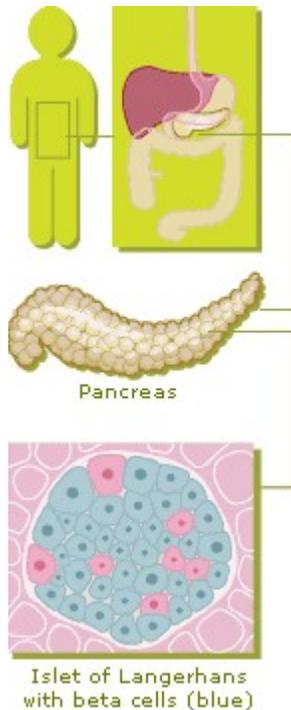


The Discovery of Insulin

(Taken From Nobelprize.org Web Site)

Before the discovery of insulin, diabetes was a feared disease that most certainly led to death. Doctors knew that sugar worsened the condition of diabetic patients and that the most effective treatment was to put the patients on very strict diets where sugar intake was kept to a minimum. At best, this treatment could buy patients a few extra years, but it never saved them. In some cases, the harsh diets even caused patients to die of starvation.



During the nineteenth century, observations of patients who died of diabetes often showed that the pancreas was damaged. In 1869, a German medical student, Paul Langerhans, found that within the pancreatic tissue that produces digestive juices there were clusters of cells whose function was unknown. Some of these cells were eventually shown to be the insulin-producing beta cells. Later, in honor of the person who discovered them, the cell clusters were named the islets of Langerhans.

In 1889 in Germany, physiologist Oskar Minkowski and physician Joseph von Mering, showed that if the pancreas was removed from a dog, the animal got diabetes. But if the duct through which the pancreatic juices flow to the intestine was ligated - surgically tied off so the juices couldn't reach the intestine - the dog developed minor digestive problems but no diabetes. So it seemed that the pancreas must have at least two functions:

- To produce digestive juices
- To produce a substance that regulates the sugar glucose

This hypothetical internal secretion was the key. If a substance could actually be isolated, the mystery of diabetes would be solved. Progress, however, was slow.

Banting's Idea

In October 1920 in Toronto, Canada, Dr. Frederick Banting, an unknown surgeon with a bachelor's degree in medicine, had the idea that the pancreatic digestive juices could be harmful to the secretion of the pancreas produced by the islets of Langerhans.

He therefore wanted to ligate the pancreatic ducts in order to stop the flow of nourishment to the pancreas. This would cause the pancreas to degenerate, making it shrink and lose its ability to secrete the digestive juices. The cells thought to produce an antidiabetic secretion could then be extracted from the pancreas without being harmed.

Early in 1921, Banting took his idea to Professor John Macleod at the University of Toronto, who was a leading figure in the study of diabetes in Canada. Macleod didn't think much of Banting's theories. Despite this, Banting managed to convince him that his idea was worth trying. Macleod gave Banting a laboratory with a minimum of equipment and ten dogs. Banting also got an assistant, a medical student by the name of Charles Best. The experiment was set to start in the summer of 1921.



Banting, right, and Best, left, with one of the diabetic dogs used in experiments with insulin.

Credits: University of Toronto Archives

The Experiment Begins

Banting and Best began their experiments by removing the pancreas from a dog. This resulted in the following:

- It's blood sugar rose.
- It became thirsty, drank lots of water, and urinated more often.
- It became weaker and weaker.

The dog had developed diabetes.

Experimenting on another dog, Banting and Best surgically ligated the pancreas, stopping the flow of nourishment, so that the pancreas degenerated.

After a while, they removed the pancreas, sliced it up, and froze the pieces in a mixture of water and salts. When the pieces were half frozen, they were ground up and filtered. The isolated substance was named "isletin."

The extract was injected into the diabetic dog. Its blood glucose level dropped, and it seemed healthier and stronger. By giving the diabetic dog a few injections a day, Banting and Best could keep it healthy and free of symptoms.

Banting and Best showed their result to Macleod, who was impressed, but he wanted more tests to prove that their pancreatic extract really worked.



Banting's and Best's laboratory, where insulin was discovered.
Credits: University of Toronto Archives

Extended Tests

For the increased testing, Banting and Best realized that they required a larger supply of organs than their dogs could provide, and they started using pancreases from cattle. With this new source, they managed to produce enough extract to keep several diabetic dogs alive.



The new results convinced Macleod that they were onto something big. He gave them more funds and moved them to a better laboratory with proper working conditions. He also suggested they should call their extract "insulin." Now, the work proceeded rapidly.

In late 1921, a third person, biochemist Bertram Collip, joined the team. Collip was given the task of trying to purify the insulin so that it would be clean enough for testing on humans.

During the intensified testing, the team also realized that the process of shrinking the pancreases had been unnecessary. Using whole fresh pancreases from adult animals worked just as well.

Testing on Humans

The team was eager to start testing on humans. But on whom should they test? Banting and Best began by injecting themselves with the extract. They felt weak and dizzy, but they were not harmed.

Collip continued his work to purify the insulin. He also experimented with trying to find the correct dosage. He learned how to diminish the effect of an insulin overdose with glucose in different forms. He discovered that the glucose should be as pure as possible. Orange juice and honey are good examples of foods rich in glucose.



In January 1922 in Toronto, Canada, a 14-year-old boy, Leonard Thompson, was chosen as the first person with diabetes to receive insulin. The test was a success. Leonard, who before the insulin shots was near death, rapidly regained his strength and appetite. The team now expanded their testing to other volunteer diabetics, who reacted just as positively as Leonard to the insulin extract.

The Nobel Prize

The news of the successful treatment of diabetes with insulin rapidly spread outside of Toronto, and in 1923 the Nobel Committee decided to award Banting and Macleod the Nobel Prize in Physiology or Medicine.

The decision of the Nobel Committee made Banting furious. He felt that the prize should have been shared between him and Best, and not between him and Macleod. To give credit to Best, Banting decided to share his cash award with him. Macleod, in turn, shared his cash award with Collip.

The Nobel Prize in Physiology or Medicine for insulin has been much debated. It has been questioned why Macleod received the prize instead of Best and Collip. However, Macleod played a central role in the discovery of insulin. It was he who supported the project from the beginning. He supervised the work and it is also most likely that Macleod's contacts in the scientific world helped the team in getting a speedy recognition of their discovery.



Frederick G. Banting and John Macleod were awarded the Nobel Prize in Physiology or Medicine in 1923 "for the discovery of insulin."

The Legacy of Insulin

Banting, Macleod, and the rest of the team patented their insulin extract but gave away all their rights to the University of Toronto, which would later use the income from insulin to fund new research.

Very soon after the discovery of insulin, the medical firm Eli Lilly started large-scale production of the extract. As soon as 1923, the firm was producing enough insulin to supply the entire North American continent.

Although insulin doesn't cure diabetes, it's one of the biggest discoveries in medicine. When it came, it was like a miracle. People with severe diabetes and only days left to live were saved. And as long as

they kept getting their insulin, they could live an almost normal life.

First published February 2009