

Frederick Banting, Charles Best, John Macleod and James Collip, who worked in the Department of Physiology at the University of Toronto, Canada, discover insulin by purifying pancreas extract from dogs and cows and injecting it into dogs with no pancreas to observe the impact on glucose levels.

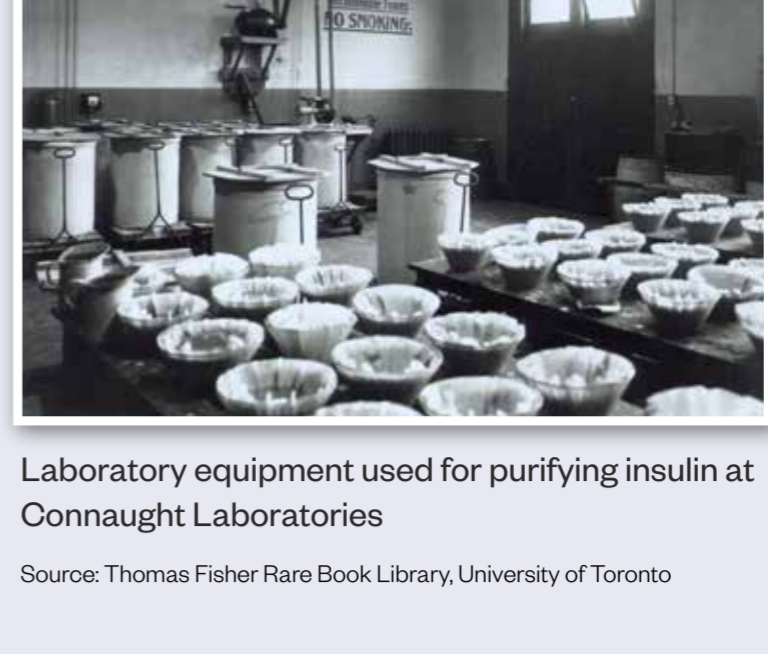
1921



Frederick Banting and Charles Best, with a dog, on the roof of the medical building, University of Toronto
Source: Thomas Fisher Rare Book Library, University of Toronto

The extract is administered to Leonard Thompson, a 14-year-old boy with diabetes at Toronto General Hospital but it produces only modest effects and the injection site abscess; Collip purifies the extract further and a second dose results in a sharp drop in blood glucose.

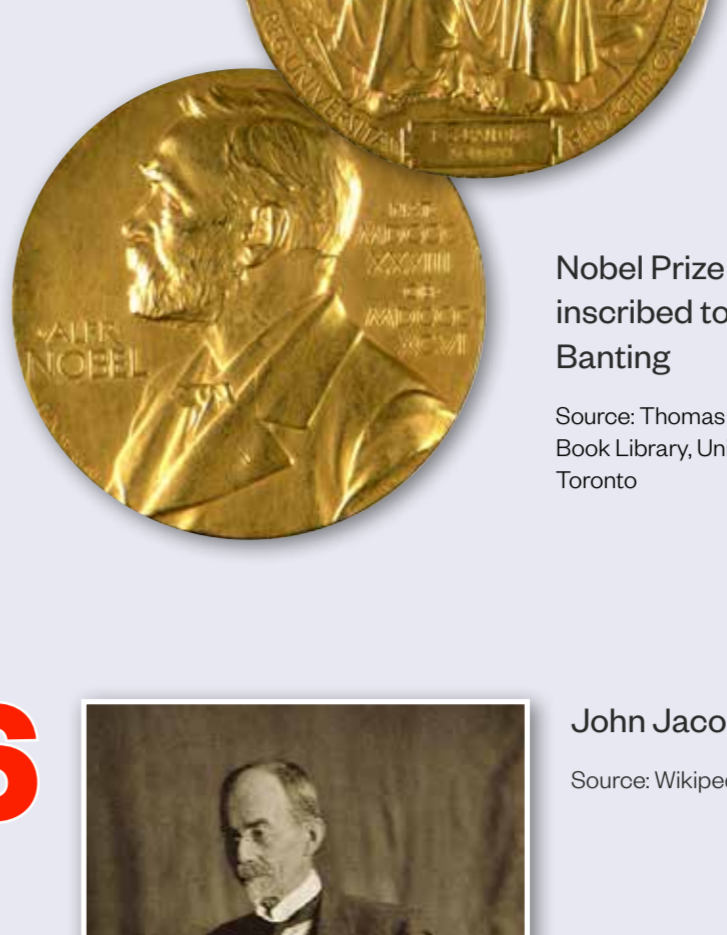
1922



Laboratory equipment used for purifying insulin at Connaught Laboratories
Source: Thomas Fisher Rare Book Library, University of Toronto

Non-profit Nordisk Insulin Laboratory, Denmark, starts insulin production. Banting, Best and Collip are awarded the Canadian and American patents for insulin, which they sell to the University of Toronto for US\$1 each; Banting and Macleod receive the Nobel Prize in Physiology or Medicine.

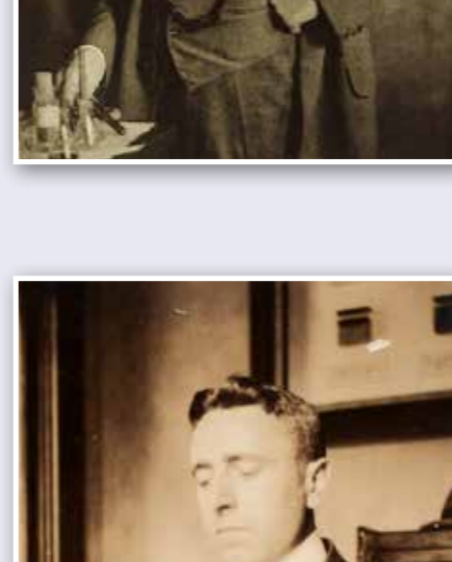
1923



Nobel Prize medal inscribed to FG Banting
Source: Thomas Fisher Rare Book Library, University of Toronto

John Jacob Abel, based at Johns Hopkins University in Baltimore, Maryland, United States, crystallises insulin for the first time, a major step in obtaining a pure insulin preparation.

1926



John Jacob Abel
Source: Wikipedia.com

Longer acting forms of insulin that last 24–36 hours (compared with 4–12 hours for short-acting insulin) are developed by Hans Christian Hagedorn and colleagues in Denmark, and separately by David Scott and Albert Fisher in Toronto, by adding protamine and zinc to stabilise the molecule.

1936



David Scott
Source: Thomas Fisher Rare Book Library, University of Toronto

Hagedorn develops an intermediate-acting insulin, neutral protamine Hagedorn (NPH) insulin, which lasts 18–24 hours and can be mixed with shorter-acting insulins.

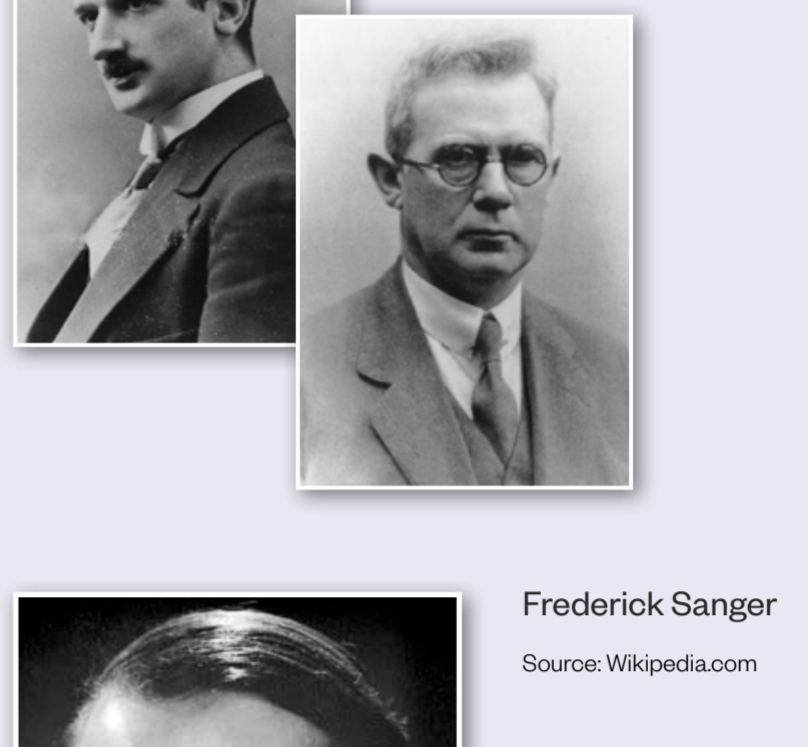
1946



Hans Christian Hagedorn
Source: Novo Nordisk

Thorvald and Harald Pedersen at Nordisk Insulin Laboratory develop semilente, lente and ultralente — long-acting protamine-free insulins that could be mixed to allow individualised regimens. The brothers later leave Nordisk and set up pharmaceutical company Novo (to become Novo Nordisk in 1989).

1951



Thorvald Pedersen (left) and Harald Pedersen (below)
Source: Novo Nordisk

British biochemist Frederick Sanger sequences insulin, the first protein to be fully sequenced, securing him the Nobel Prize in Chemistry in 1958 and paving the way for insulin to become the first human protein to be chemically synthesised in the laboratory in 1963.

1955



Frederick Sanger
Source: Wikipedia.com

Novo launches a highly purified form of insulin called monocomponent insulin to reduce insulin resistance. All insulins are standardised to a concentration of 100 units/mL.

1973



Original Novo logo

The first genetically engineered, synthetic insulin is produced by biotechnology company Genentech, with Dennis Kleid and his team using a genetically manipulated plasmid of Escherichia coli bacteria. Synthetic insulin will resolve problems with insulin resistance, allergies and lipotrophy and enable unlimited production.

1978



Dennis Kleid and a colleague in the molecular biology laboratory at Genentech
Source: Genentech Archives

Synthetic insulin is renamed 'human insulin' and Eli Lilly's Humulin R and Humulin N are the first to be approved in the UK.

1982



Source: © Copyright Eli Lilly and Company. All Rights Reserved. Photo courtesy of Eli Lilly and Company Archives

MiniMed (now Medtronic) brings the first commercial insulin pump to market, the MiniMed 502.

1983



Source: Medtronic

Novo launches the first insulin pen delivery system — NovoPen — eliminating the need for vials and syringes.

1985



Source: National Museum of American History, Smithsonian Institution

MiniMed (now Medtronic) releases the MiniMed 506 insulin pump, which delivers meal bolus memory and daily insulin totals.

1992



Source: Medtronic

The first rapid-acting insulin analogue — Eli Lilly's insulin lispro (Humalog) — is launched in the UK. Insulin analogues are modified to ensure more predictable absorption, making it easier to plan around mealtimes and avoid hypoglycaemia.

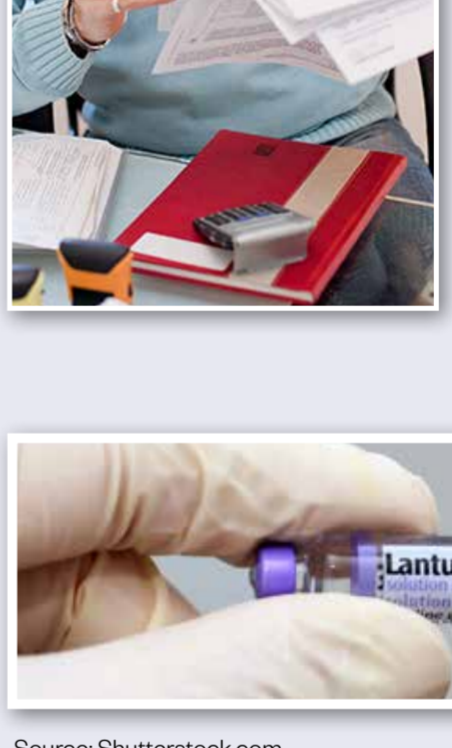
1996



Source: © Copyright Eli Lilly and Company. All Rights Reserved. Photo courtesy of Eli Lilly and Company Archives

The first continuous glucose monitoring (CGM) device is approved by the US Food and Drug Administration (FDA). The device records glucose values over three days, after which trend data are downloaded by a healthcare professional for analysis.

1999



The launch of CGM devices allows clinicians to review trend data for blood glucose values
Source: Burger / Phan / Science Photo Library

The first long-acting basal insulin analogue — Aventis's (now Sanofi) insulin glargine (Lantus) — is approved in Europe.

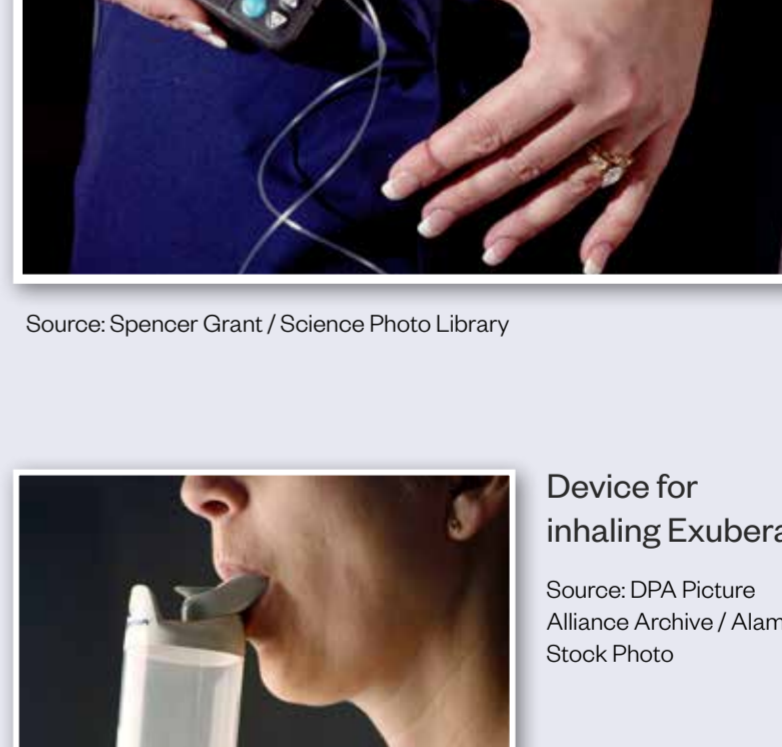
2000



Source: Shutterstock.com

Insulin pumps become available on the NHS.

2003



Source: Spencer Grant / Science Photo Library

Inhaled insulin Exubera is launched in the UK by Pfizer but rapidly withdrawn owing to poor market uptake.

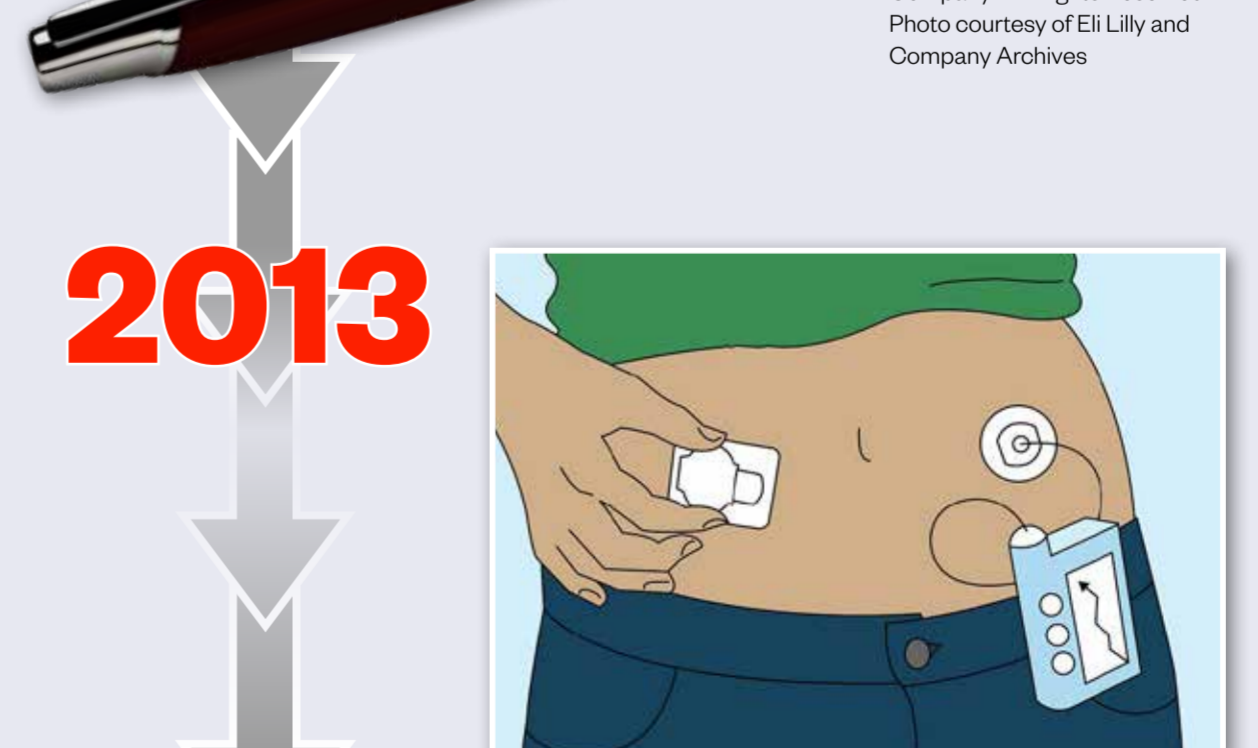
2006



Device for inhaling Exubera
Source: CIPA Picture Alliance Archive / Alamy Stock Photo

Eli Lilly launches the first multiple-dose electronic insulin pen — HumaPen Memoir — in Europe.

2007



Source: © Copyright Eli Lilly and Company. All Rights Reserved. Photo courtesy of Eli Lilly and Company Archives

Novo Nordisk's ultra long-acting insulin analogo insulin degludec (Tresiba) is approved and is the first insulin available in the UK at a higher concentration than the standard U100. A team at the University of Cambridge develops an artificial pancreas that pairs an insulin pump with a continuous glucose monitor.

2013



Sensor/delivery system for artificial pancreas
Source: US Food and Drug Administration

Abasaglar (insulin glargine; Eli Lilly and Boehringer Ingelheim), the first insulin biosimilar, is launched in the UK.

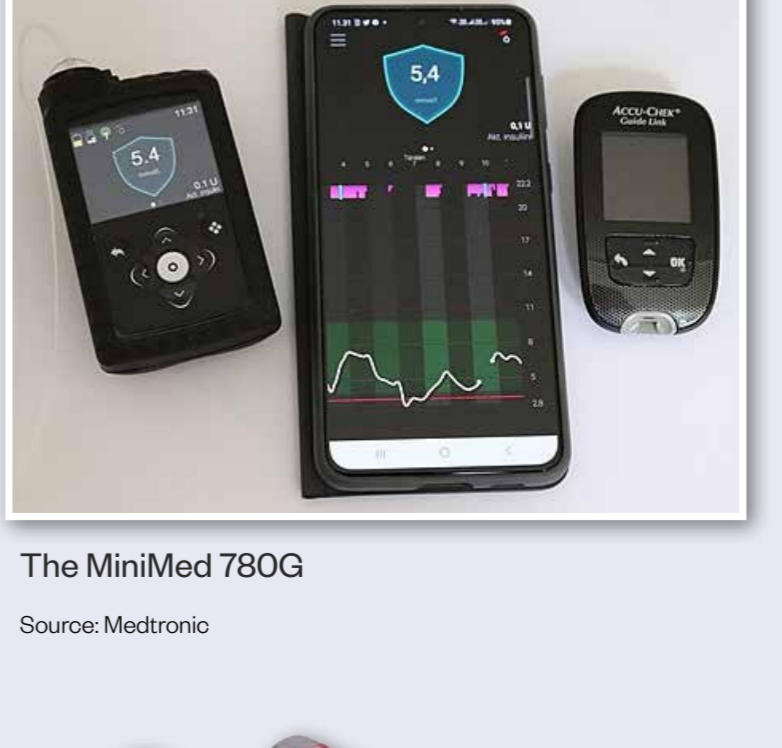
2015



Source: © Copyright Eli Lilly and Company. All Rights Reserved. Photo courtesy of Eli Lilly and Company Archives

Flash glucose monitors (Freestyle Libre; Abbott) become widely available on the NHS for patients with type 1 diabetes mellitus. Beta Bionics's iLet — a bionic pancreas that autonomously controls blood glucose through administration of insulin and glucagon — is given breakthrough device designation by the FDA. Medtronic's MiniMed 670G System becomes the first hybrid closed loop system (artificial pancreas) to be launched in the UK.

2019



The Freestyle Libre glucose monitor
D P Marazzi / Science Photo Library

Medtronic launches MiniMed 780G in Europe, a next generation closed loop system that automates delivery of basal insulin and correction boluses every five minutes. Trial results for an investigational once-weekly insulin — Novo Nordisk's loodec — suggest it is safe and effective.

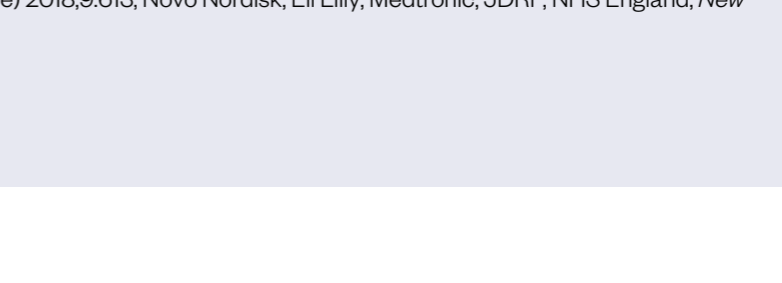
2020



The MiniMed 780G
Source: Medtronic

The NHS announces £2m for a pilot roll-out of an artificial pancreas system. A pilot of Novo Nordisk's 'smart' connected insulin pens, which automatically record the time and dose, also starts.

2021



NovoPen 6 and NovoPen Echo Plus
Source: Novo Nordisk

Editorial advisers: Philip Newland-Jones, consultant pharmacist for diabetes and endocrinology and clinical director of the diabetes and endocrine service at University Hospital Southampton NHS Foundation Trust; Hamzah Syed, pan East Sussex diabetes lead pharmacist, East Sussex Healthcare NHS Trust.
Sources: Diabetes.co.uk; Endocrine Reviews 2021;42:503; Nature Medicine 2021;27:1154; Frontiers in Endocrinology (Lausanne) 2018;9:613; Novo Nordisk; Eli Lilly; Medtronic; JDRF; NHS England; New England Journal of Medicine 2020;383:2107.