scale preparation of insulin. Dr. Collip had returned to his professorial duties and no one else was available for this work. The struggle to recover the secret of making insulin in sufficient quantities for clinical use, was for me the most difficult and trying part of the whole insulin investigations. There was no time to approach the problem systematically and the only thing that seemed worth-while was to wage a night and day struggle in the hope that we might hit upon success. It may have been that a return to the use of a 0.2 per cent of concentrated hydrochloric acid in the extractive, or the introduction of the very efficient wind tunnel for rapid evaporation of our extracts, or the substitution of the lower boiling point acetone for alcohol as the original extractive, was the secret of the success which we achieved after a few weeks. More than one of these factors may have been important. In any case a consistent production of reasonable amounts of insulin was again made possible and the clinical work was started over again. The supply was at first not large and indeed over the summer months of 1922 the records show that not very much insulin was actually produced. The following table of the amounts sent to Fred Banting each month from what we called The Insulin Division of the Connaught Laboratories may be of interest. Further small amounts were probably sent directly to the Toronto General Hospital and to the Military Hospital at Christie Street. Some insulin was also made available for experimental work. The total was, however, very small and the product was of low potency—1 to 10 units per cc. as I remember it.

Insulin Supplied to Dr. Banting

June 1922	122½	cc.
July 1922	512	cc.
August 1922	390	cc.
September 1922	1,682	cc.

The recovery of the process for making insulin bridged the gap between the laboratory preparation and the large-scale commercial production. I have paid my tribute before to Dr. G. H. A. Clowes and the chemical engineers of Eli Lilly and Company and to my working partner in the Connaught Laboratories, Dr. D. A. Scott, who helped with further modifications and improvements in the large-scale preparation of insulin. There are many other names which should be mentioned and I can select only a few. The contributions of E. A. Doisy, M. Somogyi, and P. A. Shaffer, of the late Harold Ward Dudley, of P. J. Moloney and D. M. Findlay, will not be forgotten. Many different processes were soon developed for the further purification and concentration of the active material which we had found. This is not the place to review the many important steps by which insulin has been made a more efficient therapeutic agent. When the active substance has been synthesized it is possible that modification can be introduced which will further improve the antidiabetic effects of the hormone.

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A PERSONAL IMPRESSION

It is fitting to honor Leonard Thompson, the first patient to receive insulin, by placing his picture upon the cover of DIABETES. He had the courage to volunteer for an experiment. He was not like the dog, a passive participant, but an active member of the diabetic team. He stands out as an example of thousands of diabetics who have followed their doctors' advice, often bizarre, and have lived an honest diabetic day, not for themselves alone, but for the benefit of mankind. Would that they, especially those in the starving decade before insulin, could be immortalized as Rodin did those six emaciated burghers of Calais, who with halters around their necks, expecting death after its year-long siege, surrendered to Edward III to save their city.

For a quarter of a century I had been treating, or rather fighting, diabetes, when I heard a rumor of a surprising discovery by two young men in Toronto and went to New Haven in December 1921 to hear Banting speak about his experiment before the American Physiological Society. As we listened we physicians became so excited over what we learned and asked so many questions that the customary serenity of the meeting of that elite organization was upset and some of the members showed they regretted our presence. Banting spoke haltingly, Macleod beautifully. The possibility of mistakes in the work was fully exploited by those who discussed the paper in a skeptical but on the whole in a sympathetic way. A few months later Banting and Best and their clinical colleagues, Campbell and Fletcher, in Toronto showed us their early cases, but the full impact of the discovery did not fully dawn upon me until I learned I was to receive insulin for trial with my own patients. I remember well staying awake all night the day before it was to arrive. The first unit I gave to Miss Mudge, my severest patient, a nurse, on Aug. 7, 1922. She had obeyed the rigid regime. During her five years of diabetes her weight had fallen from 157 to 72 pounds, but she remained sugar free. She was nearly bedridden and, I recall, had gone over a flight of stairs in her home (oddly enough on the site of the New Hospital Teaching Clinic), but once in nine months. I watched her come back to life and go on in later years

to care for her mother instead of her mother's taking care of her. After four weeks of insulin, she walked four miles, and in seven months she gained twenty pounds. She lived another twenty-five years happily until she died suddenly of coronary thrombosis.

By Christmas of 1922 I had witnessed so many other near resurrections that I realized I was seeing enacted before my very eyes Ezekiel's vision of the valley of dry bones—Ezekiel XXXVII, 2-10:

> ". . . and behold, there were very many in the open valley; and, lo, they were very dry.
>
> And he said unto me, Son of Man, can these bones live?
>
> And . . . lo, the sinews and the flesh came up upon them, and the skin covered them above: but there was no breath in them.
>
> . . . Thus saith the Lord God: Come from the four winds, O breath, and breathe upon these slain, that they may live.
>
> . . . and the breath came into them, and they lived, and stood up upon their feet, an exceeding great army."

Colonel Palmer, my standard Case Number 632, a most brilliant young officer in the Canadian Army whose career was shattered by diabetes just before the first World War, came back for insulin. When he saw the children, his first reaction was: "Now they make a noise." Formerly they sat with protruding bellies, silent for hours, resignedly consuming their washed 3 per cent vegetables. Yet today of those feeble creatures there is many a one alive, breathing and standing upon his own feet. Von Noorden shuddered and turned aside at the sight of one of them a quarter of a century ago, but now he has passed on, and little Ruth is now working in a doctor's office in Chicago. For Christmas in 1922 the group of my first insulin users, numbering 83, sent a "round-robin" letter of thanks to Mr. Lilly in Indianapolis. He replied with the present of a doll to the girls, which they promptly named "Lilly," and to the boys, an insulin syringe set.

There was almost a tinge of regret in several of us over the discovery of insulin, because it had come so soon. It was known that much was being learned about the disease and we feared intensive effort would stop. Children were living two years instead of one; adults six years instead of five; an occasional patient outlived a normal life expectancy and we were discovering day by day mistakes that we had made in dietetic treatment and learning how they could be corrected and the metabolism of the diabetic preserved and strengthened. We argued by analogy, if a similar improvement occurred in a group of cancer patients, how it would be acclaimed! We knew that progress was being made and that the whole field of the betterment of diabetes by existing methods had yet to be explored. Although it still was a Cyrano de Bergerac fight, the joy of working and fighting was uppermost, even though it was realized the cause might be lost. Never before had such a high pitch of endeavor been evident in all centers in diabetes.

Then came insulin and what a reaction followed. "Now, Dr. Joslin, you will have no more diabetics to treat," was the common saying. The relaxation was as great as that I saw Nov. 11, 1918, in France the day of the armistice. In the twinkling of an eye, the whole atmosphere changed. Instantly salutes, which before 11 o'clock were alert and snappy, by noon had become informal and sloppy. Only one thought possessed the thoughts of the American soldiers—namely, to get home.

The finding of insulin by Banting and Best was unusual in that it was an anticipatory discovery. Then there were comparatively few diabetics in the world, because the average age at death of people generally was around forty years, whereas the onset of two-thirds of all cases of diabetes occurs above the age of forty years. Future generations therefore will rise up and call them blessed even more than those in their own generation.

It is a great satisfaction today to sense that same old enthusiasm, zeal and endeavor to prevent and treat diabetes which existed just before insulin was discovered. But the attack upon the disease is now on a broader basis. Then we were fighting a battle, but now we are conducting a campaign. Then the object of the encounter was to defeat diabetic coma, which took the lives of two-thirds of all the patients; today our campaign is to prevent and overcome complications in the eyes, circulation and kidneys. The battle ended in a quick death in unconsciousness, the campaign involves a lingering illness often with pain and despair, yet now there is more hope because we are convinced and have found the proof that such a sad outcome can be avoided by meticulous control of the disease, particularly in its early years, temporarily utilizing undernutrition diets, supplemented by insulin.

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