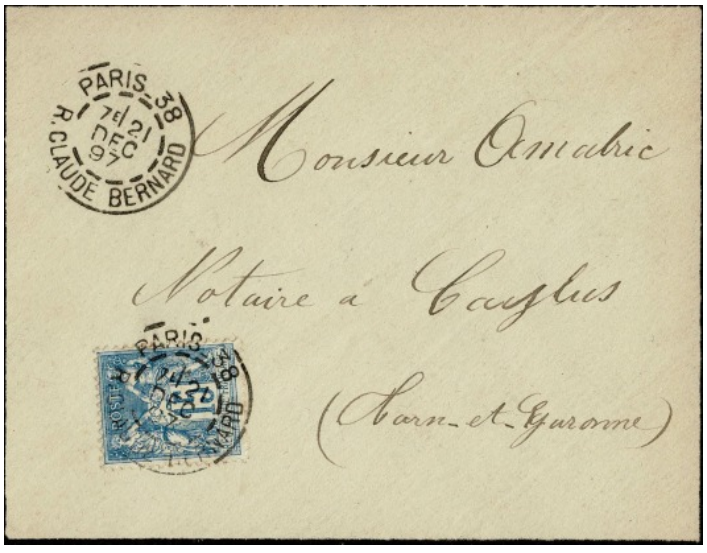

Fig 5: Rue Claude Bernard in Paris is named after the French scientist. Paris 21 Dec 1897.

Fig 6: Paul Langerhans studied the pancreas. West Berlin 1997

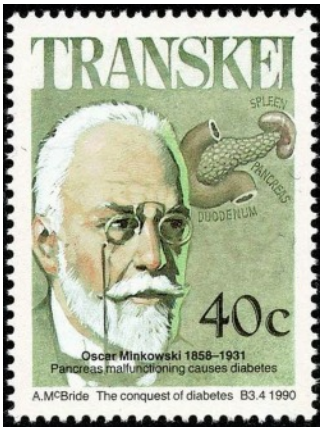

Fig 7: Oscar Minkowski. Transkei 1990

Fig 8: Nicolae Paulescu recalls the research with pancreatin. Romania 1991

Fig 9: Paulescu's discovery of insulin is perhaps not credited enough. Romania 1993

Fig 10: Frederick Banting. Canada 1991

Fig 11: A Croatian postage stamp issued to mark the 75th anniversary of insulin. Mandatory on all letters from 10 to 17 October 1996. A practice well known in the former Yugoslavia, of which Croatia is one of the successor states.

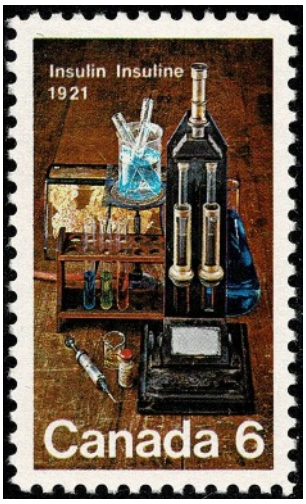

Fig 12: 50th anniversary of the discover of insulin. Canada 1971

Fig 13a: Reverse of a Portuguese postcard, issued on 22 January 2022, to mark the 100th anniversary of the first insulin injection in a human being

Fig 15: 15 Banting, one of the most famous Canadians of the twentieth century. Canada Millennium issue 2000

Fig.13b: Front of the Portuguese postcard, with the special cancellations: um passado de sucesso a criar futuros felizes = a successful past creates happy futures

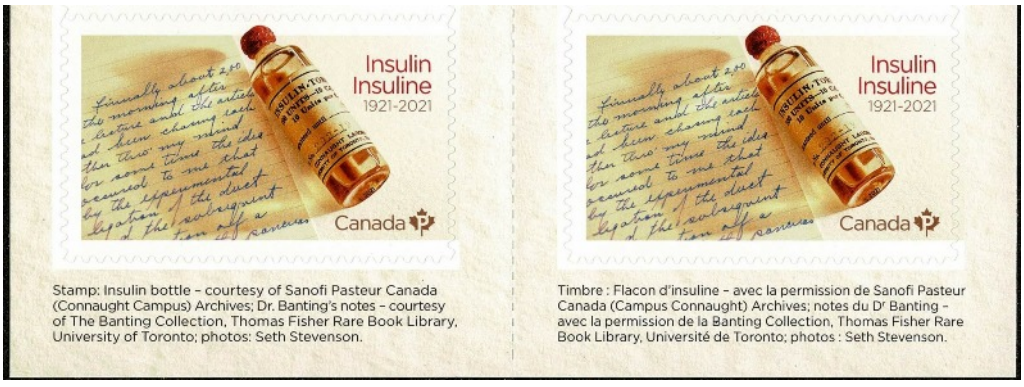

Fig 14: Part of Banting's notes. Canadian stamp booklet 2021

had come this far in 1916 when he was drafted into the army. After the war, he continued his research and published extensively in 1921. His ‘purification’ of the pancreas for insulin was a step in the right direction, but the resulting ‘concoction’ was not easy to use in humans. However, it was shown to have a beneficial effect in humans (Fig 9). He did not receive the recognition he deserved for this work.

The next group of people to venture into research were Canadians. Frederick Banting (1891-1941) (Fig 10) saw the possibilities and asked John Macleod (1876-1935), a laboratory director, for help with space and engineering aids. Experiments with dogs were carried out with his assistant Charles Best (1899-1978) (Fig 11). The pancreas was surgically removed, but the islets of Langerhans remained alive. This showed that purification of an insulin extract was better. Injecting this extract into diabetic dogs gave encouraging results.

In consultation with Macleod, the tests were tightened up. Another collaborator was involved in the research: James Collip (1892-1965). By the end of 1921, they had so much knowledge and expertise that an experiment on a human was deemed responsible (Fig 12). On 11 January 1922, 14-year-old Leonard Thompson, who was dying of diabetes, was treated with an injection of the (impure) insulin extract (Fig 13). Unfortunately, the extract was so impure that Thompson suffered a severe allergic reaction. Collip was able to obtain a completely pure extract from bovine pancreas within two weeks. The effect was very positive and trouble-free (Fig 14); Thompson lived on another thirteen years with regular insulin injections. And the rest, as they say, is history.

Collip had already shown that bovine insulin also worked well in the human body. Later it was shown that pig insulin was also effective in the human body. With today's knowledge, this is not so surprising since the composition of human, bovine and porcine insulin is very similar. Another fortunate coincidence was that bovine and porcine pancreases were widely available from abattoirs. Purification was also greatly improved, making allergic reactions rare.

Such an important result is worthy of a Nobel Prize. Indeed, the Nobel Prize in Physiology or Medicine was awarded in 1923 for the discovery of insulin. The Nobel Prize is awarded to a maximum of three (living) people. Problems were inevitable! It was eventually awarded to Banting (Fig 15) and Macleod (who was never depicted on a Canadian postage stamp; he returned to his native Scotland after some time). This caused some surprise. Banting was so angry that his collaborator Best had not been co-nominated that he shared half his prize money with him. Similarly, Macleod shared his prize money with Collip. There has been much surprise that Romanian Paulsecu was not co-nominated or at least mentioned. This is not the first (and certainly not the last) time that a Nobel Prize has been the subject of controversy. 🕮

To be concluded in December 2024 Themescene

NEDERLANDSE VERENIGING THEMATISCHE FILATELIE

The author is a member of the Nederlandse Vereniging voor Thematische Filatelie (NVTF), the Dutch Association for Thematic Philately, the Dutch equivalent of the British Thematic Association. Details about the Association will be published with part two of this article.