Fifty Years of Insulin

Emaciation, weakness, coma and death. The victims were children. The outcome was always the same. Only deliberate starvation could slow the lethal course of the disease.

This is a picture of juvenile diabetes in 1921. In that year, an obscure Canadian physician, Frederick Banting, made medical history when he discovered the hormone insulin and later provided its ability to control diabetes. Insulin, of course, has since saved millions of lives throughout the world. The year 1971 is the 50th anniversary of Banting's historic discovery.

The story of insulin actually began on the night of 30 October 1920. Young Dr Banting, then a demonstrator in physiology at the University of Western Ontario, arose at two in the morning to jot down procedures for an experiment that would eventually reveal the life-saving hormone. Banting's idea was to tie off a dog's pancreas ducts, wait until the pancreas degenerated, and then remove the organ and try to extract an elusive pancreas secretion thought to regulate the body's use of sugar and other carbohydrates. He would then inject the extract into a second dog who had diabetes. On 30 July 1921 Banting performed the experiment that confirmed the existence of insulin. He removed the pancreas of the dog Marjorie and then kept her alive and active for 76 days with injections of an extract made from the pancreas glands of other animals. He finally sacrificed her on 14 October to check for possible internal damage from the extract. He found no evidence of injury.

An impaired ability to utilize carbohydrates is, of course, the basic problem in the disease. Juvenile diabetics, especially, have a severe impairment.

Because of limited laboratory facilities at Western Ontario, Banting eventually performed his dog experiments at the University of Toronto. He was assisted throughout the work by Charles Best, a Toronto graduate-student rated by Banting as the co-discoverer of insulin. The two men began their experiments in May 1921, and had produced a crude pancreas extract by late July. On 30 July Banting injected the extract into a dog whose pancreas had been removed and who, therefore, was severely diabetic. The animal gradually became more alert and within two hours her blood sugar had dropped by 50%. This seemed to confirm the existence of a pancreas secretion that regulated sugar metabolism. Of even greater importance —it also suggested possible control of human diabetes through periodic injections of pancreas extract.

Fig. 1. Frederick Banting (right), Charles Best, and Marjorie, the dog used in the experiment of 30 July 1922.

Banting soon found that extracts made from cattle pancreas glands worked equally well. After further tests with dogs, the first human diabetics received the cattle extract in January and February 1922. Their response quickly confirmed the importance of Banting's discovery.

The success with humans triggered a massive effort by University of Toronto scientists to isolate the active principle in Banting's extract. Their immediate goal was a less toxic and more potent product. Large-scale production was also necessary to expand the human tests and eventually, to meet the needs of diabetics throughout the world. The university scientists developed a purer, and therefore less toxic, extract but could not produce the new 'insulin' in large quantities.

Before the first test with humans, Eli Lilly and Company, then a small US pharmaceutical firm, had offered Dr Banting its full assistance in developing large-scale production techniques for insulin. This offer was accepted by the University of Toronto in May 1922, and thereafter the two institutions worked jointly on the problems of purification and mass production. Lilly scientists finally broke the production impasse in November 1922 with the development of iso-electric precipitation procedures for insulin. The new technique greatly increased manufacturing yields and also improved the purity, potency and stability of the product.

In January 1923, the University of Toronto's Connaught Laboratories joined

Fig. 2. Grinding of animal pancreas glands in 1923—the first step in insulin production.

Lilly in the large-scale production of insulin; and, by May, the two groups were supplying a massive human study involving 10 000 diabetics. Lilly received Toronto's approval to market insulin in October 1923, after a clinical evaluation more extensive than that for any previous medicine.

Mass distribution of insulin was a unique event in the history of medicine. For juvenile diabetics, it was an immediate reprieve from death. To those who had developed the disease in middle life, insulin meant relief from distressing symptoms and possible avoidance of premature physical deterioration. Severe diabetics, however, often required as many as five injections of the original product each day. Scientists therefore sought chemical modifications that would delay absorption and thus give adequate control with fewer injections. They eventually so improved the absorption characteristics of insulin that today 85% of all diabetics require only one daily injection.

Price reduction went hand-in-hand with product improvement. Eli Lilly and Company, the world's leading manufacturer of insulin, today charges only one-twentieth of its 1923 price for a much-improved product. During this same period, general consumer prices have doubled in most countries. Approximately 10 000 pounds of animal pancreas glands are still required to produce one pound of insulin crystals. Yet insulin costs for the average diabetic are now less than 7 cents a day.

Frederick Banting won the 1923 Nobel Prize in medicine for his discovery of insulin. The details of Banting's life and work are now largely forgotten, yet the human impact of his discovery remains unchanged after half a century. Today literally millions of people—farmers, scientists, housewives, businessmen, children—owe their health or their continued existence to insulin.