

Is serum revival in works?

PETER HENDRA
The Whig-Standard

A Kingston ear, nose and throat specialist in the 1920s and '30s would spend his post-practice hours in a tiny lab trying to figure out a way to dissolve cataracts.

Dr. Hendry Connell came upon a method that appeared to work. Then he wondered: if it worked with cataracts, what about cancer tumours?

Soon his work led to the creation of a serum he called Ensol and, before long, desperate cancer patients were streaming to Kingston, hoping to get a dose of Connell's formula.

What happened to Ensol is a tale of science, medicine, business and not just a little intrigue, rife with greed, power and jealousy.

"This would be," says Connell's grandson, Sandy Crothers, "a great blockbuster movie."

The family has been working hard to keep Connell's legacy alive.

Katherine Connell Crothers, Connell's daughter, and her husband, Robert, have published two books — *Enzyme Solution: The Story of Ensol* and *Must not have been in vain: The lost cancer serum* — chronicling the doctor's work.

In the fall, they launched a website — www.cancerserum.ca — detailing the story of Ensol, which they refer to as the "lost cancer serum."

"What intrigued me after mom's book was, 'Wow, this is a great idea to put on a website so it's not lost,'" said Sandy, who



Sandy Crothers.

spurred the site's creation. "I would not have known about it without my parents (writing the book)."

That book may soon have an epilogue. At the famed Mayo Clinic in Rochester, Minn., Dr. Keith Knutson, an immunologist researching cancer serums, is intrigued by the work Connell did more than 70 years ago.

Particularly interesting to Knutson was Connell's inclusion of what he calls a "danger signal" protein in the formula, which stimulates the body's immune system.

"Where did he get that (idea)? What was the thinking behind that?" Knutson wondered. "That's the formulation we're using today."

"He definitely was ahead of his time because people are still using his strategy."

So what happened to Ensol?: We tell the story today. Page 9

Old formula comes off shelf

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A cancer serum developed in Kingston more than 75 years ago may soon be getting another look.

An immunologist from the renowned Mayo Clinic, Dr. Keith Knutson, said he hopes to replicate the formula for Ensol, which was created by Dr. Hendry Connell in 1935.

Knutson is curious to see what effects it has on a mouse cancer model, but that re-creation will have to wait as Knutson has some other research to conduct first — in August, it was announced that two breast cancer vaccines he helped develop are about to undergo clinical trials.

The delay hasn't dulled his curiosity about Connell's 70-year-old serum.

"One of the interesting things about Dr. Connell's approach is that he was working on a vaccine that's much like the vaccines that we're actually testing today," Knutson said.

"It's a very interesting formulation that he had, taking the tumours themselves and killing them so they release their proteins. I'm not sure he knew why and how it was working."

Knutson was initially contacted by Connell's descendants, who sent along the doctor's revised formula from the 1950s.

"We could hold onto the papers forever," his daughter, Katherine Connell Crothers, said, "but it wouldn't do anybody any good."

Knutson believes that Connell's methodology somewhat mirrors his own by deploying what he calls "danger signals."

"When you have a vaccine, you have to have something in there that the immune system is going to respond to, and usually that's proteins," Knutson explained from his office in Minnesota.

"Usually, a bacteria or virus has



Courtesy of Crothers family

Dr. Hendry Connell tested Ensol on terminally ill cancer patients.

very strange proteins and the immune system sees that the bacteria or viruses are loaded with all kinds of things that the immune system has never seen, called 'danger signals.' (The immune system) responds to these danger signals and then it attacks those signals."

Knutson believes Connell was a pioneer. "What he was doing was infecting the tumour cells and then he was taking the solution off the top of it," he explained.

"It turns out (those) are danger signals, the bacteria, mixed with the proteins of the tumours. That's exactly the type of vaccines that I'm working with. I haven't seen a lot of evidence from that time that people were doing that."

The story has humble beginnings. Dr. Hendry Connell had a private practice, working as a nose, ear and throat specialist. After treating his last patient of the

day, he would retire to a third-floor lab at Queen's University.

He was also investigating ways to dissolve cataracts and came upon a method that, he believed, appeared to work. Then he had the notion that, if he could do that with cataracts, he could apply the same idea to cancer tumours.

"He was thinking (that) if you can dissolve one kind of solid tissue using this bacterial-derived solution, maybe you can dissolve other tissues," explained Dr. Jacalyn Duffin, who is the Hannah Chair of the History of Medicine at Queen's. "and the tissue you really want to dissolve, if you can pick any tissue at all, is a tumour."

Connell set aside his practice and began focusing on his cancer research alongside bacteriology technician Bertram Holsgrove. The two men put in 16 hours a day, often seven days a week, in their laboratory.

The resulting formulation was

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called Ensol, short for "enzyme solution." In the spring of 1935, he began tests on cancer patients who had been deemed incurable by other doctors.

"After due orthodox experiments on cancerous mice, young Dr. Connell began to inject the sterile nitrate of such dissolved cancers into the muscles and veins of dying Kingston cancer victims," read an Oct. 14, 1935, article in *Time* magazine.

"One of the first was a prisoner of Ontario's dreadful Portsmouth Penitentiary, close to which the Drs. Connell have their homes."

(The other Dr. Connell was Connell's father, Dr. James Cameron Connell, who was a longtime dean of Queen's University's faculty of medicine.)

The test results were encouraging. Along with regular radiation therapy, the new solution seemed to shrink tumours in many of his cancer subjects. It was reported that those patients suffered few, if any, side-effects, regained their appetites and reported less pain.

To ensure his solution was safe, Connell would inject himself.

By now, Connell and his equipment had moved to the university's Ontario Hall, where bars were installed on the windows for fear his discovery would tempt trouble. In July 1935, it was announced that the 40-year-old Connell had concocted a treatment for cancer, which was to be used in conjunction with radiation therapy and surgery to prevent the recurrence of cancer.

He was careful not to call it a cure.

"It is altogether too soon to assess the ultimate value of the method," he cautiously wrote. "Weeks to months must elapse before we can determine if the cancer mass continues to show shrinkage and absorption till their complete disappearance."

Connell's work had been published, and endorsed, in the Canadian Medical Association Journal and subsequently drew media attention from around the world.

His discovery drew a number of those afflicted with cancer to Kingston — so many, it was reported, that students coming to the city for university found it difficult to find a place to stay.

Connell, who had since created the Hendry Connell Research Foundation, received funding from Queen's, as well as the provincial and federal governments.

Connell had also entered into a partnership with the Franklin Institute of Philadelphia, which produced the serum under the name "Rex."

By January 1936, Connell's staff had grown from two to more than 20, and operations were moved to a new lab at Kingston General Hospital. That year, more than 2,000 cancer patients were receiving injections of Ensol.

Within four years of its discovery, Ensol had 22 patents in 12 different countries (the Canadian patent was issued in 1936).

In March 1938, however, things took a turn for the worse. Ten people in Orlando, Fla., who had been injected with Connell's serum

died of lockjaw. The vial of solution from which they were injected hadn't been properly sanitized.

Even though Connell and company were absolved from any wrongdoing — the vial in question was one produced and distributed by the Franklin Institute — the solution's reputation was irreversibly sullied.

Accusations were made that Ensol had been sabotaged by those who had fallen out of favour with the foundation.

The funding he had counted upon disappeared, but for years Connell persevered, using his own money. He even sold his cherished boat. It didn't help that the Second World War was on the horizon, and money and qualified personnel would suddenly be in short supply.

Eventually, Connell transferred the rights to manufacture the serum to Baxter Laboratories Inc. The American company sent a biochemist to Kingston to work alongside Connell to learn how to produce the drug. Illness, however, forced the biochemist to return to the U.S., and he never returned.

The inventory of the formula, now known as U-10, was destroyed.

By this time, Connell had returned to his private practice at its original King Street office and he continued to work there until health problems arose. In 1958, he suffered a stroke, and, in 1961, he was again hospitalized with acute bronchitis and heart troubles. He would be back in hospital again in 1963 because of heart difficulties. Ultimately, he died the next year of congestive heart failure.

Before he died, Connell complained of abdominal pain. It turned out that Connell, who had been regularly injecting himself with his own cancer serum, was suffering from pancreatic cancer.

Doctor's work believed relevant

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On his deathbed, he repeatedly asked if any word was forthcoming from Baxter about the status of his formula.

Like the Mayo Clinic's Knutson, the director of Cancer Research Institute at Queen's, Dr. Roger Deeley, believes Connell's work is relevant.

"In many respects, the treatment, as controversial as it turned out to be, was way ahead of its time, and may have been one of the first attempts at a cancer vaccine," he said.

Nowadays, thanks to strides in both knowledge and technology, vaccines are created much differently.

"We recognize that the immune system recognizes proteins — we've known that for a long time," explained the Mayo Clinic's Knutson.

"Now we can pick out the parts the immune system is responding to, so we're not just putting in a whole bunch of proteins," he said. "We can pick the specific proteins, and we can pick the specific parts of the protein the immune system is responding to, and we can syn-

thesize those, so we don't need to use the malignancy itself to stimulate the immune system."

Barbara Clow, now the executive director of the Atlantic Centre of Excellence for Women's Health in Halifax, wrote about Connell in her book, *Negotiating disease: Power and cancer care, 1900-1950*.

"There were treatments that were considered standard for cancer at the time, and his was not one of them," Clow said.

Connell, she said, did not endure the same scrutiny other cancer researchers did.

"He was treated very differently than other practitioners were in the same period," Clow explained. "He got direct government support for his research for a number of years, he was never drummed out of the profession ... and he was never really subjected to the same kind of critique as other practitioners were."

Historian Duffin said Connell was working in an interesting era.

"The 1930s was an age of blossoming biochemistry," she said, and many of the Nobel prizes awarded around that time were presented for work in that field. The thinking at the time, Duffin

explained, was that "the body is a biochemical soup, and we just have to sort out the chemicals."

"Right around the time Dr. Connell is doing some of his work," she said, "there are notions that bacteria are going to turn out to be the causes of everything."

The way research is conducted has changed vastly since Connell's time, Duffin said. For one thing, Connell didn't use a control group to measure Ensol's effectiveness, and since it was administered in conjunction with radiation therapy, there was no way to measure the impact of the solution itself.

"He was claiming that the radiotherapy worked better because they were taking Ensol at the same time, but the radiotherapist would not say that," explained Duffin.

When he was conducting his work, Duffin said, "people were desperate."

"They didn't have rules to follow in that way and, of course, you give them everything you possibly can," she said. "It appeared that Ensol didn't hurt anyone, and it also seemed that some people got better after taking it."

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