

# Leone Farrell

Research Scientist: Mass Production of Polio Vaccine

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*The production of quantities of the polio vaccine was achieved through a process that became known throughout the world as the Toronto technique.*

**T**he mystery lady of Connaught Laboratories, or so she seemed to me when I first began probing to find out more about her. Even her name had an air of mystery about it.

I did know that she was a Canadian scientist who was an important player in the world conquest of the dread disease polio over half a century ago. Yet, no one seemed to know who she was outside of Connaught Labs, where she worked for over 35 years, and the broader community of scientists who knew about the disease. Certainly, she was not famous like hockey players are in Canada, but there is no question she should have been, given the lasting importance of her work. Curiously, there does not even seem to be a simple monument or plaque anywhere to commemorate her accomplishments. However, old Knox College, the neo-Gothic building she worked in on Spadina Avenue in Toronto, is miraculously still standing in the middle of a traffic circle north of College Street, and is a monument of sorts. The Toronto Academy of Medicine, I am told, plans to erect a commemorative plaque to Leone Farrell there.

Poliomyelitis (or simply polio) is an infectious disease caused by any one of three distinct types of poliovirus. The virus enters the body through the mouth, multiplying in the gut and, if not stopped there or in the bloodstream, invades the central nervous system, targeting the delicate nerves of the spinal cord, disrupting communication between the brain and muscles, and often leading to varying degrees of paralysis and sometimes death.

Because its victims were predominantly young people, it was mistakenly thought at first to be a children's disease (hence its earlier name, infantile paralysis), but persons of any age could be affected. It struck down its victims with little warning other than headaches, a sore neck, and a high fever, all of which could be attributed to many other things. While the disease has probably been around for a very long time, the first cases of polio in North America were first identified in the 1890s. By 1910, outbreaks were identified in many communities. A *Toronto Star* headline at the time said, "Children Attacked by Strange Epidemic" (*Star*, Aug. 10, 1910).

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While polio is now under control by the Salk and Sabin vaccines developed in the 1950s and 1960s, few of us know the full story or the importance of the Canadian connection. For those of us who were teenagers before 1955, we spent our summers in constant dread of the spectre of this terrifying disease in its annual march across the country. We all had friends, relatives, and classmates who had been its victims.

In 1953, the worst polio year in Canada, 9000 cases were reported and many more people had been touched by it. The media gave daily reports on the progress of the disease and the number of reported cases were often highlighted in a box on the front page of newspapers.

As young people at the time, we were advised not to congregate or mingle in crowds, go to movies, attend concerts, swim in public areas, play organized sports; in fact, we were advised to live generally isolated lives through the peak period of the disease in midsummer. But kids just cannot do that, and so were all at risk.

The most famous polio victim was Franklin Delano Roosevelt, the president of the United States, who contracted the disease as an adult in 1921 and was severely crippled by it. He also became the major public advocate to conquer the disease and one of the founders of the March of Dimes, also known as the National Foundation for Infantile Paralysis (NFIP).

If you did not live through those times, you could not know how polio pervaded every facet of our summer lives and how joyfully the announcement of a vaccine breakthrough was received. I remember being lined up in the school auditorium to receive that first vaccination, which we knew very little about. But we all knew what polio was.

This story, then, is about the vaccine that was created by the great Jonas Salk at the University of Pittsburgh, but it is also about the role played by the University of Toronto's Connaught Medical Research Laboratories, and Leone Farrell's team there, in making the mass production of safe polio vaccine possible. That process became known throughout the world as the Toronto Technique.

Connaught Labs, under noted virologist Dr. Andrew Rhodes, had already been conducting extensive polio research since 1947 and had established solid credentials, first by "investigating the complex problems of polio epidemiology and diagnostics" (Rutty) and then, by 1951, growing polio virus in test tubes using a method pioneered

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by the American Nobel Prize-winning scientist John Enders of Harvard. In 1949, Connaught scientists, in their cancer research work, had developed a new serum-free, chemically pure liquid synthetic nutrient base known as Medium 199, which was created from a mixture of more than 60 ingredients. It was the first synthetic medium ever produced, which meant it “did not include any additional animal serums that could render any vaccine dangerous for human use” (Rutty). Rhodes’ team proved Medium 199 to be surprisingly effective in cultivating polio virus from monkey kidney cells. (Rutty)

However, not enough poliovirus could be produced using this laborious test-tube method to ever hope to have enough virus for a vaccine for a mass immunization program — so a better method had to be found. Encouraged by the effectiveness of Medium 199 and the pioneering work being done at Connaught on polio, the March of Dimes funded a pilot project to find that better method, and Leone Farrell, with her extensive experience in vaccine production, was assigned the task.

In her previous work at Connaught on the pertussis vaccine a decade earlier, she and her colleagues had developed an incubation production method of gently rocking horizontally large, long, rectangular glass bottles that contained the bacterial culture in a liquid medium.<sup>1</sup> The process was carried out over many days and was found to stimulate bacterial growth as well as to greatly enhance production levels of the pertussis vaccine. Farrell believed it could work in producing greater quantities of the poliovirus as well. Her assumptions were eventually proven to be correct after a long process of trial and error in the lab — and testing, testing, testing.

In the chemically pure environment of Medium 199, kept at a constant body temperature and rocked gently over time on Farrell’s “rocking machine,” the production of poliovirus was greatly increased to levels sufficient to carry out the large-scale national field trial planned with the Salk vaccine.

Jonas Salk, who remained in close contact with Connaught, was delighted with the success of the process, and the American March of Dimes was so encouraged that they contracted Connaught to make all the poliovirus in Toronto for their National Field

<sup>1</sup> This was before the development of Medium 199 by Joseph Morgan, Helen Morton, and Raymond Parker at Connaught Labs in 1949.

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Trials in the United States. This was a great coup for Connaught and Leone Farrell. So, throughout the winter of 1953–54, Connaught’s production of poliovirus was carried out under the supervision of Dr. Leone Farrell. Each week on Thursday, a station wagon would pull up to the door of the Spadina Avenue lab of Connaught, load up the jars of poliovirus, and set off for the two pharmaceutical companies in Detroit and Indianapolis where the poliovirus was inactivated and turned into polio vaccine.

The first field trials were carried out in the United States in the spring of 1954 and involved about 2 million children. In appreciation for Connaught’s exceptional contribution to their field trials, the U.S. March of Dimes (NFIP) offered Canada some of the surplus vaccine, which was then used in Canadian trials in Manitoba, Alberta, and Halifax that same year. The test was a grand success in both Canada and the United States, which encouraged both countries to plan on full national programs the next year. But again, they needed even more vaccine.

In Canada, the federal government contracted Connaught to produce all the vaccine needed for the full Canadian program. In addition, scientists and health officials from the federal and provincial governments monitored the program through to its completion. At the time, Connaught was one of the world’s leading producers of vaccines.

In the U.S., the vaccine production was licensed to commercial producers who “rush-released” the vaccine to market with little government control.

Regrettably, the optimism and euphoria over the vaccine in its successful trial period suddenly evaporated when several batches of vaccine from one of the U.S. commercial producers was directly associated with 80 new polio cases, which prompted the Surgeon General of the U.S. to suspend the entire U.S. program to avert a potential catastrophe. Canada had the same decision to make. But, having had no problem with Connaught in the Canadian test, and given the fact that Connaught would produce the vaccines for all of Canada, the then-Minister of Health Paul Martin Sr. agreed to go ahead with the Canadian program. Paul Martin Sr. and his son had both been victims of polio and understood how important this program would be to millions of young Canadians. The Canadian program was carried out successfully, but the suspension of the U.S. program meant that Salk’s vaccine had been used in only one full national program — Canada.

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Without Canada, that could have ended the Salk vaccine experiment. But the Canadian results were so positive that public confidence in Salk's vaccine was restored, Salk himself was vindicated, and the Canadian results played a significant role in ensuring that the Salk vaccine would be used in many other countries. While many people played a part in the control of polio, Leone Farrell and her colleagues were major players. Jonas Salk felt that, without Connaught's Herculean effort, there would not have been a national trial or a practical vaccine in the first place. (Rutty)

In a speech he made in Canada on September 7, 1955, the medical director of the National Foundation for Infantile Paralysis in New York, Dr. H.E. Van Ripen, said that "...nowhere in the world has greater progress been made in controlling polio than in Canada... We (the U.S.A.) have much to learn from you." (*G&M*, Sept. 8, 1955)

As the Salk vaccine supply increased and more children and then adults were immunized, Canadian polio incidence declined sharply, dropping to almost 0 by the early 1960s — and 0 is where it has remained ever since. But over time, and with the glow of success elsewhere, Connaught's monumental work in the polio vaccine program seems to have been lost in the mists of time, including some Canadian mists, and the central role played by Connaught, its scientists, and Leone Farrell seems to have been filed away and forgotten.

But not in the minds of those who know the real story — because it was partly a Canadian story, as Jonas Salk himself had said. The proof is in the Connaught archives, and was in the Smithsonian Institute in Washington where a prototype reconstruction of Leone Farrell's rocking bottle machine was featured in a polio exhibit that opened in 1957.

I began this story by referring to Leone Farrell as the mystery lady of Connaught because no one there could tell me very much about her beyond her work. She was born in the small farming community of Monkland Station outside of Ottawa, Ontario, in 1905 and raised in Toronto. She earned a PhD in biochemistry from the University of Toronto in 1933, at a time when that was a rare accomplishment for women. She was hired by Connaught as only the second woman PhD on staff.

She came from a family of achievers, where books were important and education encouraged. Her three brothers all graduated from university before her. Her

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brother-in-law, who was a great influence in her life, was an editor and publisher of several scientific trade magazines that were later acquired by the Maclean's empire.

She was described by her colleagues as an elegant and fashionable lady who wore silk blouses, business suits, and heels to the office every day and whose hair was always perfect. But that was the superficial. As an administrator, she was described by her colleagues as "goal driven," a "classic researcher and disciplined in her work." She had vision and imagination in her scientific enquiry, and was a good team leader as well as a good team player. "She was totally dedicated to her work and wrapped up in what she was doing" (Daly).

In retirement, she was well known at the University of Toronto Women's Club, where she was said to be an excellent and regular bridge player. She was close to her family and had a strong influence on her niece, who is currently a writer in Toronto. One of her colleagues, now retired, told me that they often had lunch together, and he remembered her as an interesting, well-read person, but apart from being a successful scientist, he did not know that she was important.

That pretty well says it all in terms of our collective historical perception of most of our great Canadian scientists, like Leone Farrell and her colleagues: Andrew Rhodes, Robert Defries, Edith Taylor, Joseph Morgan, Helen Morton, Raymond Parker, Arthur Franklin, Frank Shimada, Eina Clark, as well as many others at Connaught Laboratories. They are mostly all forgotten now!

And yet, what would our world have been like without them?



*Knox College*