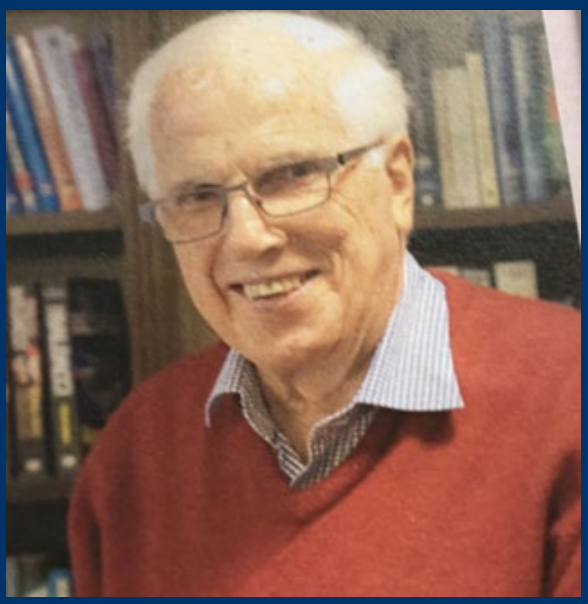
100 YEARS OF INSULIN TREATMENT

We are here to celebrate 100 years of insulin treatment for diabetes. So, what do we have to celebrate?



Dr Bob Smith

Aretaeus of Cappadocia wrote almost exactly 2,000 years ago:

> *Diabetes is a remarkable affliction, not very frequent among men, being a melting down of the flesh and limbs into urine… The course is the common one, namely, the kidneys and bladder, for the patients never stop making water, but the flow is incessant, as if from the opening of aqueducts. The nature of the disease, then, is chronic, and it takes a long period to form, but the patient is short-lived, if the constitution of the disease be completely established; for the melting is rapid, the death speedy.*

It took nearly 1,900 years for Aretaeus' wrong explanation of the cause of diabetes to be corrected. It was during the premiership here in New Zealand of Richard Seddon that a disorder of the pancreas –which makes and secretes insulin into the blood stream – was correctly identified as the cause of diabetes. The pancreas also makes a secretion of enzymes that take part in digestion of food in the intestine. When all that was understood there were attempts in many places to extract the internal secretion, which we now call insulin, from the pancreas of animals. The problem was that digestive juices destroyed the insulin.

Aretaeus of Cappadocia

Dr (later Sir) Frederick Banting, a Canadian surgeon who had been awarded a Military Cross for service as a medical officer in the British army in World War I, came up with the notion of ligating the duct that led the pancreatic digestive juices into the gut. This he hoped would result in destruction of the cells that made the digestive juices, leaving the insulin-secreting cells from which insulin could then be extracted. He sought advice from Professor John Macleod of Toronto University, who was a guru on carbohydrate metabolism. His expectation was that Banting's idea would not work, but as it had not been properly tried before he thought it was worth trying. He provided lab space, dogs and rabbits, and medical student Charles Best to help during university holidays.

Frederick Banting and Charles Best

John Macleod

James Collip

At first things did not go well but eventually they succeeded in producing an extract and were able to demonstrate that it lowered the blood sugar levels of dogs with diabetes. Macleod quickly appreciated the importance of the results and recruited James Collip, a protein chemist from Alberta, to help with insulin extraction.

With Collip's help, they found that it was possible to extract insulin from a pancreas without the need for pre-ligation of the pancreatic duct. By 1922 they were able to try the extraction on a human patient with diabetes. They succeeded at the second attempt on the same boy, Leonard Thompson.

Leonard Thompson

The rest, as they say, is history.

With help from Eli Lilly and Connaught Companies, insulin was produced from the pancreas of animals in abattoirs and made widely available after patenting in the name of the University of Toronto. This was a defensive move, not to stop anyone else making insulin but to stop anyone else from stopping anyone else! And to put this in our local context, all this was going on during the time when William Massey was Prime Minister.

One of the early patients who consulted Dr Banting in Toronto was Elizabeth Hughes, daughter of US Secretary of State Charles E. Hughes. She had been kept alive for two years after the diagnosis of diabetes, but only just, by the extreme starvation regime of Dr Frederick Allen in New York. When she reached Toronto she could barely walk. Insulin rescued her and many like her. She wrote to her parents some weeks later:

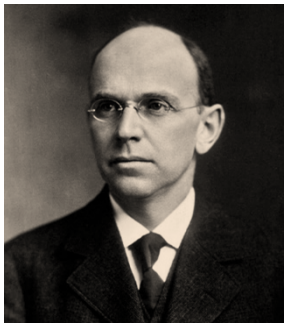
> *To think that I'll be leading a normal, healthy existence is beyond all comprehension. Oh, it is simply too wonderful for words this stuff*.

Elizabeth Hughes

In Boston, diabetes specialist Dr Elliott Joslin obtained insulin and had many near resurrection experiences. He wrote:

> *By Christmas of 1922 I had witnessed so many near resurrections that I realised I was seeing enacted before my eyes Ezekiel's vision in the valley of dry bones.*

Joslin referred to Ezekiel 37:2-10 as "the Banting chapter of the Bible".



Elliot Joslin

Insulin had been discovered, it worked, and it could be produced in commercial quantities. Diabetes research largely packed up and researchers looked for other projects. One of these was the production of long-acting insulin because there was not a lot of fun in having multiple injections each day. The chemists came up with protamine zinc insulin and a series of lente (slow acting) insulins, which meant that many patients could get by with just one injection a day. But there was a heavy price to pay. The chronic complications of diabetes such as kidney, eye and nerve damage, artery disease, and hollows and lumps under the skin had a field day now that people with diabetes lived long enough for these to develop.

I gained my own experience of diabetes in 1962 when, as a house surgeon in Palmerston North, I attended a teenage girl who was admitted in diabetic ketoacidosis on several occasions. I saw the dramatic improvement that resulted from insulin and intravenous fluids and was so intrigued that I analysed the records of more than 200 of diabetic patient admissions. I presented my report to a meeting of physicians which included Dr Graham Joplin, a New Zealander visiting from Hammersmith Hospital in London.

Following my time in Wellington as a medical registrar and research fellow, and a year in Canberra, I spent two years as a physician in the Solomon Islands. Diabetes was not common there but one young man stays in my memory. He had type 1 diabetes which we could only manage by having him attend the hospital twice daily for insulin injections. To make this convenient we arranged accommodation and a job for him at the hospital. Then one day he failed to appear. He had been seen on the wharf that morning from where a ship had departed for the island that was his home, thirty hours sailing time away. There was nothing we could do. We never saw him again.

Back in Wellington I joined Dr Verney Cable's diabetes clinic. I was helped greatly in my pursuit of diabetes experience by a six-week visit to Melbourne and by a subsequent year as a Commonwealth Medical Fellow at King's College Hospital in London with Drs David Pyke and Peter Watkins. Highlights for me were coming right up to date with the management of diabetic ketoacidosis, diabetic retinopathy, pregnancy in women with diabetes, diabetic foot problems, diabetic neuropathy, education for patients with diabetes and psychological support.

No longer was ketoacidosis treated with huge doses of subcutaneous insulin but rather with low dose insulin infusions. No longer was retinopathy effectively untreatable but eye doctors could use lasers. No longer did diabetic mothers have a higher rate of miscarriages or stillbirths than others. No longer did foot ulcers lead to early amputation. No longer did nerve damage have no real answers. No longer did patients have to be admitted to hospital to learn how to manage injections. I was at the forefront of introducing some of these advances to New Zealand. A huge benefit was the role of the Diabetes Nurse Educator which I copied from St Thomas' Hospital in London; it was Margaret Llewelyn who made such a success of that role in Wellington.

Back in Wellington I applied all I had gained from my UK stay and visits to Munich, Boston, and Minneapolis. I was able to get the agreement of colleagues, particularly Drs Jack Kilpatrick in Dunedin, Don Beaven in Christchurch and Malcolm Watson in Wellington, to set up the NZ Society for the Study of Diabetes which was modelled on a combination of the Medical and Scientific section and the Professional Services section of the British Diabetes Association. We were closely associated with the lay organisation that is now called Diabetes New Zealand. Importantly, we were able to encourage each other, especially by presentations and discussion at our annual scientific meetings.

I remember Dr Jeanette Crossley's presentation at our first annual scientific meeting, comparing the effect of drinking apple juice, eating apple purée or eating a whole apple; the last of these provided the slower rise in blood sugar levels – an advantage for people with diabetes. A further advance was the improvement in purity of insulin, so-called mono-component, which brought an end to disfiguring hollows at injection sites. Around this time, we were hearing of good results from the Diabetes and Complications Trial in North America. Here was the first convincing evidence that good control of blood glucose levels really did matter. The introduction of fine needle syringes made injections a lot less unpleasant and the availability of blood glucose testing at home revolutionised the ability to balance insulin dosage with exercise and food intake. Various iterations of syringes were made and then came insulin pumps, which Dr Peter Dunn had worked on in Boston and back in Hamilton.

I remember well a teenage boy at a diabetic children's camp in Auckland for which I was the camp doctor. He came to us from hospital where he had had his umpteenth admission for ketoacidosis. I had a medical student assisting me and I tasked him to observe closely the blood sugar testing and insulin administration for this lad. All went well for a few days but craftily he conned the student and gave himself no insulin for the last day and a half. He became ketotic of course so we had to send him back to hospital. I was glad to learn that he was referred to Dr David Scott, a very patient-centred diabetes physician. The lad had an unhappy time at home from which he sought escape by omitting to take his injections (which was the reason behind the so-called brittleness of his diabetes). David introduced him to a more positive way of living, which included using an insulin pump.

If I had ever been in doubt about pumps, it was absolutely dispelled when I met a Miss America touring New Zealand. She had an insulin pump for her type 1 diabetes and said that without it she could never have kept up her frenetic travel itinerary.

I hope that I have adequately answered the question as to why we should be celebrating the discovery and use of insulin. Where to from here? Could we accurately predict who is likely to get diabetes? Could we detect diabetes very early, before the destruction of insulin-producing cells has advanced to clinically significant damage, and arrest the process? We might continue to seek better biological or mechanical means of replacing insulin secretion. Then there are the problems of reaching patients in remote areas, now being assisted by teleheath and zoom meetings. This means supporting research, service delivery and patient education by adequate funding for health in general, and adequate sharing of funds for diabetes in particular.

Where to from here, I will leave to you. Two organizations exist that are well able to provide advice: Diabetes New Zealand (DNZ), principally serving types 1,2 and 3, and the New Zealand Society for the Study of Diabetes (NZSSD), principally involving type 4 (all health professionals assisting people with diabetes) with the goal of serving types 1 and 2 and 3. I include type 3 particularly because this group who live with and support their child or spouse are little recognised but they are the life-blood of diabetes management for so many. I recognise and applaud you mightily.

RBW Smith

August 2022

Dr Bob Smith compiled this document as a contribution to **Transforming Lives: 100 years of insulin**, a symposium held in Wellington on 24 November 2022. <https://www.otago.ac.nz/diabetes/news/otago0231654.html>