



The Discovery of Insulin: **What is the Definitive History?**

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Emirates Diabetes Society, Insulin 100th Webinar

World Diabetes Day

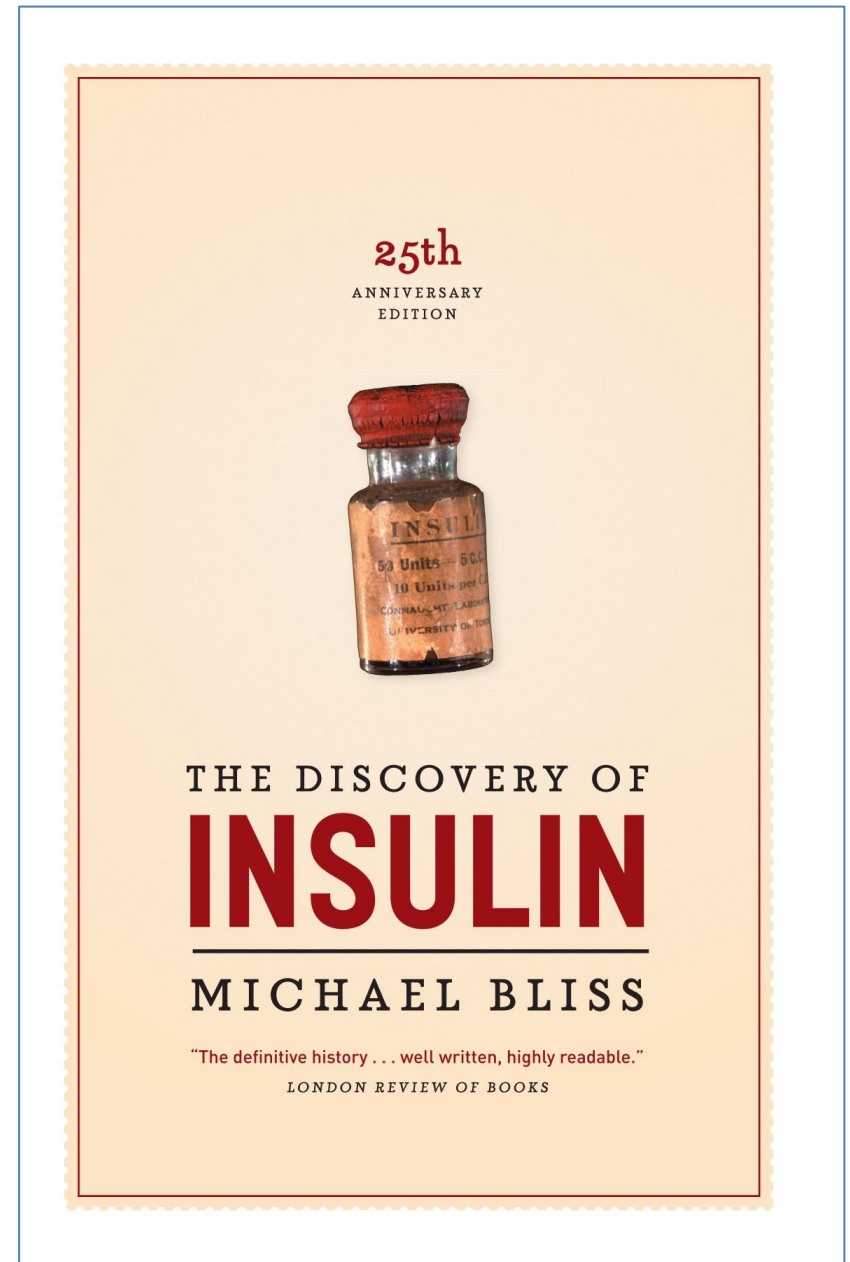
November 14, 2020



Introduction

- I was asked to give a presentation about the discovery of insulin and answer the question:

What is the definitive history?
- The short answer is quite easy
- Michael Bliss' book, *The Discovery of Insulin*, first published in 1982, certainly remains the definitive history
- Although the late Professor Bliss was my Ph.D. supervisor, colleague, friend, and at times my unofficial agent, I'm aware of no other histories that challenge its authority
- What I would like to do is recount key parts of the discovery story and highlight the many unique challenges of transitioning from the discovery of insulin to its development and production in order to expedite its equitable accessibility to diabetics globally



Introduction

- My Ph.D. with Prof. Bliss was about the history of polio in Canada, not insulin
- Since 1996 - Insulin 75th – I've conducted my own insulin historical research and curated several exhibits, such as “Insulin: Toronto’s Gift to the World” for the University of Toronto Faculty of Medicine to mark the Insulin 90th



Introduction

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Introduction



<https://definingmomentscanada.ca/insulin100/>



Insulin100: Inspiration and Innovation will share the story of the uniquely Canadian and collaborative life-saving discovery and development of insulin, follow the life of Dr. Frederick Banting as an example of a ground-breaking scientist, and encourage further exploration into Canada's rich and diverse history of scientific and medical innovations.

Defining Moments Canada brings the story of insulin into your classroom through historical content and lessons to support educators and students. ***Insulin100: Inspiration and Innovation shares the story of the life-saving discovery of insulin and follows the life of Dr. Frederick Banting in an engaging story map.*** We have developed **new lesson plans**, historical articles, and microhistories – easily adapted for both physical and digital classrooms – with multiple cross-disciplinary entry points. *Insulin100* will showcase stories demonstrating the impact that diabetes has had on Canadian communities over the last 100 years.

Dr. Chris Rutty has prepared a series of historical articles which tell the story of discovery and development in great detail. **[Start your exploration here.](#)**

— INSULIN100

SIR FREDERICK BANTING

TEACHING ABOUT
INSULIN100

INSULIN100: THE DISCOVERY
AND DEVELOPMENT

MICROHISTORIES

- I'm currently working as "Lead Historian" for the Defining Moments Canada "Insulin 100" national digital commemoration project
- My work has recently been focused on preparing a series of 14 articles that provide the core historical content for the site's online exhibition
- Currently, the first 8 of the 14 articles are posted

Introduction



<https://definingmomentscanada.ca/insulin100/timeline/context/>

SETTING THE SCENE: CANADA IN 1920

In 1920, on the eve of the discovery of insulin, Canada was hesitantly emerging from four tumultuous years of war. The final months of World War I, which ended on November 11, 1918, coincided at home with the enormous suffering caused by the global influenza pandemic of 1918-19. Emerging from the pandemic, the federal government set up a national department of health in 1919. At the same time, significant labour unrest erupted, most dramatically in the Winnipeg General Strike.

As 1920 began, so did a period of relief after many years of economic sacrifice and anxiety, and the start of what many Canadians hoped would be a bold new age. The telephone and the radio had become standard technologies in most Canadian homes. People flocked to movie theatres to watch films, which, as of 1927, also had sound. The members of the "Group of Seven" held their first exhibit of iconic Canadian paintings in May 1920. On July 1, 1920, the Dominion Elections Act came into effect, granting women the right to vote and run in federal elections. The start of the 1920s also saw growing consumer interest in the automobile and the expansion of aviation across the country. Indeed, the first airplane flight across Canada, from Halifax, N.S. to Richmond, B.C., was completed on October 17, 1920, which happened to be two weeks before Dr. Frederick G. Banting was struck by a unique idea in the middle of the night — an idea that led to the discovery of insulin.

DIABETES IN 1920: PERSONAL CONTEXT

In 1920, a diagnosis of diabetes was essentially a death sentence, especially for a child with rapid onset of what later was defined as Type 1. Life expectancy was generally less than a year from diagnosis. Slower onset diabetes, mostly among adults and later defined as Type 2, was more manageable, yet still deadly in many cases.

INSULIN100: THE DISCOVERY AND DEVELOPMENT

DIABETES BEFORE 1920

CONVINCING MACLEOD

BANTING & BEST: PROGRESS AND UNCERTAINTY IN THE LAB

IT WORKS! NOW WHAT?

THE DISCOVERY GOES PUBLIC

HISTORY OF CONNAUGHT

MAKING INSULIN

DIABETIC RESURRECTIONS

ARTICLE LIST

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- Currently, the first 8 of the 14 articles are posted
- Coming soon:
- "Patent Protection"
- "Eli Lilly"
- "Making Insulin 2"
- "Novo Nordisk"
- "Nobel Prize: Canada's Gift to the World"
- "Better Insulin, Nothing Better Than Insulin"

Deadly Diabetes, Before Insulin

- Before Insulin, the life of a person with diabetes, especially a child with type 1, was inevitably tragic and short, dominated by unquenchable thirst, starvation diets and a body that ultimately feeds on itself
- Beyond strict dietary control, very little could be done to prevent death, despite the claims of patent medicines and others offering dubious cures

3050 Walnut, Philadelphia, Pa.

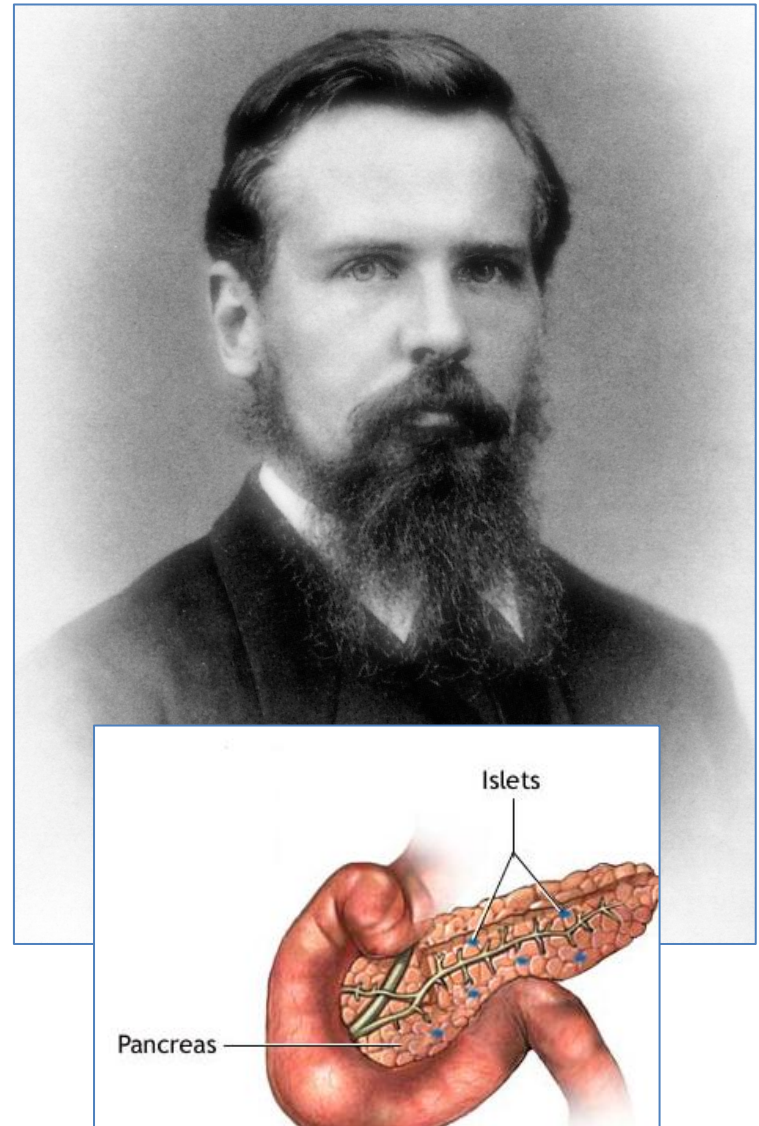
Diabetes Treated with greatest success without restricted diet. Physio-nutritive Sal-Sano removes all symptoms of the disease, produces gain in weight, muscle and nerve power and energy. At leading druggists. Write for booklet.

SAL-SANO COMPANY
11½ WEST BROADWAY. NEW YORK



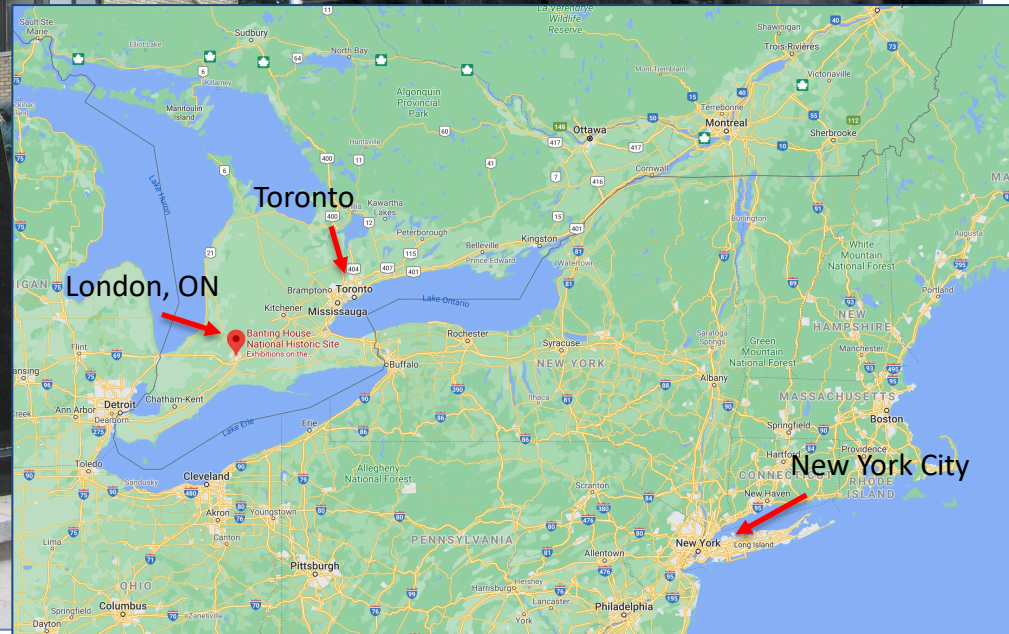
Deadly Diabetes, Before Insulin

- **250 B.C.** – First use of “diabetes” (from the Greek “to pass through”)
- **1675** – “diabetes mellitus” term first used (“mellitus” Latin for honey or sweet)
- **1869** – Paul Langerhans (right) identifies “insulin”-producing “islets of Langerhans” in pancreas
- **1889** – Role of pancreas in diabetes discovered; diabetes developed in dogs when pancreas removed
- **1910** – Discovered that diabetes caused by the lack of “insulin” in the pancreas
- This work led researchers to conduct a variety of insulin extraction experiments, but with none yielding promising results until a young Canadian surgeon was struck by a compelling idea in October 1920



Banting's Idea

- **Oct. 31, 1920 (2:00 am)** - The Insulin story began in London, Ontario, when Dr. Frederick Banting awoke with a compelling idea...



Banting's Idea

- Banting had read an article by Moses Baron about the pancreas for a lecture he was preparing at the University of Western Ontario about carbohydrate metabolism
- Baron discussed a rare case of formation of a pancreatic stone that completely obstructed the main pancreatic duct
- The blocked duct led to atrophy of the main pancreatic tissue, but the internal islet cells survived
- Baron noted that the effect of the blocked duct was similar to the effect of ligating, or tying off the duct, and supported the hypothesis that the health of the islet cells was the key factor in the development of diabetes

SURGERY, GYNECOLOGY AND OBSTETRICS

AN INTERNATIONAL MAGAZINE, PUBLISHED MONTHLY

VOLUME XXXI

NOVEMBER, 1920

NUMBER 5

THE RELATION OF THE ISLETS OF LANGERHANS TO DIABETES WITH SPECIAL REFERENCE TO CASES OF PANCREATIC LITHIASIS

By MOSES BARRON, M.D., MINNEAPOLIS, MINNESOTA

From the Department of Pathology, University of Minnesota, Minneapolis, Minnesota

ANY reference to the pancreas as secreting a hormone necessary for the utilization of sugar by the tissues of the body is misleading, as that function is, accurately speaking, exercised by only a very small portion of the organ, the so-called "islets" of Langerhans; so that what is generally understood as the relation of the pancreas to diabetes is rather the relation of the islets to that disease. And yet it should not be overlooked that in spite of a great abundance of proof from experimental and clinical studies, it has not been universally accepted that the deficiency of either the pancreas as a whole or of the specific portion of it, the islets, results in diabetes mellitus.

The purpose of this paper is to present examples of typical changes in the islets found in cases of true diabetes together with a detailed study of the histopathology found in a case of pancreatic lithiasis with special reference to the islets, and to correlate these findings with those recorded in the literature as obtained in experimental ligation of the ducts in animals. Such a combined study of clinical and experimental cases is of special advantage because of the similarity between the spontaneous and the induced conditions.

Pancreatic lithiasis is a very rare condition. Only a relatively small number of cases have been recorded in the literature, although Graaf speaks of it as early as 1667, and Mor-

gagni and Cawley recognized the condition in 1765 and 1778 respectively. Opie (35) found two cases in 1,500 autopsies. Rindfleisch (39) found 3 cases in a series of 2,000 autopsies. Zesas (45) in 1903 collected only about 70 cases from the literature. Of these, 7 had been diagnosed clinically. Einhorn (10) states that the clinical recognition of this disease is exceedingly rare; much rarer than the very rare condition itself. In our own laboratory, this was the first case found in a series of several thousand autopsies.

Gall-stones are generally found in the gall-bladder; they are rare in the ducts. Pancreatic stones, on the other hand, are found lodging in the ducts in the absence of a cystic diverticulum. It is probable that pancreatic lithiasis is more common than is suspected, but the condition is not recognized unless the stones are large enough to meet resistance. Small stones may be expelled into the intestine without any symptoms. A few large stones have also been found in the faeces (13), but this is very much rarer than in the case of gall-stones.

In contrast to the relative frequency of gall-stones in the female, more than 75 per cent of cases of pancreatic lithiasis occur in the male. Lazarus (25) collected 57 cases from the literature of which 47 occurred in the male. He states that about 60 per cent are found during the fourth decade.

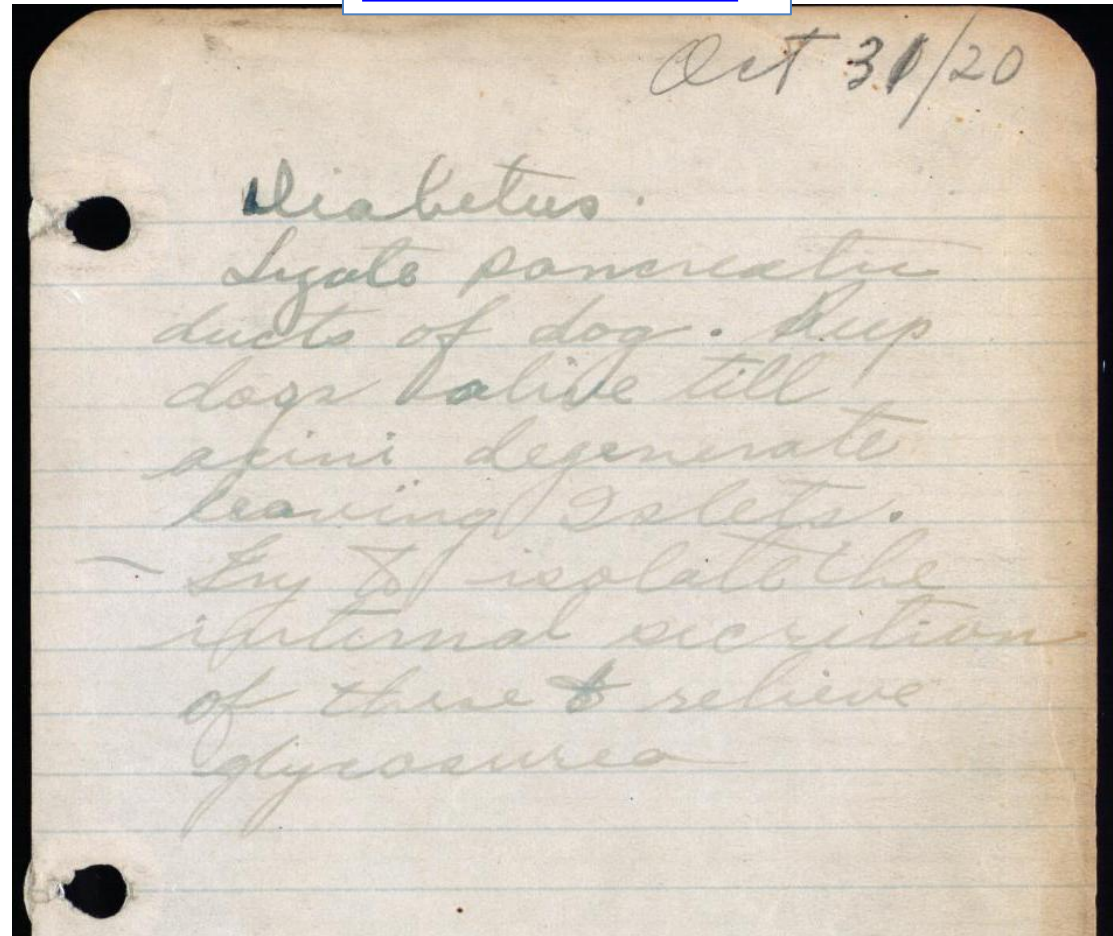
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Reprinted with permission from *Surgery, Gynecology and Obstetrics*, now called the *Journal of the American College of Surgeons*.

Banting's Idea

- Banting fell asleep after reading this article, and also after studying about carbohydrate metabolism and diabetes
- At about 2:00 am he suddenly woke up with an idea for a novel surgical method and experiment to isolate the internal secretion from the pancreas that might control diabetes
- He jotted down in a notebook,

<https://insulin.library.utoronto.ca/>



“Diabetes: Ligate pancreatic ducts of dog. Keep dogs alive till acini degenerate leaving Islets. Try to isolate the internal secretion of these and relieve glycosurea”

Banting's Idea

- Born on November 14, 1891 (now World Diabetes Day) in Alliston, Ontario, Dr. Frederick G. Banting brought a surgeon's perspective to the problem of diabetes
- **1912** - He entered the University of Toronto and graduated with an expedited class because of WWI
- After the war, he worked at the Hospital for Sick Children in Toronto before moving to London, Ontario
- **1920** - Banting started his own practice, but lack of patients led him to work as a demonstrator in the University of Western Ontario medical school's physiology department



<https://bantinghousehsc.wordpress.com/>

Banting's Idea

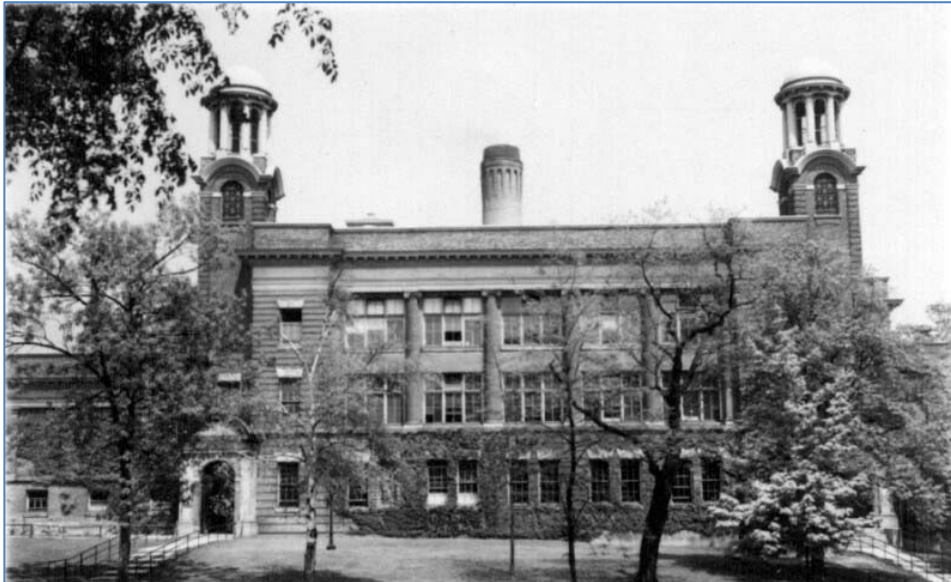
- Today, Banting's London home and medical practice in 1920 is known as "Banting House," which includes a museum and a diabetes education centre operated by Diabetes Canada
- A prominent feature of Banting House is the "Flame of Hope," which will burn until a cure for diabetes is found



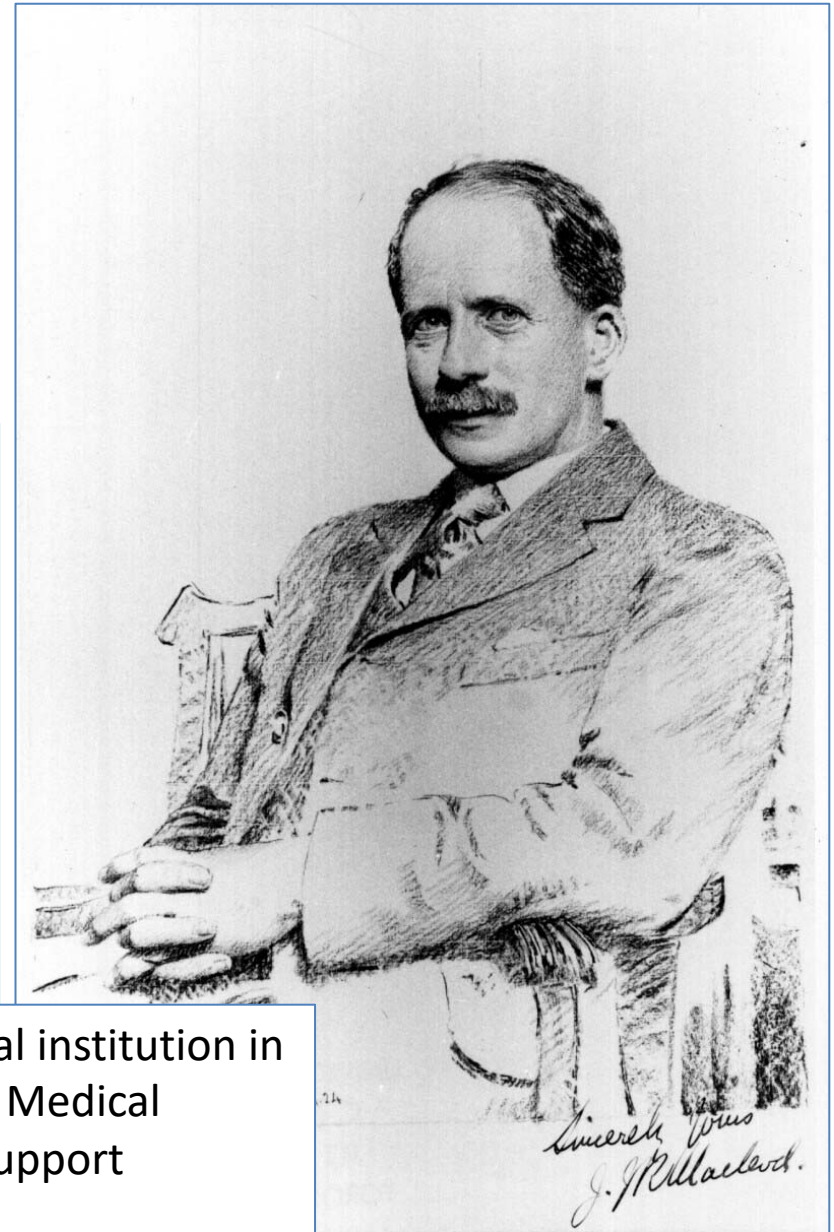
<https://bantinghousehsc.wordpress.com/>

Banting's Idea

- **Nov. 6, 1920** – Banting took his idea to the University of Toronto and presented it to Dr. J.J.R. Macleod, Professor of Physiology and a specialist in the study of diabetes



- **Early 1920s** - The University of Toronto an ideal institution in which Banting could develop his idea, with its Medical Building, built in 1903, specially designed to support scientific research



Banting's Idea

- U of T stood at the centre of a uniquely linked group of medical and scientific institutions -- Toronto General Hospital (r), the Hospital for Sick Children (l), and its singular public health biologicals producer, Connaught Antitoxin Laboratories -- each ready to play key roles in the insulin story



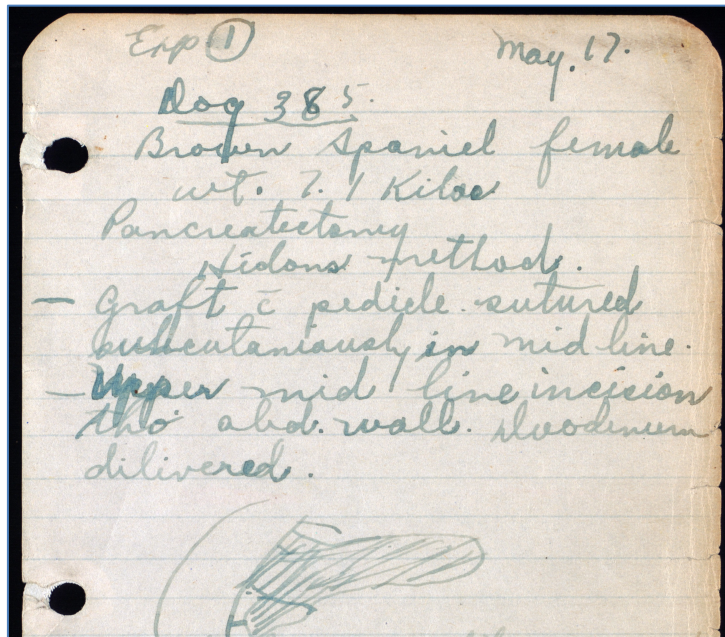
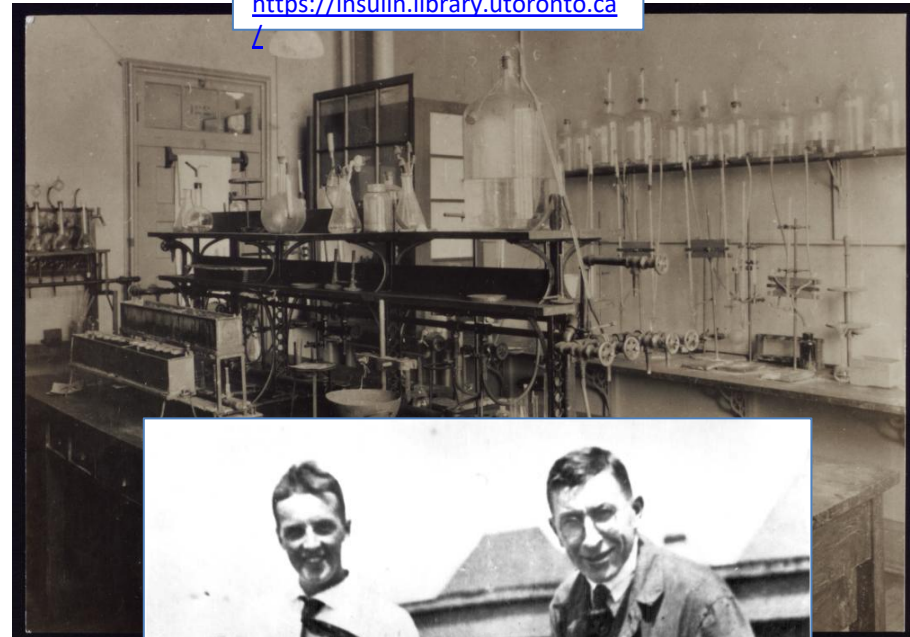
Sanofi Pasteur Canada Archives



Discovering Insulin in Toronto

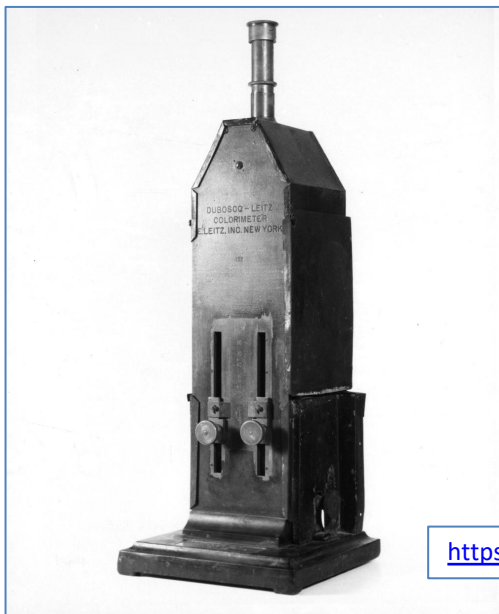
- After meeting Macleod, who was intrigued, though skeptical, Banting was soon given a small lab, access to experimental dogs, a \$100 budget, and the assistance of Charles Best, a recent graduate in Physiology and Biochemistry
- They got started on May 17, 1921

<https://insulin.library.utoronto.ca>



Discovering Insulin in Toronto

- **May-Aug 1921** – During an especially hot summer, Banting and Best reported encouraging results with a pancreatic extract controlling blood sugar levels in de-pancreatized dogs.



<https://insulin.library.utoronto.ca/>

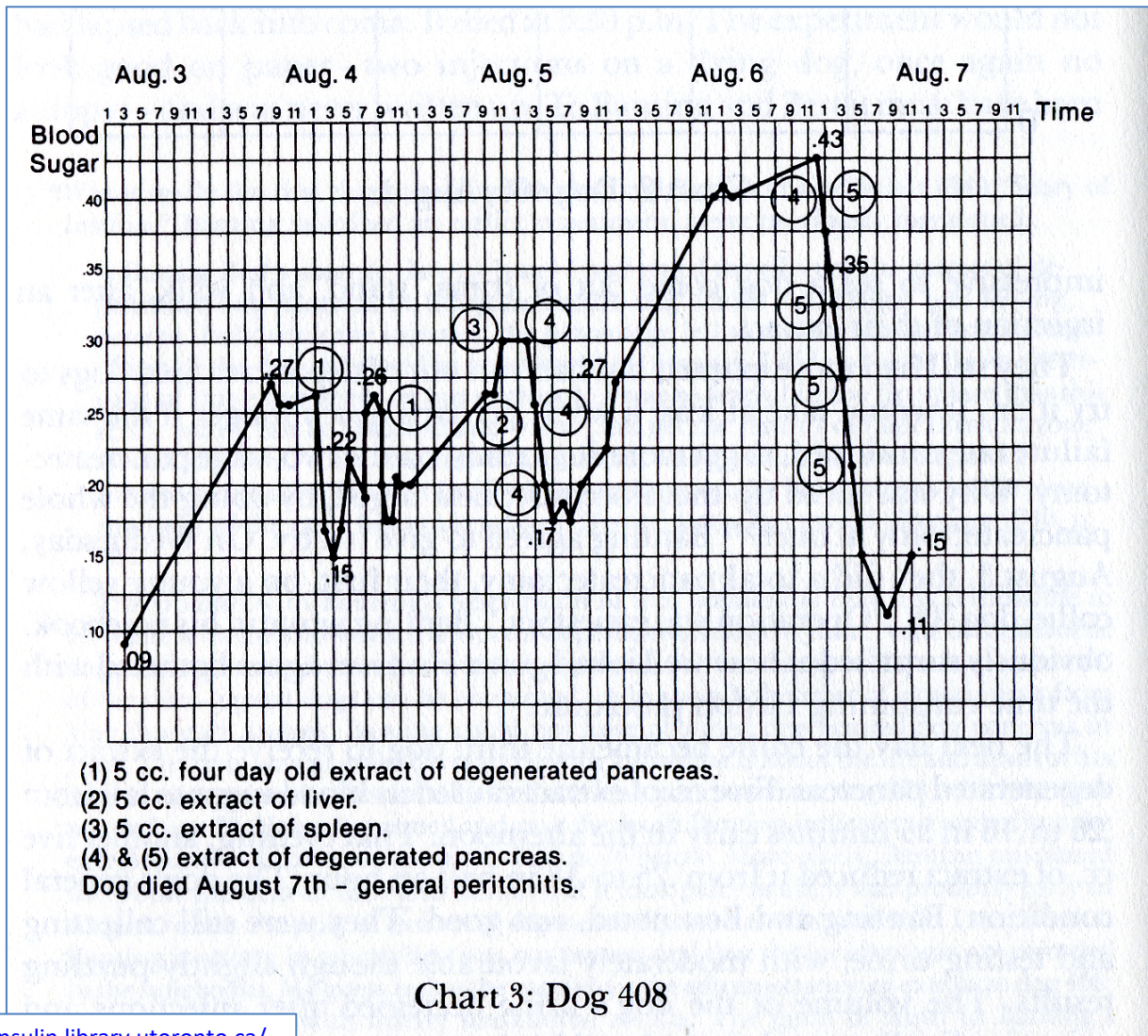


Chart 3: Dog 408

Discovering Insulin in Toronto

<https://insulin.library.utoronto.ca/>

- **Nov 14, 1921** – Banting and Best – on Banting's 30th birthday -- gave the first presentation about their pancreatic extract research to the Journal Club of the U of T Department of Physiology

- The presentation prompted a suggestion of a longevity experiment with the extract given regularly to a diabetic dog over an extended period

- But where would the extract come from?

- The duct-ligation process was time consuming and expensive on several levels, not least of which involved the reliance on dogs
- There had to be a better way

(1) This is the original manuscript on Insulin which was presented as an oral communication by Banting and Best on November 14, 1921 to the University of Toronto Physiological Society. The hand-written paper was then typed and sent as the first report on Insulin to the *Journal of Biological and Clinical Medicine*.
The Internal Secretion of The Pancreas F.G.B.

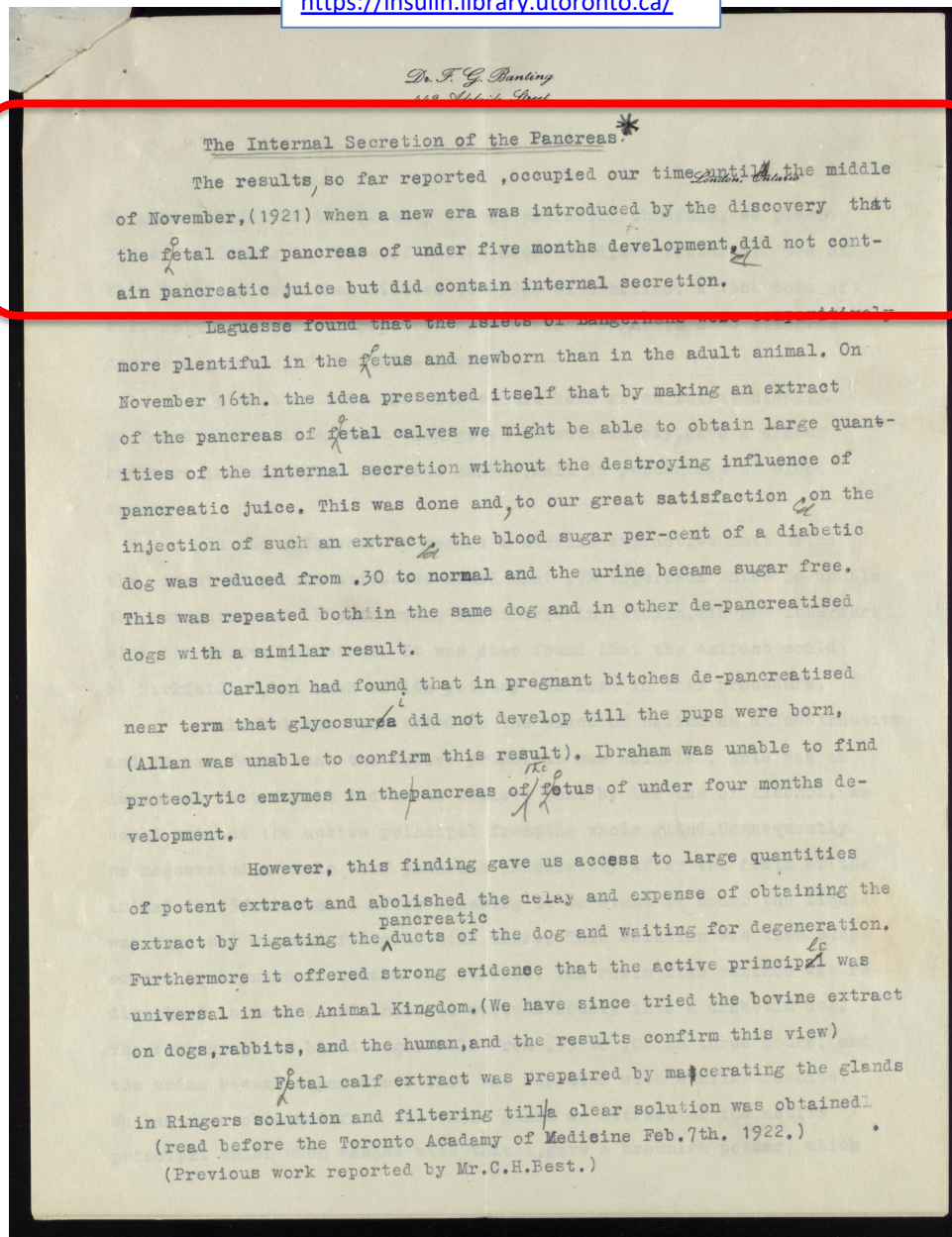
By F. G. Banting, M.B. and C. H. Best, B.A.

The hypothesis underlying this series of experiments was first formulated by one of us in November, 1920 (F.G.B.) while reading an article dealing with the relation of the islets of Langerhans to diabetes. From the passage in this article, which gives a résumé of degenerative changes in the islets of the pancreas following ligation of the ducts, the idea presented itself that since the acinus, but not the islet tissue, degenerates after this operation, advantage might be taken of this fact to prepare an active extract of islet tissue. The subsidiary hypothesis was that Trypsinogen or its derivatives was autolytic to the internal secretion of the islets. The failure of other *investigators* in this *worked* field were thus accounted for. Feasibility of the hypothesis having been ascertained by Professor J. J. R. Macleod, work was in his direction, in May 1921, in the Physiological

Discovering Insulin in Toronto

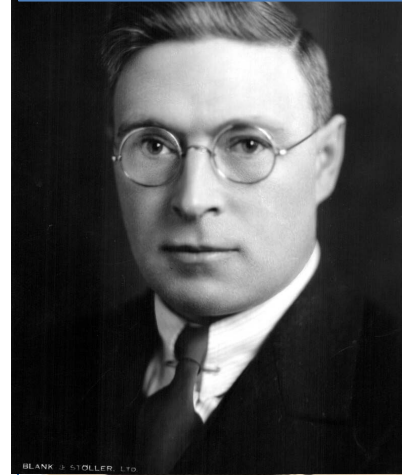
<https://insulin.library.utoronto.ca/>

- **November 16, 1921** - Banting was struck by another idea that led to preparing the extract from foetal calf pancreas
- It soon became clear that fresh whole beef pancreas would prove to be a much more readily available source of the extract



Discovering Insulin in Toronto

- **Dec. 1921** - Dr. James Bertram Collip, a biochemist from the University of Alberta on sabbatical in Toronto, joins Banting and Best to help purify the extract.
- Encouraging results with dog #33, "Marjorie," lead to the extract's first human use (administered orally), but it was unsuccessful

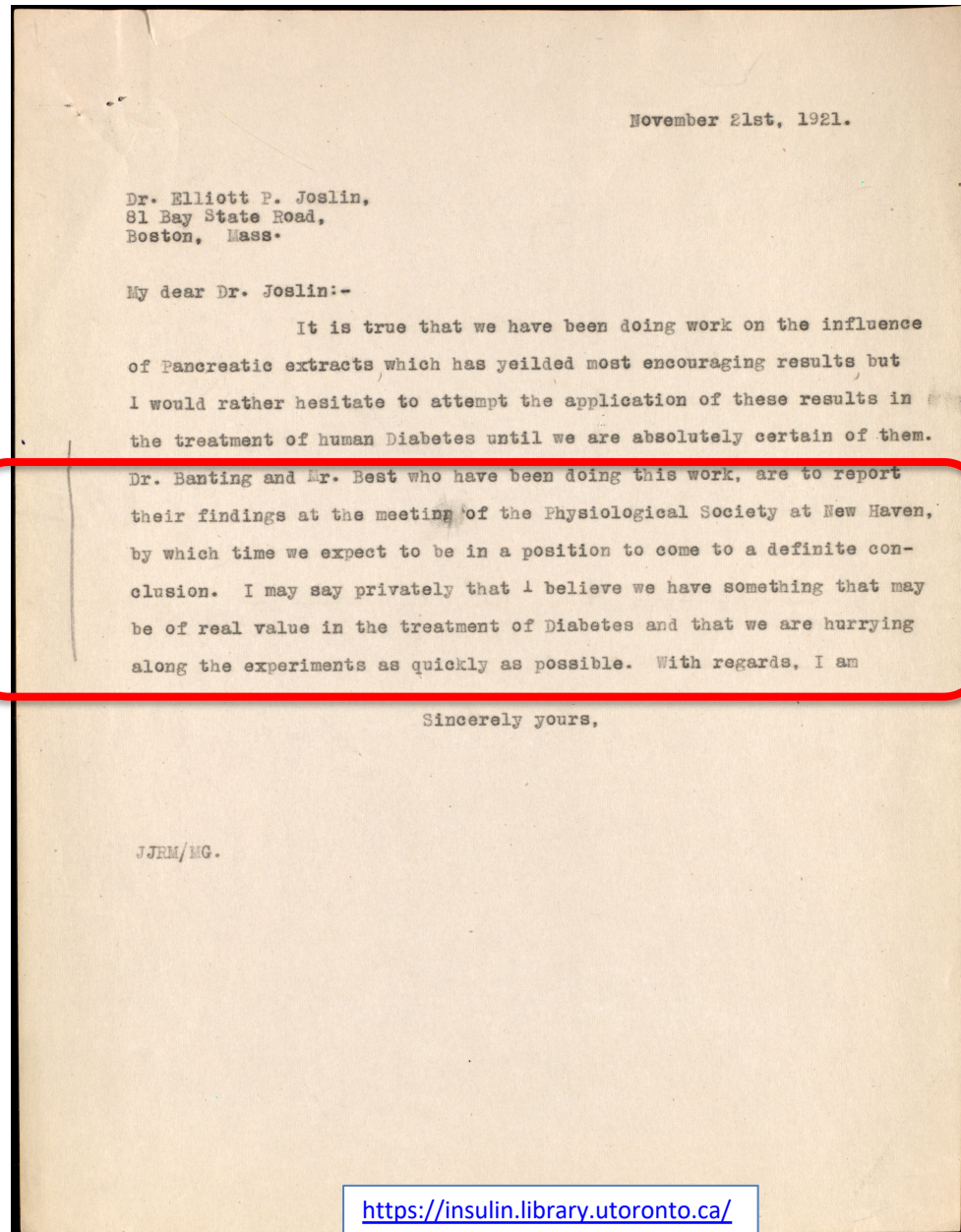


Clinical Use.
Dec. 20. Phoned for Filchrist -
gave him extract that we knew to
be potent. - by mouth - empty stomach.
Dec. 21 - no beneficial result.

<https://insulin.library.utoronto.ca/>

Discovering Insulin in Toronto

- **Dec. 30, 1921** –The work of the Toronto group presented at the Annual Meeting of the American Physiological Society in New Haven, CN, and attended by the leading diabetes specialists
- Banting was nervous giving the presentation and Macleod stepped in to help answer questions
- Dr. George Clowes, research director of Eli Lilly & Co, of Indianapolis was impressed with the work's potential and closely followed its progress



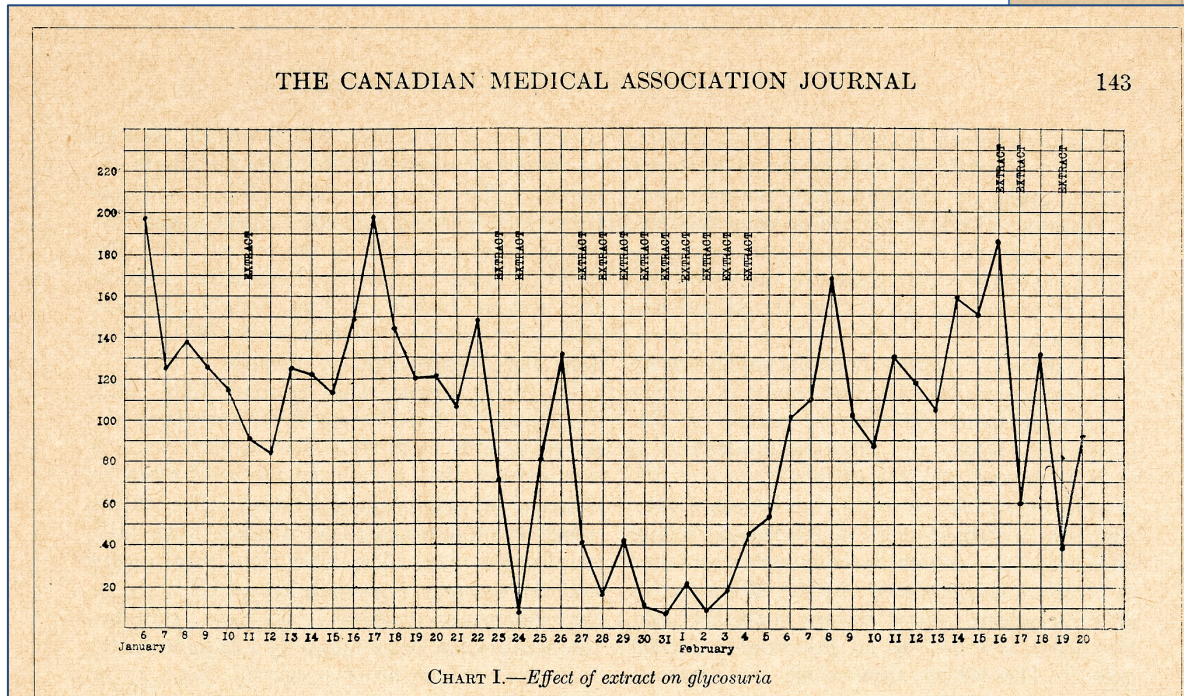
Discovering Insulin in Toronto

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- **Jan. 11, 1922** - 13-year-old Leonard Thompson is the first to receive an injection of the extract, but with limited effect, and with some reaction (abscesses)
- **Jan 23, 1922** – Leonard receives Collip's more purified extract, with striking results



LEONARD THOMPSON
First patient to receive insulin in
Toronto.



Developing Insulin in Toronto

- **Jan 25, 1922** - Encouraged by Leonard Thompson's successful treatments, but concerned about the future control of the new extract's production, the director of U of T's Connaught Laboratories, John FitzGerald (right), facilitated an agreement with Banting, Best, Collip and Macleod
- He offered them funds and the Lab's facilities in the Medical Building, not far from Banting & Best's lab, to help develop methods to produce the extract for clinical trials

<https://insulin.library.utoronto.ca/>

January 25th 1922.

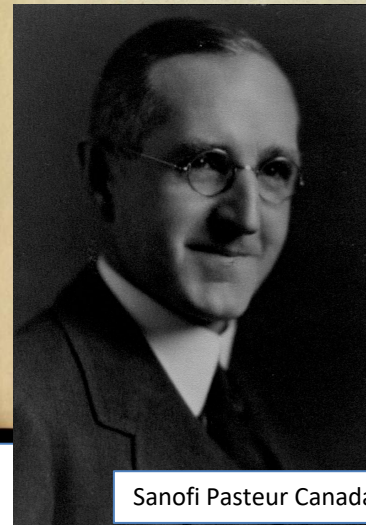
MEMORANDUM IN REFERENCE TO THE CO-OPERATION OF THE CONNAUGHT ANTITOXIN LABORATORIES IN THE RESEARCHES CONDUCTED BY DR. BANTING, MR. BEST AND DR. COLLIP UNDER THE GENERAL DIRECTION OF PROFESSOR J. J. R. MACLEOD TO OBTAIN AN EXTRACT OF PANCREAS HAVING A SPECIFIC EFFECT ON BLOOD SUGAR CONCENTRATION.

The Connaught Antitoxin Laboratories will co-operate under the following conditions with the above mentioned workers:-

1) Dr. Banting, Mr. Best and Dr. Collip each agrees not to take any steps which would result in the process of obtaining an extract or extracts of pancreas being patented, prepared by any commercial firm with the aid of any of the above, or otherwise exploited during the period of co-operation of the Connaught Antitoxin Laboratories.

2) That no step involving any modification in policy concerning these researches be taken without a preliminary joint conference between Dr. Banting, Mr. Best and Dr. Collip, and Professor MacLeod and Professor FitzGerald being held.

in Laboratory is prepared in the Antitoxin Laboratory of the extract or extracts being shown due the Connaught Antitoxin Laboratories of the above outlay without any return.

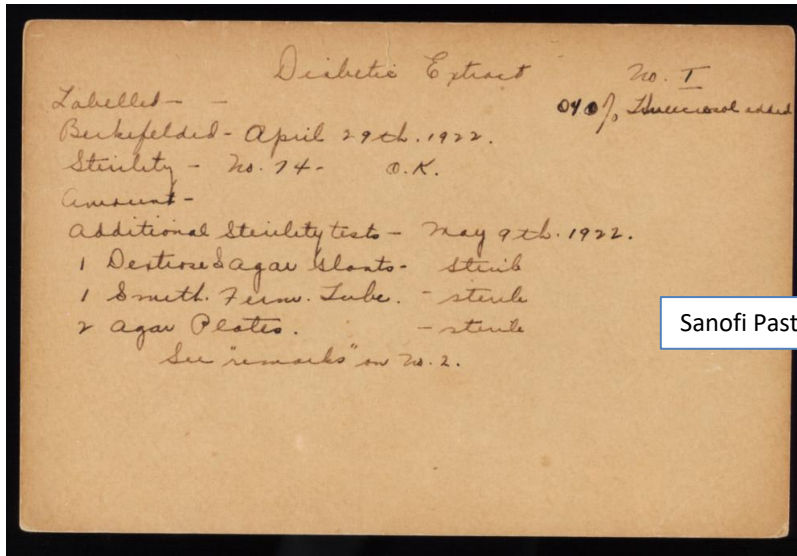


Sanofi Pasteur Canada Archives

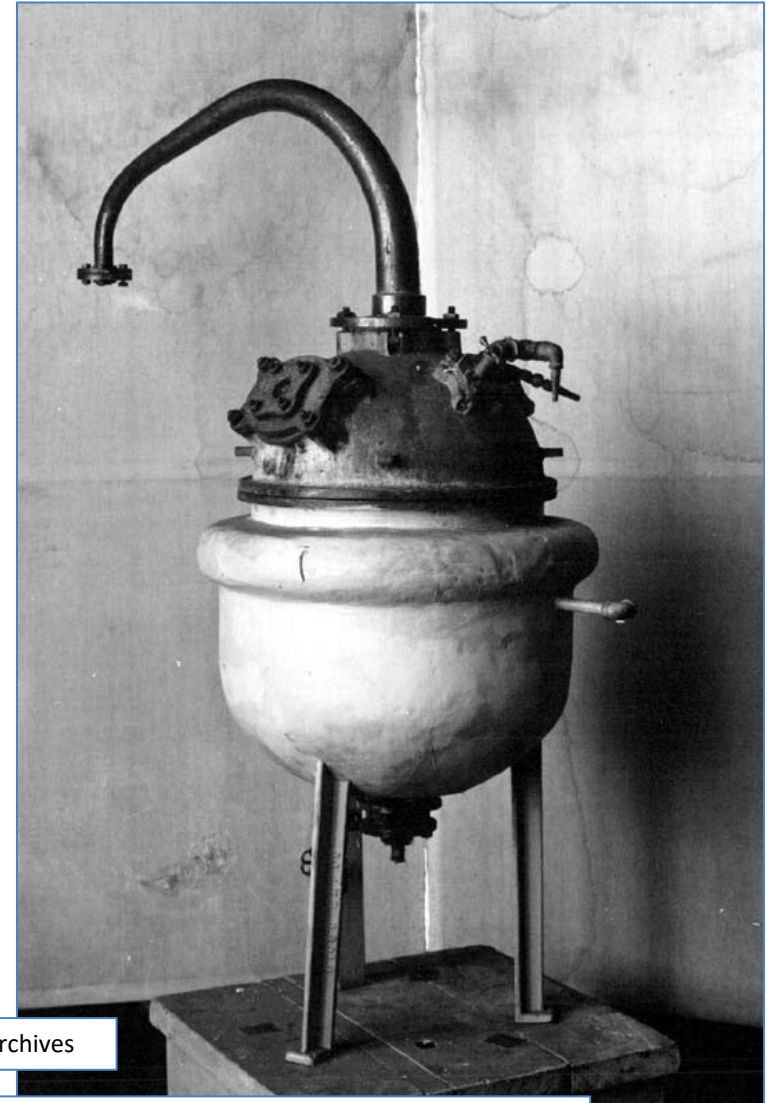
J. J. R. MacLeod
C. H. Best
J. B. Collip
F. G. Banting

Developing Insulin in Toronto

- Moving from lab to clinical trial scale, and then to large-scale production of the extract was a major challenge for Connaught Labs
- **March-May 1922** - After frustrating failures, production was restored under Best's direction
- Connaught then dedicated its full, though modest, resources to insulin production and output rose steadily



Sanofi Pasteur Canada Archives



- **May 1922** - The extract was given the name "Insulin"

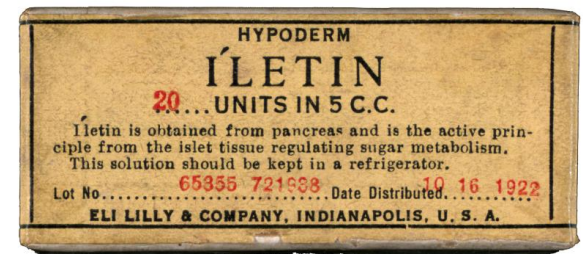
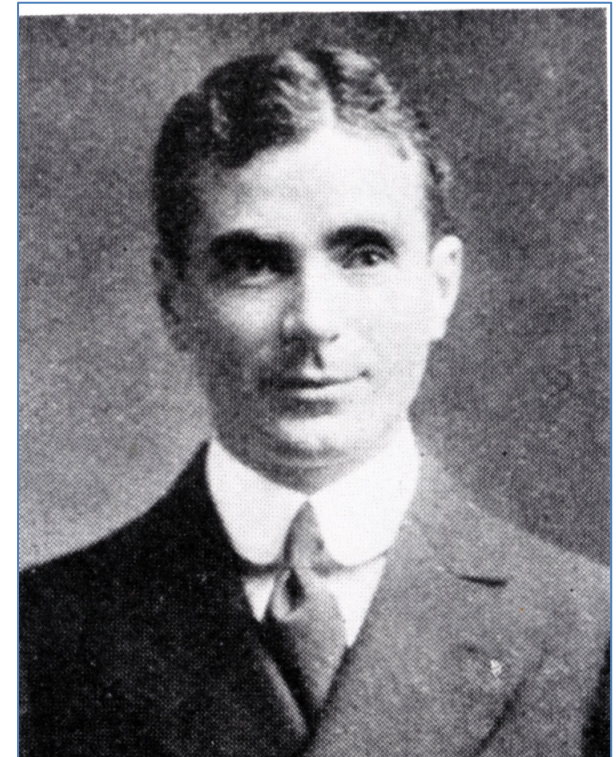
Developing Insulin in Toronto

- **May 3, 1922** – The insulin success story with the first human diabetic cases – and the first public use of the “insulin” name – was told in a seminal presentation by Macleod in Washington, D.C. at a major conference attended by physicians and the leading diabetes specialists from across North America
- Macleod’s presentation prompted a wave of letters to the Toronto team from physicians on behalf of their desperate diabetic patients, pleading for insulin, although the supply was very limited
- **May 21-26** - The first American treated with insulin was 22-year-old Jim Havens of Rochester, NY



Developing Insulin in Toronto

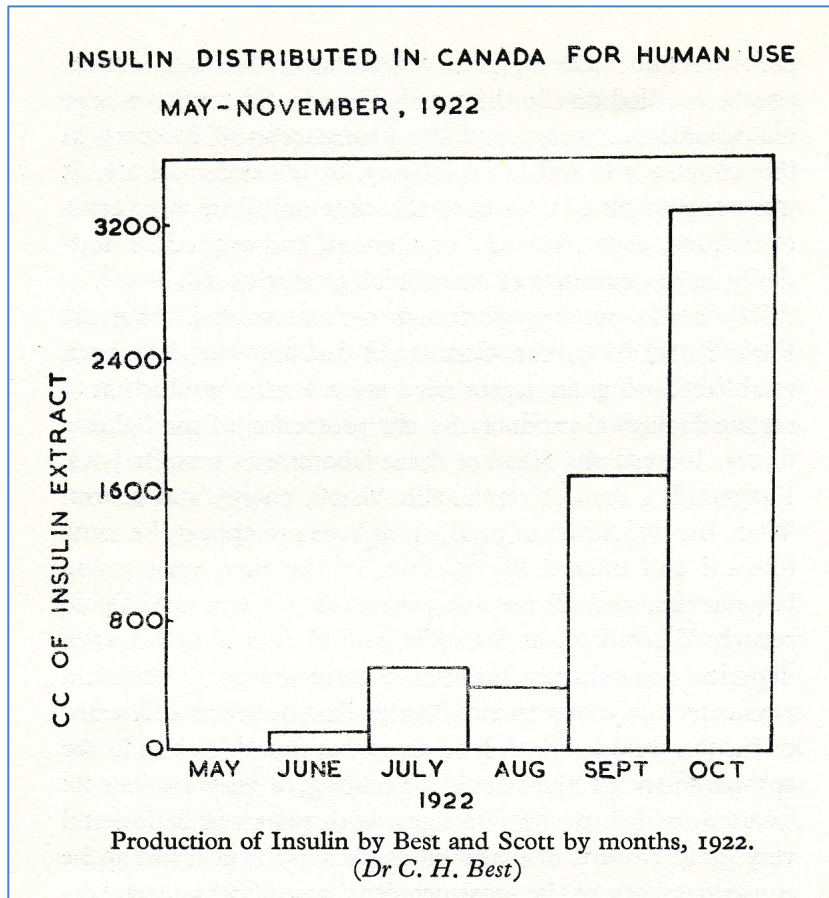
- **May 30, 1922** - A unique collaboration agreement arranged between the University of Toronto and Eli Lilly & Co. of Indianapolis, designed to expedite the the development of large-scale insulin production methods
- This and other agreements relating to insulin production, licensing and patent protection was negotiated by the University of Toronto's Insulin Committee
- Charles Best assumed leadership of Connaught's Insulin production and worked closely with Eli Lilly, especially the company's Research Director, Dr. G.H.A. Clowes (right)
- The agreement granted Eli Lilly exclusive rights to supply Insulin (branded as "Iletin") in the U.S. to diabetic specialists until June 1923



Sanofi Pasteur Canada Archives

Developing Insulin in Toronto

- The severe insulin supply challenges during the spring and summer of 1922 meant only a few critically ill patients, mostly children, could be treated



HAVE THEY ROBBED DIABETES OF ITS TERRORS?
Shown in these pictures are the four Toronto medical men on the University staff who figure most prominently in the discovery of a pancreatic extract to be used in the clinical treatment of diabetes in human beings. This is one of the most important medical discoveries of modern research, whose possibilities as an ultimate cure of this dread disease are very encouraging. It may be gathered from the announcement to-day of the success of the extract on seven human patients at the Toronto General Hospital since January this year, Dr. F. G. Banting on the upper left, a young man of 30, a graduate from Toronto University in 1916, brought his hypothesis on the basis of the experiments with him from London, Ontario, last May. Associated with him in all the experimental work has been a younger man still, Dr. C. H. Best, only 23 years of age, on the upper right, a nephew of Mrs. Prof. Hallam, of Wycliffe College, and a son of Dr. H. H. Best, of Maine. Dr. Best on account of the promise of his work, was chosen by Prof. J. J. R. MacLeod, associate Dean of Medicine at the University, and one of the most eminent authorities on diabetic research, to assist Dr. Banting in his experiments. Dr. J. B. Collip, on the lower left, professor of bio-chemistry at the University of Alberta, on leave of absence this year as assistant-professor of pathological chemistry at Toronto, a graduate of 1912, has greatly facilitated the work in refining and concentrating the extract from ox pancreas that was finally used on human beings for the first time in January at the General Hospital.

Star Weekly

Toronto Star Weekly, March 26, 1922

Insulin Resurrections

- **June - July 1922** – The rapidly growing attention to the Toronto insulin discovery brought desperate pleas from diabetics, their doctors and families, few of whom Banting could help due to a limited supply of insulin
- However, Banting was able to help three severe diabetic cases who came to Toronto from the U.S. for insulin treatment
- Ruth Whitehall (8 years old), treated in Toronto June 17 to the end of September
- Myra Blaustein (11 years old), treated in Toronto July to the end of September
- Teddy Ryder (6 years old), treated in Toronto July 8 through October



<https://insulin.library.utoronto.ca/>

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- Teddy Ryder (6 years old), treated in Toronto July 8 through October
- Teddy would live until March 1993

Insulin Resurrections: Banting's living miracle

U.S. man, 67 was near death at the age of 6 but insulin was discovered in the nick of time

By Frank Jones Toronto Star
HARTFORD, Conn.—A 67-year-old bachelor living quietly in an apartment here is a chapter of Canadian medical history.
 Teddy Ryder, by all odds, should have died years ago. He was one of the first diabetics to be treated by Dr. Fred Banting in the body-moulding era of the dramatic discovery of insulin in 1922.
 His mother brought him to Toronto, a walking skeleton, to Toronto when he had only weeks to live. Three months later he went home, able to run and play, his cheeks filled out, a child as if resurrected from the grave.
 Even so, the odds against him living this long were great — especially because insulin doses in the early days were widely erratic in quality and quantity.
 Yet Toronto historian Michael Bliss, author of *The Discovery of Insulin*, and I, intrigued, listening not only to Teddy's story, but that of his mother, who is very much alive and alert at the age of 92.

Mother's determination

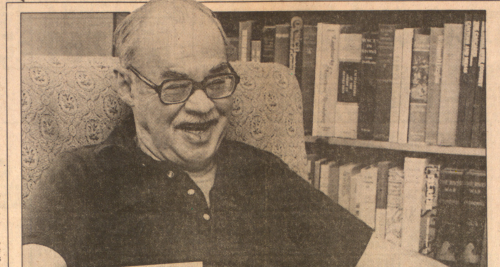
There is an amazing story of a mother's determination that her son would not die, and along the way it provides some surprising insights into the personality of Canada's most famous doctor, Fred Banting.
 Teddy's existence came to light when two physicians approached Bliss, a University of Toronto history professor, three weeks after he had given a lecture in Toronto on the discovery of insulin at the Medical History Club at Yale University.
 "I have a patient who has been using insulin for more than 60 years," one of them said. "His name is Teddy Ryder."
 Bliss couldn't believe. In his files were copies of letters written between Banting, the co-discoverer of insulin, and the Ryder family, and there was even a children's note to Banting from Teddy after he went home.
 It said: "Dear Dr. Banting, I wish you could come to see me. I am fat but now I feel fine. I can climb a tree. Margaret (his sister) would like to see you. Lots of love from Teddy Ryder."
 But Elizabeth Hughes, daughter of Charles Evans Hughes, the one-time U.S. secretary of state who heretofore had been the main reason for Banting's later fame, had told Bliss shortly before she died in 1981 that Teddy Ryder had died long since.
 When Bliss and I came to Hartford to meet the remarkable mother and son, we first met at the airport on the way to the physicians who had approached him. It was Dr. Loyal H. Harrison, an 80-year-old man, Wardner told us as we drove through snowy Connecticut scenery that he had attended Teddy's mother, Mildred Ryder, for 35 years.
 First stop was the Brightview Retirement Home where, after a while, Wardner emerged with a delicate, upright lady who laughed gingerly across the aisle as he led her to a room. Her hair, which he had, by her mind is sharp, her manner gracious.

Never married

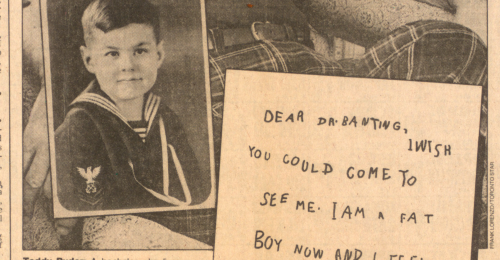
"I've so looked forward to this," she said when settled in the back of Wardner's Jeep Waggoner. With Bliss now writing a biography of Banting and also planning an item about Teddy in the next edition of *The Discovery of Insulin*, she felt happy, she said, that Teddy would finally get his footnote in medical history.
 Teddy, she said as we drove to his apartment, had never married, but had come close a couple of times. She had been particularly opposite to one man because the lady was a Christian Scientist and might have persecuted him. And because insulin, Mrs. Ryder still phones her son twice a day to make sure she's well.
 As we helped Mrs. Ryder up the path, Teddy, a chubby, shy man, emerged wearing a shirt and tartan pants. "Now wouldn't you think he would put a sweater on," she said. "Now isn't the mother me?" she laughed, and recalls the broad didn't have a mother he wouldn't be alive, would he?
 While Teddy served coffee his mother settled herself in an armchair, her hands resting on a box from which, as she told her story, she produced photographs of Teddy at various stages of his childhood.

No Christmas tree

The only man who offered any hope was Dr. Frederick Allen, a gruff, herbivorous researcher who had discovered he could extend the life of diabetics by starving them almost to death. Many doctors deplored Allen's ruthless methods, but Mildred and Earle decided to take Teddy to stay at Allen's Psychiatric Institute in Morristown, N.J.
 "He had no bedside manner to speak of," Mrs. Ryder said, "but he was very kind to us. When he heard I had a baby he insisted I could bring her along too so that she wouldn't be lonely."
 Teddy's memories of that period are not the happiest, but he recalls the broad laws and handsome man that housed them, and when he was treated even patients but his first breakfast of oatmeal he said, "Mama, they don't know how to feed little boys like me." It was until May 27.
 "From the time he arrived there in September, 1923, his



Teddy Ryder: A bachelor who lives in Hartford, Conn., he was a walking skeleton when brought to Dr. Frederick Banting in Toronto in 1922. But, as he said in a letter after his return home, he soon gained weight and by the age of 3, was a happy, healthy youngster.



Teddy remembered drives in the country around Toronto — "When we stopped at a soda fountain I was only allowed to buy water" — and especially loved the Japanese armor on the trips they made to the Royal Ontario Museum.

Drives in country

Some nights, Mrs. Ryder said, after she'd put Teddy to bed in their single room and was sitting reading by the green-shaded light she used to go to visit him. Banting would drop by to talk. "He would tell me about his trip to a particularly interesting place. He'd take her a dozen letters to marry him in the past and he'd always been there when she wanted to come back and he didn't know what to do" (finally Banting rejected the woman, Edith, because she was married someone else).
 Banting would also go on at length about Prof. J. J. R. Macleod, who had reluctantly given Banting laboratory space, but who now seemed determined in Banting's view, to take credit for the discovery.
 On one occasion, Mrs. Ryder said, Banting took her and Teddy to show them the laboratory in the Medical Building where he and Best had set with their drugs and cooked their food on a kerosene burner while they experimented.

Never gave up

"I think Mama deserves extraordinary credit," she said. "She never gave up. She never despaired of my living. Even though people say what a miserable-looking thing I was, she figured the doctor knew best. She never paid any attention to conventional wisdom."
 "Well, we were lucky," Mrs. Ryder said, gathering her souvenirs together. "We had Uncle Morton to back us up. I look on it as Dr. Banting's miracle. We have lived through it and I'm glad." "And you know," she added, "I have never heard Ted say they did this thing to me." He has never resented having taken insulin, I am proud of that fact.
 "So to insist he put his number on to come out to see us in St. As. At the retirement home she took us to in St. As. We had a photo taken there. We had a good party. I know what this day has meant to me," she said as she spoke.

Not a Christmas tree

They didn't have a Christmas tree that year, Mrs. Ryder said, because they thought Teddy might not last until Christmas Day.
 Teddy's uncle, Dr. Morton Ryder, had been searching high and low for an answer while the life of his first and favorite nephew drained away. In February, 1922, there was a break. Roy Greenaway, a Toronto Star reporter, secured a Banting's and Charles Best's experiments with insulin.
 Dr. Ryder got in touch with Banting, who was being bombarded with queries from diabetics all over the continent. Banting was treating seven patients but then, unaccountably, they lost the knack of making insulin. It wasn't until May 27 they were in production again.
 In June Dr. Ryder came to Toronto to

to have three or four injections a day. Nothing was standardized at all," Mrs. Ryder said. "Dr. Banting would say, 'Well, we tried this on a rabbit and would better go easy on this lot. It may be too strong. But if there was any more of Teddy having a reaction, he would come running.'
 It was a summer of miracles in Toronto. The few patients Banting agreed to treat were arriving like walking skeletons then magically filling out as the insulin allowed them to start eating again.
 They became the Mecca for worldwide families seeking help for their stricken children. Earle Ryder, on a visit in September, met Charles Hughes, the secretary of state, and found him afraid. The wealthy Baltimore parents of Ruth Whitehall, another of Banting's small patients, brought their father and maid and rented an eight-room apartment. The Ryders were then invited over and on Sept. 14 the Whitehalls gave a birthday party for Teddy.
 "I wore an Indian suit and I think even the help was in costume," Teddy recalled. "Then the doorman rang. I opened it and there was a tall lady in a row gown and a large hat and wearing white gloves.
 "I couldn't figure — she looked somewhat familiar. Then I realized — it was Dr. Banting dressed up!"

Not a Christmas tree

By the time Mildred returned to New Jersey with Teddy at the beginning of October, 1922, the change in the little boy was dramatic. "I can't tell you too strongly how much pleased I am with what you have accomplished," Morton Ryder wrote to Banting.
 When Banting addressed a packed hall of medical men in New Jersey in January, 1923, he had Teddy, now a chubby little boy, come on and sit on his knee.
 In 1929, the Ryders were in Toronto again when Teddy's grandfather, who had paid much of the cost of his treatment and attended a bankers' conference at the Royal York Hotel, went to see Dr. Banting, food which was probably the earliest model of him wearing it in his laboratory, and invited him to a banquet. "I was very pleased," Mrs. Ryder said. "I never heard Ted say they did this thing to me." He has never resented having taken insulin, I am proud of that fact.
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Insulin Resurrections

- August 15 – November 30** – Banting's most famous diabetic patient was 15-year-old Elizabeth Hughes, press attention to her heightened by her being the daughter of the U.S. Secretary of State, Charles Evans Hughes

Toronto Star, Aug 17, 1922



HELPED BY INSULIN 'CURE'

Daughter of Secretary of State Hughes Recovers From Diabetes

Toronto, Oct. 16.—Miss Elizabeth Hughes, fifteen-year-old daughter of the American Secretary of State, Charles E. Hughes, has been taking the Insulin treatment for diabetes for about two months under the personal attention of Dr. F. G. Banting, discoverer of the treatment.

She has gained sixteen pounds and is eating everything, was the way one who knows her described her condition.

When she came here she was suffering from the malady in acute form. As is customary with patients of this type, she was unable to assimilate the staple foods which contain carbo-

SCIENCE'S NEW CURE LEADS HUGHES'S CHILD TO HEALTH

Toronto, Oct. 15.—A gain of sixteen pounds in two months shows the remarkable response of Miss Elizabeth Hughes, fifteen, daughter of Charles Evans Hughes, Secretary of State, to the Insulin treatment for diabetes, which she has been taking here under the personal attention of Dr. F. G. Banting, who discovered the method.

When Miss Hughes came here she was unable to assimilate any of the staple foods which contain carbohydrates, and as a consequence she was forced to a diet which bordered on starvation.

After a few injections of the extract which forms the basis of the treatment, her improvement was marked. These injections provided the element in her blood which oxidized the sugar and after the first week she has been extending her diet to now it embraces all the staple foods.

Miss Hughes is making her home in Toronto with a nurse, Miss Burgess, who has been with the Hughes family for some years. Mrs. Hughes visited the city in August, expecting to take her daughter to the Toronto General Hospital, and was overjoyed when she found that this step was unnecessary.



Miss Elizabeth Hughes

Insulin Resurrections

- **August 15 – November 30** – Banting's most famous diabetic patient was 15-year-old Elizabeth Hughes, press attention to her heightened by her being the daughter of the U.S. Secretary of State, Charles Evans Hughes

Toronto Star, Aug 17, 1922



- Elizabeth documented her recovery story in many letters she wrote from Toronto to her parents

<https://insulin.library.utoronto.ca/>

78 Grosvenor Street,
Toronto,
Canada.

August 22nd, 1922.

Dearest, dearest Mumsey,

I hope to goodness this does reach you safely for it carries in it some very interesting news I think. Dr. Banting came in as usual last night about 5.30 P.M. and said he had a good report to make. The insulin which they have been working on for so long will now be ready for use in a couple of days at the most, and it is the most powerful that has yet been made. So much so, in fact, that I will only have to take 1 C.C. at a time when I begin on my two doses, which will be very soon, I think. He is getting enough of it so that his three outside patients, Ruth Whitehill, Teddy Rider, and myself will not have to change our insulin for a month or so, which is a very good thing as you know. He was so happy over that part of it, and he really feels that it is becoming more stabilized all the time. He said, you can tell your Mother that I can promise her that with this new extract, the next time you see me I will be on 2240 calories the full amount that a girl of my age should be having. It will be divided like this: 60 of protein, 50 of carbohydrate, and 200 of fat. Now if I don't begin to gain weight on that I will be crazy. The power of this new insulin is so strong that he expects me to carry all that on only 2 C.C.'s per day, one in the morning and the other at night. You see what he's so happy about, is that once he finds out my balance on that, why he has enough insulin on hand now, so that I won't have to change for at least a month, anyway. If I once get on 2240 calories, it will be an established diet plenty of calories for me, and maybe then I can live at home with Blanche to give me the extract and tend to all my food, for once my diet is established like that I wouldn't need a doctor unless something went wrong.

Insulin: From Toronto To The World

SEEK PATENTS AS PROTECTION FOR DISCOVERY

Originators of "Insulin"
Offer to Assign Them
to U. of T.

AN OFFICIAL STATEMENT

The Globe has received from authorities at the University of Toronto the following statement on the Insulin treatment for diabetes. This may be regarded as an official statement by the University.

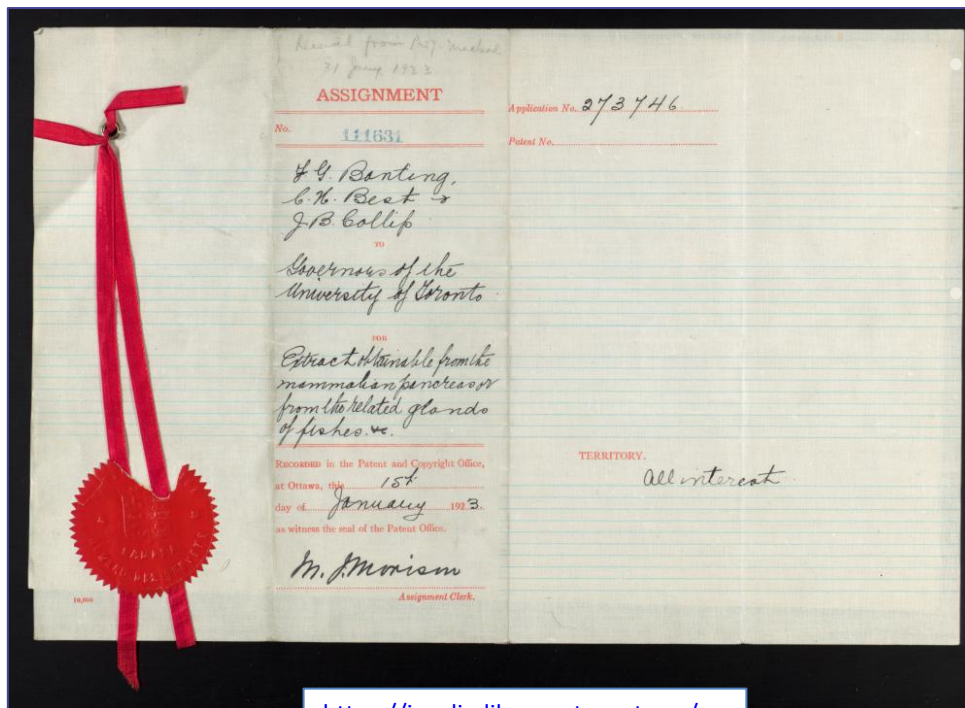
"The originators of the method of preparation of Insulin have applied for patents in Canada and other countries, and have offered to assign these, when granted, to the University of Toronto, to administer in whatever way it deems best, so as to prevent commercial exploitation of the product and to safeguard the production of a standardized extract.

Accepts Trust.

"The University, through the Board of Governors, has accepted the trust and has appointed a committee composed of representatives of the Board of Governors and of those who participated in the researches to advise it as how best to carry the above purposes into effect. The first step in large-scale production of Insulin was taken by the Connaught Anti-toxin Laboratories, but it was found that experimentation on a still wider scale was necessary to master the unexpected technical difficulties encountered in the work. It was found with each attempted expansion of the scale of production that fresh difficulties were encountered, and that products of unequal potency and of uncertain clinical value were obtained. It was decided, therefore, to collaborate with some large firm in the United States experienced in the preparation of extracts from slaughterhouse material, so that enough Insulin could be produced in the country to supply it to a selected group of physicians, so as to test its therapeutic value in diabetes, its proper dosage and so forth, before it on the market.

The Globe, Oct. 21, 1922, p. 23

- **Oct 1922** – Banting, Best & Collip assign Insulin patent to the University of Toronto Board of Governors for \$1 as a public trust, "so as to prevent commercial exploitation of the product and to safeguard the production of a standardized product"



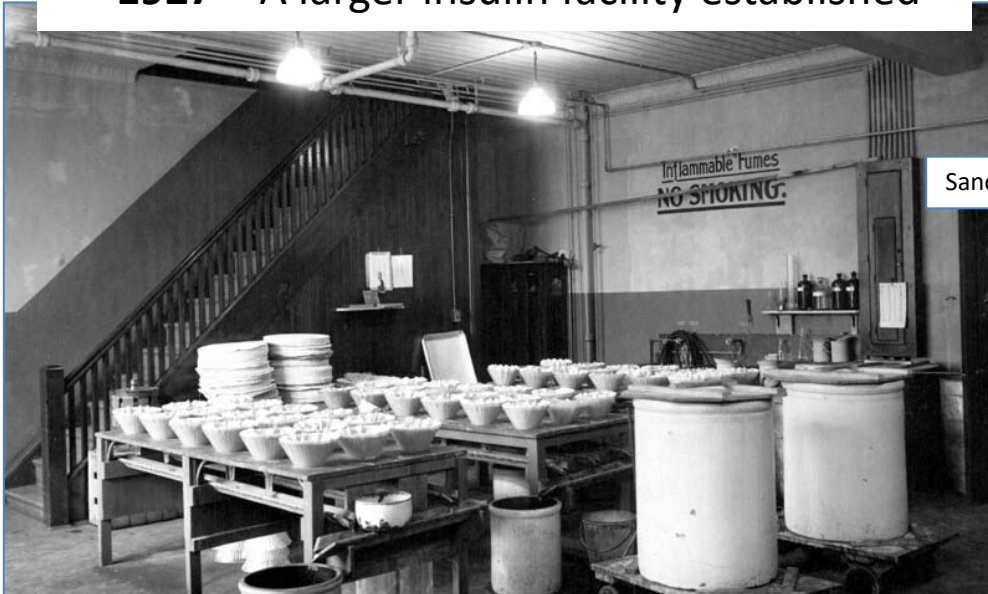
<https://insulin.library.utoronto.ca/>

Jan 1923 – Canadian and U.S. patents for insulin granted

April 1923 – Unique "patent pooling" policy established by Insulin Committee to assure the sharing of any insulin production advancements among licensed producers

Insulin: From Toronto To The World

- **August 1923** - Canada's insulin supply found a firm foothold with a larger insulin production plant for Connaught Labs, thanks to funds from the Ontario government and the Labs' reserves; the plant established in U of T's vacant YMCA building on campus
- **1927** – A larger insulin facility established



Sanofi Pasteur Canada Archives



To-morrow the Ontario Government will open the former Y.M.C.A. building at the University of Toronto as headquarters for the free distribution of insulin to those unable to pay for it. This is due to the initiative of the new Provincial Minister of Health, Hon. Dr. Forbes Godfrey, who by his prompt recognition of the duty devolving upon the state in such matters has the satisfaction of having blazed the trail for the provinces in the Old Land, who are to adopt a similar policy.

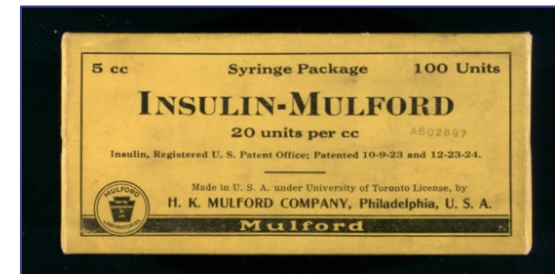
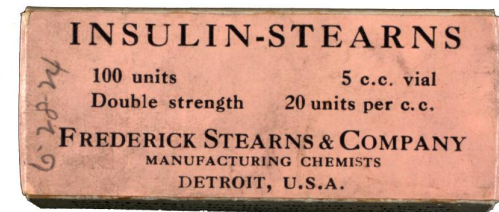
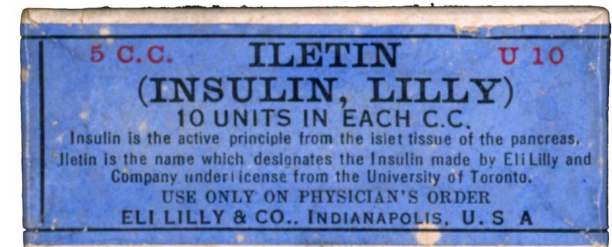


- Connaught was supplying insulin for all of Canada, and exporting it to many countries without their own production facility

Insulin: From Toronto To The World

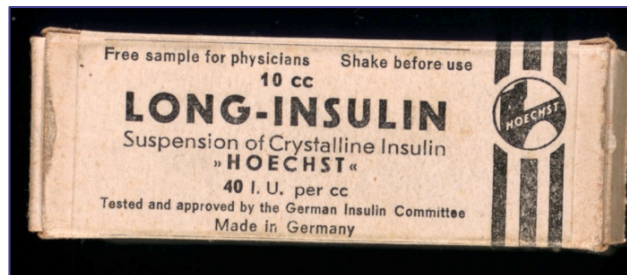
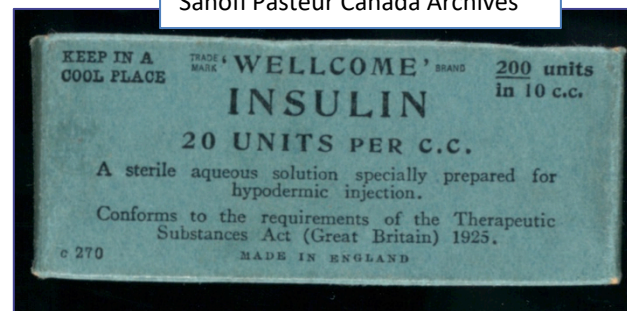
- As Insulin production steadily grew in Canada and the U.S., the University of Toronto Insulin Committee facilitated insulin patents and the licensing of production in other countries
- The Insulin Committee oversaw insulin quality control and licensing rights in North America
- In Canada, Connaught Laboratories held exclusive insulin production and distribution rights (until 1980); Connaught remained part of U of T until 1972 and today its legacy is part of Sanofi Pasteur Canada/Sanofi Canada
- Eli Lilly held sole U.S. rights until June 1923, when other firms were able to apply to the U of T Insulin Committee for licenses

Sanofi Pasteur Canada Archives



Insulin: From Toronto To The World

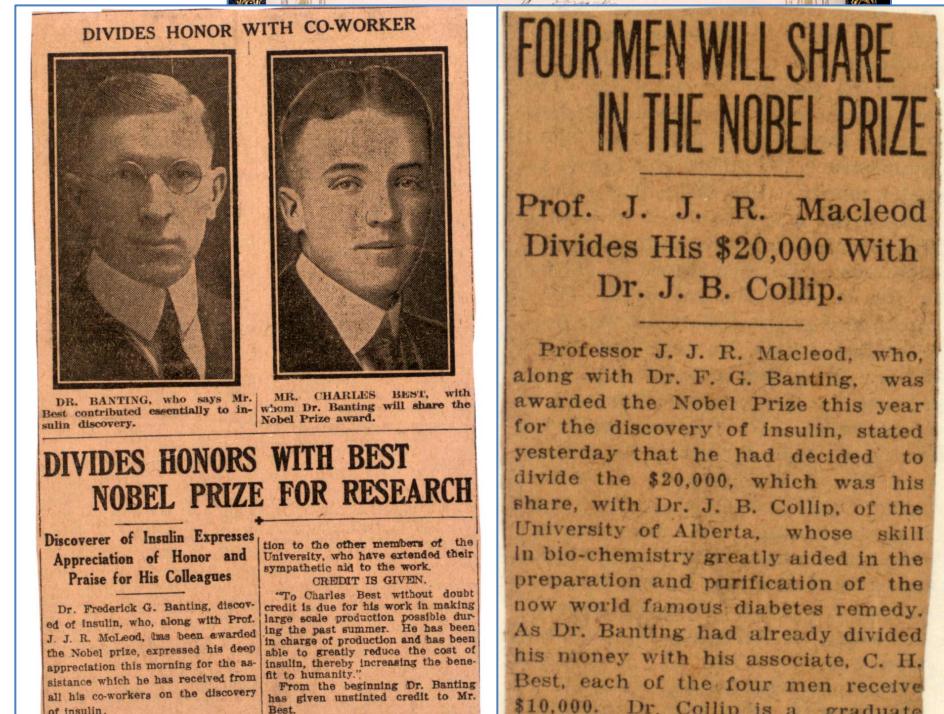
- U of T Insulin Committee also granted patent/licensing authority to carefully selected public bodies in several countries, i.e.:
 - **Nov 1922** – U.K. Medical Research Council (first insulin prepared in hospitals Jan 1923, then Burroughs Wellcome main producer April 1923)
 - **Nov 1922** – Nordisk Insulin Laboratory (Scandinavia) (first Nordisk insulin late 1923)
 - **July 1923** – German Insulin Committee (Hoechst first insulin Oct 1923)
 - **July 1923** – Gov't of Australia (Commonwealth Serum Laboratories first insulin Sept 1923)
- By 1926, insulin was patented and trademarked in 44 countries, with the Insulin Committee carefully regulating who produced it



Insulin: Honouring the Discoverers

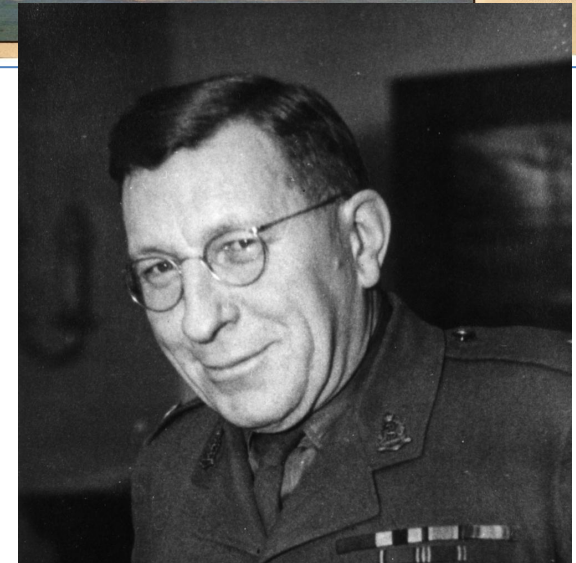
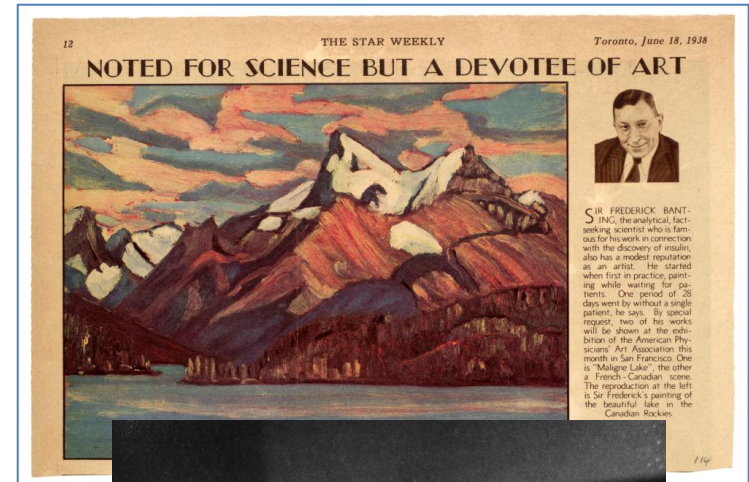
- The insulin story attracted significant international attention to Toronto, most notably,
- **Oct. 25, 1923** – The greatest global honour came when Banting and Macleod won the Nobel Prize for Medicine for the discovery of insulin

- However, recognizing that two others were similarly deserving, Banting shared his half of the Prize with Best, while Macleod shared his with Collip



Epilogue: Discoverers After Discovery

- Frederick Banting would focus on medical research, but was drawn to a growing interest in art, especially painting
- There were great expectations that Banting would make another major medical discovery, which proved quite frustrating, and art provided an important escape
- When World War II started, Banting became involved with aviation medicine studies
- He also worked closely with the British Air Force and was on a secret flight to Britain on February 20, 1941, when his small plane crashed shortly after taking off from Gander, Newfoundland; he died the next day



Epilogue: Discoverers After Discovery

- **1925** – Charles Best completed his M.D. amidst the insulin development period and then pursued postgraduate studies in Europe
- **1927** - Best returned to Toronto to continue as Connaught's Assistant Director until 1929, and to also serve as Head of the Department of Physiological Hygiene at the School of Hygiene
- **Late 1920s** - Best also initiated studies of liver extract as a treatment of anemia, and he focused especially on the development of Heparin to control blood coagulation, this work very much involving Connaught; Best died in 1978



Discover More About the Discovery of Insulin



- To learn more about the discovery and development of insulin, and the discovery team, explore the Defining Moments Canada "Insulin 100" national digital commemoration project, the first phase of which recently launched,
- <http://definingmomentscanada.ca>

INSULIN100

SIR FREDERICK BANTING

TEACHING ABOUT
INSULIN100

INSULIN100: THE DISCOVERY
AND DEVELOPMENT

MICROHISTORIES

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